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EFFECT OF PESTICIDES UPON THE CORTICAL POTENTIALS EVOKED BY VARIABLE FREQUENCY AUDIO AND VISUAL STIMULI.

Iowa State University, Ph.D., 1969
Physiology

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EFFECT OF PESTICIDES UPON THE CORTICAL POTENTIALS EVOKED BY VARIABLE FREQUENCY AUDIO AND VISUAL STIMULI

by

Charles Hutchings Bonney, D.V.M.

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
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Major Subject: Veterinary Physiology

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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Ames, Iowa

1969

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INTRODUCTION

Several topics will be discussed in this introduction. A brief comparison is presented of engineering and biology with reference to their common areas. An introduction is given to the scope of pesticide usage and to some of the controversy surrounding this usage. The purpose and scope of the laboratory in which this work was done is also presented.

The preparation of this dissertation was with the awareness that the reading of it would be done by members of two general areas, life science and physical science. Therefore, introductory material is presented in the literature review with respect to the pertinent anatomy and physiology involved as well as basic material on the analytical technique. If the material is from the reader's particular area it no doubt will be quite familiar to him but perhaps when the material is representative of an area in which he has had less association it will be helpful in interpretating that which follows.

A few recognized texts and articles will be mentioned at the close of the introduction for those who wish to do additional reading. These are deemed suitable starting points for persons who are attempting to gain further insight into a secondary or tangent area.

Biomedical Engineering

In introducing this dissertation some mention should be made of the nature of a biomedical engineering program. It

was by this avenue that this topic of research was approached. Coming from a multidisciplinary curriculum the tone of the investigation varies from the more traditional descriptive physiological approach.

Originally the areas of engineering and biological investigation developed along very dissimilar paths. Engineering sciences are particularly characterized by a heavy reliance upon mathematical analyses and models. These analyses and models are useful to the engineering disciplines as an aid to the design of functioning systems. Biological studies for the most part have been descriptive in nature. The natural variability of life systems produced an essentially experimental field of activity which deals with biological trends and ranges of values.

Within the last decade, however, these rather diverse areas have found some common ground. The advent of control systems analysis in engineering produced techniques and analytical approaches which were of interest in the investigative pursuits of the experimental physiologist. Physiological systems are in essence interacting regulatory control systems. In this case the use of mathematics is for empirical analyses. The experimental biologist is not attempting to design or construct a system but rather is attempting to gain a deeper insight of the existing life systems.

The area of electroencephalographic analysis is one which

has particularly benefited as engineering techniques have been applied. Study of the evoked potential has been enhanced with the application of suitable electronic recording equipment (Barlow and Brown, 1955; Barlow, 1959; Dawson, 1954).

Computer usage has increasingly become a part of physiological experimentation. The small digital computers offer the investigator increased capability in on-line experimental control as well as data acquisition. Larger computers allow vast amounts of physiological data to be processed.

Computer technology and résumés of its application to neurology have been compiled by Brazier (1960), and Farley et al. (1962). Brazier and Casby (1951) utilized a digital computer to conduct one of the early electroencephalographic correlation studies. Utilization of computers has made possible the application of autocorrelation and crosscorrelation techniques to analysis of the electroencephalogram (Barlow, 1959; Brazier and Casby, 1951; Campbell et al., 1967).

The Psychotoxicology Laboratory

This research effort was conducted using the laboratory facilities of the psychotoxicology group. The purpose of this research unit has been to evaluate the effects on the electroencephalogram by those pesticides which exhibit clinical signs of central nervous system involvement. Fundamentally, their efforts have been to establish criteria which will accurately reflect the level and degree of central nervous system effect

as a result of pesticide exposure. This purpose has been pursued by bringing to bear the disciplines of physiology, toxicology, pharmacology, and psychology. The experimental animal has been the mature female sheep.

In the conduct of this project the major theme of the laboratory is approached through the realm of linear systems analysis techniques.

Problems of Pesticide Usage

Pesticide usage is widespread on a worldwide basis. The benefits from the use of these chemicals have been clearly visible as man has improved the quality and quantity of food and fiber. Less clear, however, is the range and magnitude of the problems associated with their use. Undeniably, there is a calculated risk associated with the use of pesticides. The risk rests primarily with the problem of chemical residues. However, the world's production of food and fiber has become irrevocably tied to the use of pesticides, and the likelihood is not great that these chemical agents will at some future time be eliminated from use (Lehman, 1950; Richardson and Foter, 1966).

Little is known about the least level of a pesticide in animal tissue that may exert a biological effect. Pesticide residue in food, water, and air subjects large populations to exposure and intensifies the question of least significant level (Breidenbach, 1965; Durham, 1963; Frazier, 1967;

Nicholson and Thoman, 1964; Richardson and Foter, 1966; Tabor, 1966). The need for a more accurate nationwide survey of morbidity and mortality has been cited by Reich et al. (1968).

When used appropriately some researchers feel that there is little hazard associated with the use of pesticides. Several surveys have indicated that there may be a tolerance on the part of the animal body to chronic levels of some pesticides. Jegier (1954) examined workers applying insecticides to orchards. Despite the use of few protective measures no workers were found to experience acute toxicity. Hoffman et al. (1967) assayed 994 specimens of human abdominal fat. These examinations revealed the sum of DDT and DDE averaged 9.6 parts per million. Hoffman also found that there had been no progression of body storage in the general population since 1951. He also concluded that these levels for this agent had not been proved biologically harmful. Durham (1963), however, has pointed out that the question of subtle long range effects has yet to be resolved. Although the principle clinical signs of toxicity are in the form of central nervous system involvement, little research has been done in the realm of electroencephalography and central nervous system effects. It was the purpose of this research to examine the evoked cortical potential for qualitative changes which could be correlated with clinical signs of pesticide toxicity. Dieldrin, DDT, and Rulene® were used in this study as representative of particular

families of compounds discussed later in the literature review sections on chlorinated hydrocarbons and organophosphorous compounds.

Additional Reading

Basic material on neurophysiology may be found in the texts by Ruch and Patton (1965), Brazier (1968) and in the Handbook of Physiology, Section of Neurophysiology (Field et al., 1959). A presentation concerning the Fourier series is available in the text by Kreyszig (1967). Brown and Nilsson (1962) have a readable text which also discusses the Fourier series and transform with an emphasis on the interpretation of these functions. Portions of Hancock (1961) will be of interest to neurophysiologists who wish to adapt principles of communication theory to their area of investigation. A tutorial article on the problem of noise has been written by Bennett (1956) which deals with the mathematical aspects of the signal-to-noise ratio problem. Signal averaging is discussed in articles by Chaykowsky and Moore (1968), and Nittrouer (1968). A text by Bendat and Piersol (1966) is devoted to the area of random processes and analysis.

REVIEW OF THE LITERATURE

History of the Clinical Electroencephalogram

Examining the brain for an analog to the action potential of peripheral nerves, Richard Canton in 1875 first observed spontaneous electrical activity in the exposed cortex of a rabbit. Canton observed an irregular oscillation when he placed two electrodes onto the cortex. It was established by Canton that these fluctuations were not related to either respiration or cardiac function but rather were a biological property of the cerebral cortex (Chang, 1959). In his experimentation Canton also observed changes in this spontaneous electrical activity as a result of sensory stimulation. This was the beginning of electroneurophysiology and the original work with potential changes due to sensory stimuli (Brazier, 1959).

In 1929 Hans Burger recorded this spontaneous electrical activity by the use of electrodes placed on the skin overlying the skull. It was Burger who gave to these tracings the term electroencephalograph, a term which is often abbreviated EEG. In his work Burger described two rhythms in normal patients, the alpha and beta rhythms. A major discovery by Burger was that the electroencephalogram varies from the norm in patients suffering from epilepsy. Thus, it was Burger who laid the foundation for the use of electroencephalography in clinical medicine (Brazier, 1957; Chang, 1959).

Since 1930 the EEG has become increasingly more a part of clinical medicine as electronic devices for detecting and recording the EEG have become common and more reliable.

Recordings of the electrical activity of the brain are composed predominately of irregular waves. The analysis of these tracings is more art than science. The origin of this electrical activity has yet to be defined, making a precise interpretation of the waveforms extremely difficult. Classification of the EEG waveforms by frequency has produced the classes alpha, beta, theta, and delta. Alpha waves are in the range of 8-14 Hz., beta 14-60 Hz., theta 4-8 Hz., and delta 1-4 Hz. (Ruch and Patton, 1965).

The Evoked Potential

A measurable electrical change in any portion of the brain due to a controlled deliberate stimulation of a peripheral sense organ is known as an evoked potential. This detectable electrical change within the brain differs from the spontaneous ongoing activity in several ways. The evoked potential bears a temporal relationship to the stimulus i.e., it has a definite latency. An evoked response will have a waveform that is characteristic for a specific sensory system and the waveform is generally predictable and reproducible when produced under similar conditions. Localization within the brain is usually exhibited by the evoked potential (Chang, 1959; Ruch and Patton, 1965).

Investigation of changes in the electroencephalogram due to a known sensory input is often hampered by the random background activity of the cortex. Using anesthetics to depress the unwanted electrical background activity, early workers were able to selectively examine the electroencephalogram for changes related to stimulation of one of the peripheral sensory receptors. This review of literature does not deal with anesthetized preparations of the earlier form. Later studies involving averaging or summation techniques are more closely related to the study presented here and are described.

More recently electronic signal averagers have been used to eliminate the undesirable background and to detect signals the amplitude of which may be masked by the intrinsic noise. Utilizing an averaging or summation technique allows one to conduct an investigation of evoked cortical potentials without the use of drugs. Coupled with the use of chronically implanted electrodes an animal may be examined while fully conscious. A brief discussion of the averaging technique is presented in Appendix A.

Characteristically the evoked response is described as having two components, the presynaptic and postsynaptic. The presynaptic component is attributed to the arrival of impulses as they pass along the axon and its terminals. The postsynaptic component reflects the activity of the cell body and the dendrites (Bremer, 1958).

When examining the evoked potential recorded from the cerebral cortex the characteristic response is initially a surface-positive wave often followed by a series of rhythmic after-discharges (Ruch and Patton, 1965). The initial wave is a product of presynaptic potential resulting from activity in the thalamocortical fibers. The after-discharge is produced by activity in the intracortical neurons (Chang, 1959).

Genesis of the cortical evoked response

The electrogenesis of the evoked cortical response is postulated by applying what is known about the cyto-architectural relationships and established principles of electrophysiology.

Two features must be considered in discussing the cortical evoked response: (1) the cortical response to afferent stimuli is remarkably constant over the entire sensory cortex, (2) the cortex possesses an extremely well developed granular layer.

Afferent stimuli reach the cortex by means of specific thalamic fibers which terminate principally in the fourth cortical layer synapsing with Golgi type II cells. Golgi type II cells possess short profusely arborizing axons. Dendrites are few and poorly developed. Anatomically, these cells appear to be poorly equipped and to transmit impulses. They are thought to serve principally as amplifiers. It is also unlikely that surface potential changes could be recorded from these cells. Rather, these cells seem to serve the purpose of stimulating

other cell types within this same layer, notably the star pyramids which in turn activate the medium pyramid and small pyramid cells. From these pyramid cells comes the activation for the large pyramid cells of the fifth and sixth layers (Sholl, 1956). See Figure 1 (Ham, 1966).

Propagation of nerve impulses along the vertically oriented apical dendrites is the source of the detectable surface positive potential (Bremer, 1958). Thus, following indirect activation of the pyramidal cells by way of a chain of internuncial neurons, the postsynaptic activity begun at the soma will act as a sink and the apical dendrites as a source of current flow (Ochs, 1965). This then will produce a surface positive wave. Polarity of the waveform will be reversed as soon as the impulse reaches the plexus of the apical dendrites at the surface of the cortex (Chang, 1951).

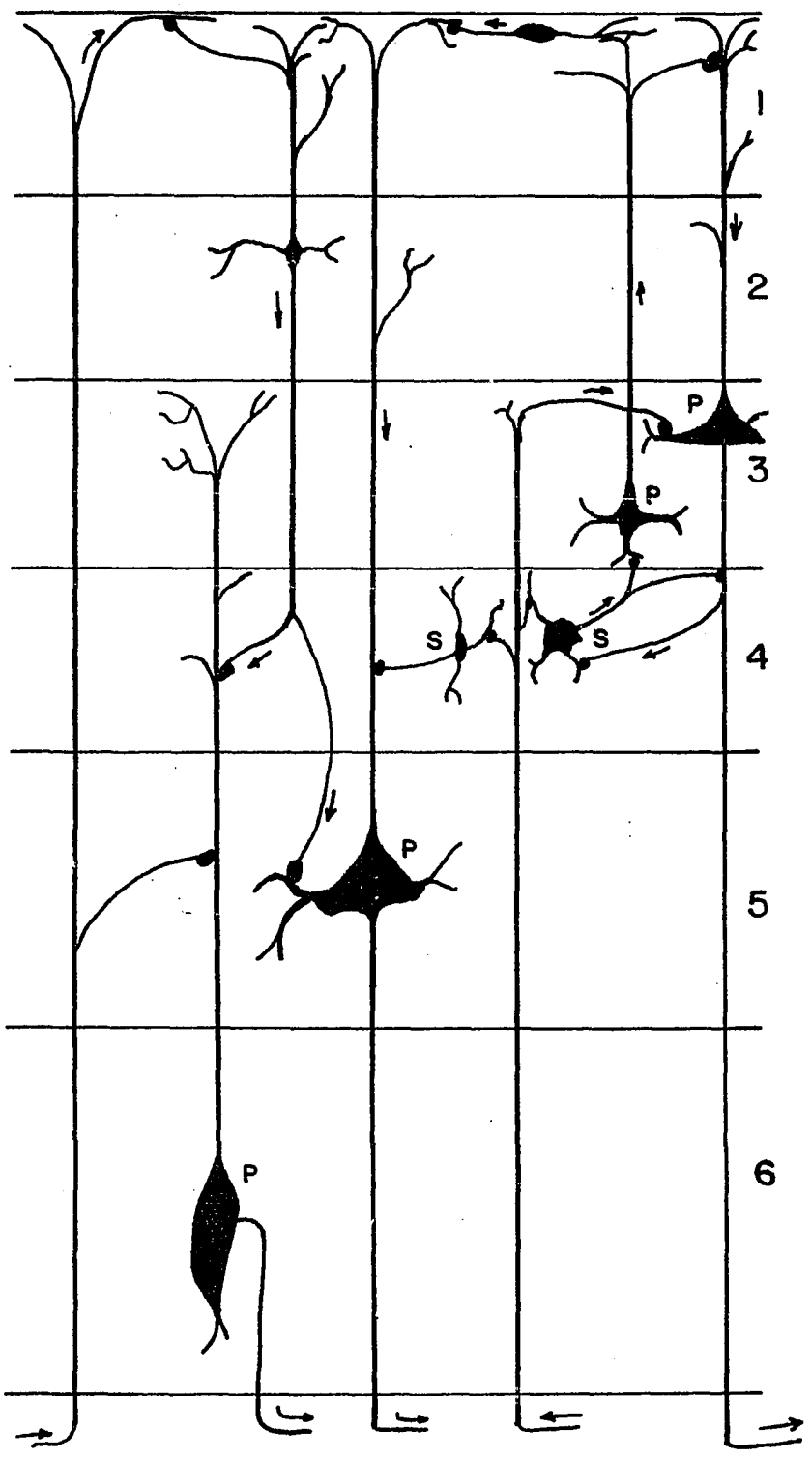
Neuronal discharge following the evoked potential

Three forms of after-discharge may follow the cortical response: (1) a self-sustained repetitive firing of single elements, (2) local after-discharges which involve activity of closely situated intrinsic neurons, and (3) after-discharges which involve reverberating circuits which interconnect distant structures producing a periodic form of after-discharge.

Rose and Mountcastle (1954) utilized microelectrodes to study the repetitive firing of an individual neuron. This study revealed that a thalamic unit may fire as many as seven

Figure 1. Diagramatic representation of some of the connections in the cerebral cortex and cell types. Pyramidal cells, P, and stellate cells, S, are represented. Arrows represent possible paths of transmission. The layers are numbered on the right side of the diagram:

1. molecular layer
2. outer granular layer
3. pyramidal layer
4. inner granular layer
5. internal pyramidal layer
6. layer of polymorphous cell


1
2
3
4
5
6
P
P
P
P
S
S

times in response to a single stimulus. Amassian and Devito (1954) found a similar response of units in the reticular formation.

A hypothesis for the self-generating mechanism of after-discharge has been presented by Burns (1955). It has been suggested that the recovery rates of the resting membrane potentials following stimulation take place non-uniformly. Thus, one end of a cortical neuron is repolarized more slowly than the other. Utilizing microelectrode techniques it was established that a flow of extra-cellular current is established between cellular areas of rapid repolarization and areas of slower activity (Brazier, 1968).

Neurons within the cortex arranged in a closed circuit configuration can produce a longer lasting form of after-discharge activity than the single neuron which may discharge repetitively. The closed circuit provides an anatomical basis for an auto-reexcitation of the neurons within the circuit. Axonal stimulation of the large pyramidal neurons can be followed by an auto-stimulation of the same neuron by its own collaterals. A shock stimulus applied to a point on the medullary pyramid can be followed by a discharge detected at this same point as a result of internuncial activity completing an auto-excitatory circuit.

Periodic evoked after-discharges are dependent upon intact pathways between the cerebral cortex and the thalamic

nuclei (Burns, 1955). Similar waves have been recorded from appropriate thalamic nuclei and the sensory cortex. Upon removal of the cerebral cortex the waves disappeared. Specific periodic after-discharge activity may be due to the action of reverberating circuits between the sensory cortex and the thalamus. Spontaneous cortical activity and the evoked after-discharge activity may well have the same frequency which lends difficulty to the recognition and interpretation of these waves. An aid to interpretation is the fact that the evoked wave is always surface positive while spontaneous activity is not (Brock et al., 1952).

Many factors have been shown to influence the activity of evoked periodic and after-discharge waves. If an anesthetic is used, the stage of anesthesia may affect the frequency of the after-discharge activity. The variation in size of fibers which provide the interconnections between the thalamus and the cortex as well as the variable number of synapses in the possible circuits may introduce a degree of temporal dispersion. Kristinnsen and Courtois (1949) found impulses traveling in such circuits may not all be effective in initiating or continuing the cyclic activity. Impulses which reach a neuron at various points in the cycle of neuronal excitability or those which reach the cortex during post-excitatory depression will make no contribution to the auto-excitation of the circuit.

Excitability changes associated with the evoked cortical potential

Neurons of the cortex exhibit properties similar to peripheral nerves following stimulation. Changes in excitability include a refractory period, and a recovery period as well as a period of post-excitatory depression.

In the vast majority of work done on evoked potentials an anesthetic agent has been employed. Barbiturates have been widely used and have been found to alter the recovery time by lengthening it (Kristinnsen and Courtois, 1949; Krendel, 1959-1960). These agents have been used with the thought that depression occurs through action on the internuncial cortical neurons rather than on the afferent pathways. This is supported by the suppression seen in the spontaneous cortical activity while the primary evoked response is left unaffected.

Post-excitatory depression has been observed in the cortex following the evoked response and is linked to the intensity of the stimulus. A weak cortical response to stimulation may produce no observable cortical depression whereas an intensely strong response may be followed by a phase of post-excitatory depression lasting for several hundred milliseconds to as long as a full second (Clare and Bishop, 1952; Marshall, 1949).

The periodic after-discharge activity and the phenomenon of post-excitatory depression have been linked by the work of Jarcho (1949). As the corticothalamic reverberating waves rise and fall there is a concomitant rise and fall in cortical

excitability (Chang, 1950; Chang, 1951). When compared on the same time scale, the excitability curve and the reverberating waves are found to be 90^{o} out of phase. That is to say that the maximum increase in excitability is found to coincide with the midpoint of the returning or downward portion of the reverberating wave (Chang, 1951).

Chlorinated Hydrocarbon Insecticides

Under this heading exist two subgroups: the chlorophenothane (DDT) group and the cyclodiene group. These may be differentiated on the basis of symptoms. Convulsions occur earlier in toxicity related to the cyclodiene than in the chlorophenothane group. A member of each group was used in this study and will be discussed more fully in sections to follow.

Although the use and investigation of these insecticides has been widespread, the exact mode of action for these compounds is essentially unknown. In both insects and mammals these agents are recognized as neurotoxicants with the central nervous system the primary target organ (Isaacson, 1968).

Electroencephalographic changes in chlorinated hydrocarbon insecticide toxicity

Spiotta (1951) presented a case of aldrin poisoning in which cerebral dysrhythmia developed following acute toxicity in the human. The EEG activity was characterized by bilateral synchronous spike and wave complexes. Five months following

the ingestion of aldrin the EEG rhythm of the patient returned to normal.

Human patients poisoned by chlorinated hydrocarbons have been described by Princi (1957) as having diffuse cortical discharges.

Hoogendam et al. (1962) recorded EEGs from workers engaged in the manufacture of aldrin, dieldrin, and endrin. The frequency of bilateral synchronous theta activity suggested to Hoogendam that brain stem injury was a part of the intoxication. Of those workers exposed to chlorinated hydrocarbons and manifesting convulsion, 20 percent of them showed slow, high voltage theta waves.

Chlorophenothane group

DDT is the oldest and most widely known and used compound of this group. Synthesis of DDT was accomplished in 1874 by Zeidler but its application as an insecticide was not discovered for another half century (Radeleff, 1964).

DDT poisoning in mammals is manifest by what is often termed a "fear" response. This anthropomorphic term denotes a restless state in the animal and an arousal and response to stimuli which would evoke less activity or no response in an animal which was not poisoned (Bing et al., 1946; Buck, 1965; Radeleff, 1964). A heightened response to all stimuli is indeed a characteristic early sign of DDT poisoning. An increase in the frequency of spontaneous movements is evident

initially as fine intermittent muscle tremors which progress to coarse continual tremors. Shankland (1964) found a consistent symptom pattern in chronic spinal rats poisoned with DDT. A very noticeable hyperresponsiveness to audio stimuli was reported which was followed by a fine muscle tremor of the head and shoulders. This progressed to coarse tremor and convulsions.

Absorption of DDT powder in mammals is poor through the intact skin and irregular from the intestinal tract. However, oil solvents promote absorption both from the skin and intestinal tract. Storage of DDT takes place in all body tissues especially the fatty tissue (Jones, 1965).

Dale et al. (1963) was able to correlate the symptoms of acute DDT poisoning of rats with the levels of DDT found within the brains of the affected animals. Higher concentrations of DDT were found to reside within those areas of the brain composed of gray matter. Using radioautography Bäckstrom et al. (1965) found a higher DDT concentration in the gray matter of the central nervous system. Woolley and Runnells (1967) compared DDT concentrations in the spinal cord. They reported that lipids of the central nervous system take up DDT rapidly. Such areas are represented by the gray matter of the neocortex and cerebellum. Areas of high myelin content such as the brain stem and spinal cord are much slower in their

uptake of DDT.

The mechanism of DDT toxicity has been pursued by numerous investigators. Hille (1968), Narahash and Haas (1968) have found that DDT affects the sodium channels in the nerve membrane. Membranes poisoned by DDT possess sodium channels which remain open during impulse transmission so that an abnormally long sodium current is produced. Gordon and Welsh (1948) found nerves of the crayfish, when poisoned with DDT, react to an impulse by initiating a repetitive train of impulses. An increase in concentration slows the rate of impulse frequency but increases the time duration of these impulses. Hayes (1959) reviewed investigations of DDT sites of action. The brain was considered by some to contribute greatly to the symptoms seen in DDT poisoning. Other sites of action have also been established. Bromily and Bard (1949) induced tremors with DDT in decerebrate, decerebrate-decerebellate, and spinal cats and dogs. Shankland (1964) attributed a role in the symptomatology of DDT poisoning to the spinal cord. He noted a prolongation of hind leg reflexes and the occurrence of spontaneous tremors in the hind legs of spinal rats when poisoned with DDT.

Woolley and Barron (1968) studied changes in electrical activity of the brain of DDT poisoned rats and compared them with spontaneous behavioral changes. Voltages of greatly

increased amplitude of high frequency were recorded from the cerebellar vermis and neocerebellum. This change was attributed to proprioceptive input and DDT excitatory effects acting on cerebellar neurons. Of all the sites monitored in this study, the greatest changes were seen in the cerebellum. Most of the changes seen in other sites resembled the EEG activity seen with arousal. These workers concluded that DDT acts to stimulate the reticular activating system. This activation perhaps is the basis of the hyperirritability seen in DDT poisoning. An increase in the frequency and amplitude of the electrical activity of the motorcortex and cerebellum was observed in DDT poisoned cats by Crescitelli and Gilman (1946) and in DDT poisoned dogs by Pollack and Wang (1953). Desi et al. (1966) also noted an increase in frequency and amplitude of EEGs of rats poisoned with DDT. From this work Desi postulated that DDT poisoning may result in an accumulation of acetylcholine which is known to increase the frequency and amplitude of cortical electrical activity.

Cyclodiene group

Dieldrin is representative of the cyclodiene group of chlorinated hydrocarbons. This compound was named for Otto Diels a codiscoverer of the diene synthesis in 1948 (Zavon, 1963).

As with other members of the chlorinated hydrocarbon family, dieldrin has central nervous system disturbances as

its symptomatic manifestations. Dieldrin toxicity, however, is more prone to produce convulsions earlier in the course of toxicity than is DDT. Generalized stimulation or depression of the central nervous system is characteristic of dieldrin. Symptoms will vary among animals (Radeleff, 1964).

Although the mechanism of action has yet to be delineated there is little question that the site of action is the central nervous system.

Gowdey et al. (1954) demonstrated the effects on the central nervous system of dieldrin in cats and rabbits. Intravascular injections of dieldrin produced increased reflex excitability leading to convulsions and death.

Convulsive seizures have been induced by photic stimuli in sheep exposed to dieldrin (Van Gelder et al., 1969). Three exposed animals were presented a high intensity flash of light in the range of 11 to 14 Hz. These animals began to convulse during stimulus presentation and continued until the stimulation was discontinued. Prior to this convulsive episode the animals had presented no signs of clinical insecticide toxicity.

Crevier et al. (1954) found dieldrin to increase the activity of non-specific serum esterases. Hosein and Proulex (1960) have found that in rats dieldrin may be the factor responsible for the release of betaine esters which have been shown to have the ability to produce convulsions and to have

effects similar to acetylcholine (Burger and Hobiger, 1949).

Human cases of toxicity have shown excitation, muscular twitching, convulsions, and loss of consciousness following exposure to dieldrin (American Medical Association Committee on Toxicology, 1960; Hosein and Proulex, 1960; Patel and Rao, 1958).

Hayes (1959) presented a worldwide survey of human exposures. The people involved were employed to apply dieldrin as a part of a malaria control project. Two to 40 percent of the workers were poisoned with 47 to 100 percent of the cases involving convulsions.

Twenty cases of human poisonings by dieldrin have been described by Patel and Rao (1958). In these cases the appearance of convulsions was a universal and diagnostic sign.

The symptomatology in animals is similar. Hypersensitivity is usually seen first with clonic muscle spasms following. The spasms generally involve the cervical musculature and forequarters first and progress to the hindquarters. Loss of coordination leads to abnormal walking or running. With the onset of generalized body convulsions, death usually follows shortly (Hayes, 1959; Jolly, 1954; West and Campbell, 1946; Wolfe et al., 1963).

In those cases which take the form of severe depression, the animal may show drowsiness and a reluctance to move. There is a loss of appetite with a resultant emaciation and

dehydration. These symptoms may be evident until the time of the animal's death although death is usually accompanied by convulsions (Radeleff, 1964).

Reoccurrence of symptoms and convulsions have been recorded following long periods of time from the last exposure (Conley, 1960; Gowdey et al., 1954; Hayes, 1959; Patel and Rao, 1958).

Storage and elimination of dieldrin has been shown to be slow and the basis of a cummulative effect (Gannon et al., 1959; Jolly, 1954; Wolfe et al., 1963).

In addition to the physiological signs of nervous system involvement, several behavioral studies have been conducted. Sandler et al. (1969) showed a deleterious effect on vigilance behavior related to chronic dieldrin toxicity. Maland (1968) found a high correlation between dieldrin exposure of sheep and the ability of the animal to relearn a visual discrimination task.

Organophosphorous Compounds

All members of the organophosphorous group of compounds inhibit a neural enzyme, acetylcholinesterase. Organophosphorous compounds are oxidized in the biological system to form an oxygen analogue which is responsible for the principle toxic effects. These compounds in mammals inhibit a family of enzymes, the cholinesterases. The most important member of

this family of enzymes is acetylcholinesterase.

Acetylcholine is a chemical mediator released from presynaptic neurons. This agent is released at all synapses between preganglionic and postganglionic fibers of the autonomic system, the myoneural junction, at all postganglionic parasympathetic and some postganglionic sympathetic endings. Those neurons which release acetylcholine are termed cholinergic (Ochs, 1965). Following synaptic transmission acetylcholine must be removed if repolarization is to occur. This removal is accomplished by hydrolysis of the free acetylcholine. Acetylcholinesterase is the enzyme which serves as a catalyst for the process (Ganong, 1967). Hence, without the effect of cholinesterase there is an accumulation of acetylcholine in the body which will produce a general picture of cholinergic stimulation (Jones, 1965).

In organophosphate poisoning the excessive parasympathetic function dominates the symptomatic picture. Muscarinic, nicotinic and central nervous system classifications have been given to these symptoms based on the neuro-anatomical site of action (Radeleff, 1964).

Symptoms of the muscarinic class involve the postganglionic nerve elements with a resultant excessive stimulation of autonomic effector cells. Manifestations of these symptoms includes anorexia, nausea, vomiting, abdominal pain, cramps,

gastrointestinal hypermotility, diarrhea, dyspnea, miosis, pulmonary edema and cyanosis.

Nicotinic effects result from preganglionic and somatic nerve elements. Stimulation followed by paralysis of skeletal muscle is characteristic.

Central nervous system effects are mediated through direct action on sites of nervous control. Headache, apprehension, ataxia, generalized tremor, drowsiness, mental confusion, convulsions, loss of reflexes and coma are signs of the central nervous class of symptoms.

Rulene®

Rulene® is used in the livestock industry as a systemic agent against Hypoderma bovis as well as a conventional general insecticide.

Symptoms of poisoning are variable. Salivation and abdominal distress typify one class of symptoms while alternating periods of depression and excitement characterize another. Some cases exhibit disfunction of labyrith activity. Little is known about this compound and no studies of its effect on EEG activity appear in the literature.

Pertinent Anatomy of Hearing and Vision

Hearing

Transmission of sound from the cochlea to the auditory cortex involves at least four neurons and upwards to as many

as six.

Fibers from the organ of Corti enter the dorsal and ventral cochlear nuclei. All fibers synapse at this point. Most of the second order neurons cross to the opposite side of the brain stem through the trapezoid body to terminate in the superior olivary nucleus. A few fibers pass ipsilaterally to terminate in the superior olivary body on the same side. The major portion of the auditory pathway then courses upward through the lateral lemniscus to end in the inferior colliculus. Some fibers terminate in the nucleus of the lateral lemniscus while others cross to the contralateral nucleus. From the inferior colliculus the fibers of the auditory pathway pass to the medial geniculate body by way of the peduncle of the inferior colliculus. In the medial geniculate body all fibers synapse before the pathway continues on to the auditory cortex by the auditory radiations (Elliott, 1963; Guyton, 1966).

In this pathway several sites provide fibers to both hemispheres. An abundance of collateral fibers also pass into the reticular activating system of the brain stem. The pathway may or may not contain synapses in such sites as the superior olivary nuclei, lateral lemniscial nuclei or in the nuclei of the inferior colliculi. This variability produces some tracts which are more direct than others.

The projection area in the auditory cortex in man lies

predominantly on the supratemporal plane of the superior temporal gyrus and extends over much of the lateral border of the temporal lobe (Guyton, 1966). The temporal lobe is generally regarded as the site for the auditory projection area in all animals. An accurate mapping of this area, however, is not available for the sheep.

It was shown by Rose (1960) that neurons within the auditory pathway respond to a characteristic frequency such that a tonotopic organization is represented. Woolsey (1960) has shown the auditory cortex of the cat to have an organized tonotopic representation.

Greatest cortical response to sound was shown by Bremer and Dow (1939) to be present in the contralateral auditory cortex. Confirming reports of this work have been published by Tunturi (1944), and Rosenzweig and Rosenblith (1950). In all of these reports the experimental procedures were carried out with the animal under anesthesia.

Geisler et al. (1958) reported that the transcranial response in man to a monaural click is bilateral. This work was conducted using an averaging technique to obtain the response. Bickford et al. (1964) undertook a reexamination of averaged evoked potentials in man. Using scalp electrodes Bickford found that the recorded wave forms were contaminated by myogenic activity which contributed greatly to the recorded response. Bickford concluded that the Geisler response is not

cortical but myogenic in origin. The aspect of signal contamination in other reports must be considered.

Vision

Basically the human visual pathway has three neurons from the sense organ to the cortex and unlike the auditory path, has them throughout (Elliott, 1963). The primary cell body, the bipolar cell, lies outside the central nervous system as does the secondary nerve cell body, the "ganglion" cell. Fibers from each nasal hemiretina cross in the optic chiasm (Elliott, 1963; Netter, 1962). These fibers form the optic tract which terminates in the lateral geniculate body of the thalamus. Within the lateral geniculate body of the thalamus lies the tertiary nerve cell body. In the lateral geniculate body fibers from the nasal half of one retina and the fibers from the temporal half of the opposite retina synapse to form the geniculocalcarine tract. This tract passes from the geniculate body to the occipital lobe of the cerebral cortex (Elliott, 1963; Ganong, 1967; Netter, 1962).

Evoked cortical responses to light have been shown to have a variability based on the maturity of the subject. The human infant has been shown to have a greater amplitude and longer latency in transcranially recorded light evoked responses than the mature adult (Ellingson, 1960).

Mimura et al. (1967), using rabbits, showed that cortical potentials evoked by light flashes varied with various activity

levels of the brain. Progressing from high to low phases of brain activity increases the latencies of the evoked potentials. The latencies of the repetitive afterwaves, however, exhibited a prolongation with a decrease in EEG activity. This work presented no mechanism to explain the observations but rather pointed to the effect of central nervous system interactions on the evoked potential.

METHODS AND MATERIALS

Electrode Preparation

The electrodes were fabricated from a nylon screw[1] (1/4 x 8-32 or 3/8 x 8-32) which was drilled longitudinally (1/16 inch diameter). Through this hole in the nylon screw was placed a two inch stainless steel wire which was doubled on itself. The loop end of the wire was passed from the head down the shaft. After exiting from the shaft the tip of the loop was bent at a right angle so that the wire would be carried ahead of the screw as it was screwed into the skull. The single ends of the wire were left above the screw. An open loop was fashioned in one of the free ends and was pre-soldered.[2] See Figure 2. As the electrodes were implanted the ability of the wire to be moved up and down through the hole in the screw was monitored. When the wire came into firm contact with the dura, the wire would no longer move.

Surgical Preparation

Mature female sheep were used as the experimental animal in this study.

Each animal was held off feed twenty-four hours prior to surgery. One hour prior to surgery 30 milligrams of atropine

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[1]Small Parts, Inc., Box 792, Biscayne Annex, Miami, Florida 33152.

[2]Ersin, LMP (62% tin, 36% lead, 2% silver) Allied Electronics, Chicago, Illinois.

were administered subcutaneously to the animal. Induction of anesthesia was produced by the use of an ultra-short acting barbiturate[1] administered intravenously. The animal was then intubated and anesthesia was maintained by the use of methoxyfluorane[2] administered with a closed system inhalation machine.[3]

The animal was placed in a recumbent position with its head supported firmly in a stereotoxic frame.[4] See Figure 5.

The entire dorsum of the head was clipped and scrubbed. Three applications of 70% ethanol was used as a disinfectant of the skin. A medial longitudinal incision was made from the posterior border of the frontal sinus to the external occipital protuberance. The initial incision was toweled off and the skin freed from the underlying tissue by blunt dissection. A medial longitudinal incision between the muscles was made down to the cranium. Periosteal elevators were used to free the periosteum from the dorsal surface of the cranium. All tissue freed from the cranium and the overlying muscles were excised as far laterally as possible, exposing the entire dorsum of the skull. The bony surface was then thoroughly scraped with

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[1]Pento Short, Haver-Lockhart, Kansas City, Missouri.

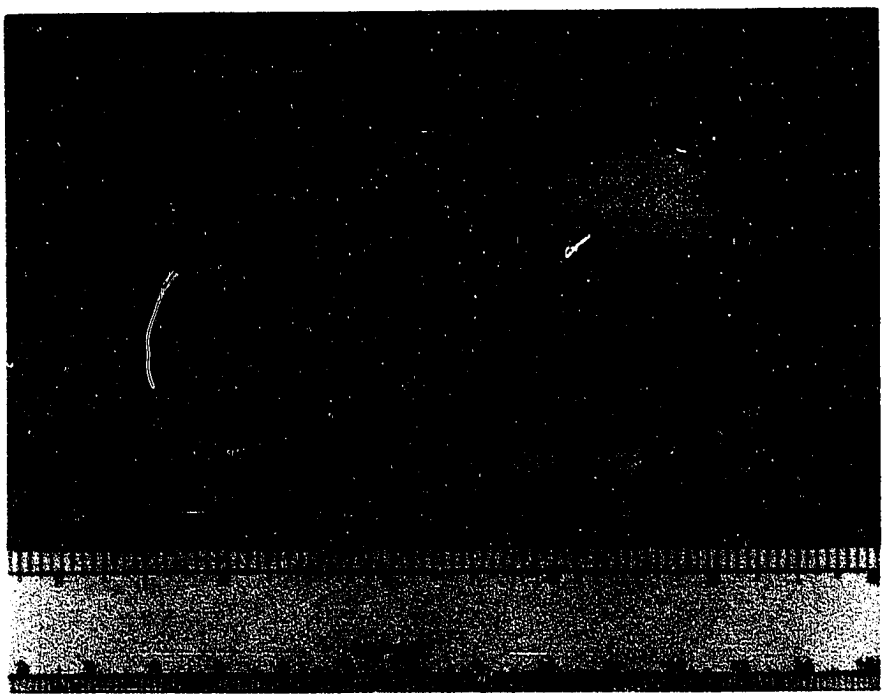
[2]Pitman-Moore Co., Indianapolis, Indiana.

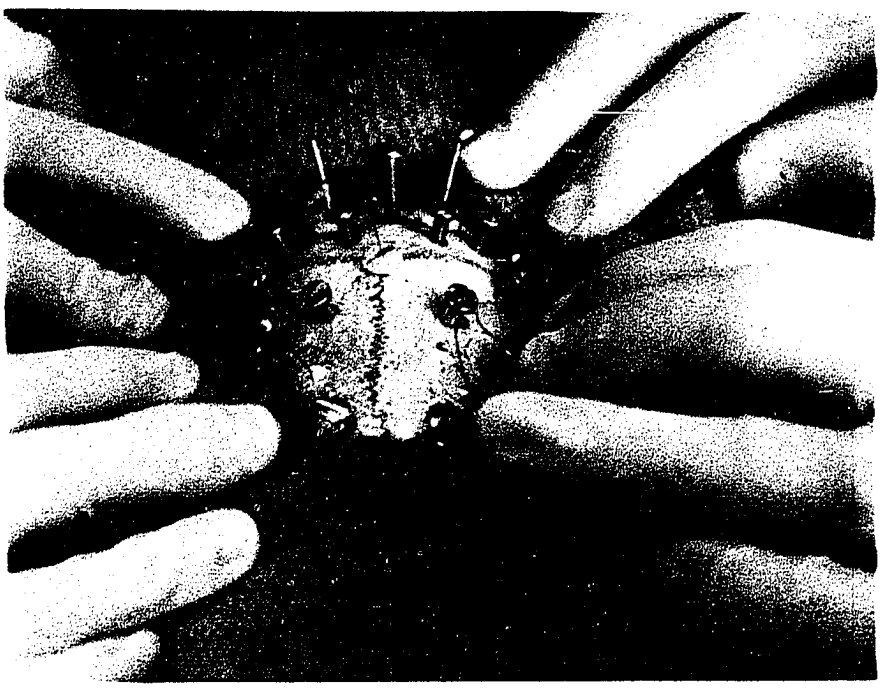
[3]Veterinary Anesthesia Machine, (Heidbrink Model 960), Ohio Chemical Co., Youngstown, Ohio.

[4]David Kopp Instruments, 7324 Elmo Street, Tujunga, California 91042.

Figure 2. The head plug is shown at the top of the picture. Stainless steel anchoring screws are to the bottom left. Three dural electrodes are shown on the bottom right.

Figure 3. Dural electrodes and anchoring screws are shown following surgical placement.





a scalpel to insure a tissue-free surface.

Six electrodes were placed through the skull onto the dura mater. Electrodes were placed over both left and right frontal, temporal, and occipital cortex. A seventh electrode was placed at bregma to serve as a reference electrode. In this study, however, recordings were taken only from the temporal and occipital electrodes.

A surgical hand drill was used to drill holes 9/64 of an inch in diameter through the skull for each dural electrode. Careful manipulation of the drill permitted this procedure to be executed without penetrating the dura. The reference electrode was placed in the bony skull. Bregma was the point from which measurements were made for electrode placement. The occipital electrodes were placed two centimeters caudally and one and a half centimeters laterally; the temporal electrodes were placed one centimeter anteriorly and two centimeters laterally; the frontal electrodes were placed three centimeters anteriorly and one centimeter laterally. See Figure 3. Each hole was threaded using a machine tap which was disinfected by cold sterilization solution.

In addition to the electrodes *per se* a dozen stainless steel anchoring screws[1] were placed into the skull.

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[1]Small Parts, Inc., Box 792, Biscayne Annex, Miami, Florida 33152.

A plastic acrylic material[1] was placed over the electrodes and anchoring screws. The anchoring screws were to facilitate the adherence of this material. Enough of this material was used at this time to thoroughly cover the electrodes but not the free end containing a pre-soldered loop.

A prepared autoclaved head plug[2] was soldered to the pre-soldered loops. Hemostats were placed on the electrodes prior to soldering to serve as a heat sink. A color code was used with the wires from the head plug. Pin representation was standardized throughout the investigation. See Figure 4.

Following the soldering of the electrodes to the head plug, the plastic acrylic was used again to cover the remaining wires. The incision was sutured anteriorly and posteriorly with simple interrupted sutures of Vetafil.[3] The suturing was done so as to pull the skin firmly against the acrylic. See Figure 5.

On the day of surgery, and for three days following, each animal received 600,000 units of procaine penicillin-G and 750 milligrams of streptomycin[4] intramuscularly.

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[1]Cranioplastic, Plastic Products Co., P. O. Box 1204, Roanoke, Virginia.

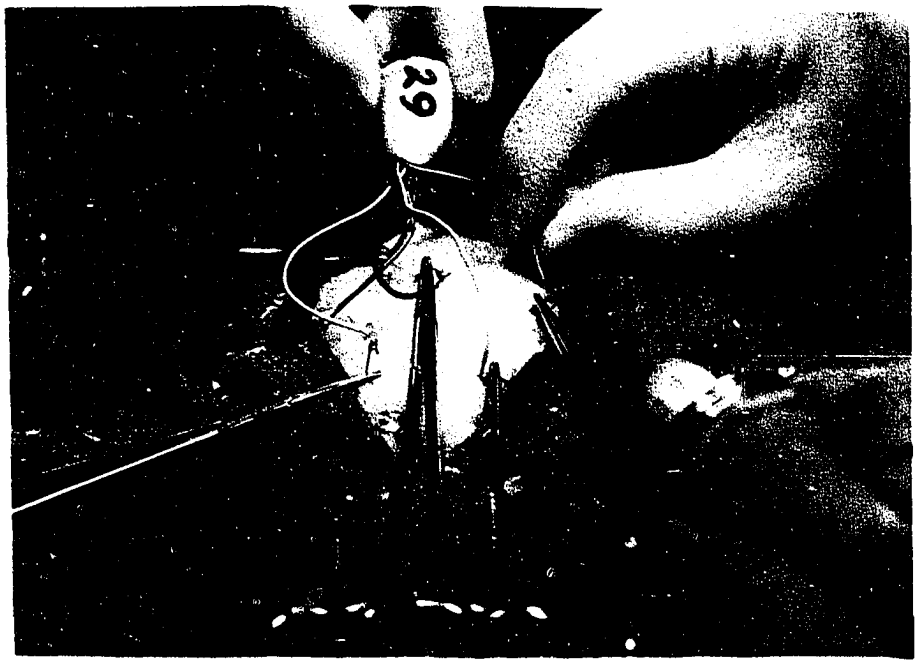
[2]Amphenol 126-198, Allied Electronics, 100 N. Western Ave., Chicago, Illinois 60680.

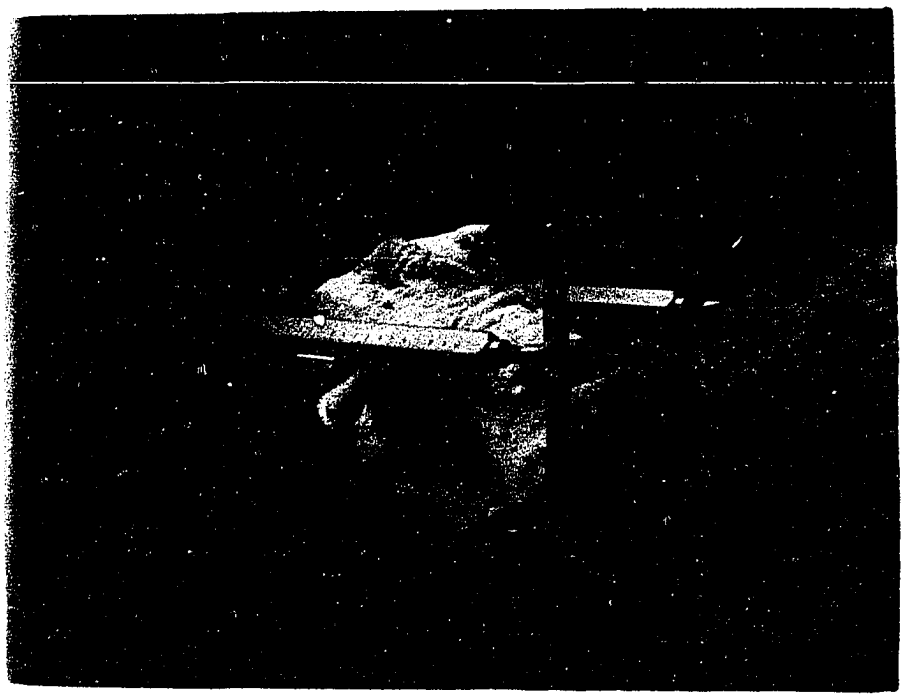
[3]Arista, Surgical Co., 67 Lexington Avenue, New York, New York 10010.

[4]Antibiotic Combination 1. Corvel Co. (A division of Eli Lilly & Co.), Indianapolis, Indiana.

Figure 4. The head plug is shown being soldered to the electrodes. The skull has been covered with the first layer of acrylic. Hemostats are used as heat sinks.

Figure 5. Completed surgical implantation of dural electrodes. The head plug is directed posteriorly. The animal is positioned in a stereotoxic frame.


29



Each animal was allowed at least two weeks of post-operative recovery time before entering the data collection phase.

Experimental Procedure

Light and sound served as the stimuli for the cortical evoked response. The cortical electrical activity was recorded by means of chronically implanted electrodes as described above and was telemetered to the pen recorders[1] (See Figure 6) and an on line digital computer.[2] Telemetry was effected by a pair of two channel battery-powered FM transmitters[3] carried on the backs of the animals. The electrodes and transmitters were connected by means of a head cable (See Figure 6).

The light and sound stimuli were presented in two forms. A short duration burst of light and sound described classically as a flash and a click were used. A modulated form of both the light and sound were also presented to the animals.

Collection of the evoked responses was accomplished through the use of programs written for each of the stimuli. Prior to exposure of the animal to the stimulus, the appropriate program was loaded into the computer. On a trial and error basis the figure twenty-five was found to be a suitable

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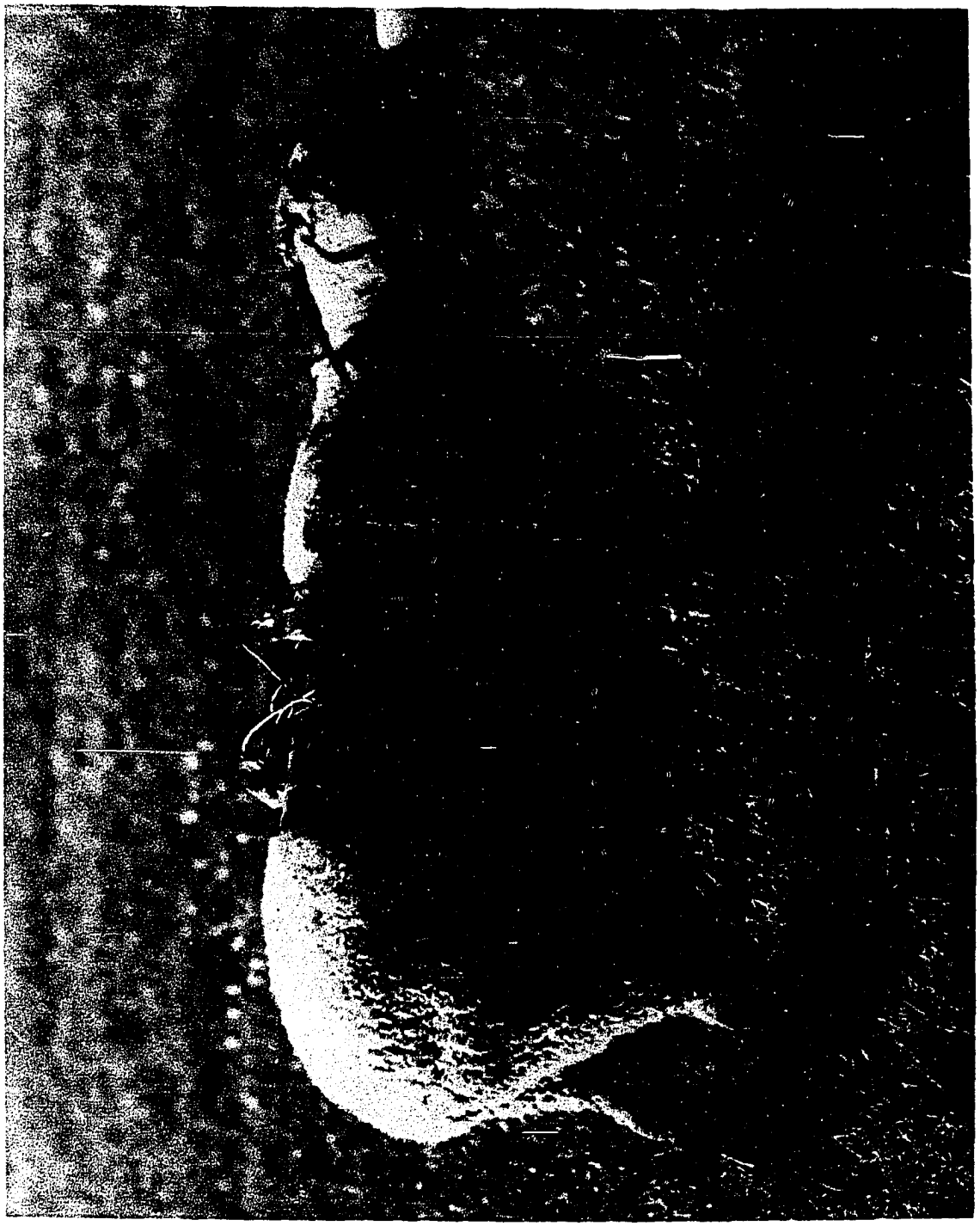
[1]Model 7, Grass Instruments, Quincy, Massachusetts.

[2]Linc-8, Digital Equipment Corporation, 146 Main Street, Maynard, Massachusetts 01754.

[3]Bio Com., Inc., Culver City, California.

Figure 6. An animal with implanted dural electrodes is shown carrying a harness with the transmitters.



number of responses to summate and was used in each program. See Appendix B.

Two hundred fifty-six data points were collected and summated for each response. During the presentation of the modulated stimuli these data points were collected over a time span of one second. When the flash or click were used the time span was reduced to half a second.

Each animal was given a capsule placebo of dextrose four hours before the collection of control data.

The animals were handled while the radio transmitters were harnessed to them. Once in the restraining cage the animals were not disturbed during the data collection period.

Presentation of stimuli was in a random pattern so that there would be no association with a repeated format. A number from one to four was assigned to each stimuli (two modulated stimuli and two pulsed stimuli) and a table of random numbers was used to determine the random sequence of stimuli presentation.

Control information was collected from each animal of the group. Following the collection of the control data the group was exposed to a pesticide given in capsule form daily four hours before collection of data. Exposure continued until the animals showed signs of clinical toxicity.

Three animals were exposed to dieldrin[1] at the rate of

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[1]Technical Dieldrin (100%) was supplied through the courtesy of the Shell Chemical Company, New York.

20 mg/Kg. Three animals were exposed to Rulene®[1] at the rate of 150 mg/Kg., and two animals were exposed to DDT[2] at the rate of 500 mg/Kg.

Table 1. Dosage schedule

Animal	Weight	Doseage rate	Dose
111	47.7 Kg.	500 mg/Kg.	24.00 g DDT
322	39.9 Kg.	500 mg/Kg.	19.90 g DDT
334	34.8 Kg.	150 mg/Kg.	5.60 g Rulene®
337	46.7 Kg.	150 mg/Kg.	7.00 g Rulene®
320	43.1 Kg.	150 mg/Kg.	6.48 g Rulene®
498	73.1 Kg.	25 mg/Kg.	1.83 g Dieldrin
455	65.2 Kg.	25 mg/Kg.	1.63 g Dieldrin
339	41.2 Kg.	25 mg/Kg.	1.03 g Dieldrin

Modulated stimuli

The use of a sinusoidally modulated input was chosen for its desirability in evaluating a physical linear system. In the realm of linear physical systems only a sine wave input will be processed by the linear system to produce an output of the same form as the input, i.e., a sinusoidal output for a sinusoidal input.

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[1]Technical Rulene® (100%) was supplied through the courtesy of the Dow Chemical Company, Midland, Michigan.

[2]Technical DDT (100%) was supplied through the courtesy of the Geigy Chemical Corporation, Ardsley, New York.

Analysis of non-linear systems is extremely difficult in general. However, many non-linear systems under particular conditions may behave in a linear fashion. Under these conditions linear analysis techniques may be employed.

Although the brain as well as most other life systems fall into the class of non-linear systems, there may be conditions under which some linearity may be discovered and through which a better understanding of the system may be gained.

Thus, by using a sinusoidal input of light and sound some assumption of linearity might be made if the system output replicates the input.

Modulated light

Light from a tungsten bulb was passed through sheets of polaroid film.[1] One sheet was cut as a circle of ten inch diameter and sandwiched between two 1/32 inch pieces of plexiglas. This sandwich was mounted on the shaft of a motor equipped with a variable speed controller.[2] As this disc rotated a variable intensity was produced ranging from 2 Hz. to 15 Hz.

The light source was mounted in a box fabricated of wood. The interior of the box was lined with a fiberglas insulation

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[1]American Science Center, Inc., 5700 Northwest Highway, Chicago, Illinois 60646. No. 70419 polarized sheets.

[2]B & B Motor and Control Corp., 96 Spring Street, New York, New York 10012.

to deaden sound. Light passed from the box through a three inch by three inch opening. See Figure 7. The exterior of the box was painted a dull black. A photocell[1] was mounted at the opening for the light source to record the variations in light intensity.

The data from the photocell was recorded as a channel of information representing the system input.

An eccentric was produced on the motor shaft which activated a micro-switch[2] with each revolution of the shaft. The signal from this switch was fed into the computer and served to synchronize the data collection.

The animals were placed in a rectangular restraining cage which prevented the animal from turning around and assured that the animal would face the stimuli. The restraining cage was open at one end so that the animal could see the light. The opening of the box containing the light source was placed two feet from the restraining cage. Room lights were turned off during the entire procedure. The modulated light stimulus was activated by a remote switch. This light was turned on only during periods of data collection. The variable speed controller was also remote. Once the animal was in position the only change effected was the appearance and disappearance of the light.

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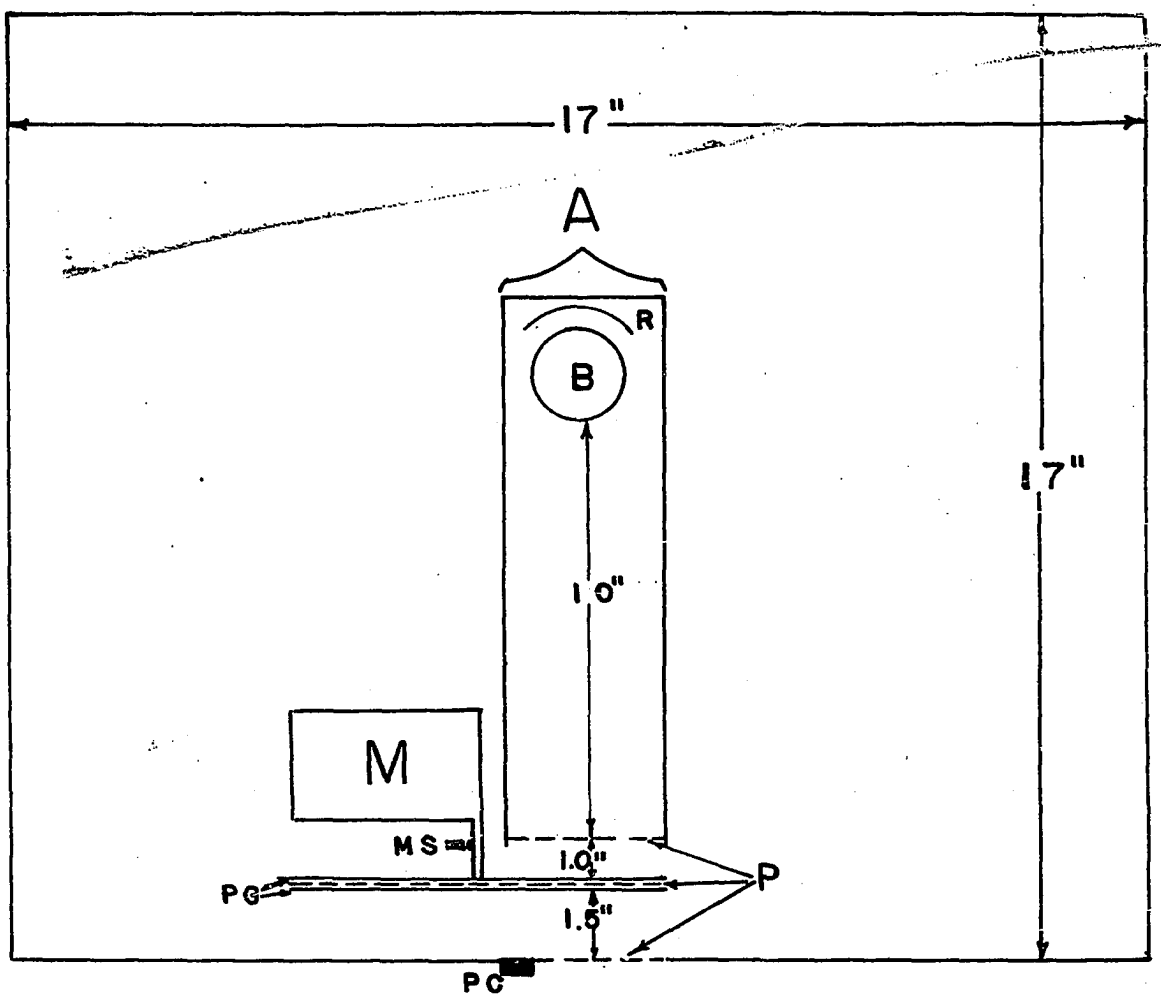
[1]RCA Electronic Components, Harrison, New Jersey 07029. KD 2106.

[2]Robertshaw, Acro Division, Columbus, Ohio.

Figure 7. Schematic representation of the equipment used to produce a modulated light source. A is composed of sides and a top with the floor of the box providing the fourth side. B is the tungsten bulb. R is a reflector. M is the variable speed motor. MS is the microswitch. PG is the plexiglass. PC is the photocell. P is the polarized film.


17"
A
R
B
17"
1.0"
M
MS
1.0"
PG
P
1.5"
PC

Modulated sound

A modulated wave of 5 KHz was varied between 2 Hz and 15 Hz. The amplitude modulated 5 KHz signal was amplified[1] and presented to the animal through a wall mounted speaker.[2] See Figure 8.

Audio stimulation was presented to the animal positioned as it was for the modulated light study. Control of the stimulus was remote. Room lights were off during the entire procedure.

Synchronization for the sample collected was based on a zero crossing of the modulation wave and was detected by a subroutine written into the computer program.

Pulsed light

The source of the burst of light was a variable frequency strobe light.[3] Flashes were presented at the rate of one per second for a time span of ten milliseconds at a peak intensity of 1,500,000 candle power.

The light unit was mounted overhead and directed toward the animal.

Synchronization of data collection was effected by feeding

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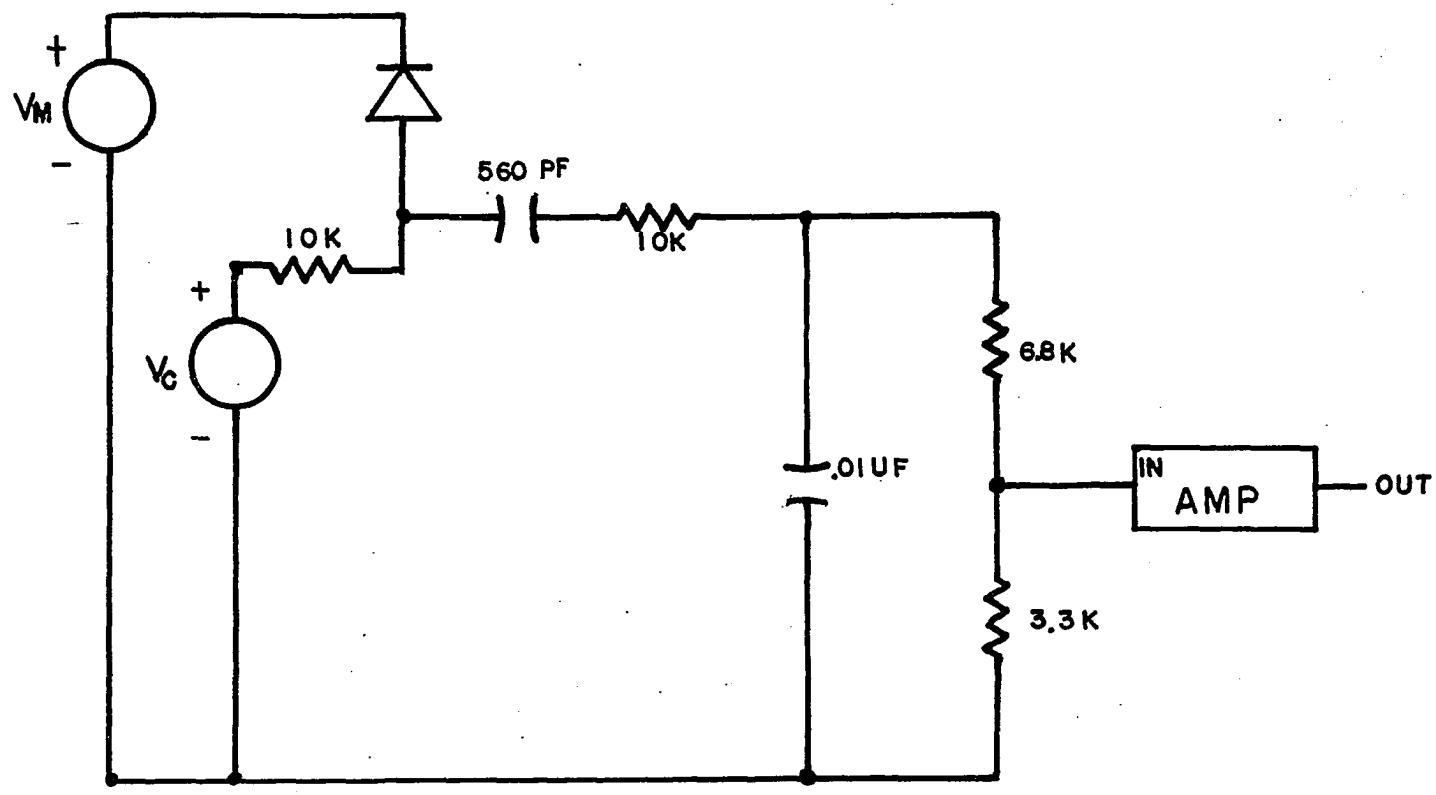
[1]Scott 299F, Allied Electronics, 100 N. Western Avenue, Chicago, Illinois 60680.

[2]Utah C8HC-2, Allied Electronics, 100 N. Western Avenue, Chicago, Illinois 60680.

[3]Model PS2. Photo Stimulator, Grass Instruments, Quincy, Massachusetts.

Figure 8. Circuit used to modulate a 5KHz signal. V_C is the carrier signal. V_M is the modulating signal.


+
VM
−
10K
560 PF
10K
+
VC
−
6.8K
.01UF
IN
AMP
OUT
3.3K

the triggering pulse of the photo stimulator into the computer. The computer was programmed to accept this as the synchronizing pulse.

Pulsed sound

The 5 KHz signal used as the carrier wave in the modulated sound stimuli was fed through a relay so as to produce a tone at the rate of one per second at a duration rate of 50 milliseconds. The same speaker system was used to present the pulsed sound as was used in the modulated sound presentation.

The relay closure was the triggering input to the computer to synchronize the data collection.

Data Processing

Using several computer programs[1] available for the LINC-8 the waveforms of the collected responses were processed block by block. The low pass filter capabilities of the DATAM program was used to smooth the waveform.

Responses from the modulated stimuli were processed by a fast Fourier transform (FFT) program[2] to compute the power spectral density function of the response. See Appendix C. A print-out of the magnitude of the power spectral density

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[1]Digital Equipment Corporation, 146 Main Street, Maynard, Massachusetts 01754.

[2]This unpublished program was kindly provided by Dr. P. M. Handler of the Computer Science Department of Washington University, St. Louis, Missouri.

computation was obtained by using the OLIST program.

The decimal representation of the power spectral density magnitude was put onto computer cards. These cards were then processed by an IBM-360 computer.

Responses from the pulsed light and sound were processed by a program written especially for this purpose. Latencies, amplitude values, and zero crossings were computed by this program. See Appendix B.

Verification of the evoked potential

All equipment for producing the modulated stimuli and the animal was set up and a summated evoked potential was collected using both the modulated light and sound stimuli. The procedure was repeated with each stimulus blocked but with all other aspects of the experiment in operation. In the case of modulated light the opening from which the light emerged was taped so that although the light was on none could be seen by the animal. With the light source blocked no evoked cortical response was obtained. In the case of modulated sound the speaker was replaced by an eight ohm resistor. With the sound removed no evoked cortical response was obtained.

An additional check of the validity of the modulated light response was made. The acrylic head plug was masked with heavy dark material prior to collecting an evoked response. The masking of the acrylic material did not affect

the collection of the response indicating that there was no photoelectric effect taking place between the light and the electrodes.

RESULTS AND DISCUSSION

The three animals exposed to dieldrin were showing clinical signs of toxicity on the third day of exposure. Restlessness and muscle tremors were seen in each animal. Animal 455 convulsed on the afternoon of the third day of exposure and was given no further administration of dieldrin. Animal 339 convulsed on the fifth day of exposure and administration of dieldrin was discontinued on the same day.

Two animals exposed to Rulene®, 334 and 320, showed a generalized muscle stiffness on the second and third day of exposure. Excessive salivation and diarrhea was seen in all animals by the fifth day of exposure. Depression was also evident for the group on the fifth day. On the morning of the eighth day animal 320 convulsed and died.

One of the three animals in the DDT group was removed from the experiment after showing depression and elevated body temperature. Of the two classes of stimuli used in the study, the most pronounced and reproducible response occurred with light. Both the impulse and modulated forms of light produced a more consistent evoked cortical response than did the counterparts of audio stimuli.

Pulsed Stimuli

Response to pulsed sound was most infrequent. A total of 14 summated responses were collected over all animals and

treatments. The sparseness of data was the basis for discounting an attempt at analysis.

Results of the pulsed light summated responses are presented in Figures 9 to 22. The amplitudes are on a scale of relative values. Two latencies are presented and are in millisecond units. The single term latency denotes the time period between stimulus and the onset of the response. Peak latency is a term denoting the time period from the onset of the response to the time the response reaches its maximum value. See Appendix B.

For the animals in the dieldrin exposure group a wide variation in the amplitude of the summated response was recorded. The range of relative values for the amplitudes varied between 39 and 220 for animal 498 and between 16 and 205 for animal 455.

A narrower range of values may be found for the latencies. Onset latencies varied between 13 and 56 milliseconds for animal 498. The same latency period varied between 14 and 70 milliseconds for animal 455. Peak latencies varied between 4 and 41 milliseconds for animal 455 and between 8 and 26 milliseconds for animal 498.

The left and right temporal electrodes and occipital electrodes tended to record lower amplitudes in the summated responses following exposure to dieldrin. This was not the case however for the amplitude recorded from the left temporal

electrode in animal 455. The right temporal electrode recorded little change between the pre-exposure and post exposure values.

A decrease in amplitude recorded from the left temporal electrode of Rulene® animal 334 is marked from day 6 to day 15. The relative variation in this record is between 187 and 86. The downward tendency, however, began on the day prior to exposure to Rulene®. A similar set of values was recorded from the right temporal electrode. The relative amplitude variation for the right temporal electrode is 120 to 28.

Latencies for the right temporal electrode of animal 334 increased over the course of the experiment. The greatest increase occurred on the first day of exposure to Rulene®. The latency recorded on the last day of control was 20 milliseconds. The first day of exposure revealed a 38 millisecond increase to 58 milliseconds. The subsequent latencies for this particular electrode remained above a value of 55 milliseconds.

Marked variation in relative amplitude was recorded from the left occipital electrode of animal 334. Amplitudes ranged between 180 and 12 for this electrode site. On the occipital electrode on the right side the relative range was from 154 to 28.

As noted earlier, animal 320 died on the eighth day of the experiment. A sharp decrease in the left temporal

amplitude values was recorded between the sixth day and the seventh day. This range was from 150 to 100. Much less variation was recorded from the right temporal electrode. At this site values of 109 to 106 were recorded.

Animal 377 exhibited on day one of the experiment large amplitudes from all four electrode sites. The temporal electrodes recorded more homogeneous amplitudes from day six to the end of the experiment. These more uniform amplitudes began prior to the period of pesticide exposure. Amplitudes recorded from the occipital electrodes bear no relationship to those from the temporal areas. A sharp downward tendency in relative amplitude was noted in the left occipital electrode between days seven and nine. From day nine to fifteen the amplitude returned to within the range seen on the first day of exposure.

From the DDT exposure group another wide variation in amplitudes was recorded. A sharp reduction in amplitude was recorded in animal 111 for both the left temporal and the left occipital electrodes on the fifth day of the experiment. On the two successive days following this decline the amplitudes were recorded at higher values. No trend or relationship to insecticide toxicity was evident from this information.

Amplitude variation in animal 322 exhibited little homogeneity between electrode pairs. Onset latency values recorded from the right temporal electrode increased slightly

over the course of the experiment from 17 milliseconds to 60 milliseconds. This tendency began in the control period and showed no alteration following the administration of DDT.

The lack of a definite trend in the pre-exposure Figures 9 through 22 encouraged the computation of ensemble averages in an attempt to find a pre-exposure standard against which to compare the exposure data. Two subsets of animals were formed. Animals 322, 334, 337, and 111 were one subset and animals 320, 498, and 455 were the second subset. The ensemble averages for the relative amplitudes were tabulated. These values are taken over only the control data. The last day is the day prior to exposure for all animals. Data was taken from this point and extended toward the first experimental day so that the same relative days were used for each animal. The graphical results are presented in Figures 23 and 24.

A similar curve is found between the left temporal electrode of subset one and the right temporal electrode of subset two. No similarity is seen between left and right electrodes of either subset one or subset two.

Subset one shows a trend in values for left and right occipital electrodes. The averages for subset two shows no similarity between left and right temporal electrodes or to the occipital electrode plots of subset one.

As a result of the variability in the data, no pre-exposure standard was revealed either by single electrode data analysis or by ensemble averages.

Figure 9. Animal 455. Latencies and relative amplitudes from the temporal electrodes. Dieldrin exposure.

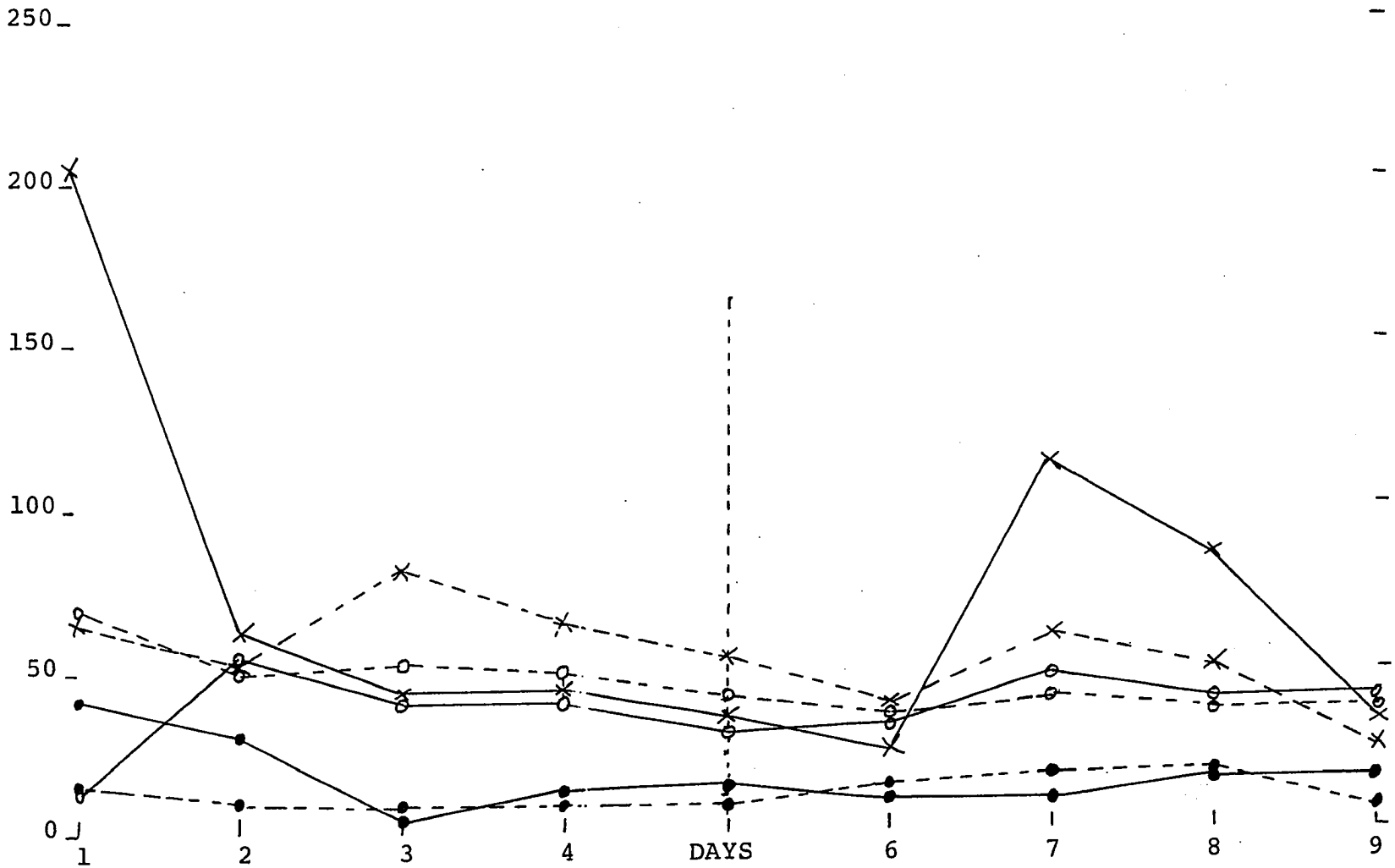
The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊛ = peak latencies

The broken vertical line marks the exposure date.


250
200
150
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50
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1
2
3
4
DAYS
6
7
8
9

Figure 10. Animal 455. Latencies and relative amplitudes from the occipital electrodes. Dieldrin exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊙ = peak latencies

The broken vertical line marks the exposure date.

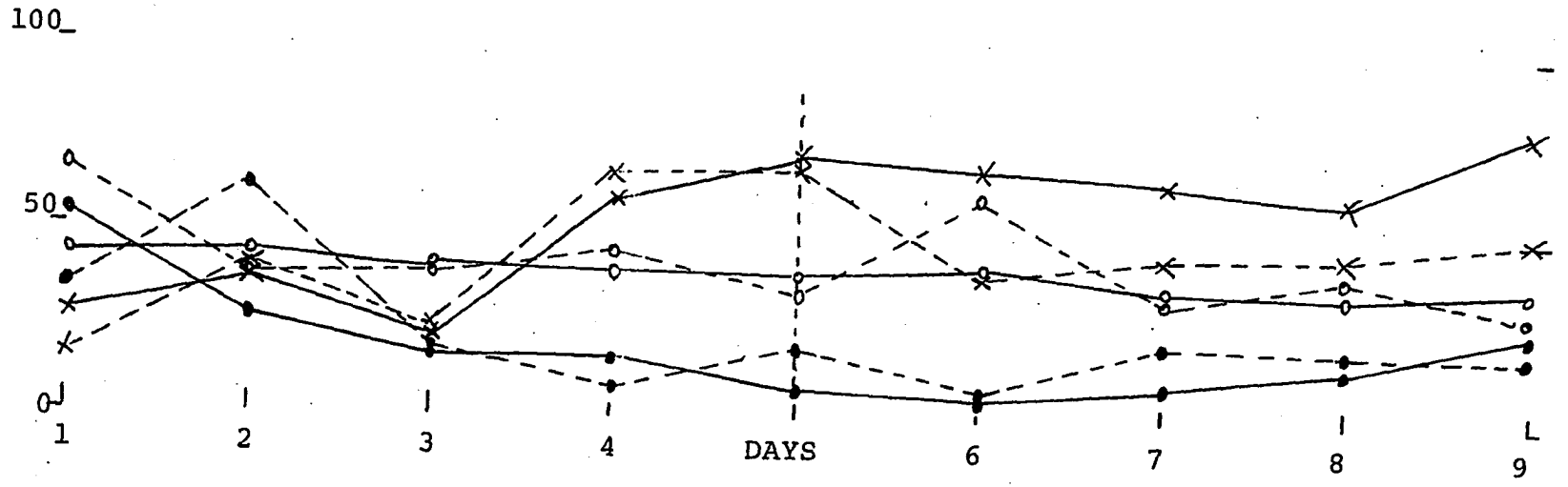

100
50
0
1
2
3
4
DAYS
6
7
8
9
L

Figure 11. Animal 498. Latencies and relative amplitudes from the temporal electrodes. Dieldrin exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

● = peak latencies

The broken vertical line marks the exposure date.

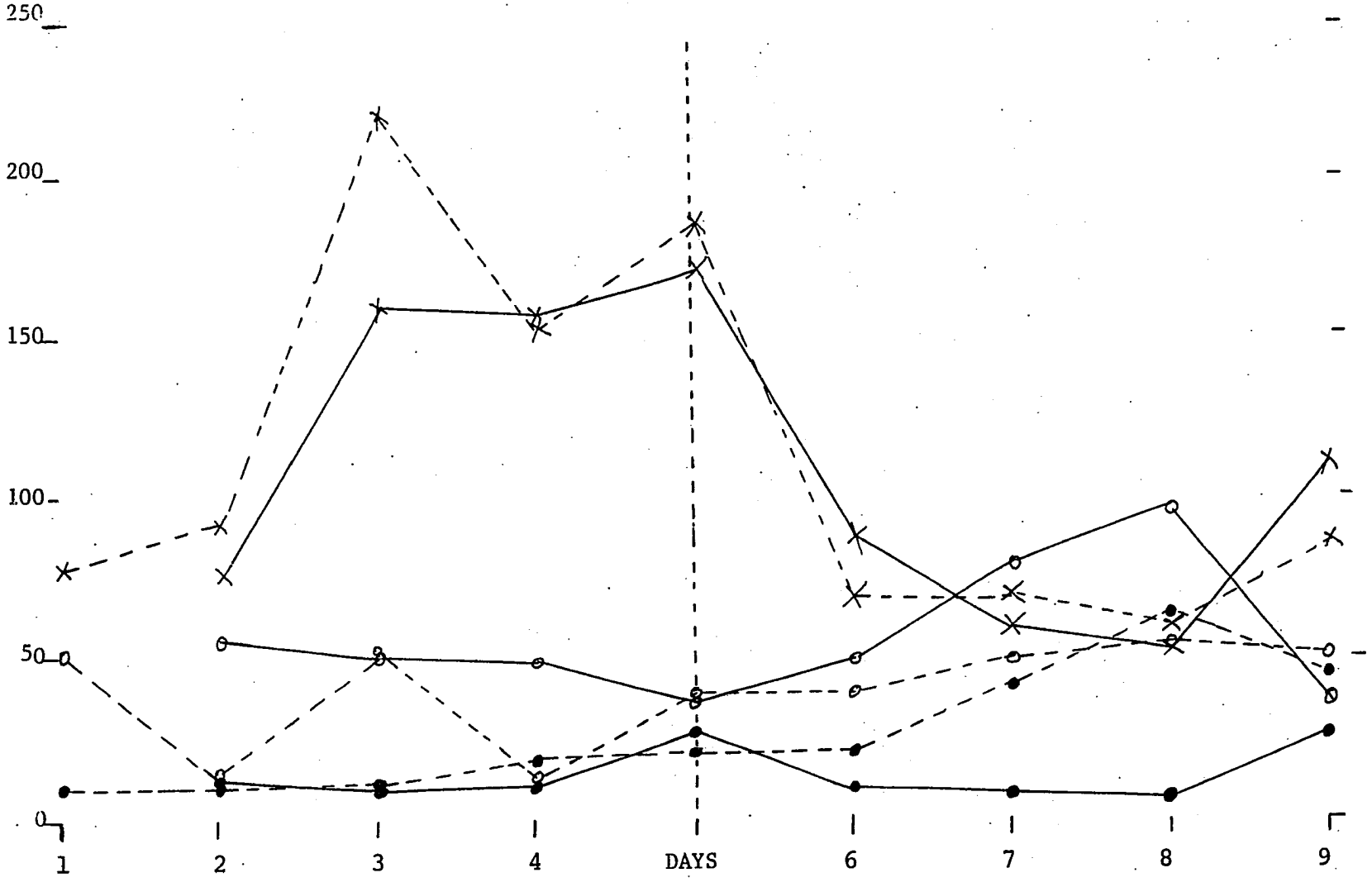

250
200
150
100
50
0
1
2
3
4
DAYS
6
7
8
9

Figure 12. Animal 498. Latencies and relative amplitudes from the occipital electrodes. Dieldrin exposure.

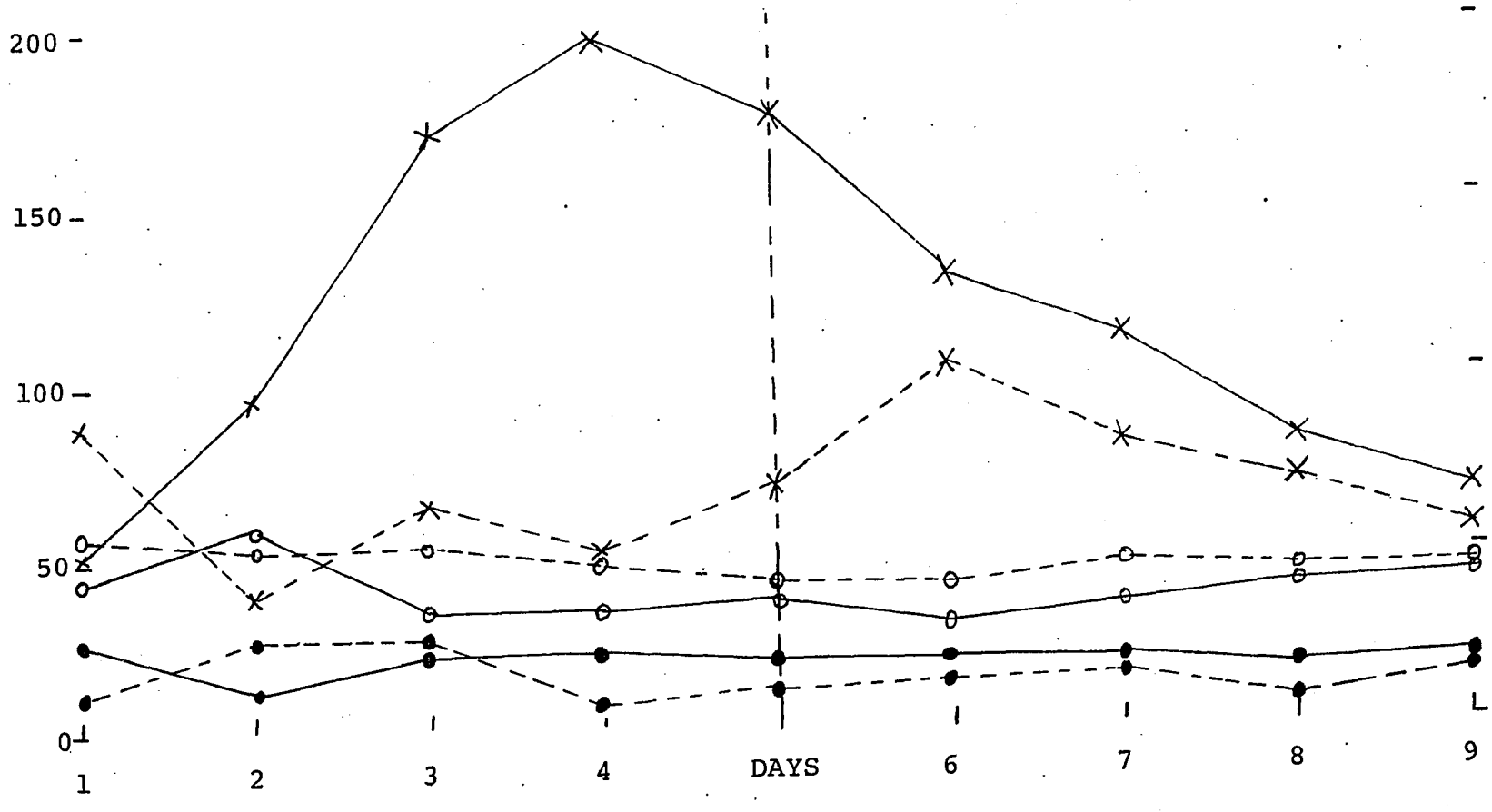
The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊛ = peak latencies

The broken vertical line marks the exposure date.


200
150
100
50
0
1
2
3
4
DAYS
6
7
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9
L

Figure 13. Animal 334. Latencies and relative amplitudes from the temporal electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊛ = peak latencies

The broken vertical line marks the exposure date.

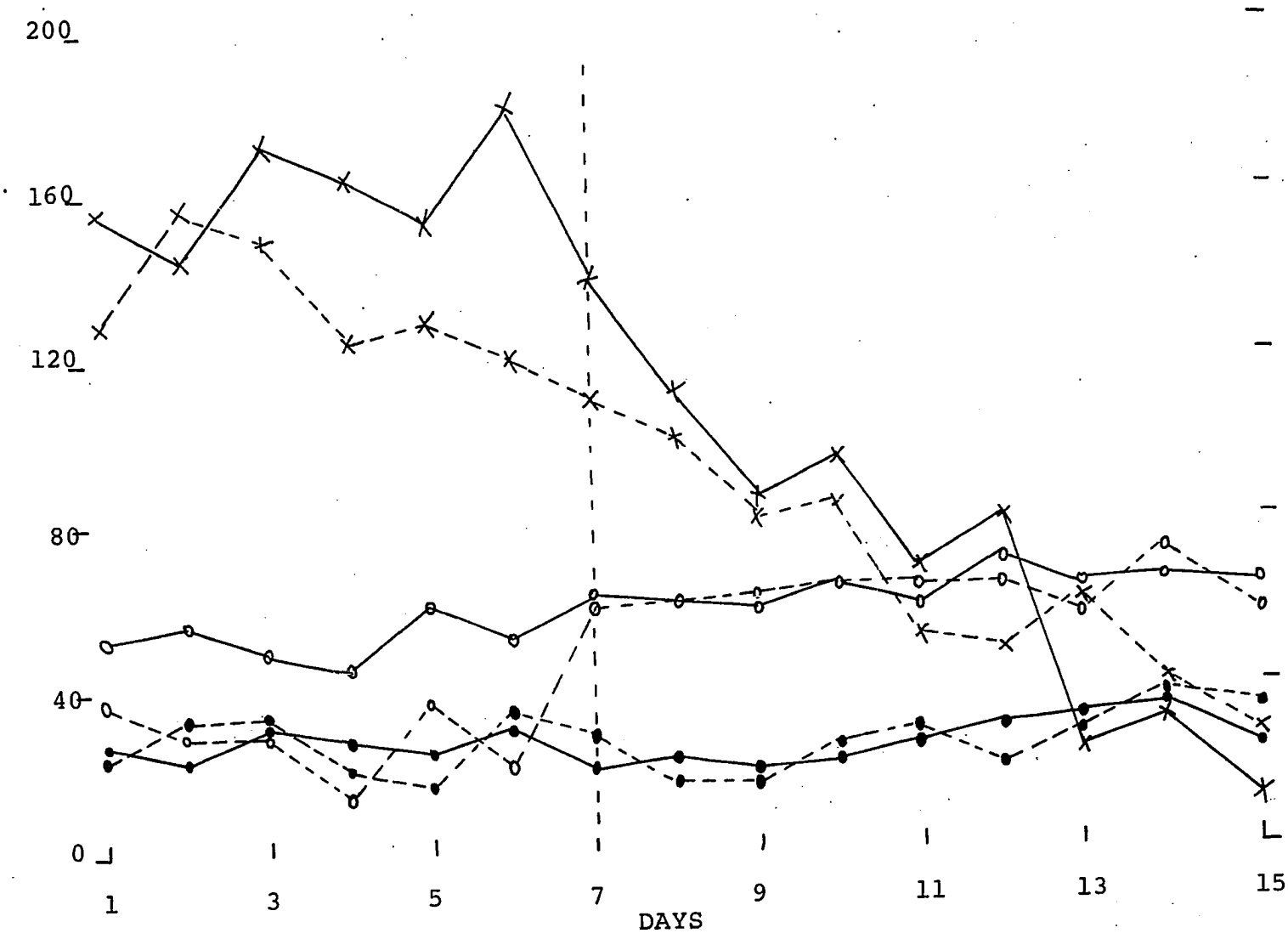

200
160
120
80
40
0
1
3
5
7
9
11
13
15
DAYS

Figure 14. Animal 334. Latencies and relative amplitudes from the occipital electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊛ = peak latencies

The broken vertical line marks the exposure date.

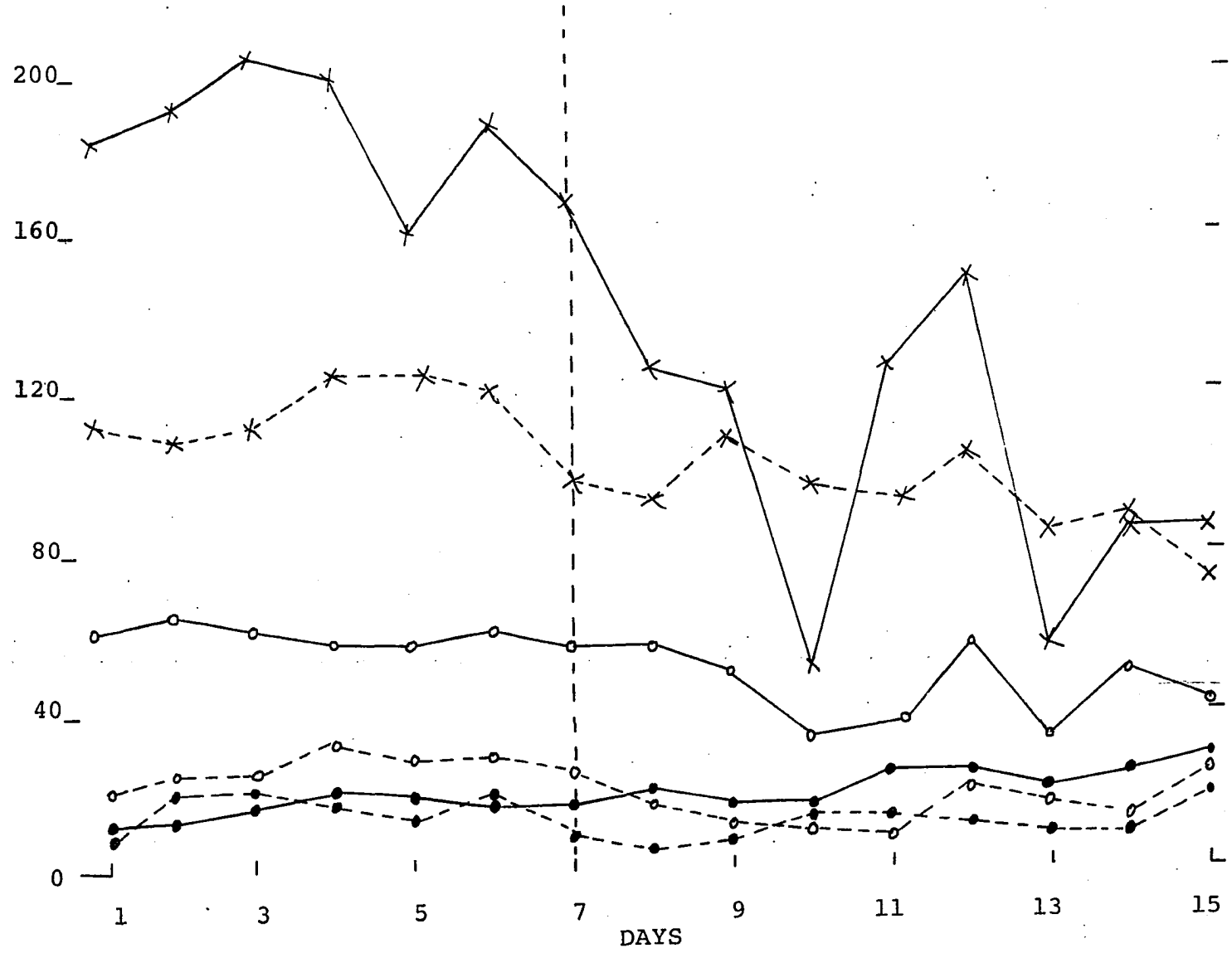

200
160
120
80
40
0
1
3
5
7
9
11
13
15
DAYS

Figure 15. Animal 320. Latencies and relative amplitudes from the temporal electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊘ = peak latencies

The broken vertical line marks the exposure date.

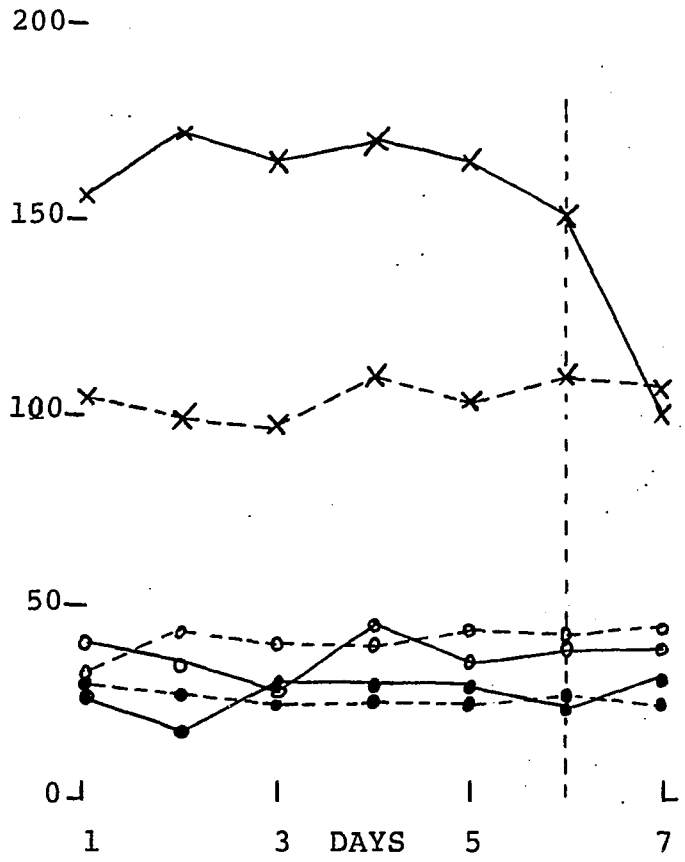

200
150
100
50
0
1
3
DAYS
5
7

Figure 16. Animal 320. Latencies and relative amplitudes from the occipital electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊙ = peak latencies

The broken vertical line marks the exposure date.

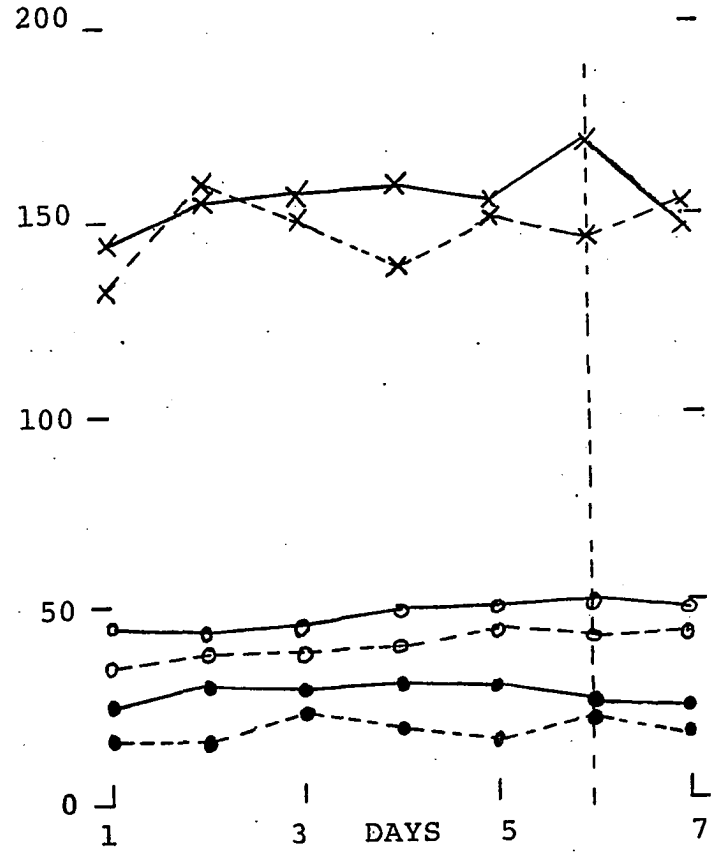

200
150
100
50
0
1
3
DAYS
5
7

Figure 17. Animal 337. Latencies and relative amplitudes from the temporal electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

⊙ = peak latencies

The broken vertical line marks the exposure date.

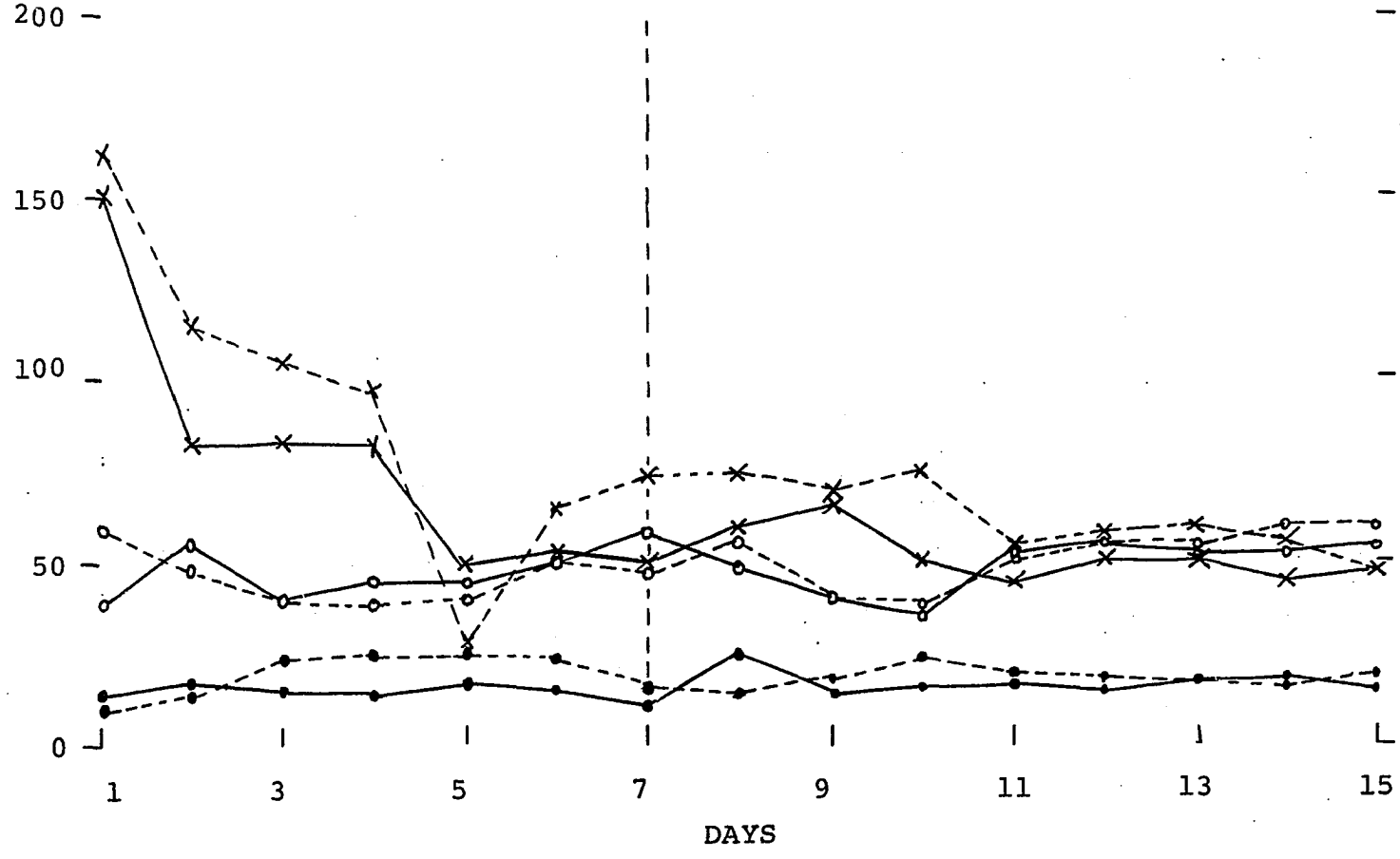

200
150
100
50
0
1
3
5
7
9
11
13
15
DAYS

Figure 18. Animal 337. Latencies and relative amplitudes from the occipital electrodes. Rulene® exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative latencies

O = latencies

⊙ = peak latencies

The broken vertical line marks the exposure date.

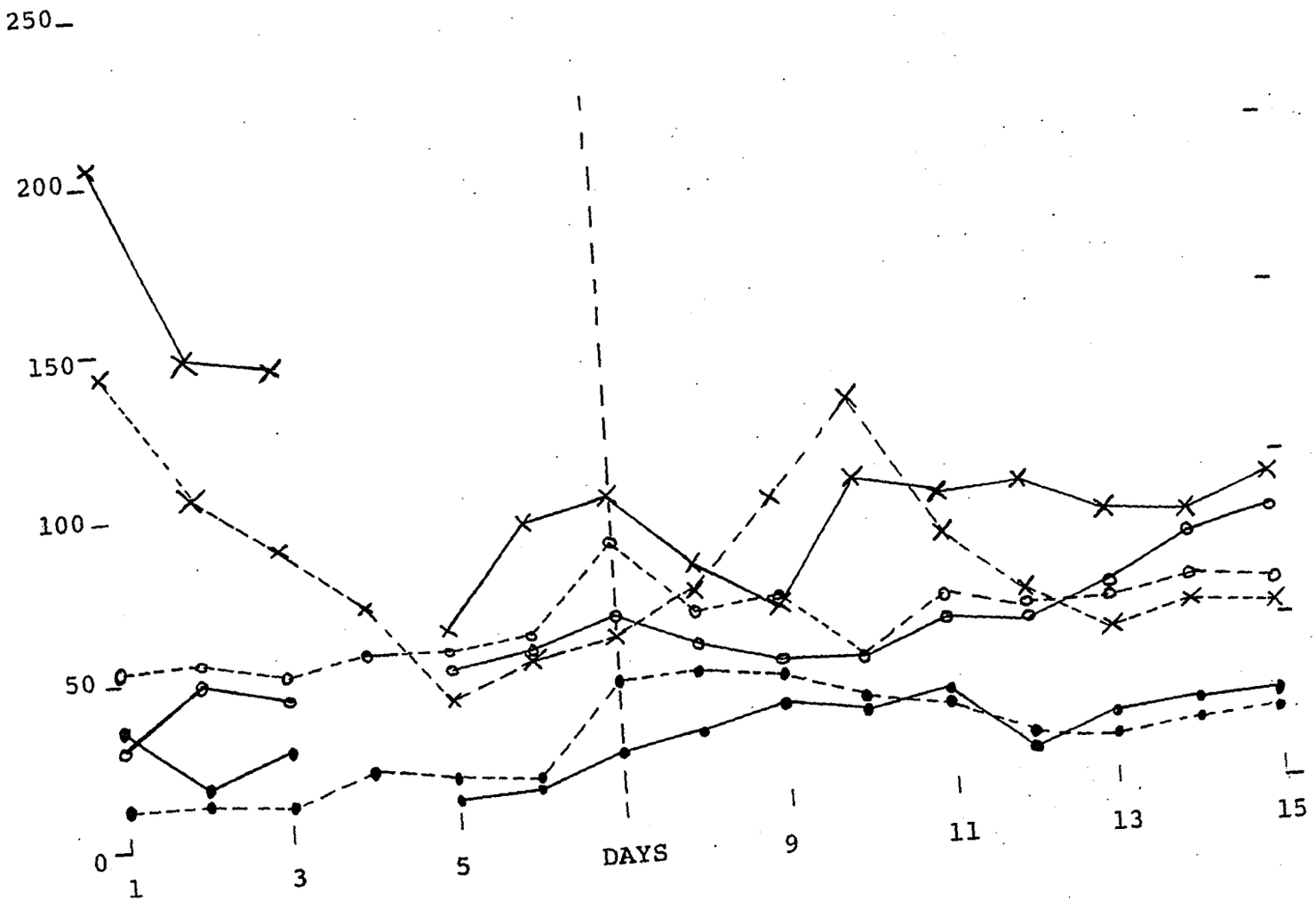

250
200
150
100
50
0
1
3
5
DAYS
9
11
13
15

Figure 19. Animal 322. Latencies and relative amplitudes from the temporal electrodes. DDT exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

● = peak latencies

The broken vertical line marks the exposure date.

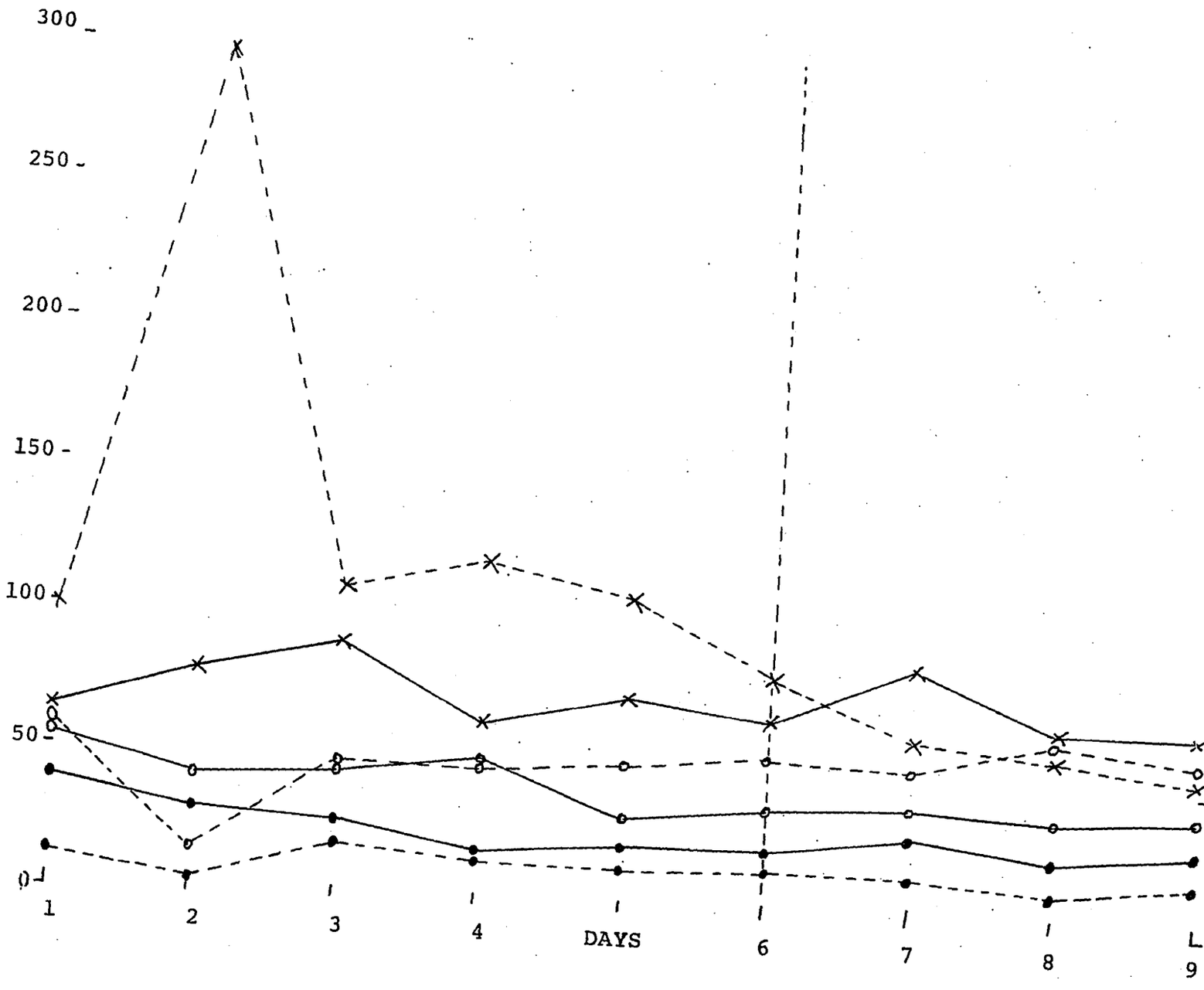

300
250
200
150
100
50
0
1
2
3
4
DAYS
6
7
8
9

Figure 20. Animal 322. Latencies and relative amplitudes from the occipital electrodes. DDT exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative latencies

O = latencies

● = peak latencies

The broken vertical line marks the exposure date.

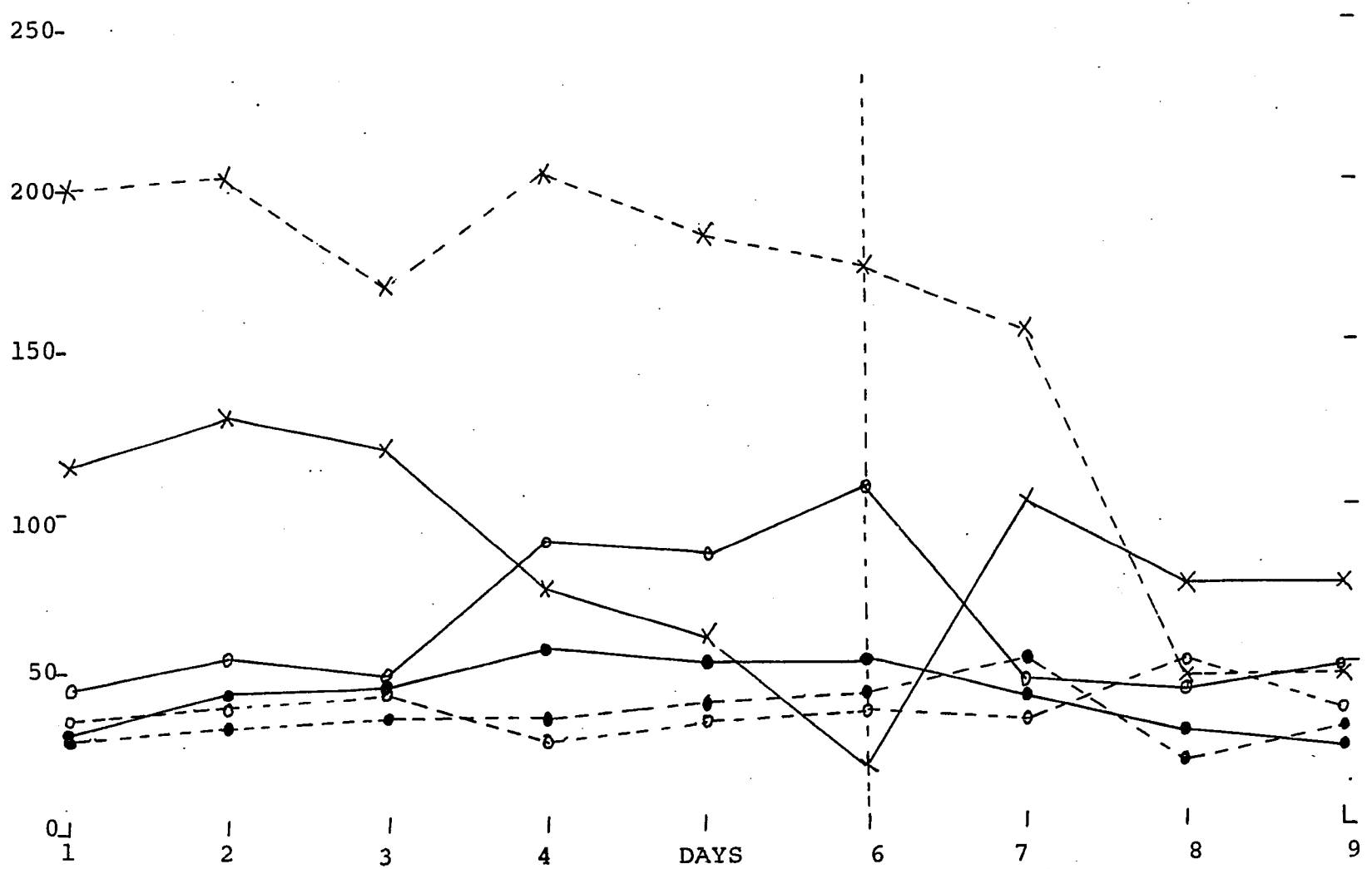

250
200
150
100
50
0
1
2
3
4
DAYS
6
7
8
9

Figure 21. Animal 111. Latencies and relative amplitudes from the occipital electrodes. DDT exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative latencies

O = latencies

● = peak latencies

The broken vertical line marks the exposure date.

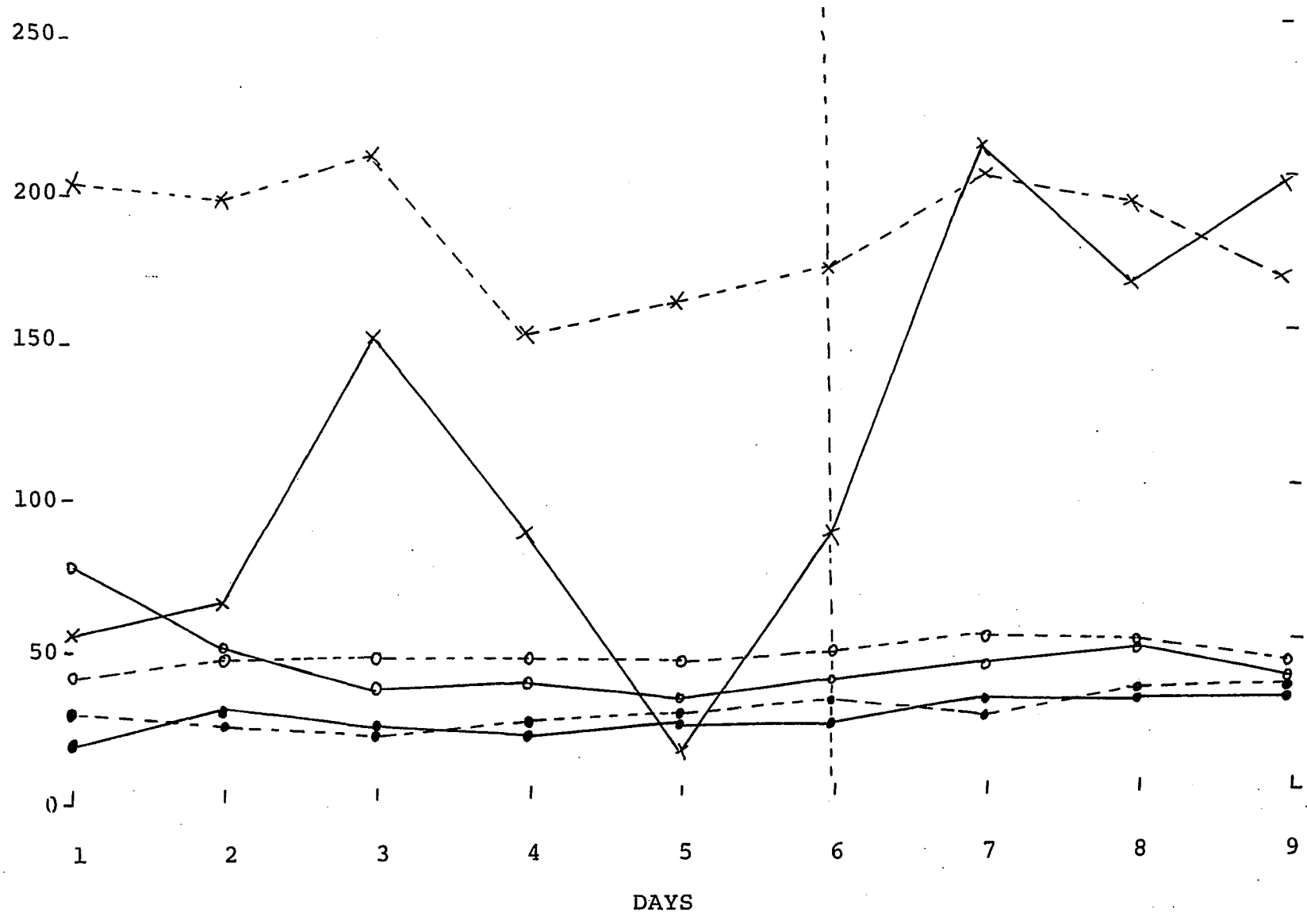

250
200
150
100
50
0
1
2
3
4
5
6
7
8
9
DAYS

Figure 22. Animal 111. Latencies and relative amplitudes from the temporal electrodes. DDT exposure.

The left electrode is depicted by the solid line and the right by the broken line. The vertical scale is a relative scale for the amplitudes and is read in milliseconds for the latencies.

X = relative amplitudes

O = latencies

● = peak latencies

The broken vertical line marks the exposure date.

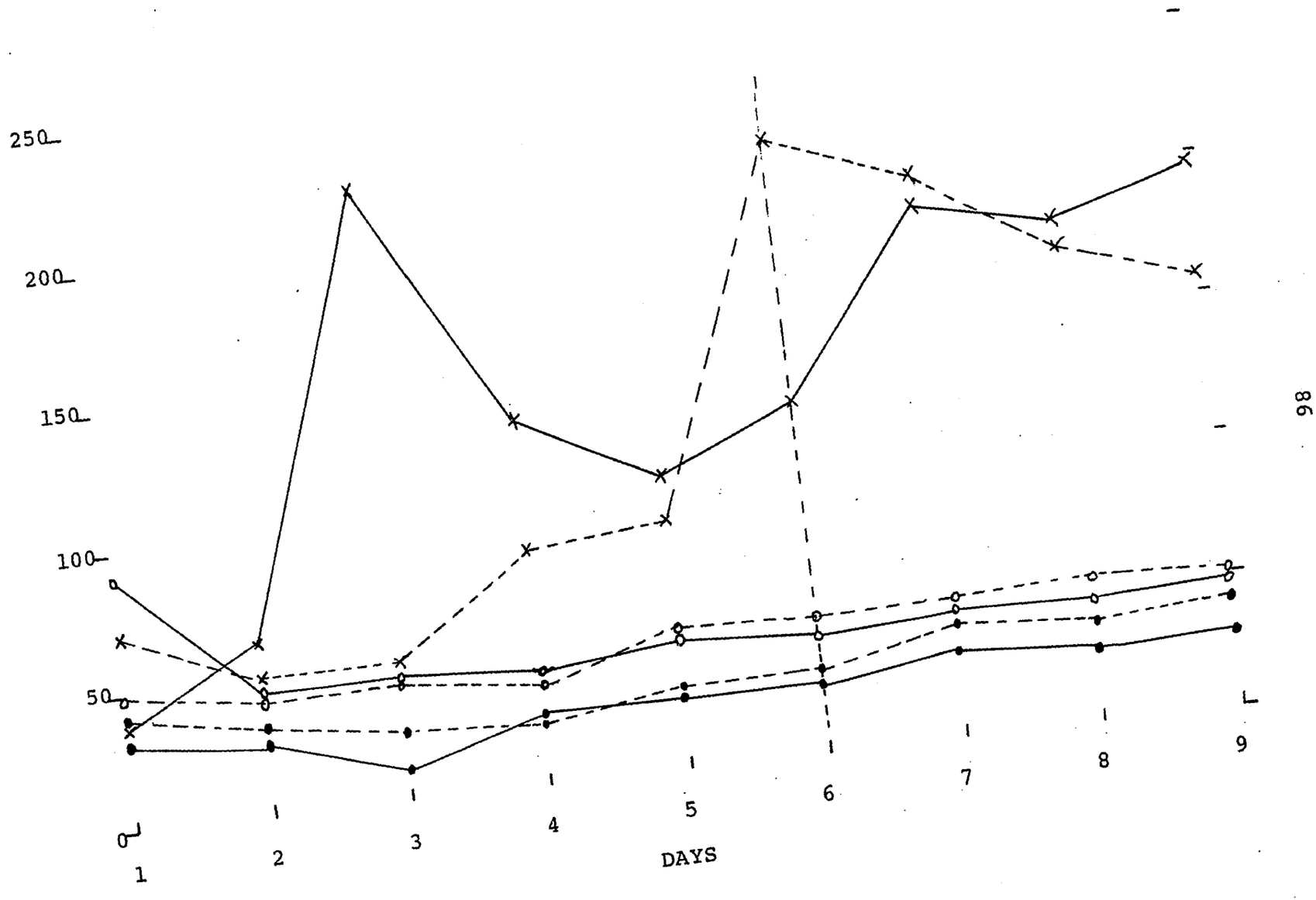

250
200
150
100
50
0
1
2
3
4
5
6
7
8
9
DAYS

Figure 23. Ensemble average of relative amplitudes from the temporal electrodes.

Solid lines denote ensemble one; broken lines denote ensemble two. The left side is represented by open circles, the right side by closed circles.

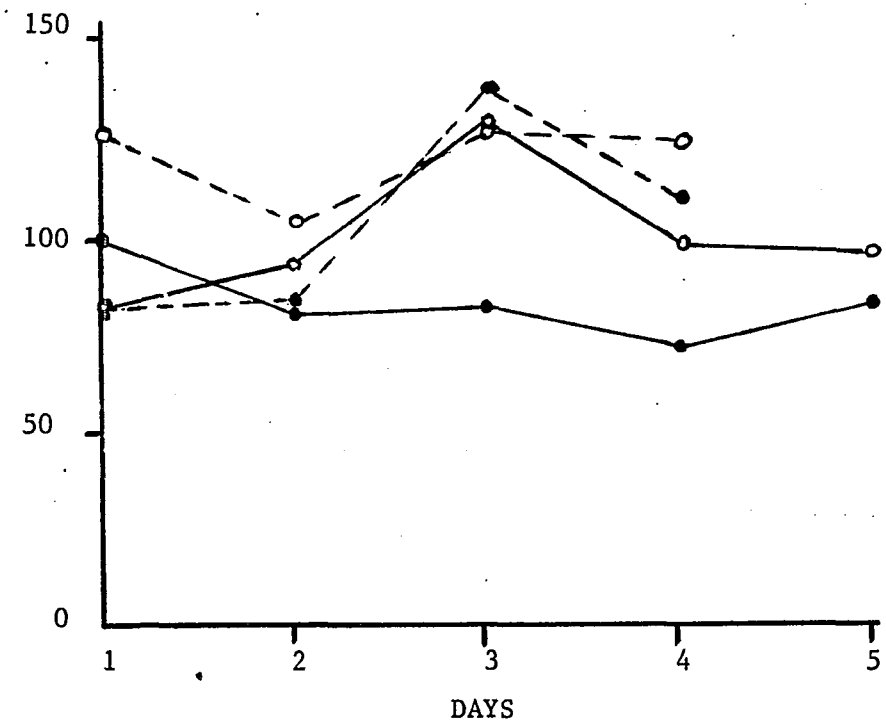
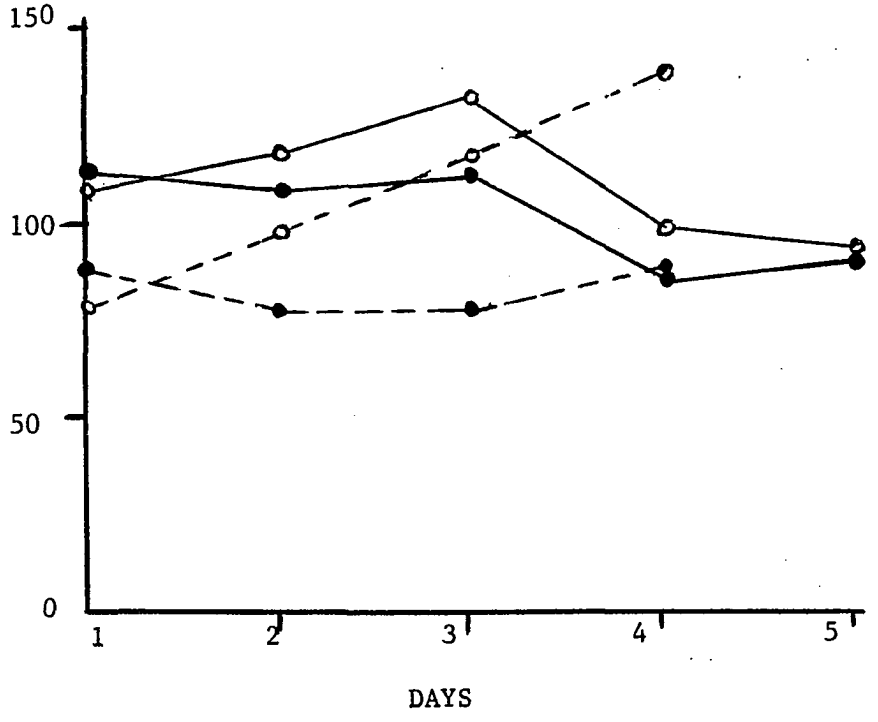

150
100
50
0
1
2
3
4
5
DAYS

Figure 24. Ensemble average of relative amplitudes from the occipital electrodes.

Solid lines denote ensemble one; broken lines denote ensemble two. The left side is represented by open circles, the right side by closed circles.


150
100
50
0
1
2
3
4
5
DAYS

Modulated Stimuli

The modulated light produced the more consistent summated evoked response of the two continuously modulated stimuli. The response to sinusoidally modulated light did not appear in all electrodes but was seen principally in the occipital electrodes. A high degree of variability existed when the recordings and the power spectral density plots were examined electrode by electrode. Consequently, examination of the power spectral density computations from individual electrodes revealed no trends. However, by having all the power spectral density computations for all active electrodes plotted on the same axes several trends were noted across treatments. Plotting the average value for the power spectral density a representation was derived for the average power spectrum for all electrodes. Typical representations are presented in Figures 25 to 72.

Modulated light

Over the course of the experimentation involving exposure to dieldrin a tendency toward an increase in higher frequency activity in the power spectrum was noted. See Figures 25 to 36.

The response during the control period was derived predominately from the occipital electrode sites. Following exposure to dieldrin, the contribution to the spectrum became either mixed, both occipital and temporal, or predominately

temporal. The temporal electrode contributions were of low amplitude.

Response to the fundamental driving frequency was consistent during the control periods but became variable following exposure. On the fourth day of exposure no response was recorded at the fundamental frequency. See Figure 35.

When the response to the fundamental frequency was recorded, during both the control and the experimental periods, it was seen predominately in the occipital electrodes.

The tendency to higher frequency response following dieldrin exposure indicates that the evoked cortical response from the visual system had begun to reflect a change or addition to the eye-cortex axis. A shift to higher frequencies may be due in part to either a basic change in the primary visual pathway or it may reflect changes in other areas of the brain which have been superimposed on the visual cortical response. The appearance of the temporal activity reflects a recruitment response and may be an evoked manifestation of the general hyperexcitability seen in cases of dieldrin toxicity.

In the course of the experiment the group of animals exposed to Rulene® recorded little change in the character of the total power spectral density plot was noted. See Figures 37 to 46. A tendency to reduction of amplitude following exposure with some higher frequency activity was recorded. During the exposure the animals exhibited restlessness,

excessive salivation, and a fetid diarrhea. Over the control period the activity was composed of either occipital activity or a mixed occipital-temporal activity. In the exposure phase the activity was mixed or predominately temporal. Response to the stimulus at the fundamental frequency was constant for an animal throughout the experiment. Animal 337 showed a predominant occipital response to the stimulus in both the control and exposure periods. Animal 334 also responded to the modulated stimulus with a strong occipital response. Some variability in this response was noted in this animal on the third day of exposure, but a response was not seen in other animals of this group. A mixed response to the stimulus was seen in animal 320 over the entire experimental procedure.

An increase or shift to temporal activity would appear to reflect, at the cortical level, activation of other areas of the brain. The lower amplitude of the spectrum occurred with the clinical observation of central depression.

Following exposure to DDT an increase of activity was seen across the spectrum. Higher frequency response with higher amplitude was the trend noted. Occipital contributions to the spectrum were more prominent during the control period. A mixed response, contributions from both the temporal and occipital areas, characterized the recordings following exposure. The response to the fundamental driving frequency

remained relatively constant across the treatment. A variation to the evoked response at the driving frequency was noted in animal 111 for the fundamental frequency of 2 Hz. This variation consisted of a response which was less than responses recorded at other frequencies. See Figures 47 to 60.

This period of increased power spectral activity corresponded to the observations of hyperirritability to external stimuli on the part of the exposed animals.

The summated evoked potentials from modulated light when viewed on the oscilloscope display of the computer also showed some of the higher frequency shift following pesticide exposure. See Figures 73 and 74.

Modulated sound

Less response was seen in the animals when subjected to the modulated sound stimuli. Little temporal response was recorded across treatments. Most of the power spectral activity following stimulation with modulated sound was from the occipital electrode sites. See Figures 61 to 72.

Following exposure to dieldrin an increase in higher frequency activity was recorded with a greater amplitude recorded on the last day of exposure. No relationship was seen between the recorded cortical activity and the fundamental driving frequency. Little or no response was seen in the summated recordings from animals exposed to Rulene®. During the control periods low amplitude activity at low frequencies

was recorded. Over the exposure period this activity disappeared. The small amount of activity recorded over the control period bore no relationship to the fundamental driving frequency.

The principle activity across the DDT experiment with modulated sound was about the fundamental driving frequency. Recordings from the occipital electrode sites were the predominant source of activity during the control periods. Following DDT exposure temporal activity became a more predominant portion of the power spectrum. Increased activity at the higher frequencies was also recorded following the exposure to DDT.

Information about the sensory projection areas of the cortex of the sheep is lacking. The electrode placement most particularly in the cases of the temporal sites may be more anatomical than physiological. That is to say, the electrodes were placed over the temporal lobes but this may not have been the area of greatest cortical activity for audio stimuli. It was thought that this was the most likely basis for the lack of consistent auditory evoked response.

Figure 25. Animal 498. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz. Two days pre-exposure.

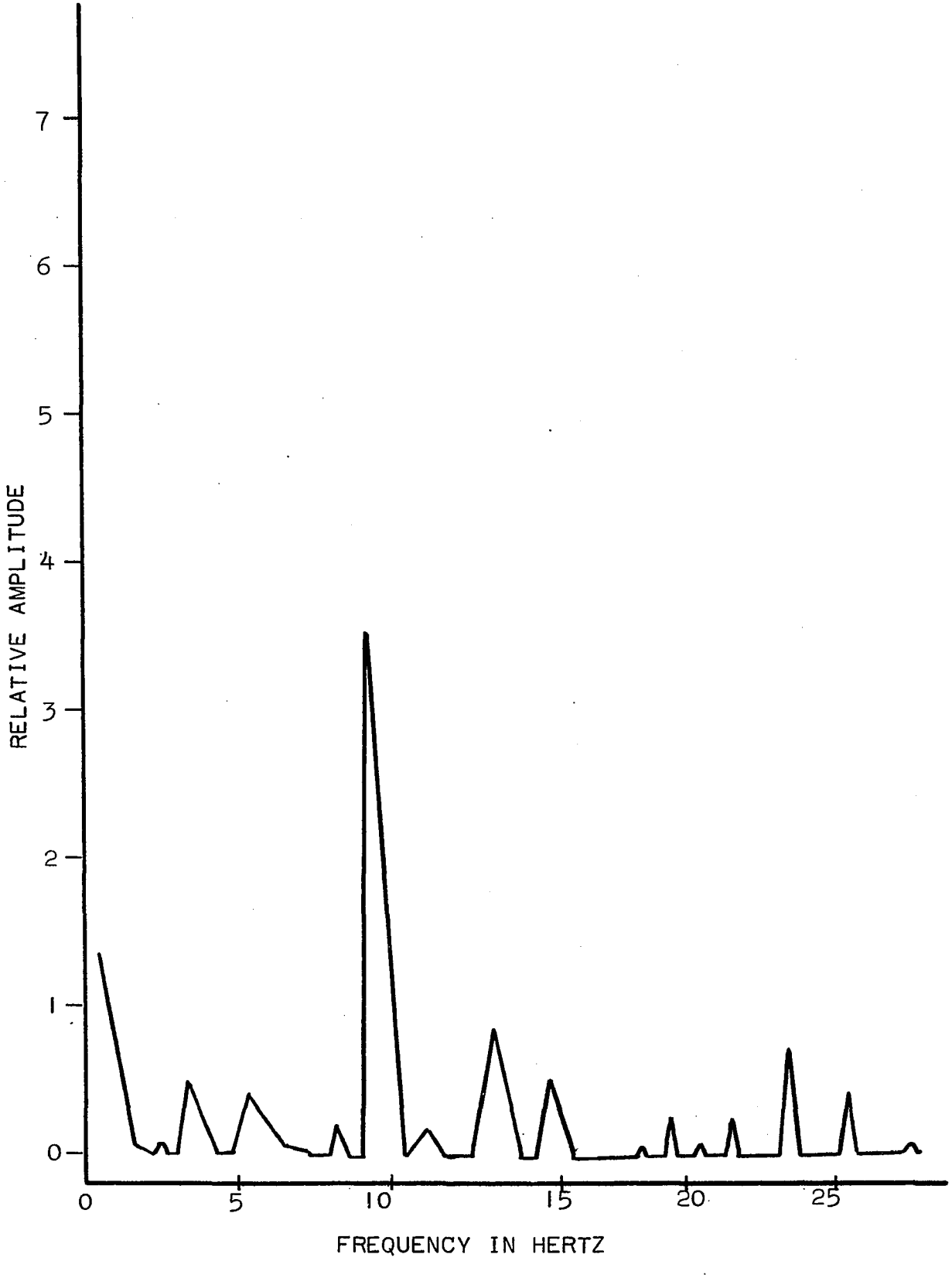

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 26. Animal 498. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz. One day pre-exposure.

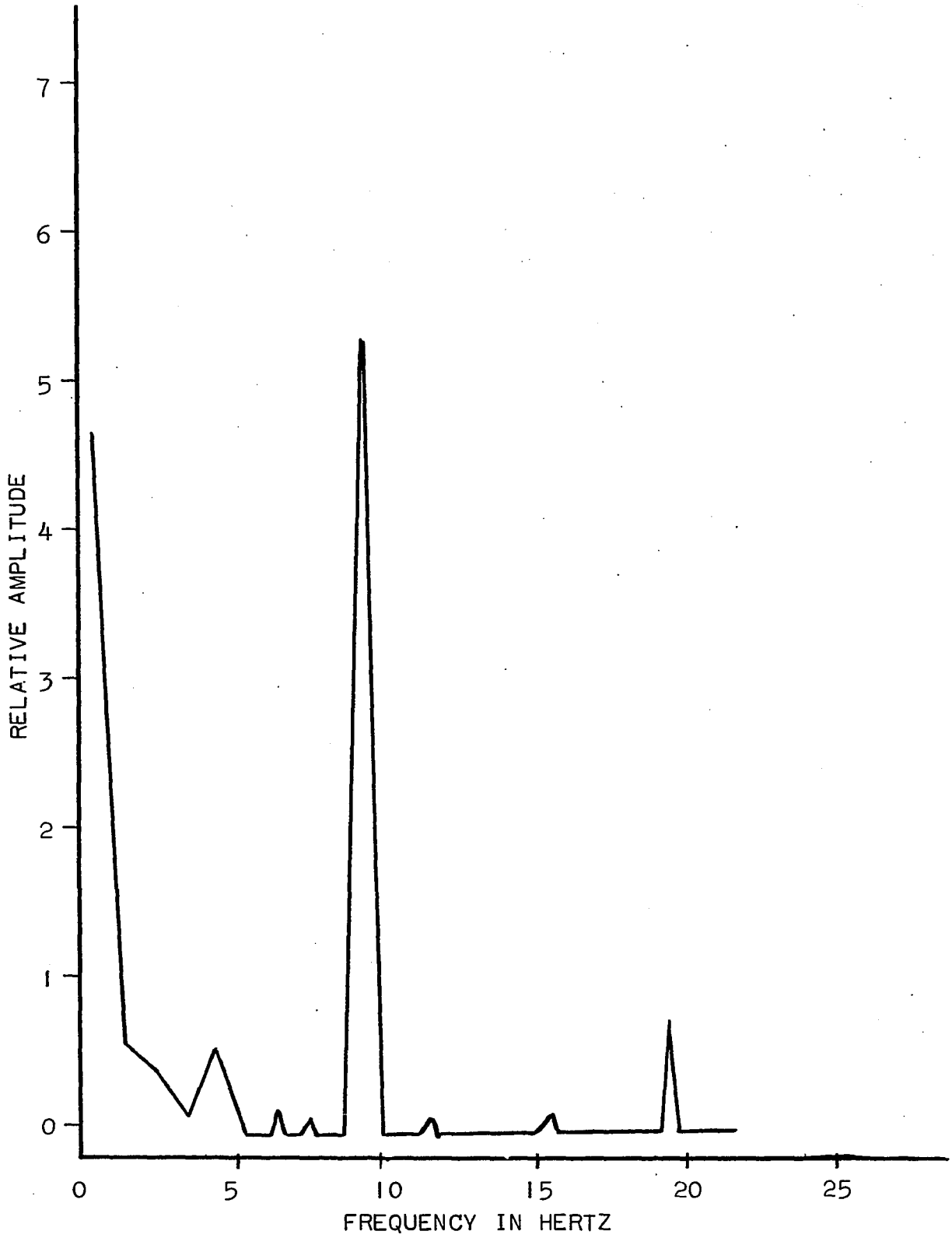

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 27. Animal 498. Fourth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

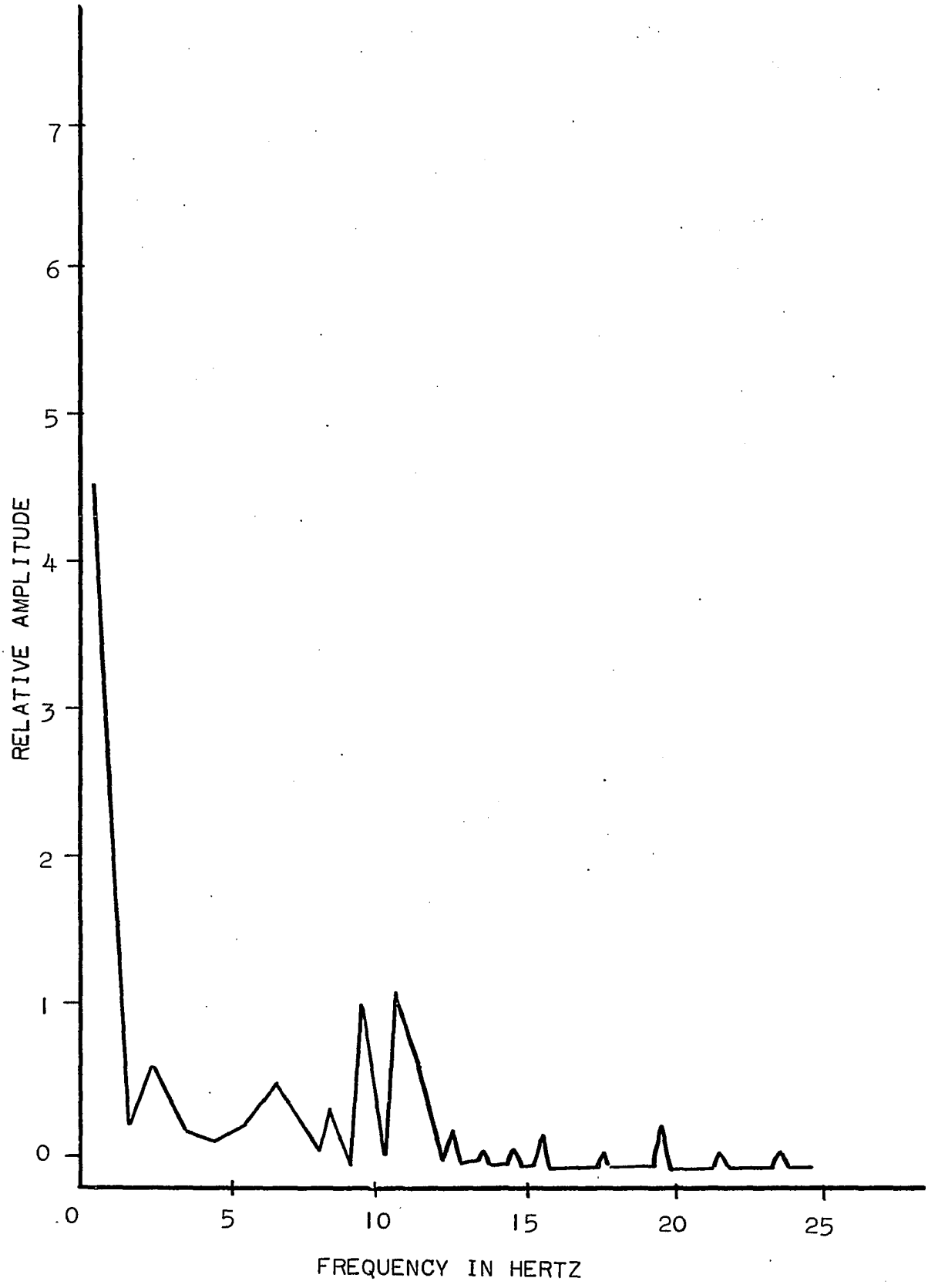

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 28. Animal 498. Fifth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

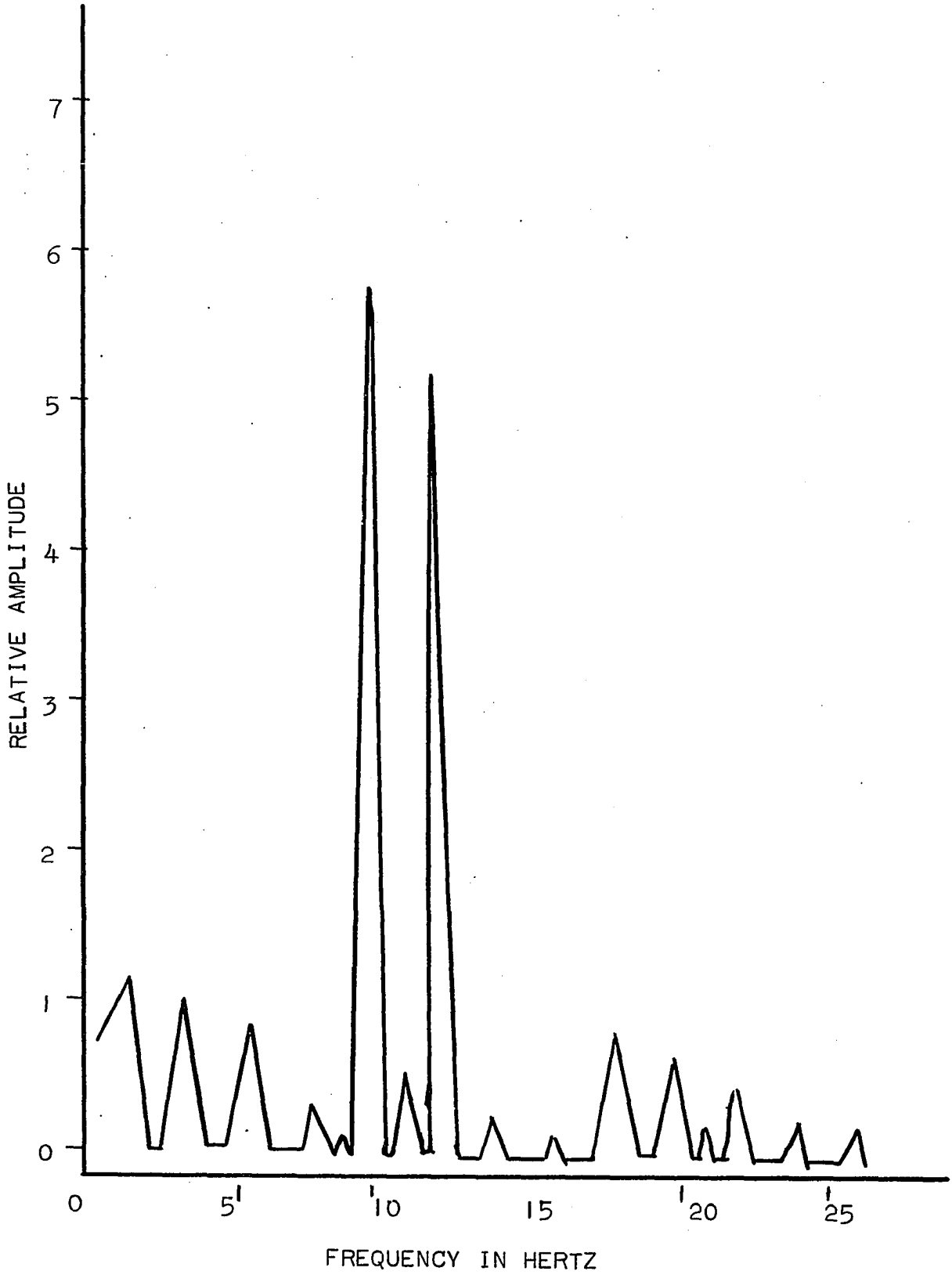

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 29. Animal 455. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz. Two days pre-exposure.

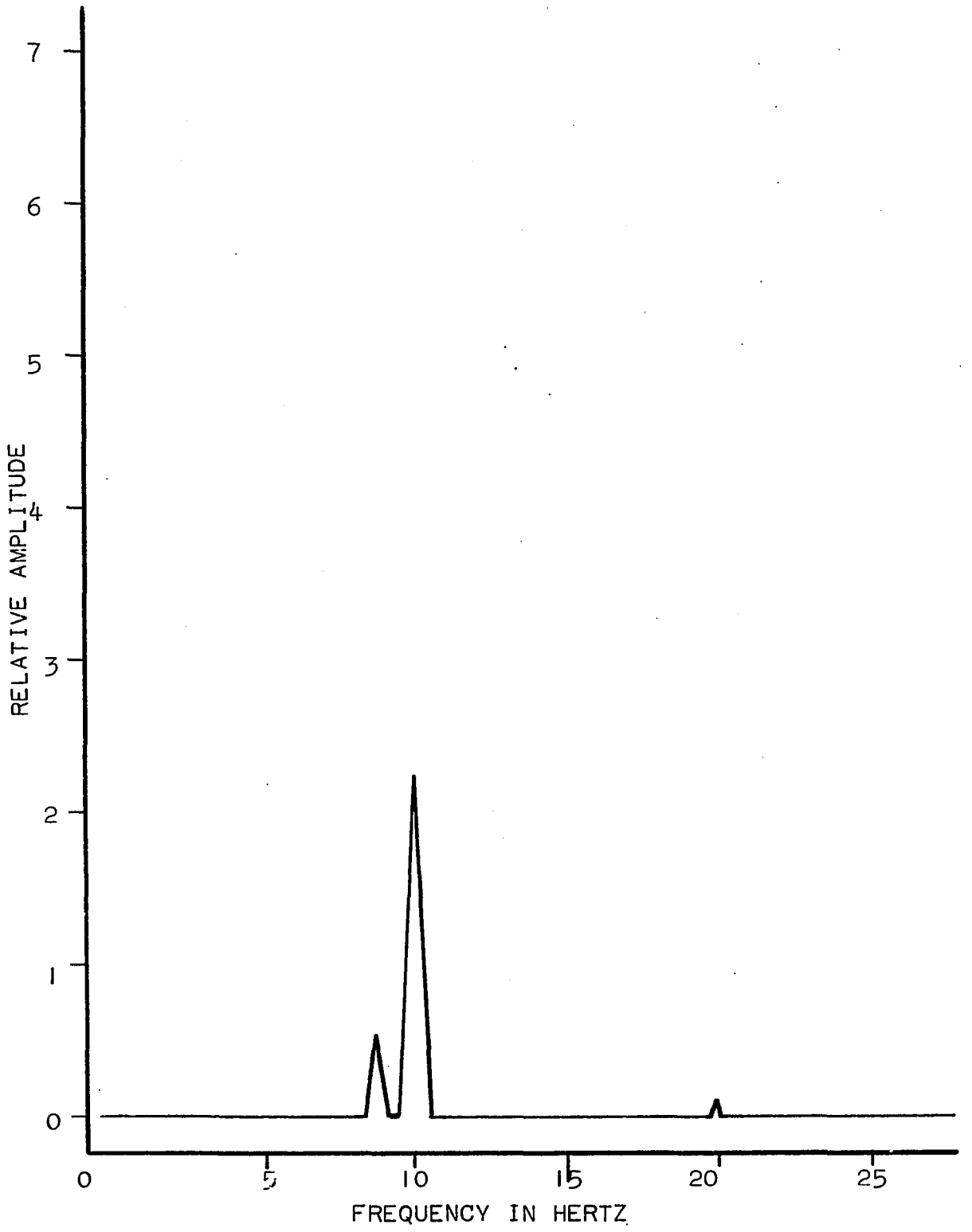

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 30. Animal 455. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz. One day pre-exposure.

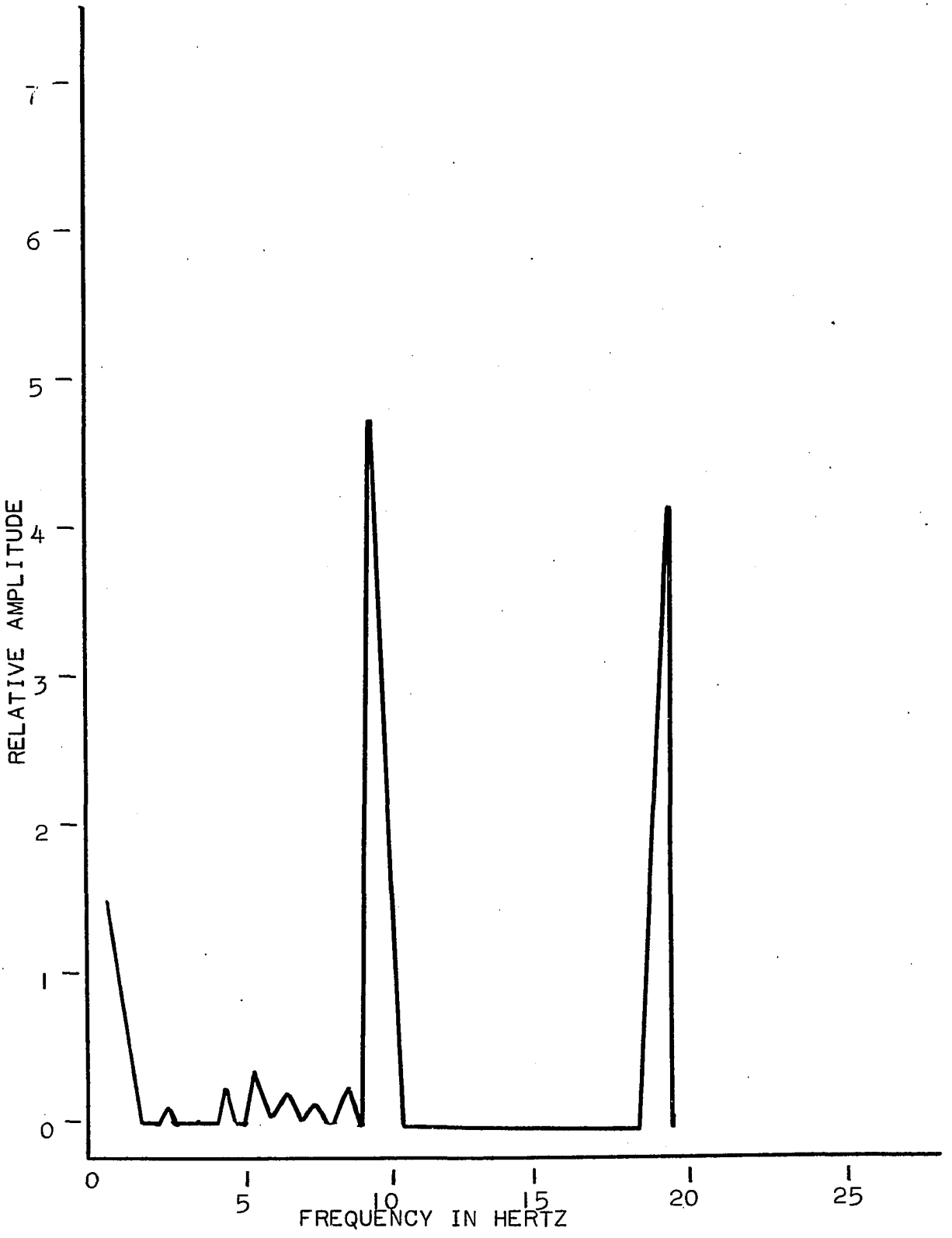

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 31. Animal 455. Second day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

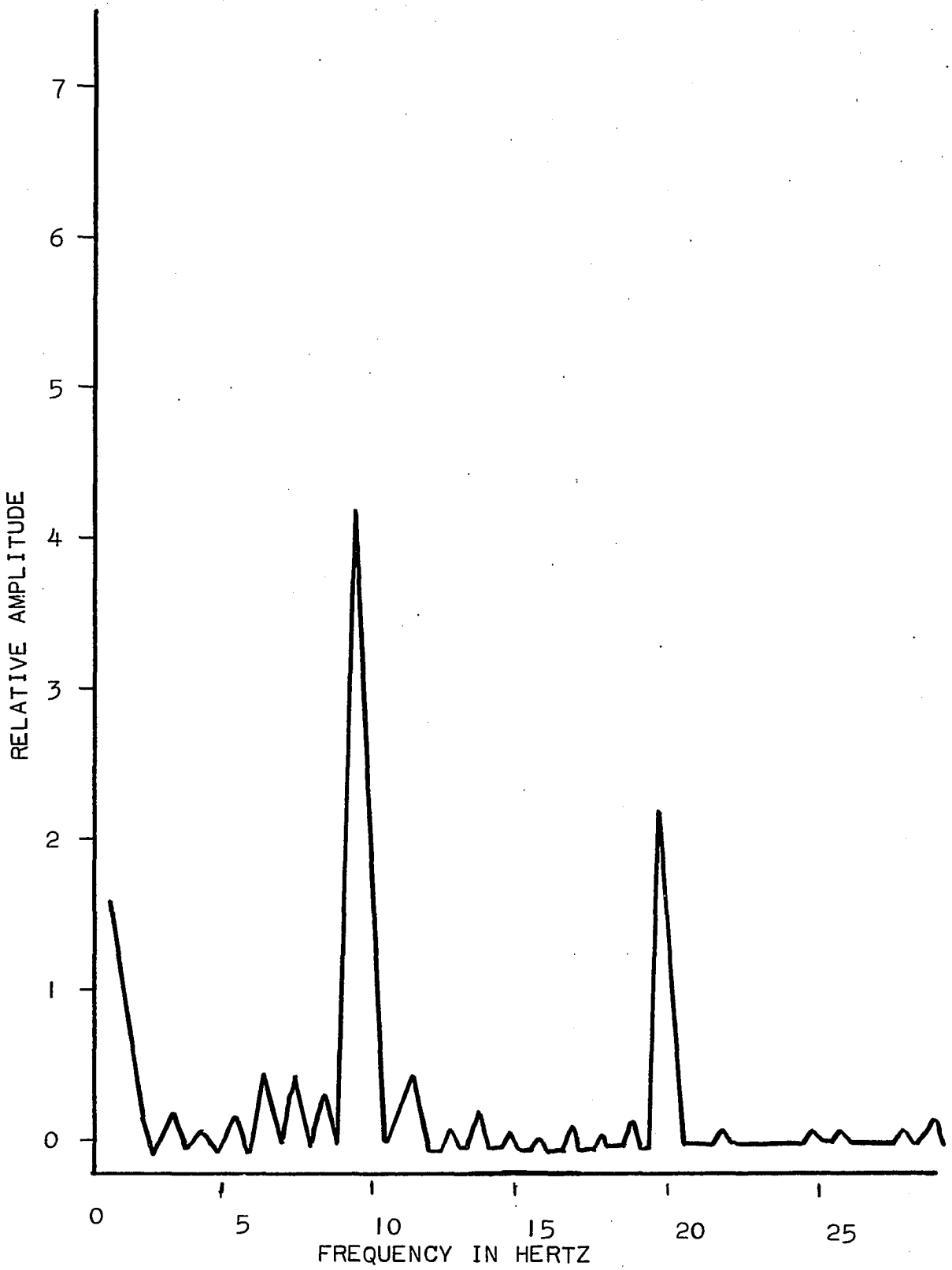

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 32. Animal 455. Third day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

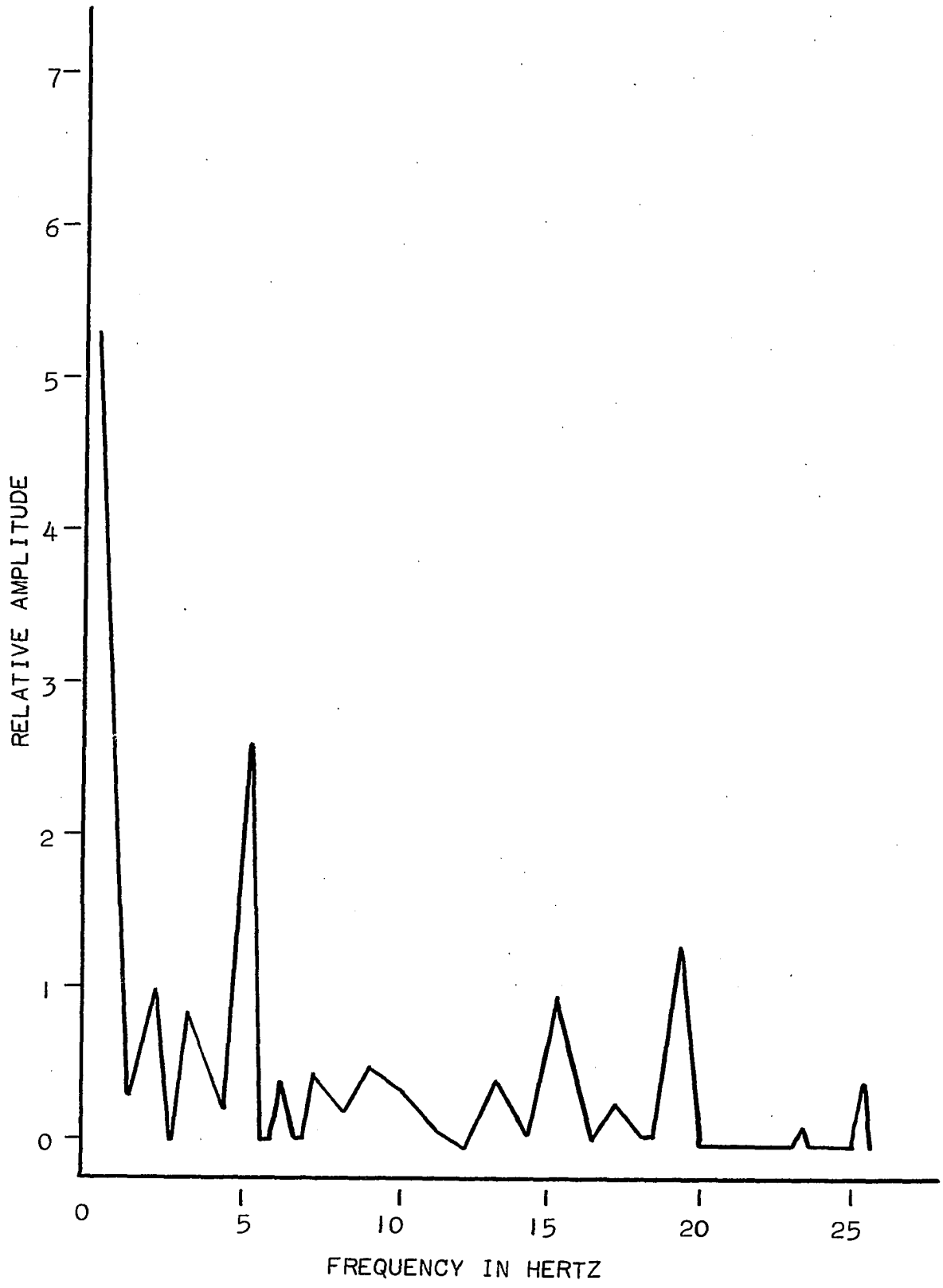

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 33. Animal 498. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz. Two days pre-exposure.

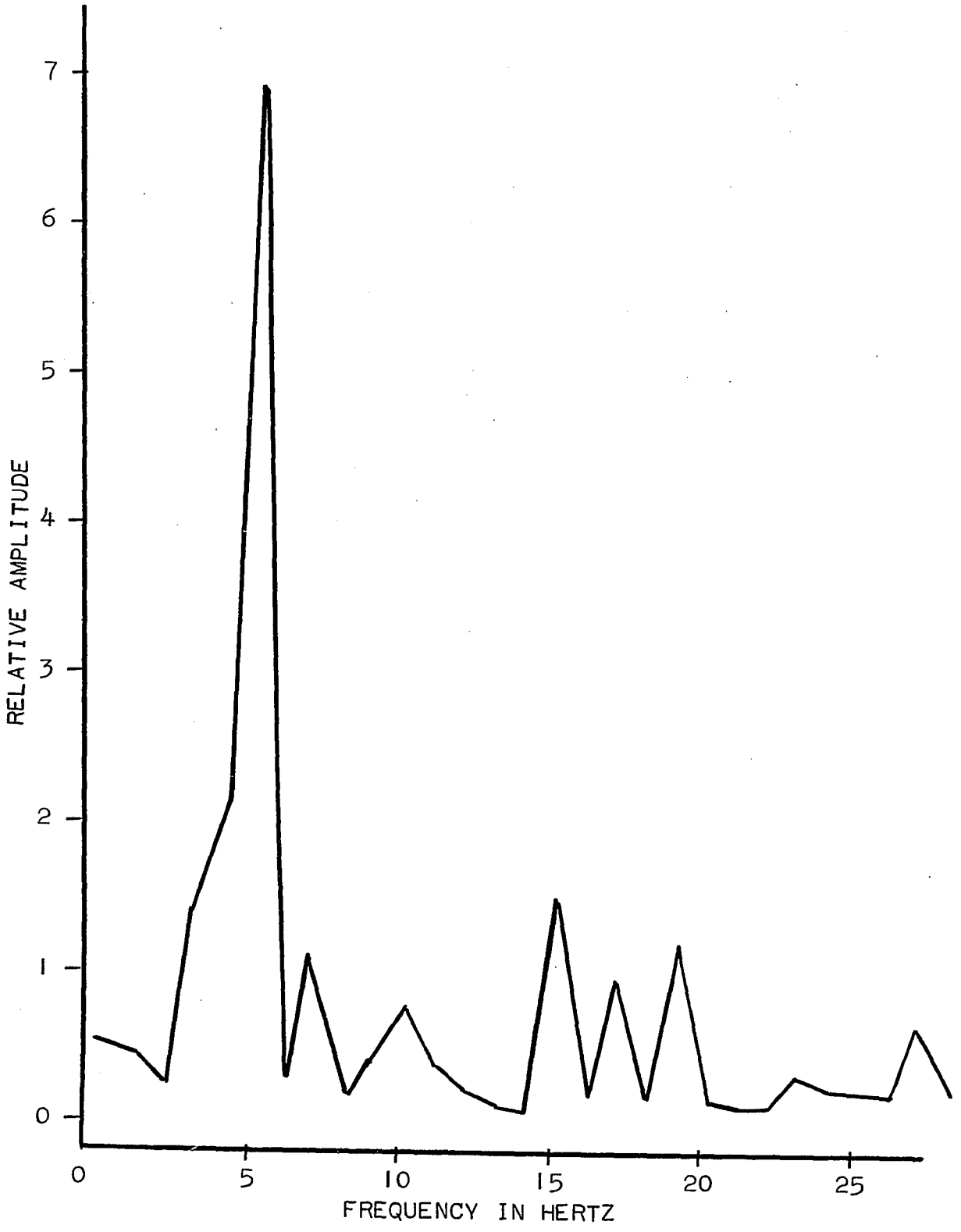

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 34. Animal 498. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz. One day pre-exposure.

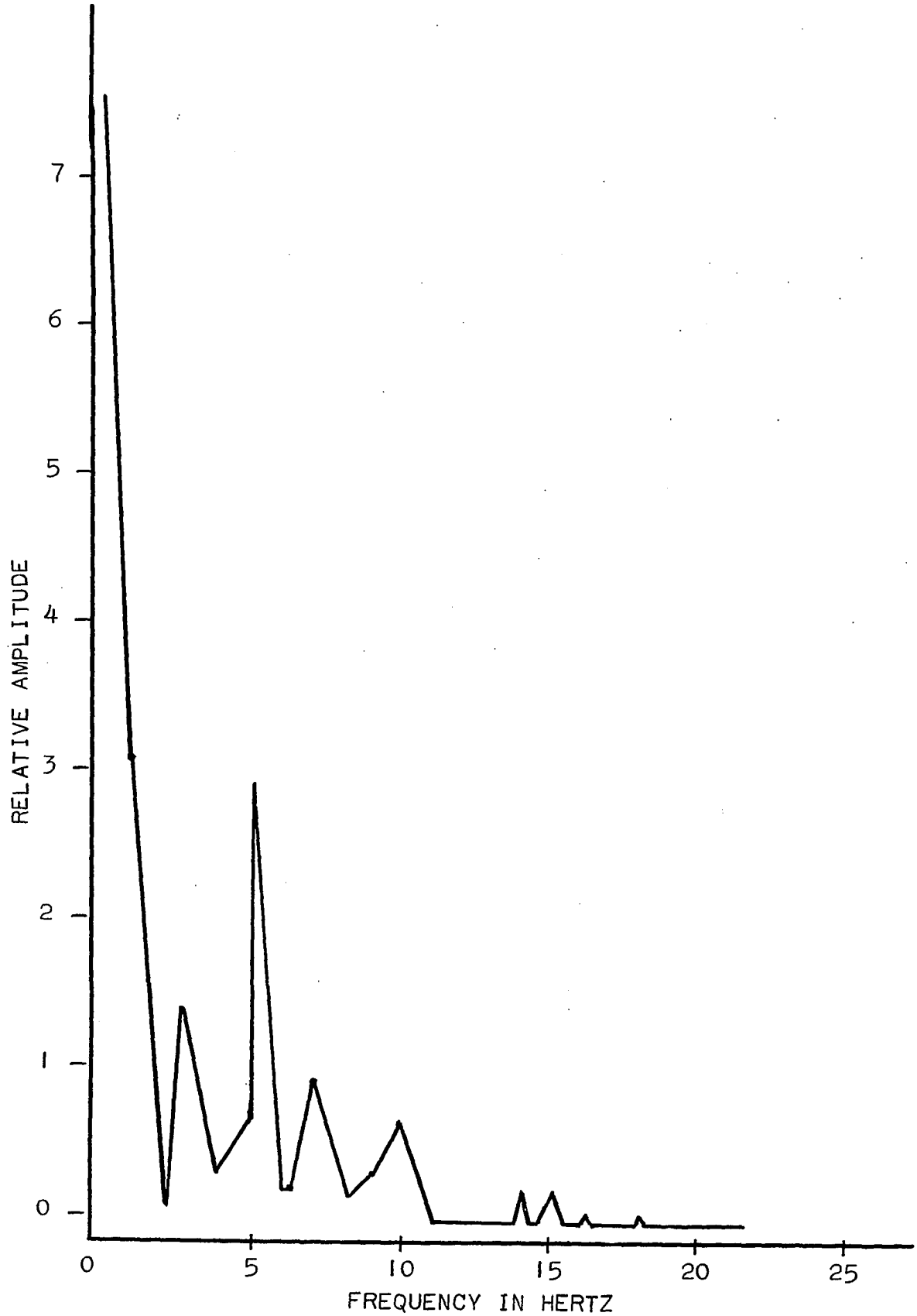

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 35. Animal 498. Fourth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

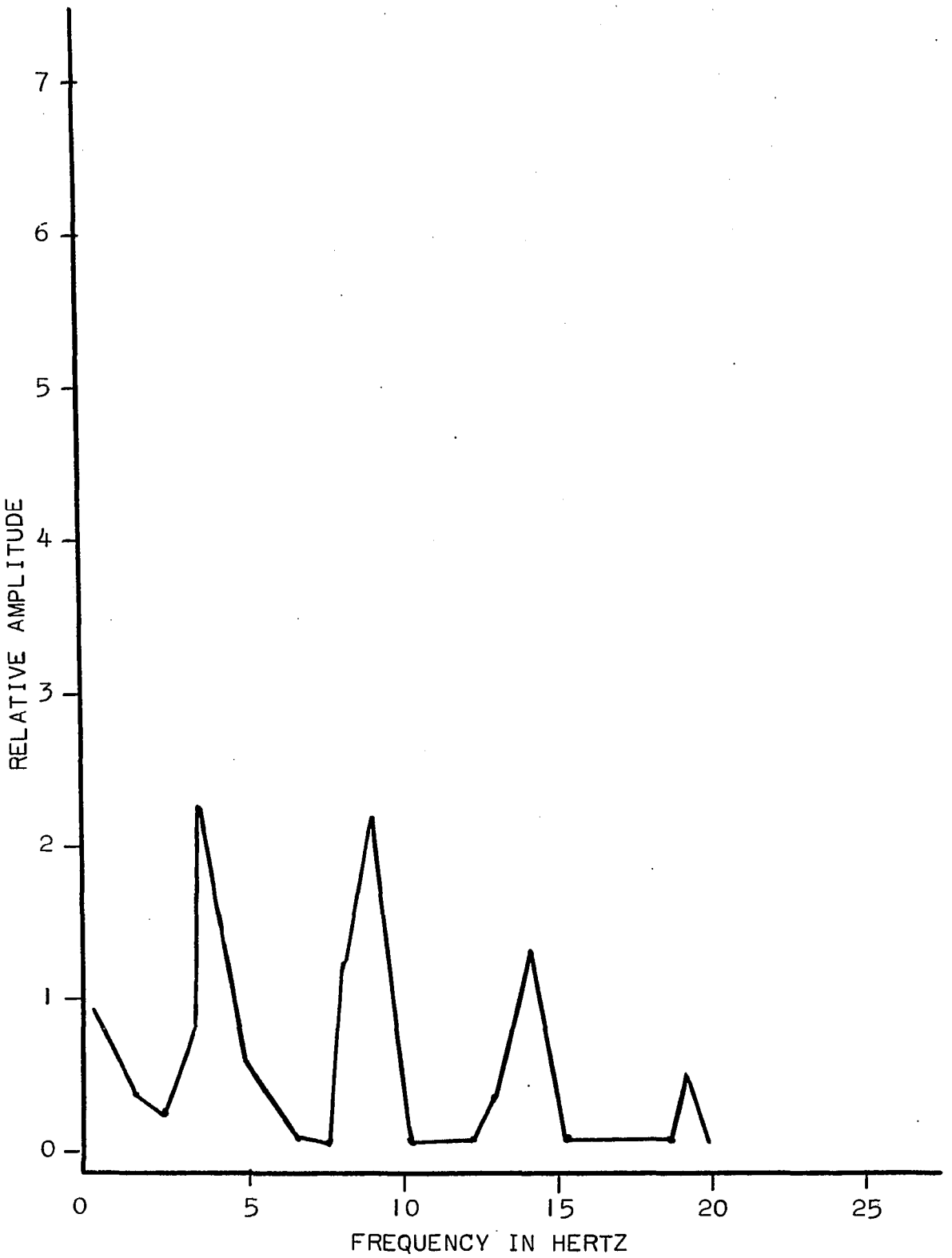

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 36. Animal 498. Fifth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

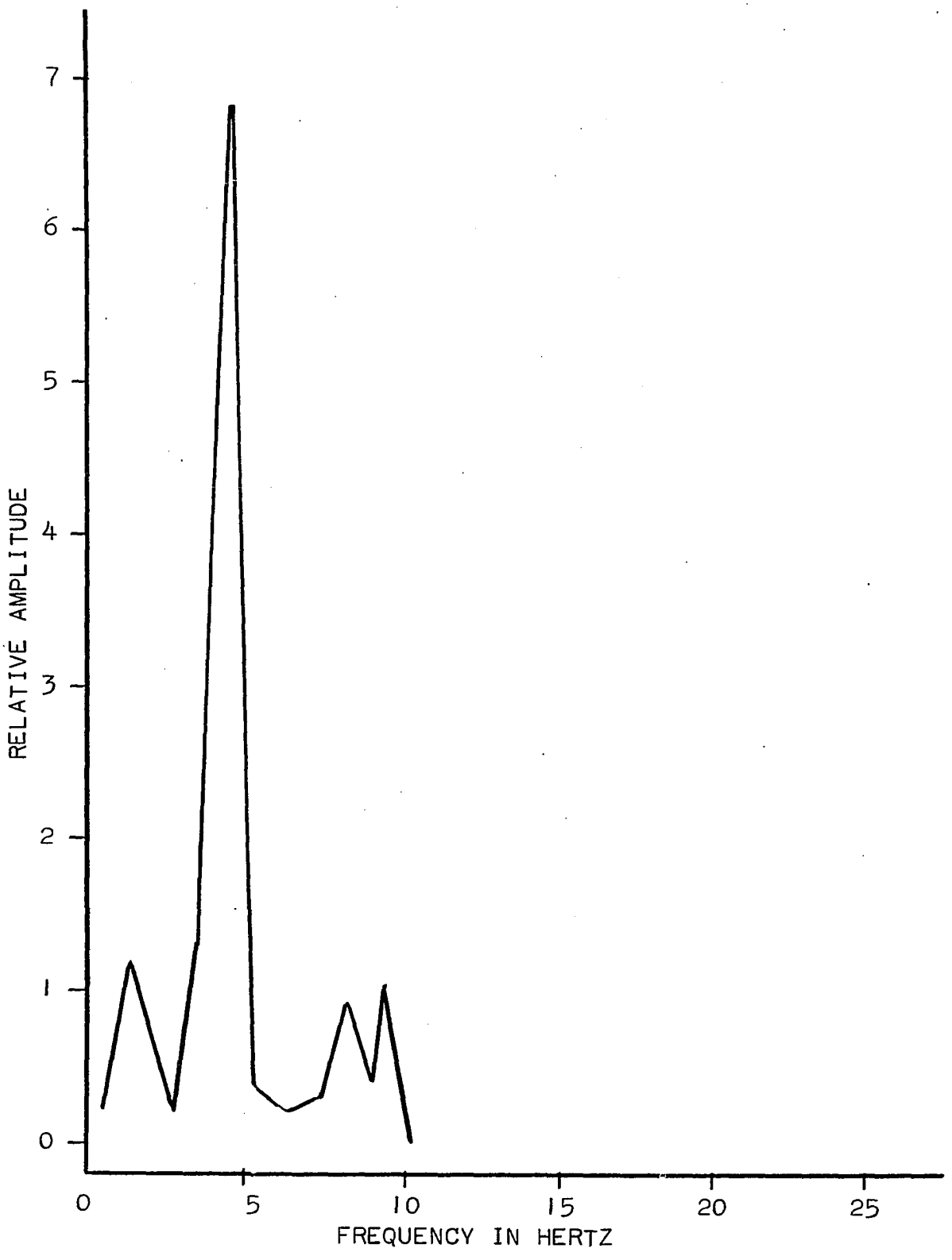

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 37. Animal 337. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

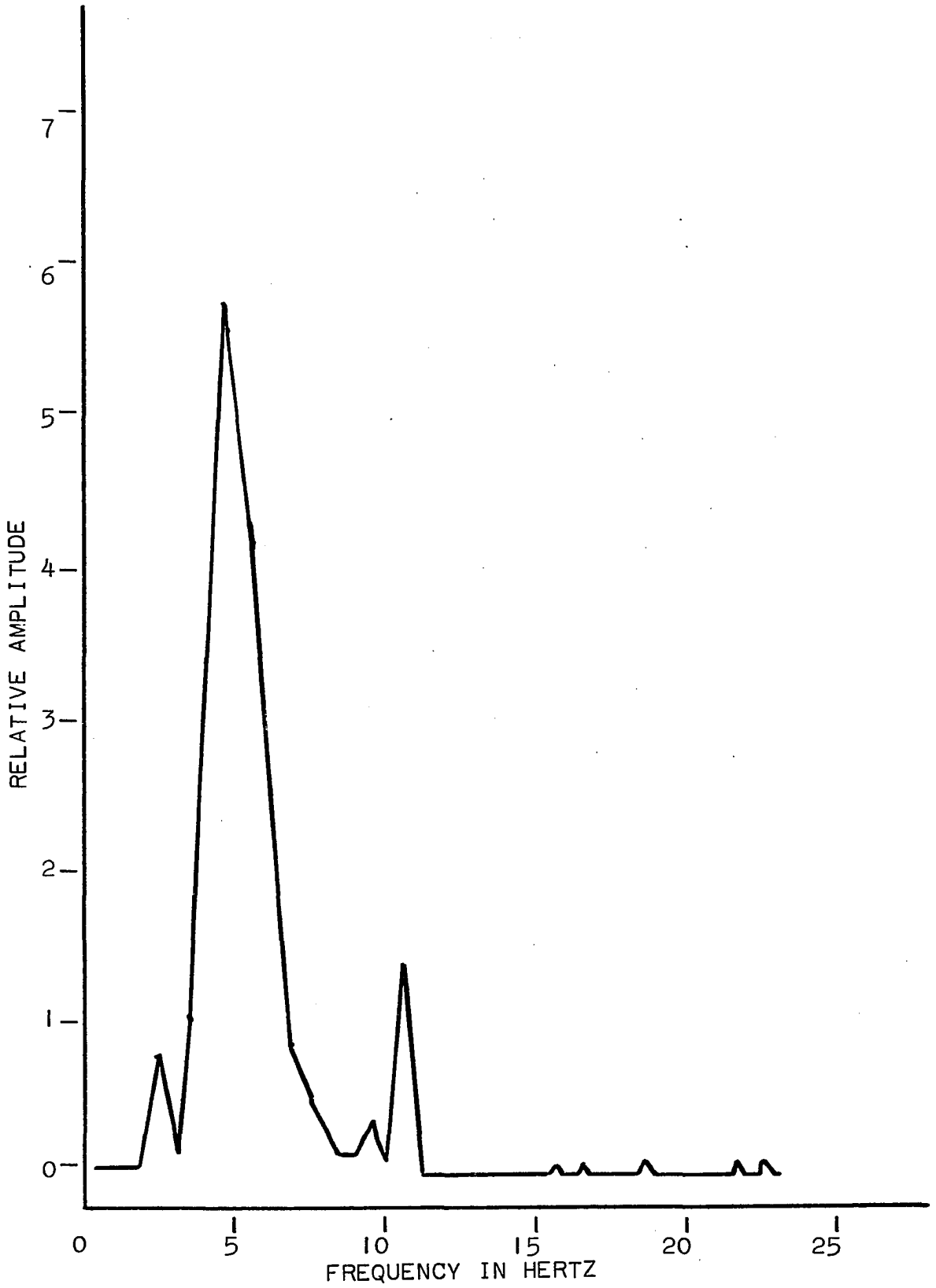

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 38. Animal 337. Third day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

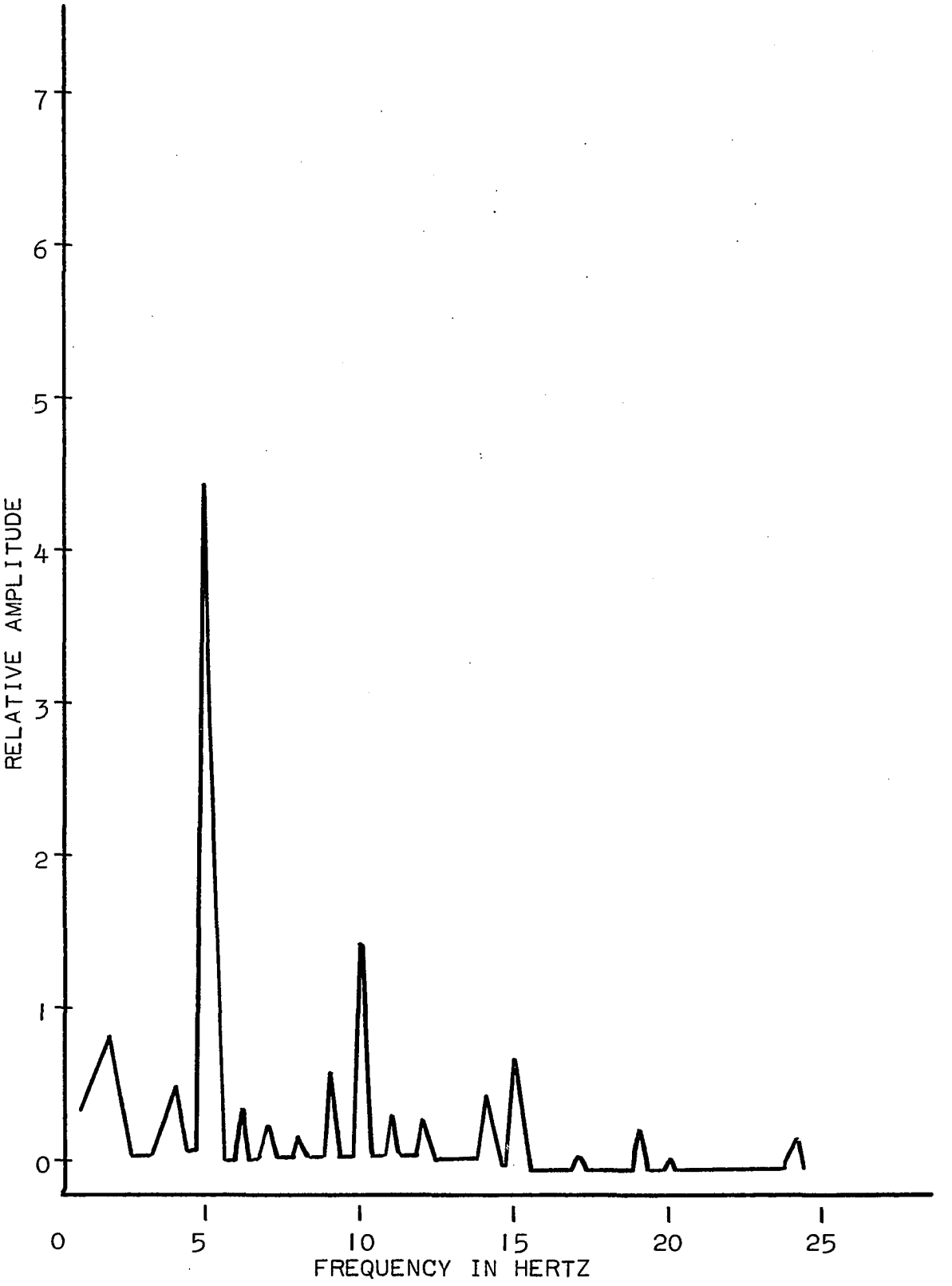

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 39. Animal 337. Fourth day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

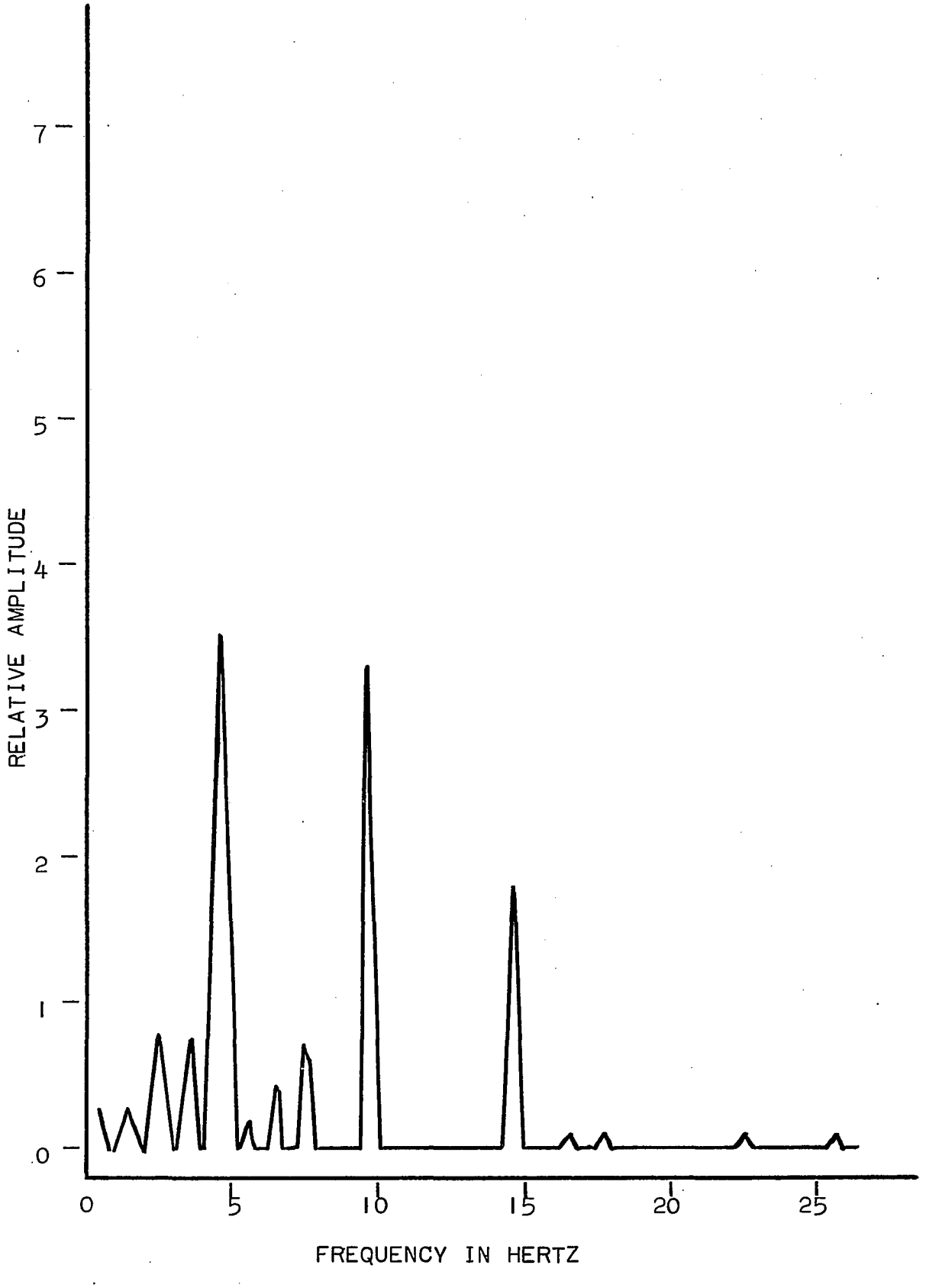

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 40. Animal 334. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 15 Hz. Two days pre-exposure.

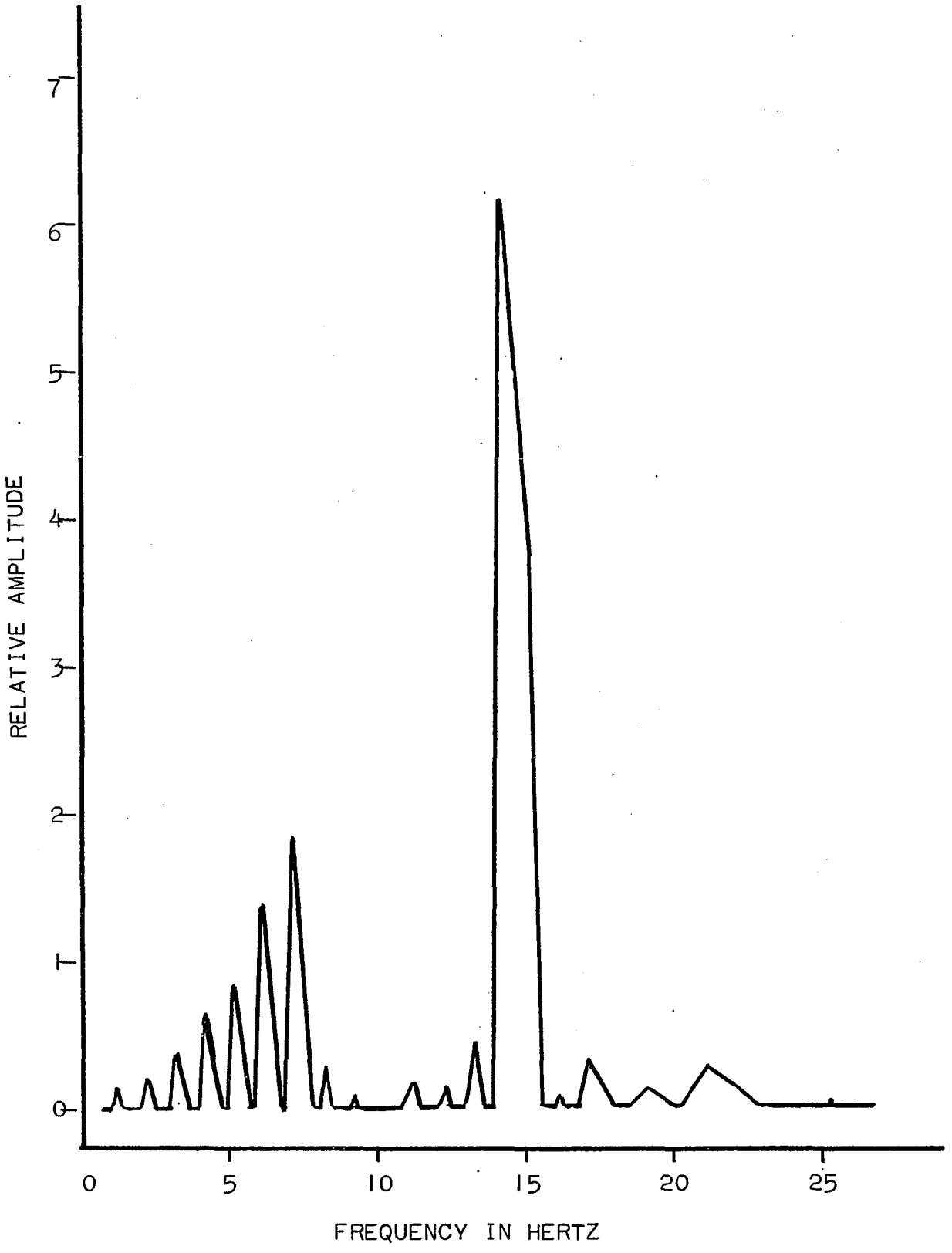

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 41. Animal 334. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 15 Hz. One day pre-exposure.

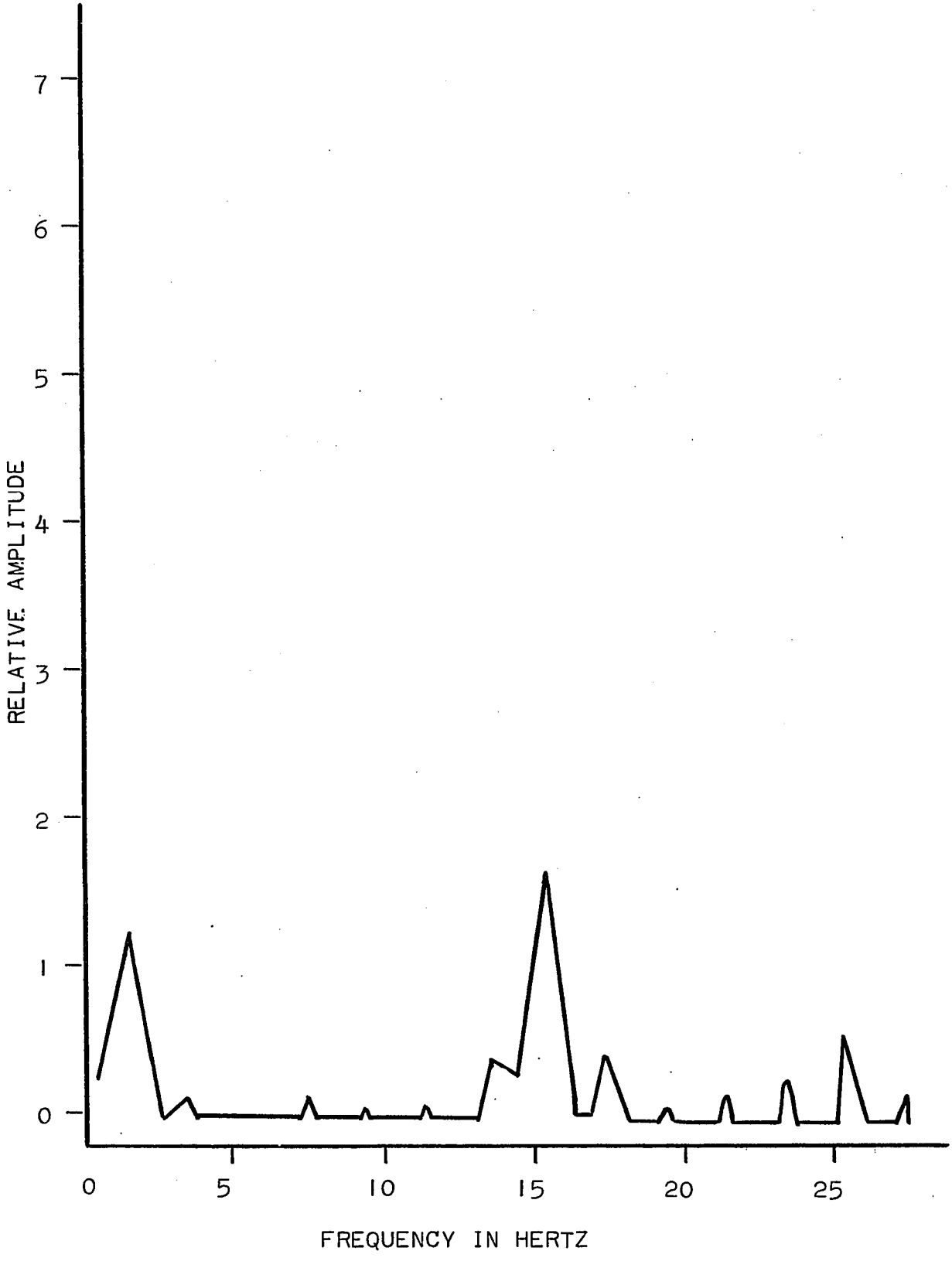

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 42. Animal 334. Third day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 15 Hz.

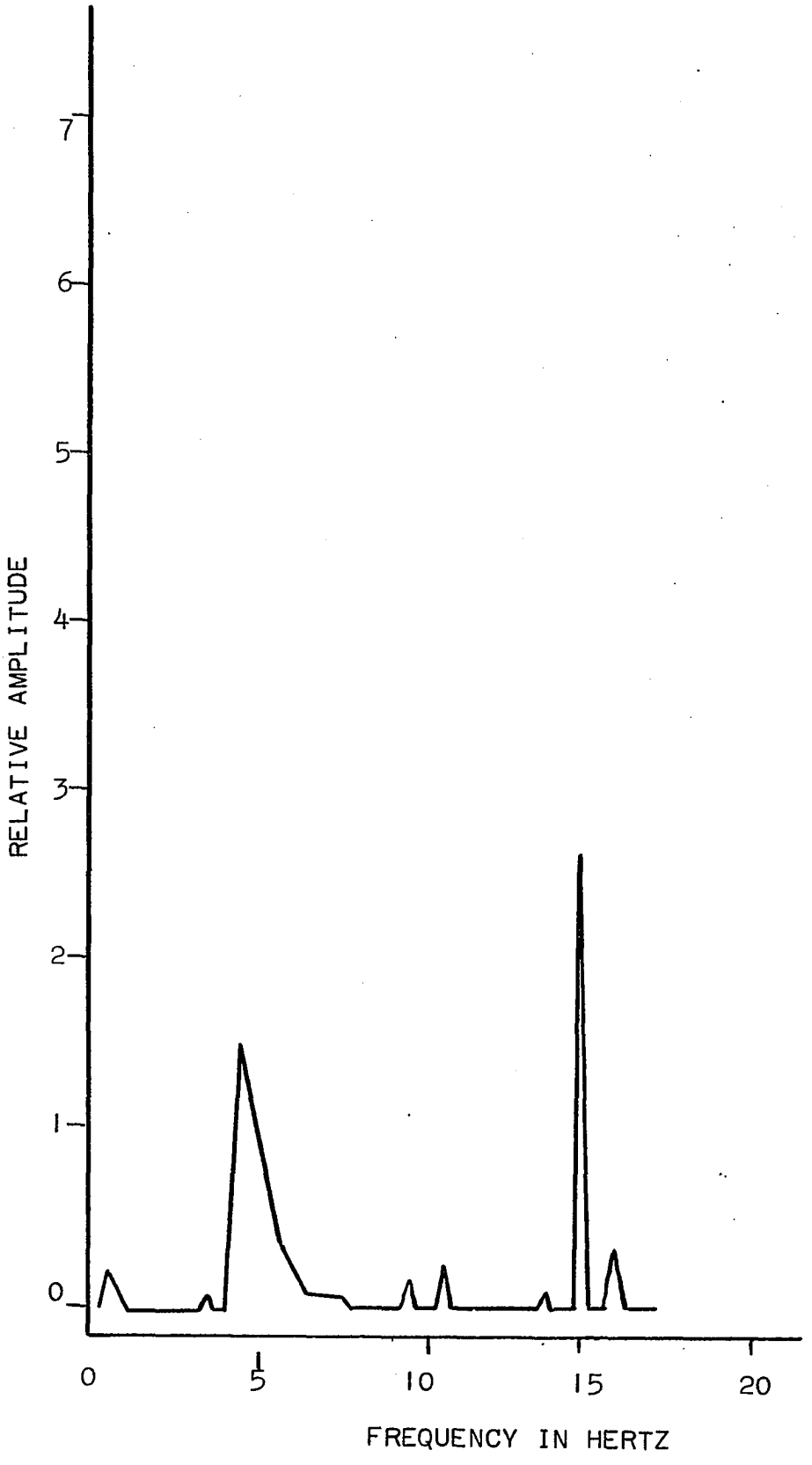

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
FREQUENCY IN HERTZ

Figure 43. Animal 334. Fourth day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 15 Hz.

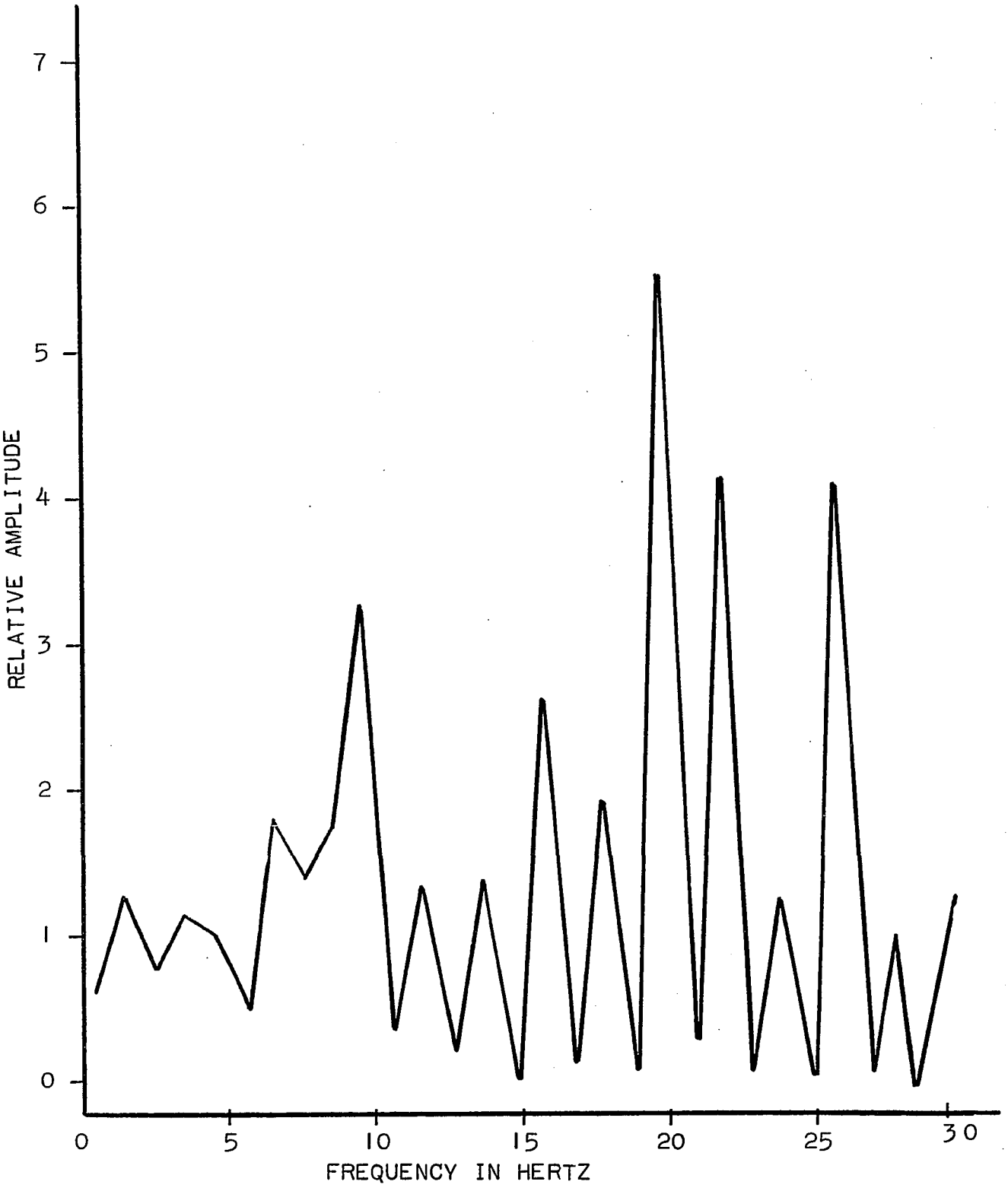

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
30
FREQUENCY IN HERTZ

Figure 44. Animal 320. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz. Two days pre-exposure.

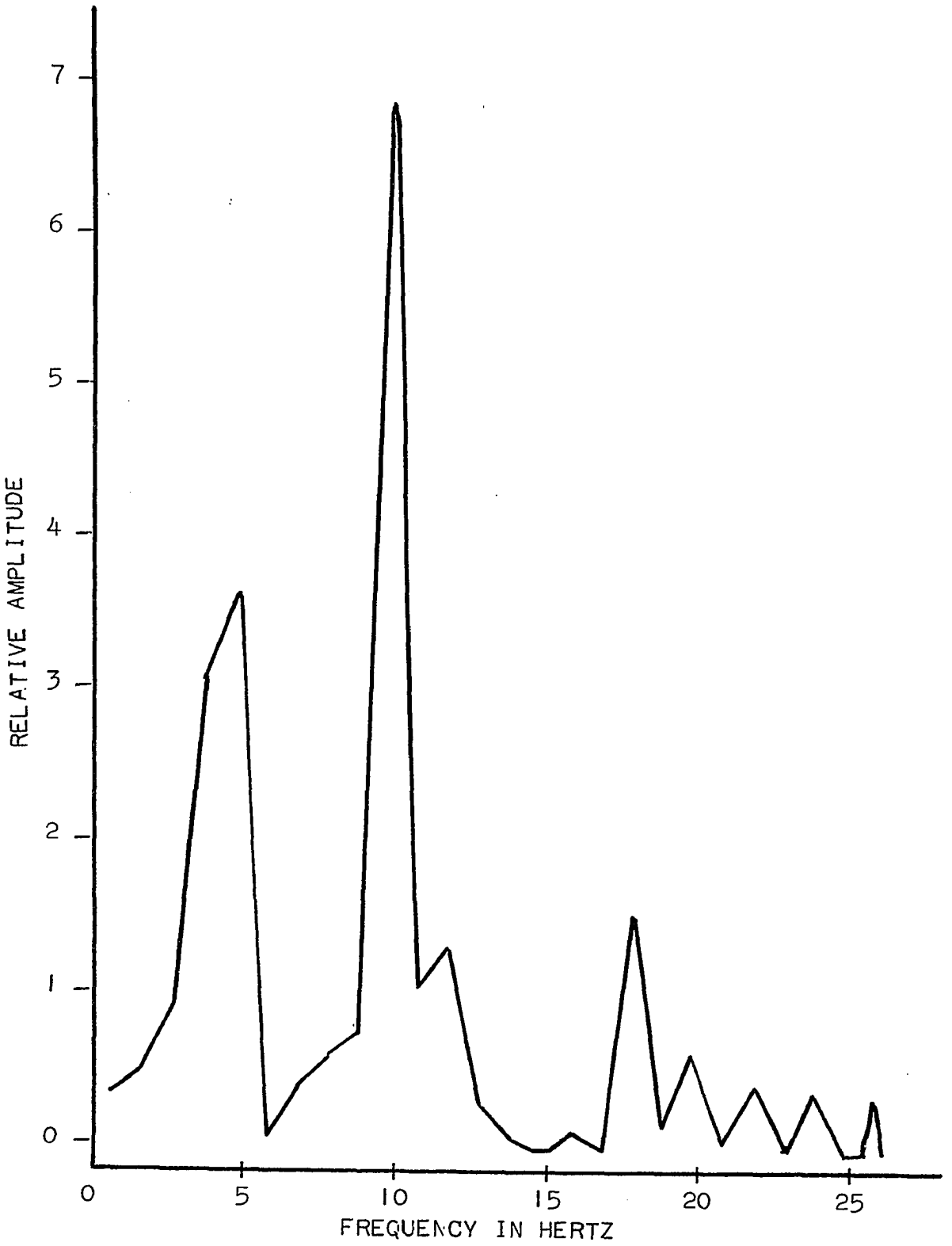

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 45. Animal 320. First day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

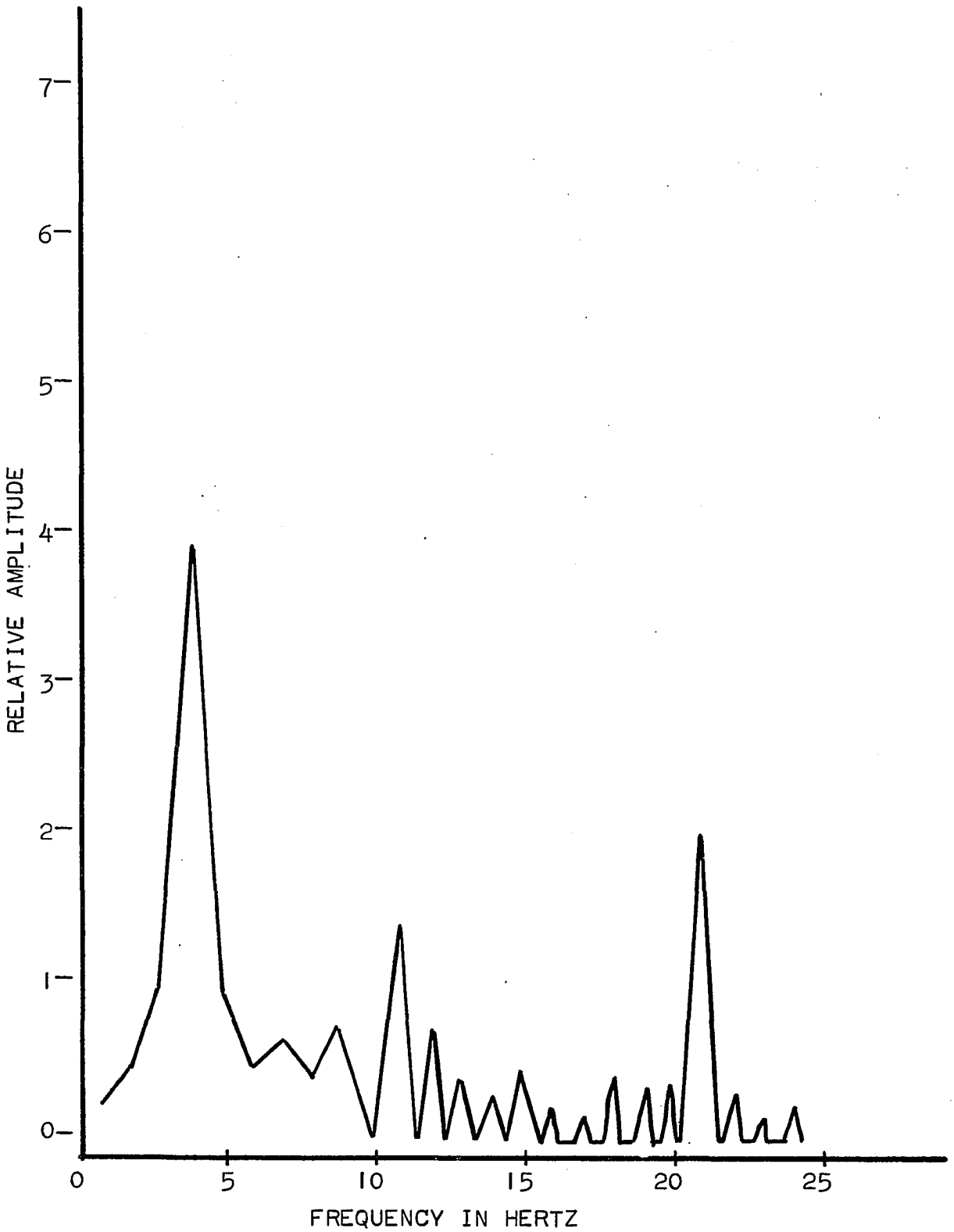

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 46. Animal 320. Second day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 10 Hz.

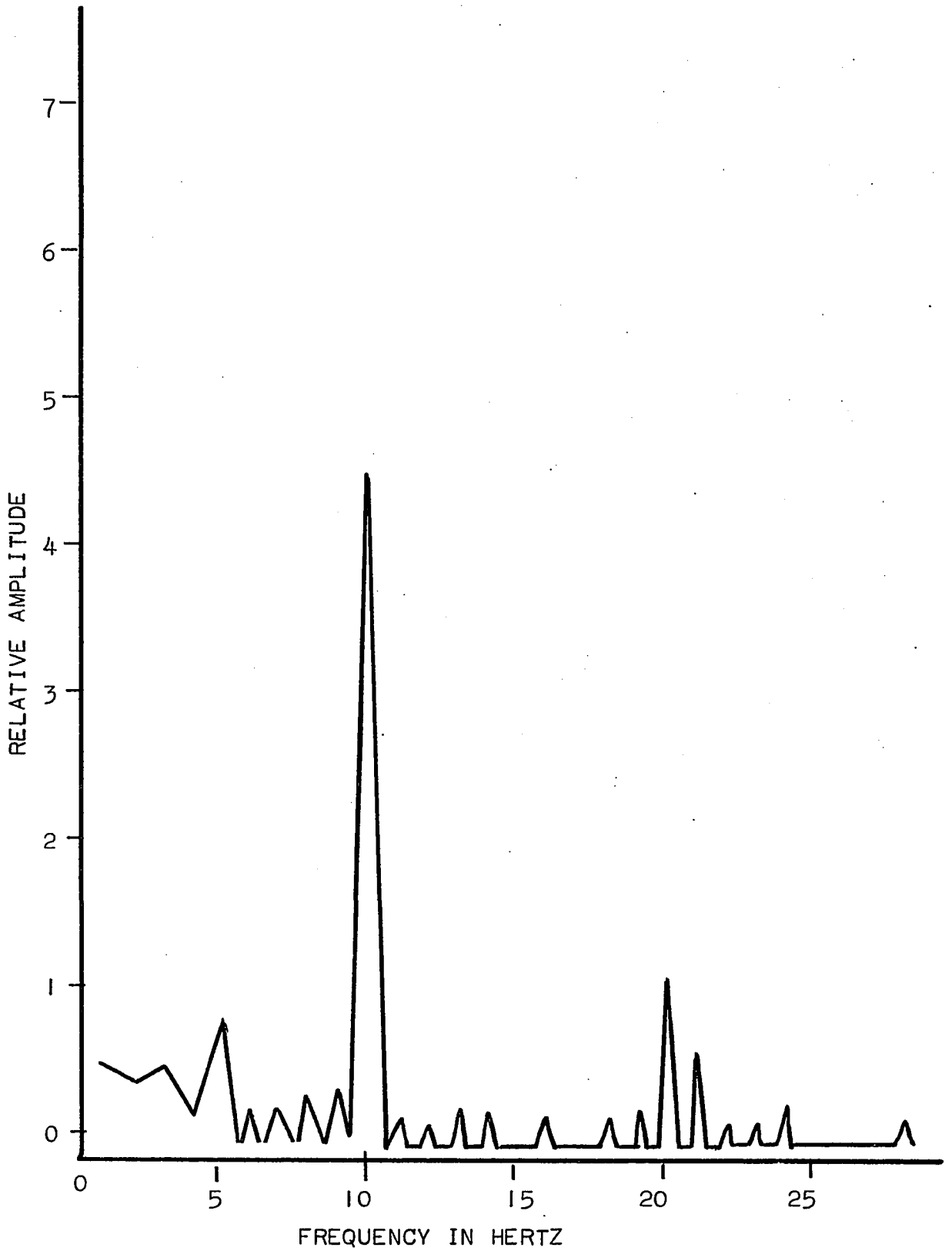

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 47. Animal 322. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 7 Hz. Two days pre-exposure.

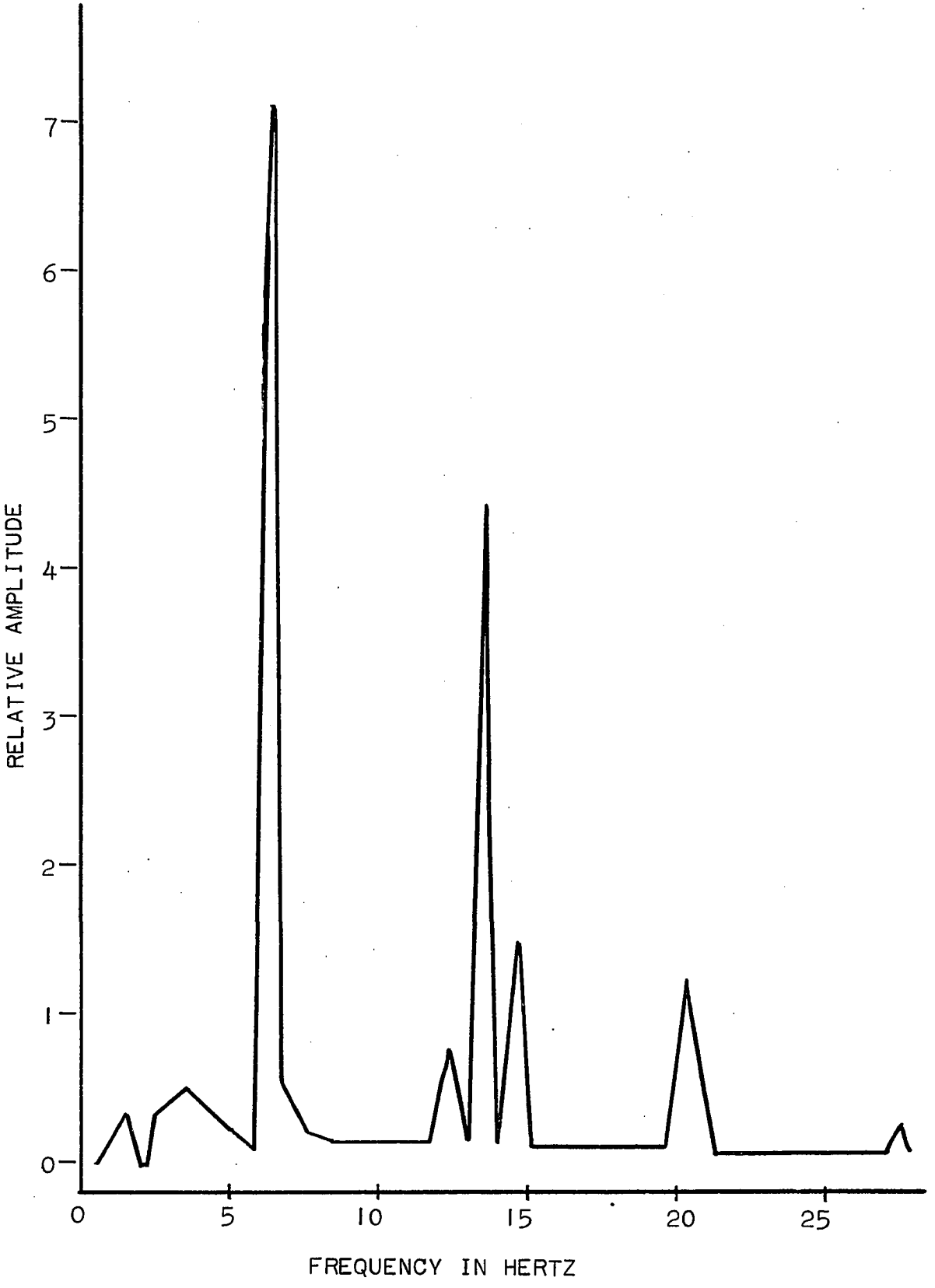

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 48. Animal 322. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 7 Hz. One day pre-exposure.

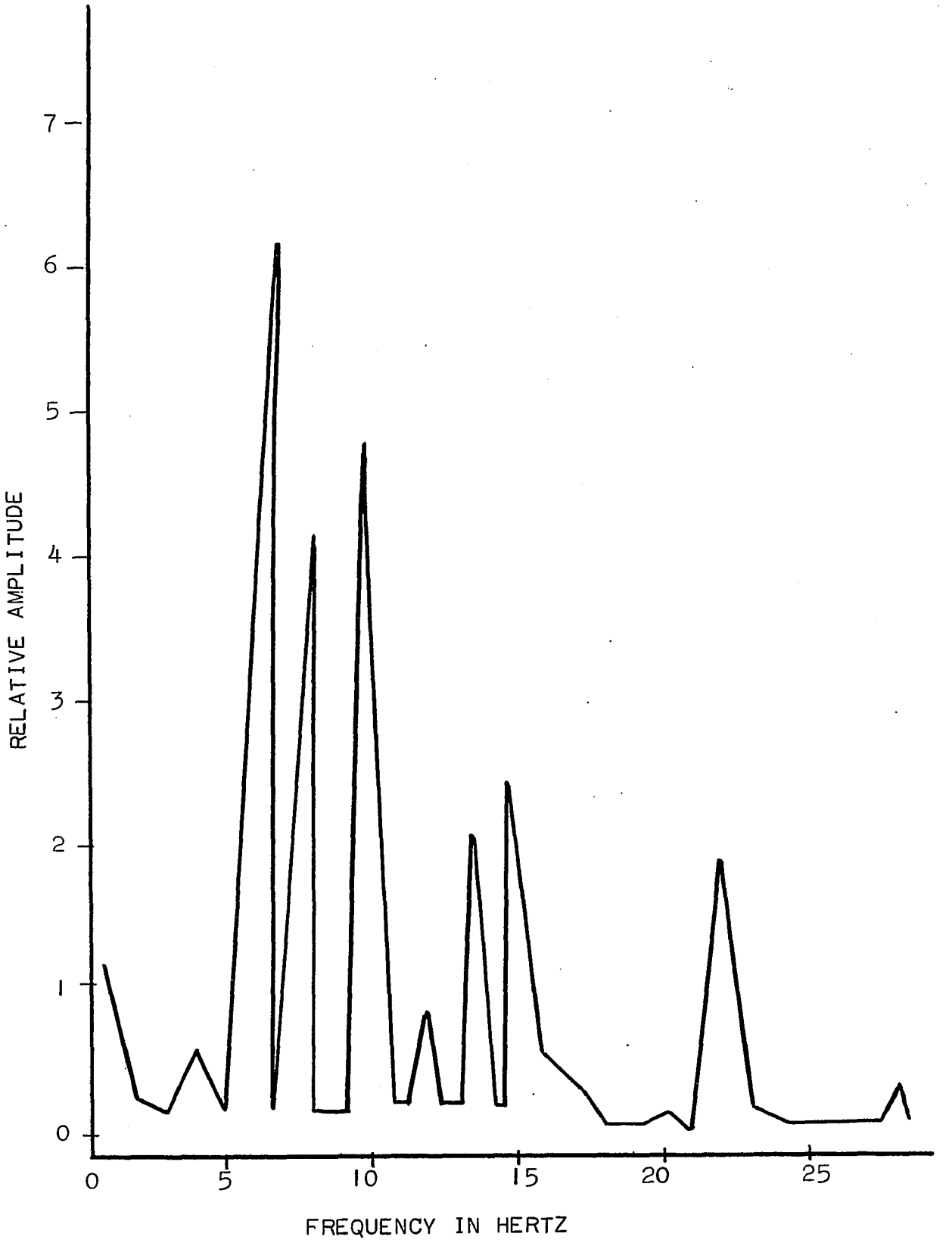

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 49. Animal 322. First day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 7 Hz.

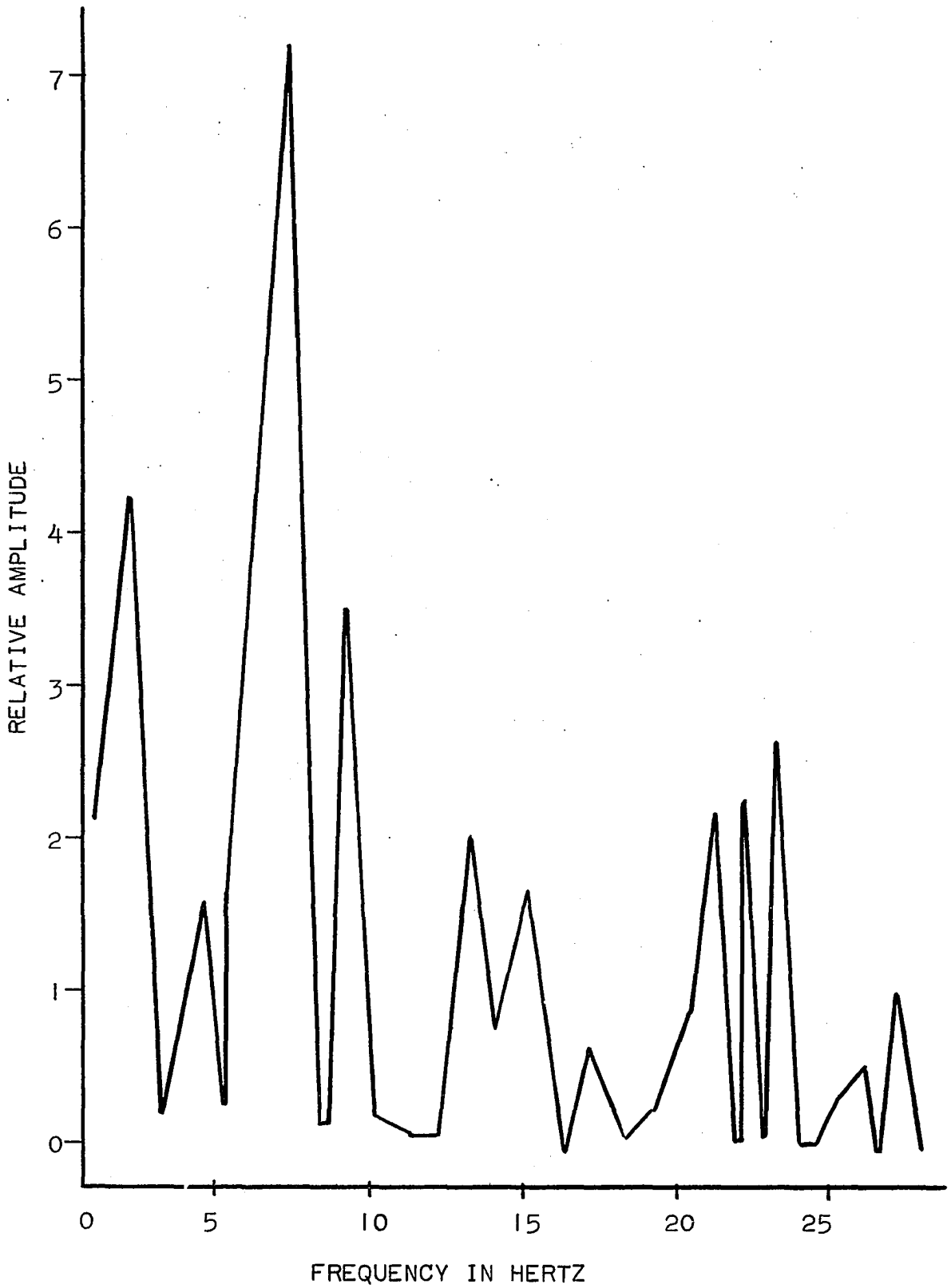

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 50. Animal 322. Second day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 7 Hz.

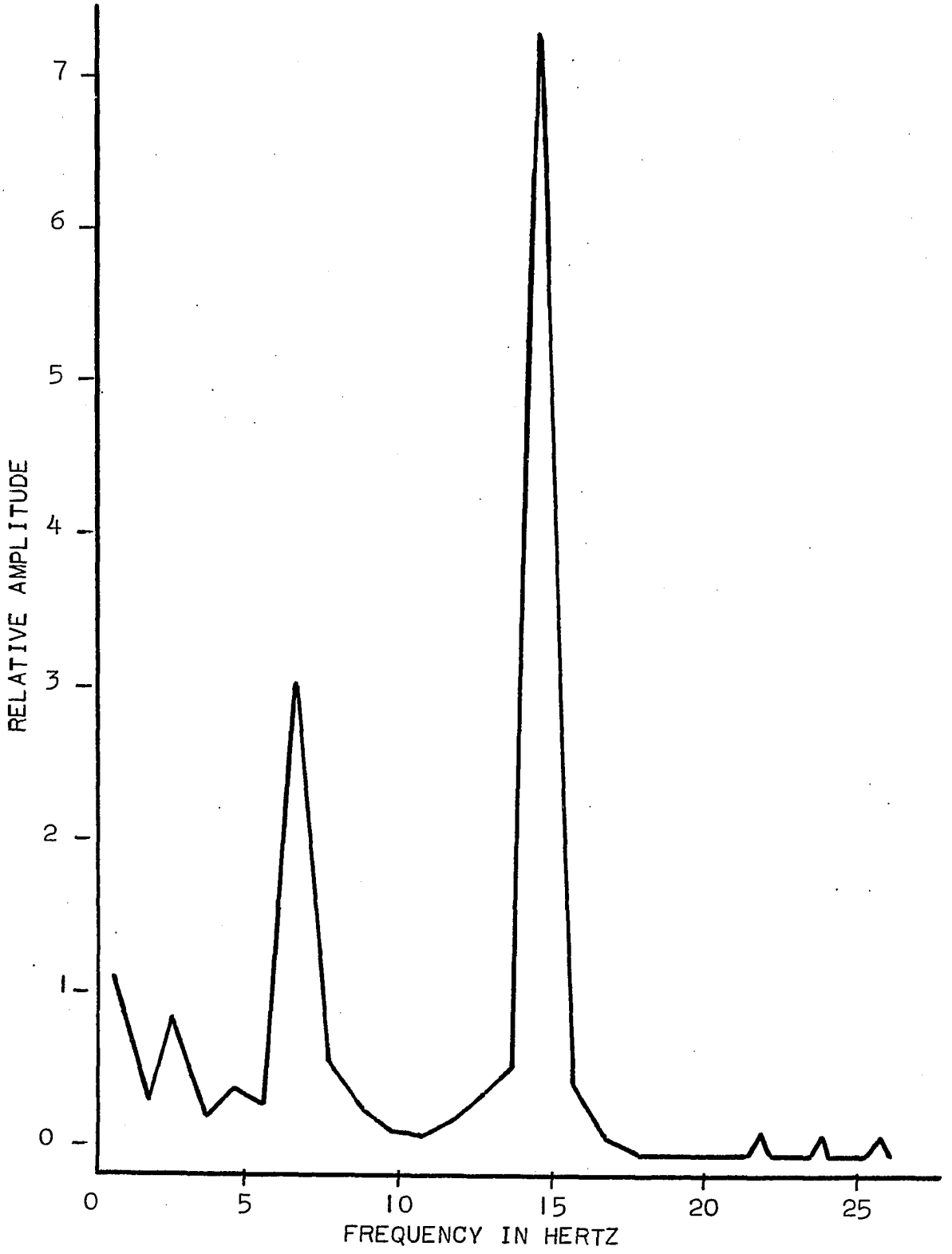

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 51. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 15 Hz. Two days pre-exposure.

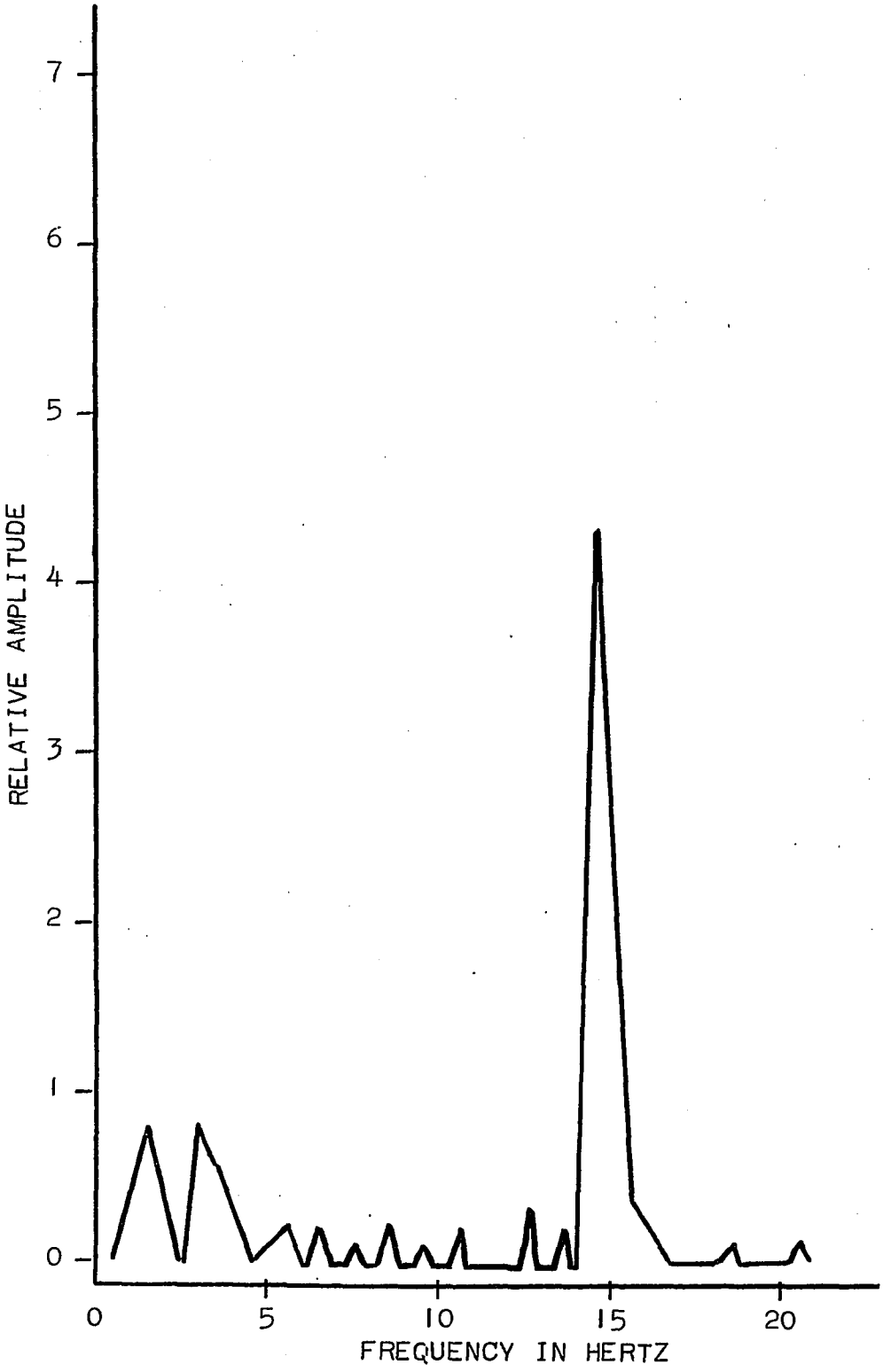

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
FREQUENCY IN HERTZ

Figure 52. Animal 111. Eighth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 15 Hz.

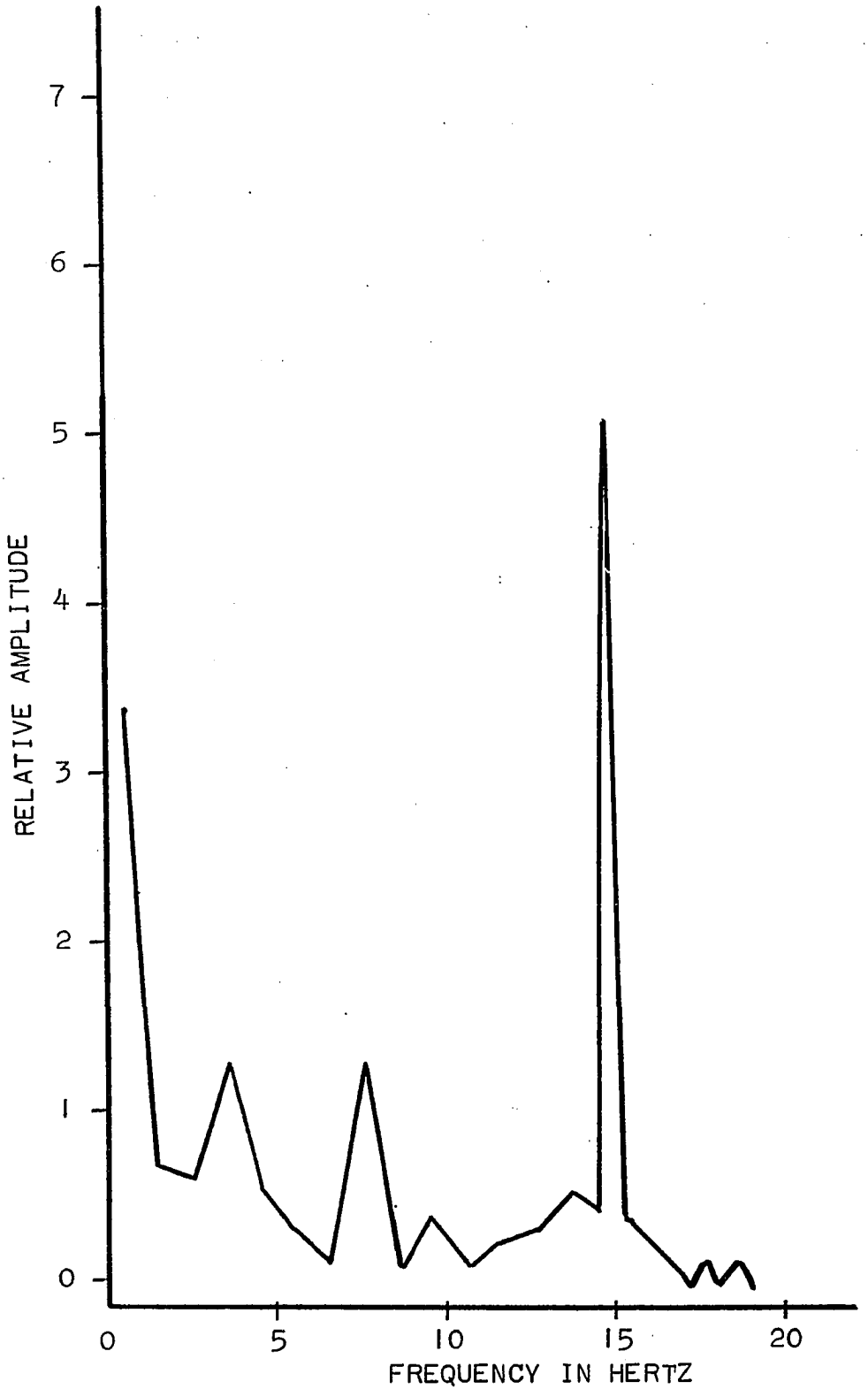

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
FREQUENCY IN HERTZ

Figure 53. Animal 111. Ninth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 15 Hz.

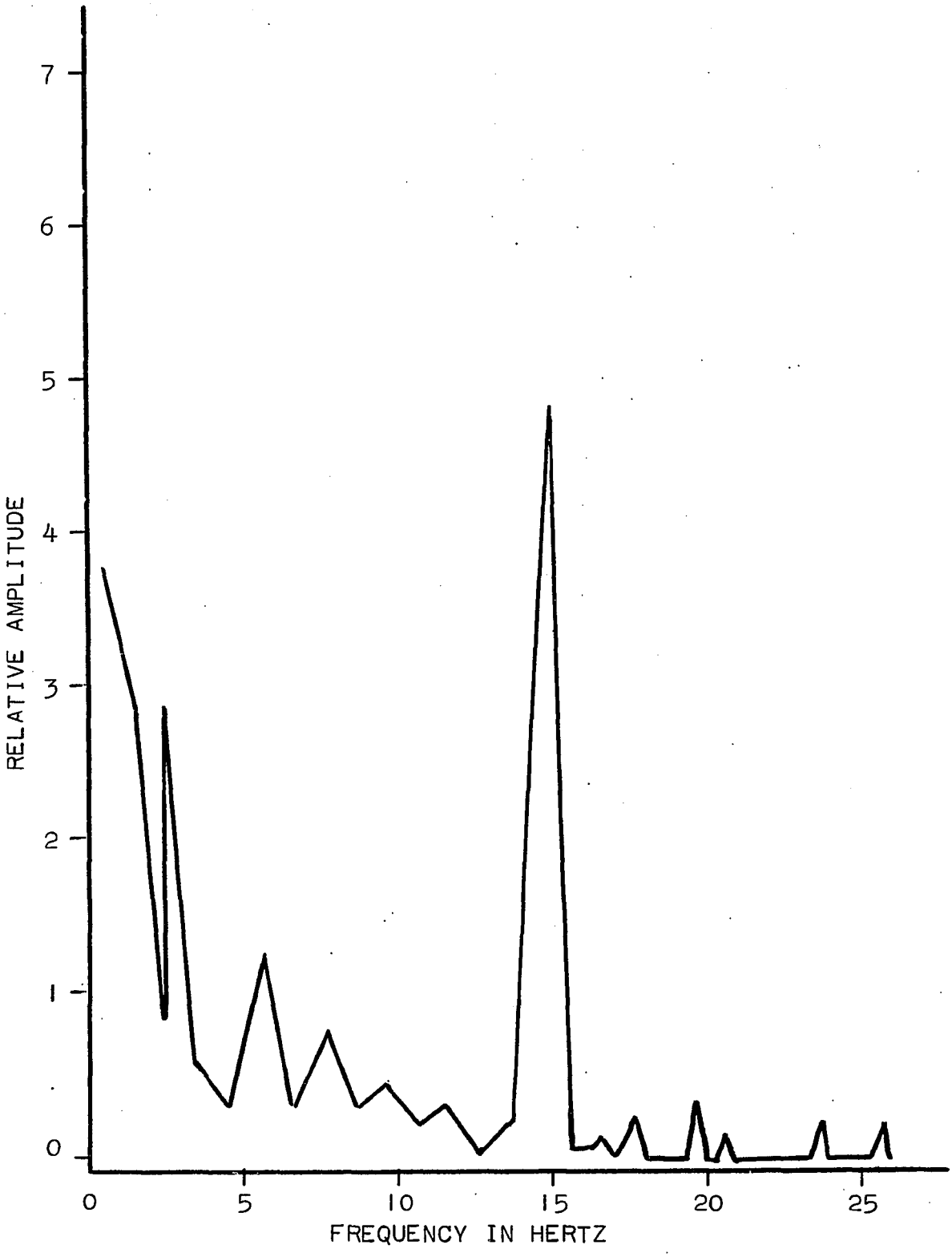

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 54. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 2 Hz. Two days pre-exposure.

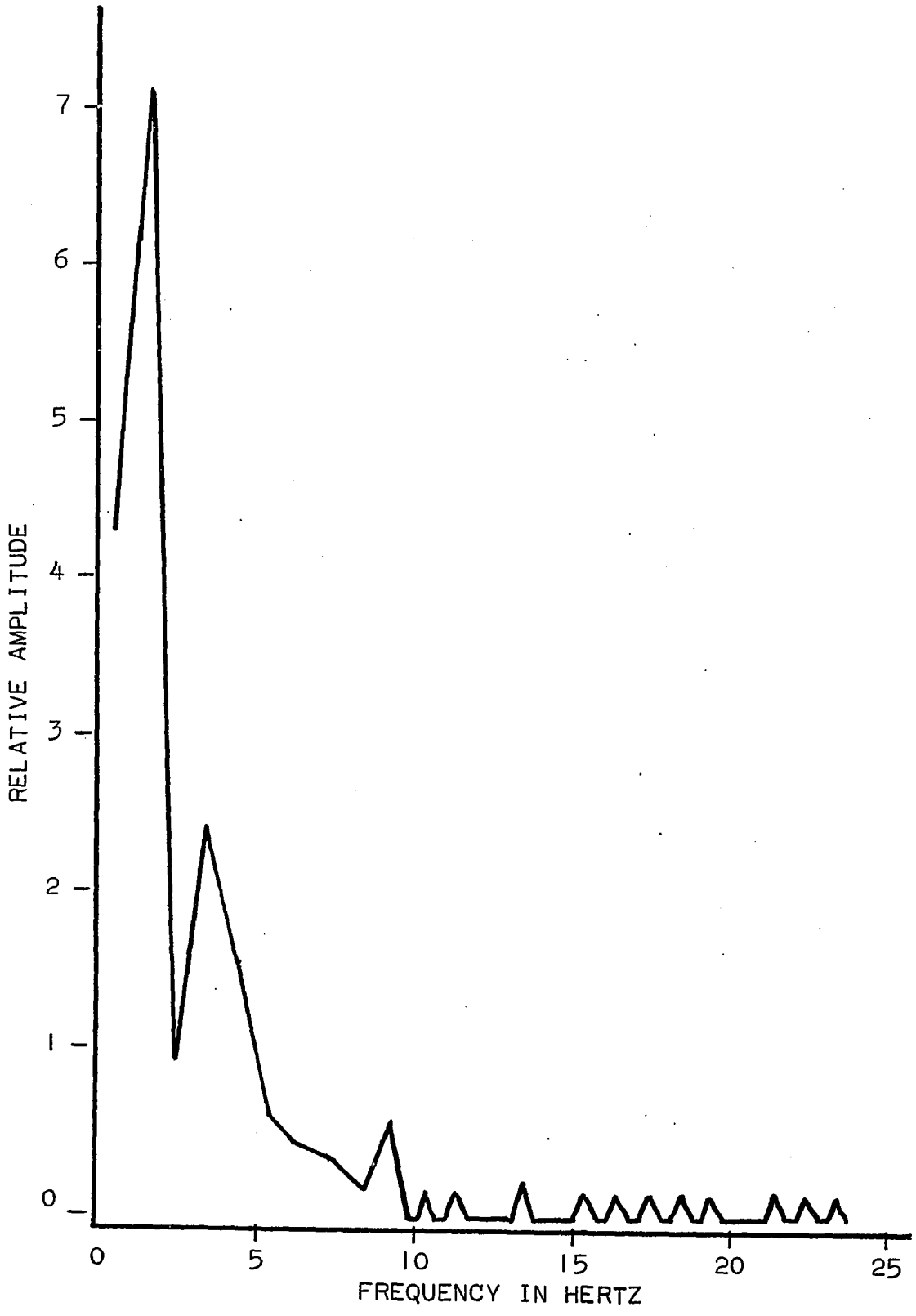

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 55. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 2 Hz. One day pre-exposure.

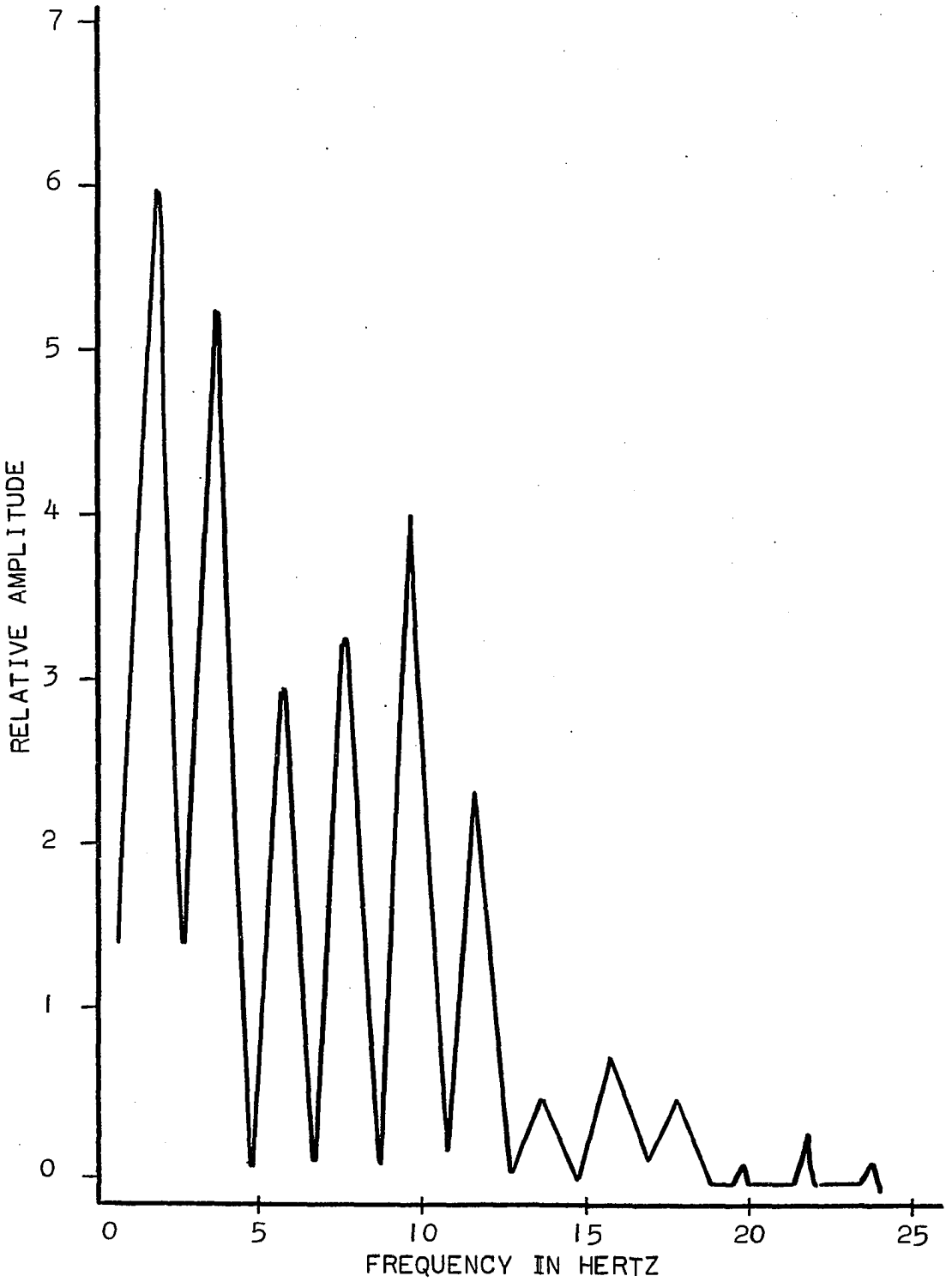

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 56. Animal 111. Eighth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 2 Hz.

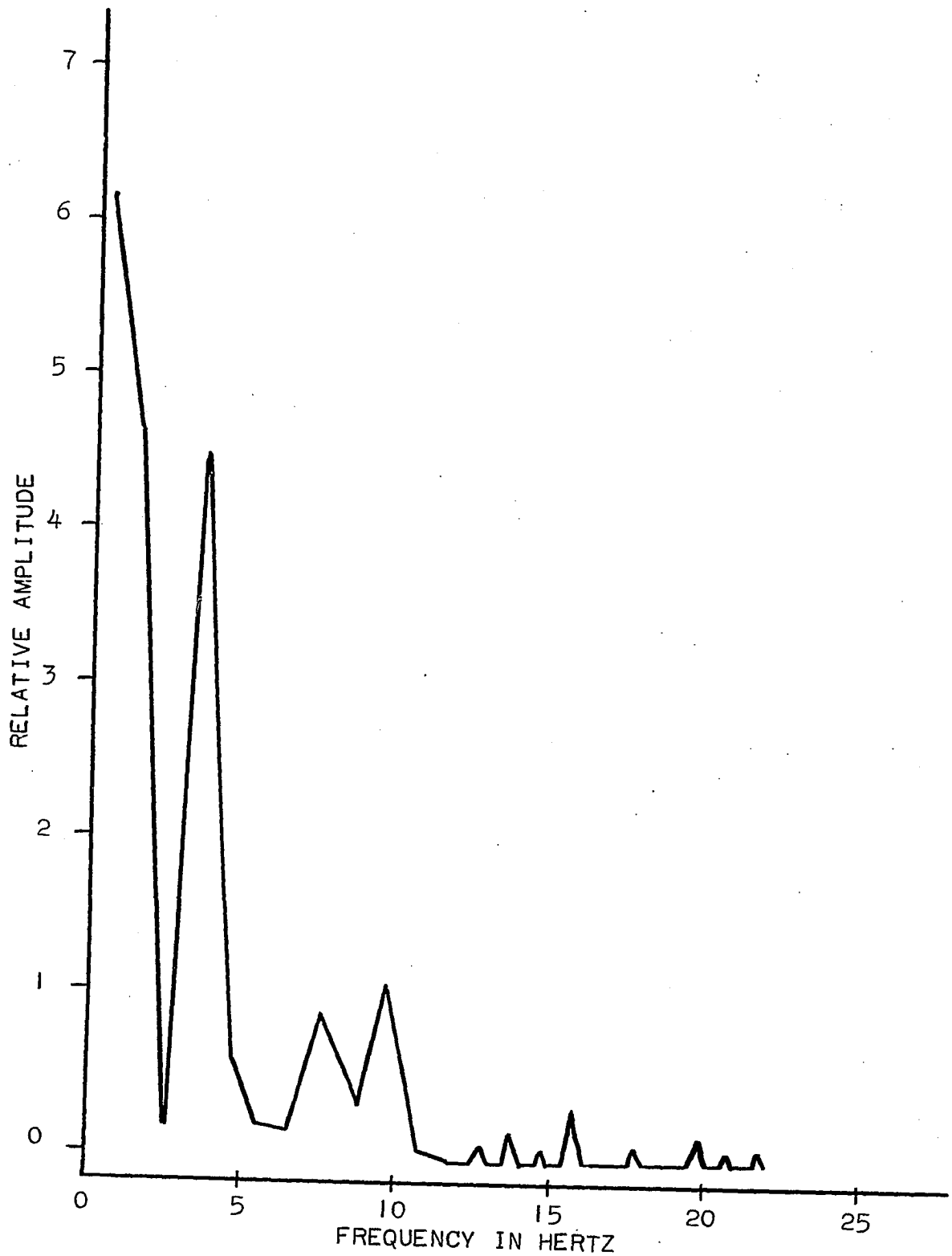

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 57. Animal 111. Ninth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 2 Hz.

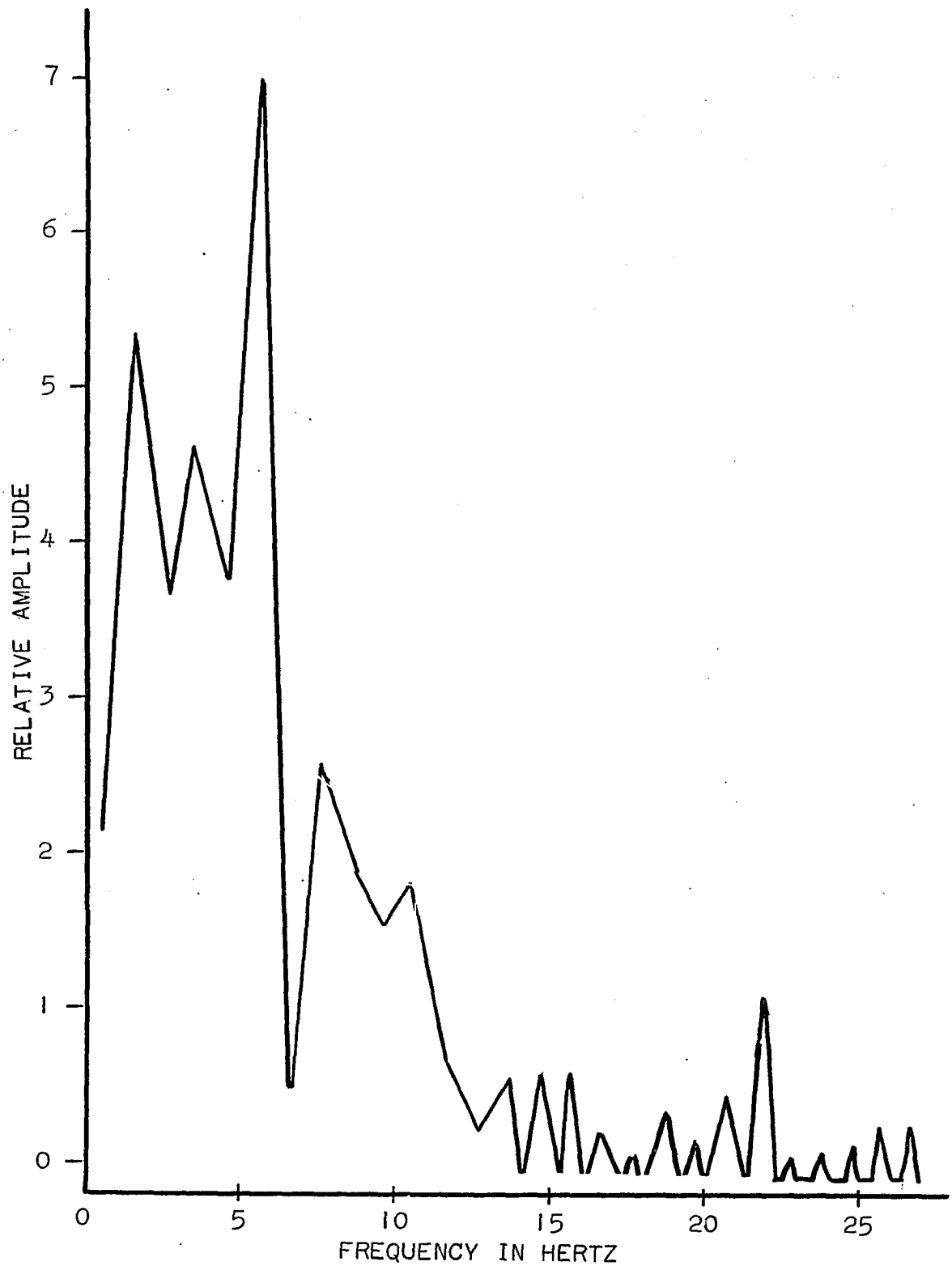

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 58. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz. Two days pre-exposure.

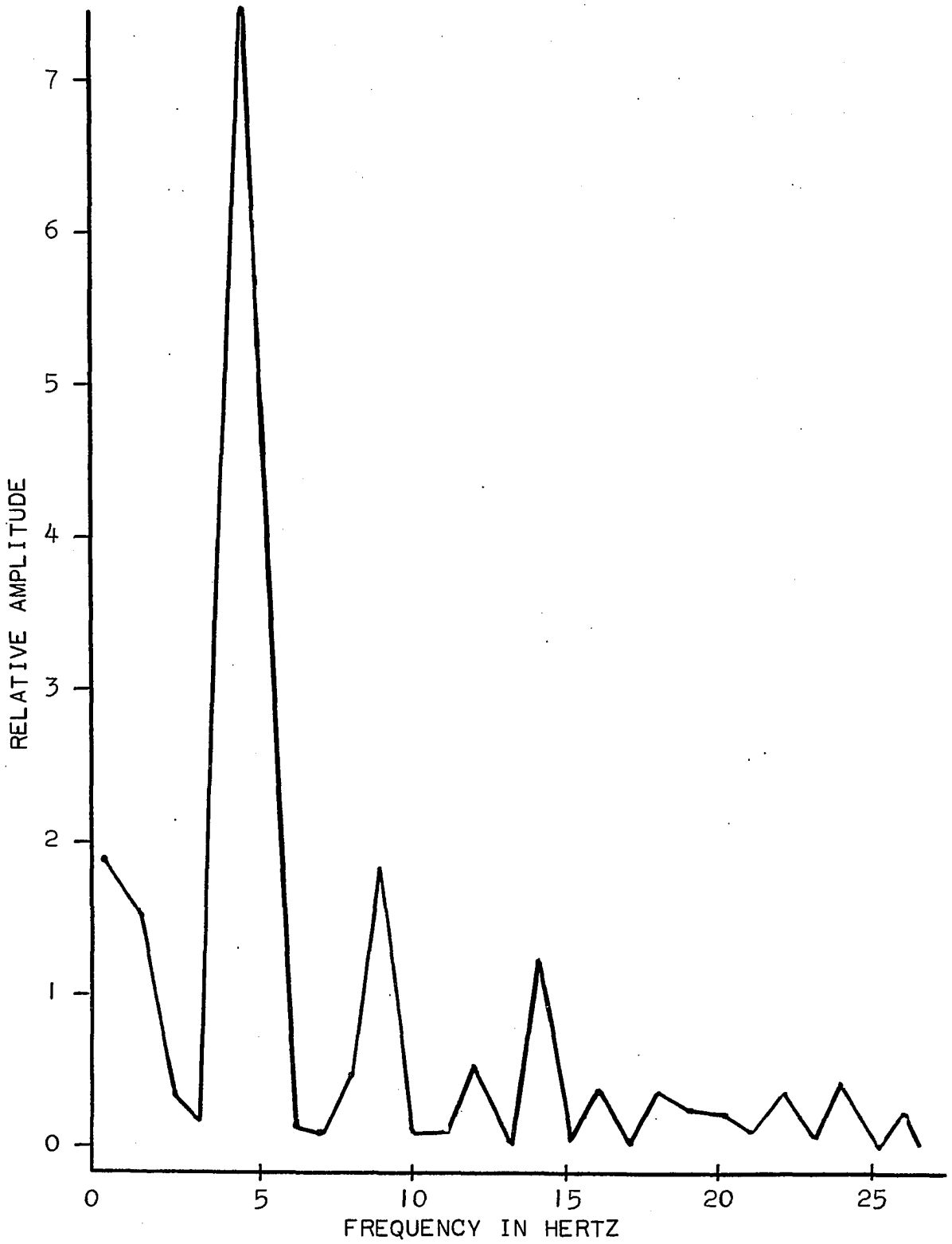

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 59. Animal 111. Eighth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

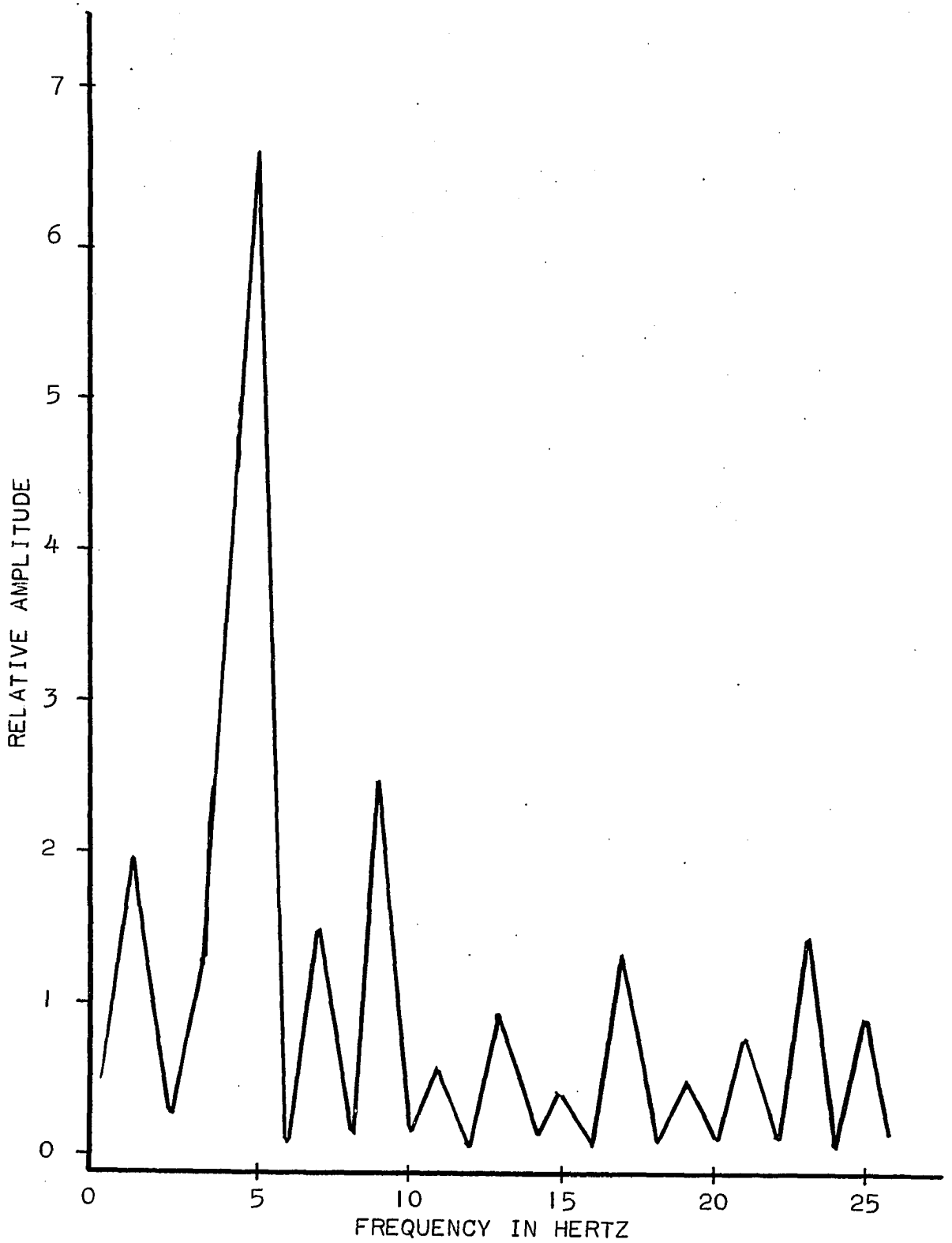

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 60. Animal 111. Ninth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated light at 5 Hz.

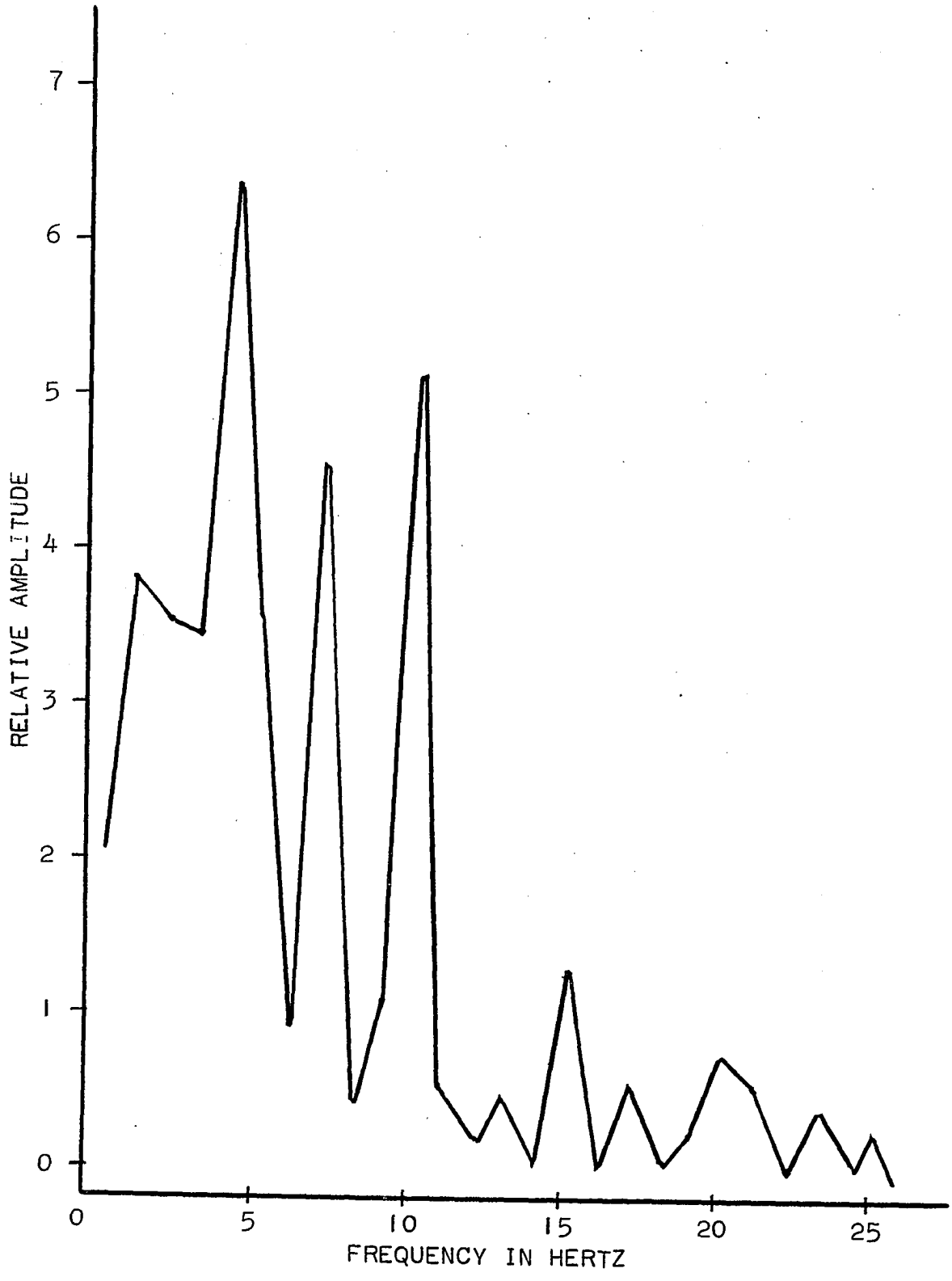

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 61. Animal 339. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz. Two days pre-exposure.

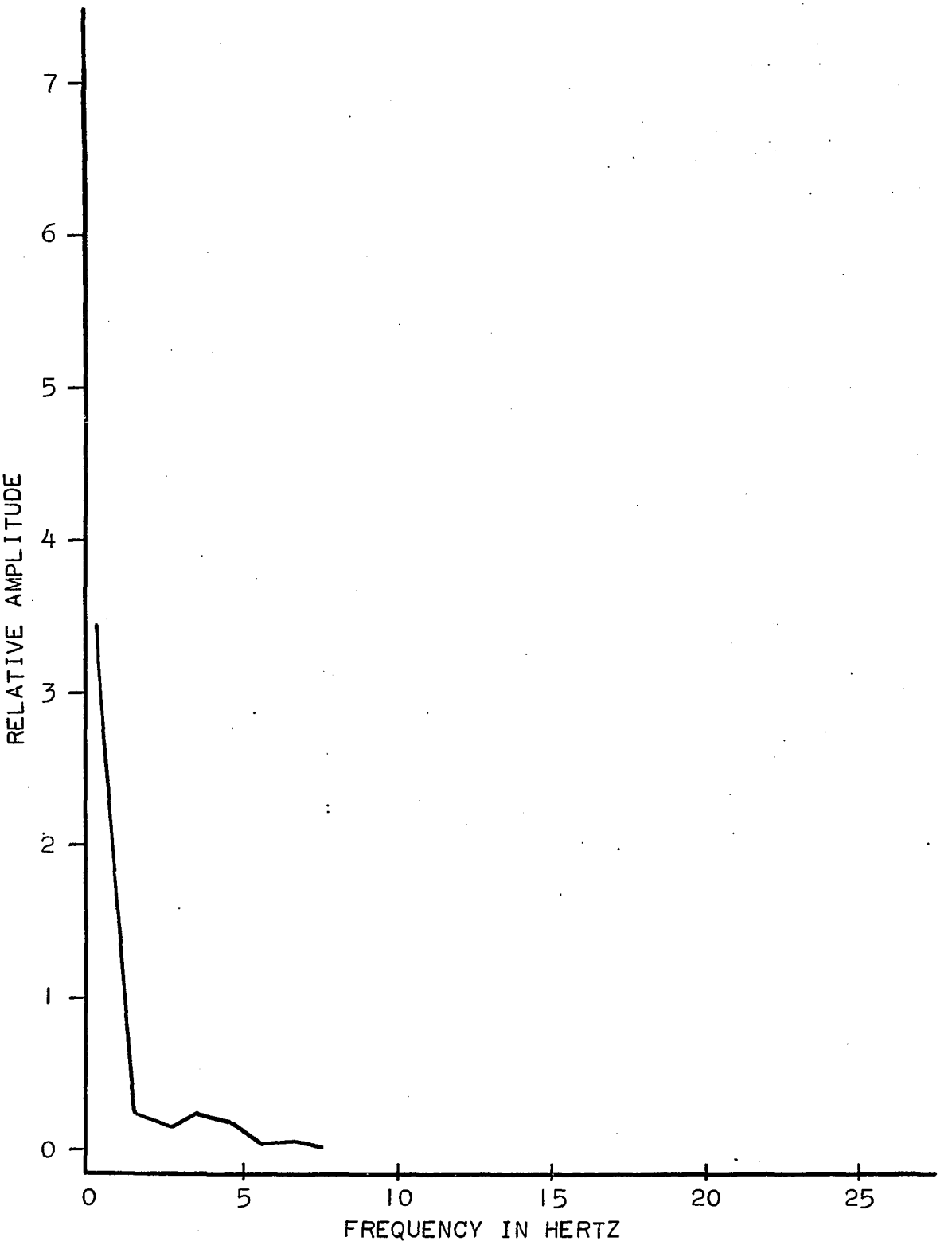

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 62. Animal 339. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz. Two days pre-exposure.

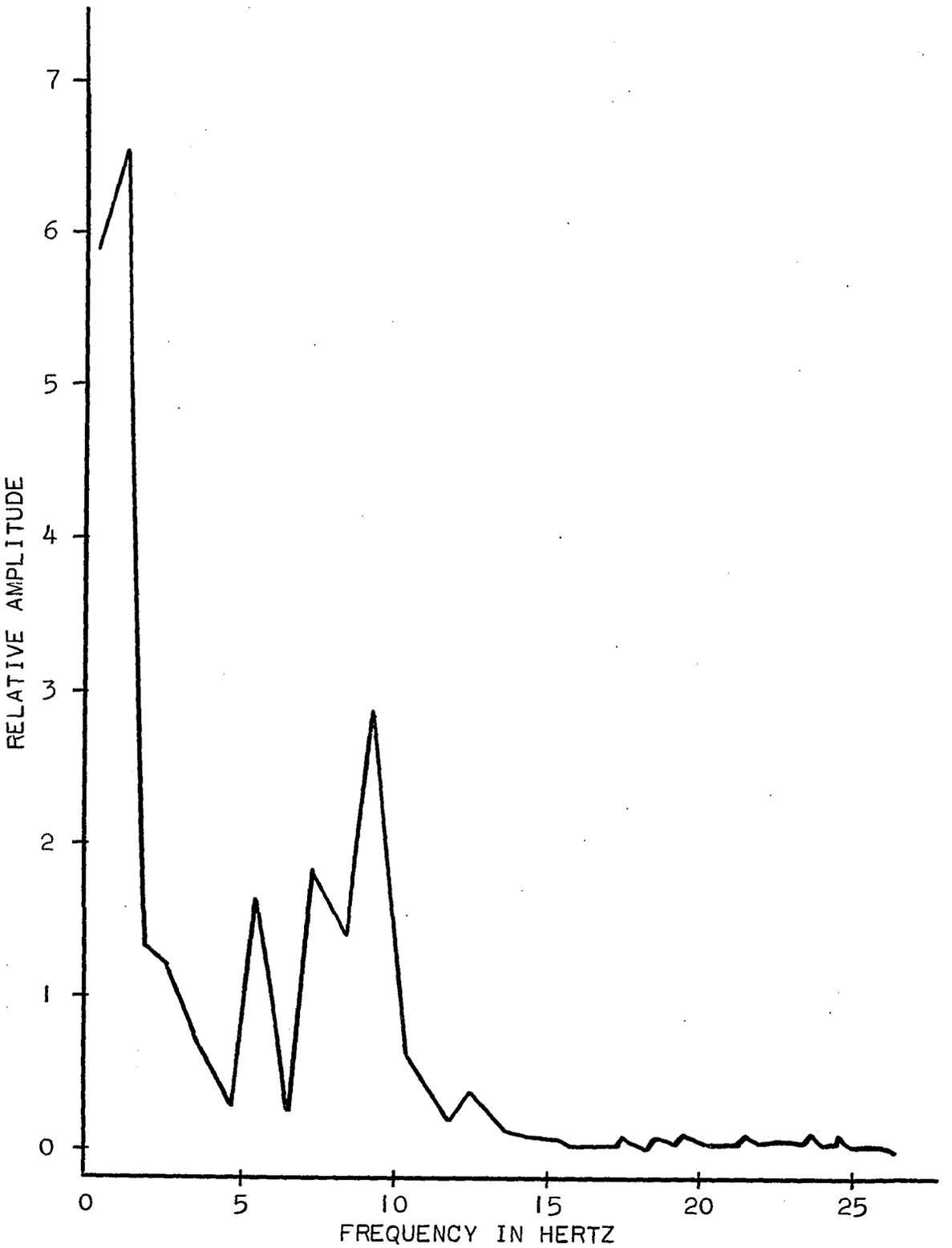

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 63. Animal 339. Fourth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz.

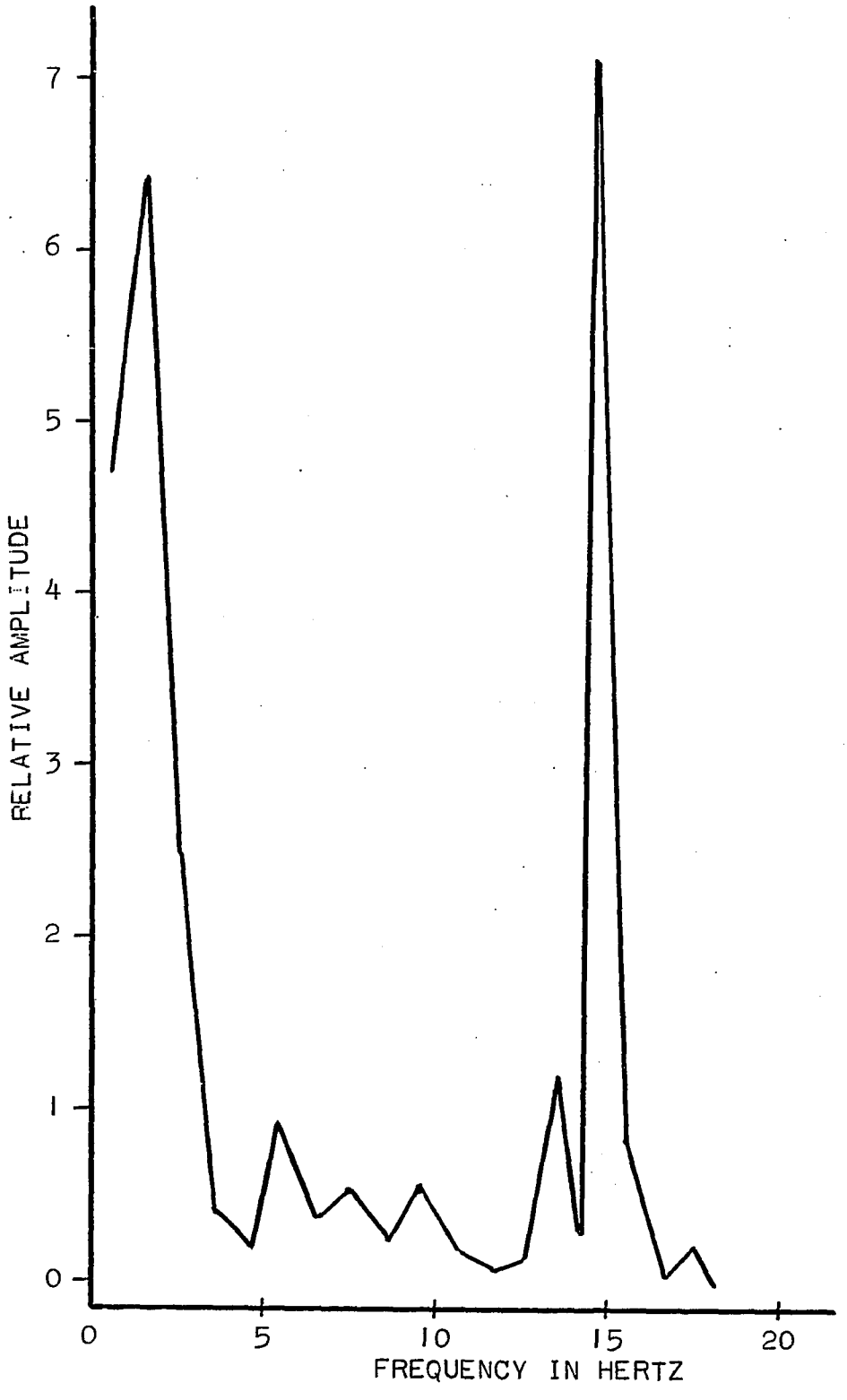

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
FREQUENCY IN HERTZ

Figure 64. Animal 339. Fifth day of dieldrin exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz.

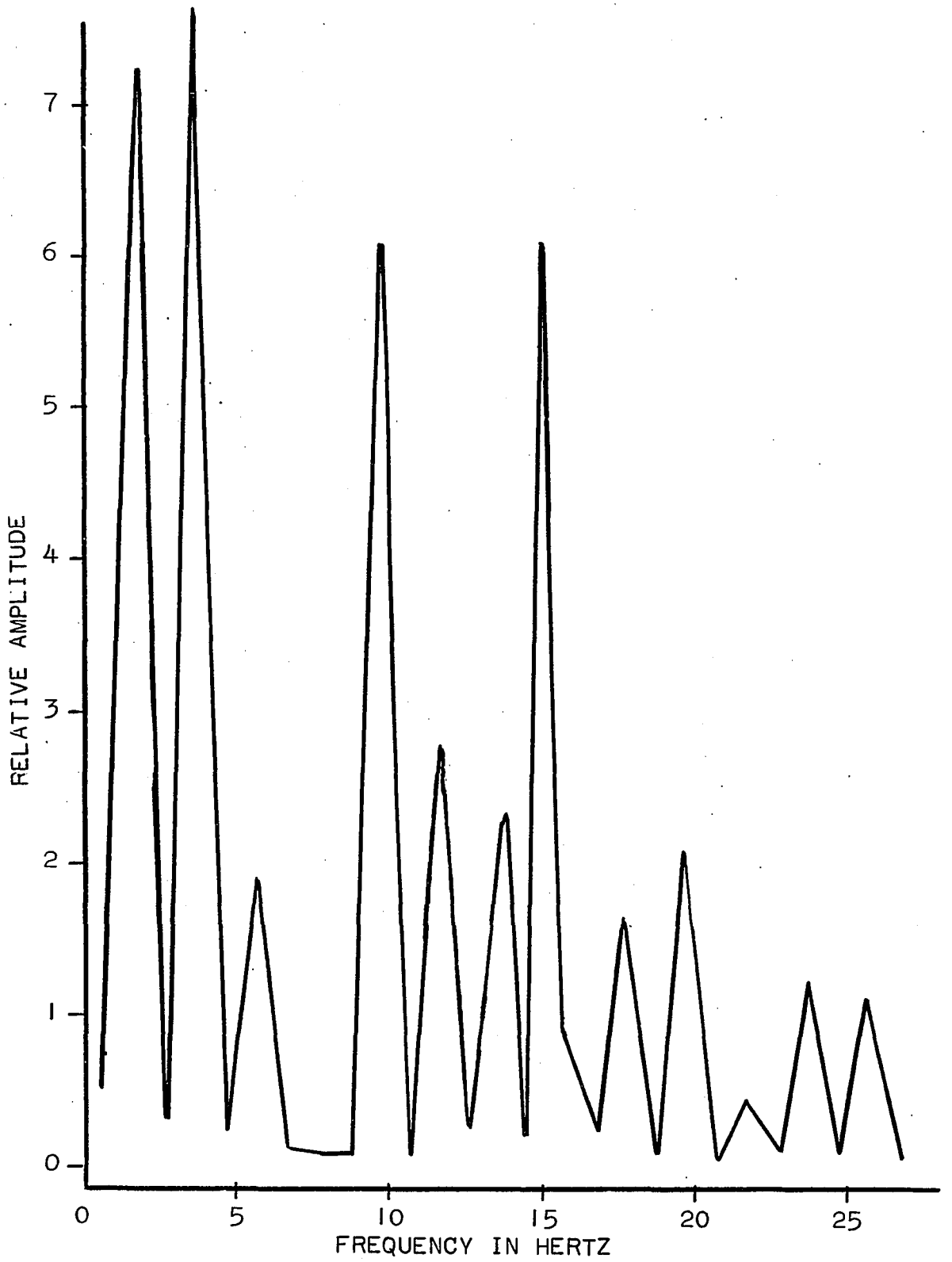

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 65. Animal 337. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz. Two days pre-exposure.

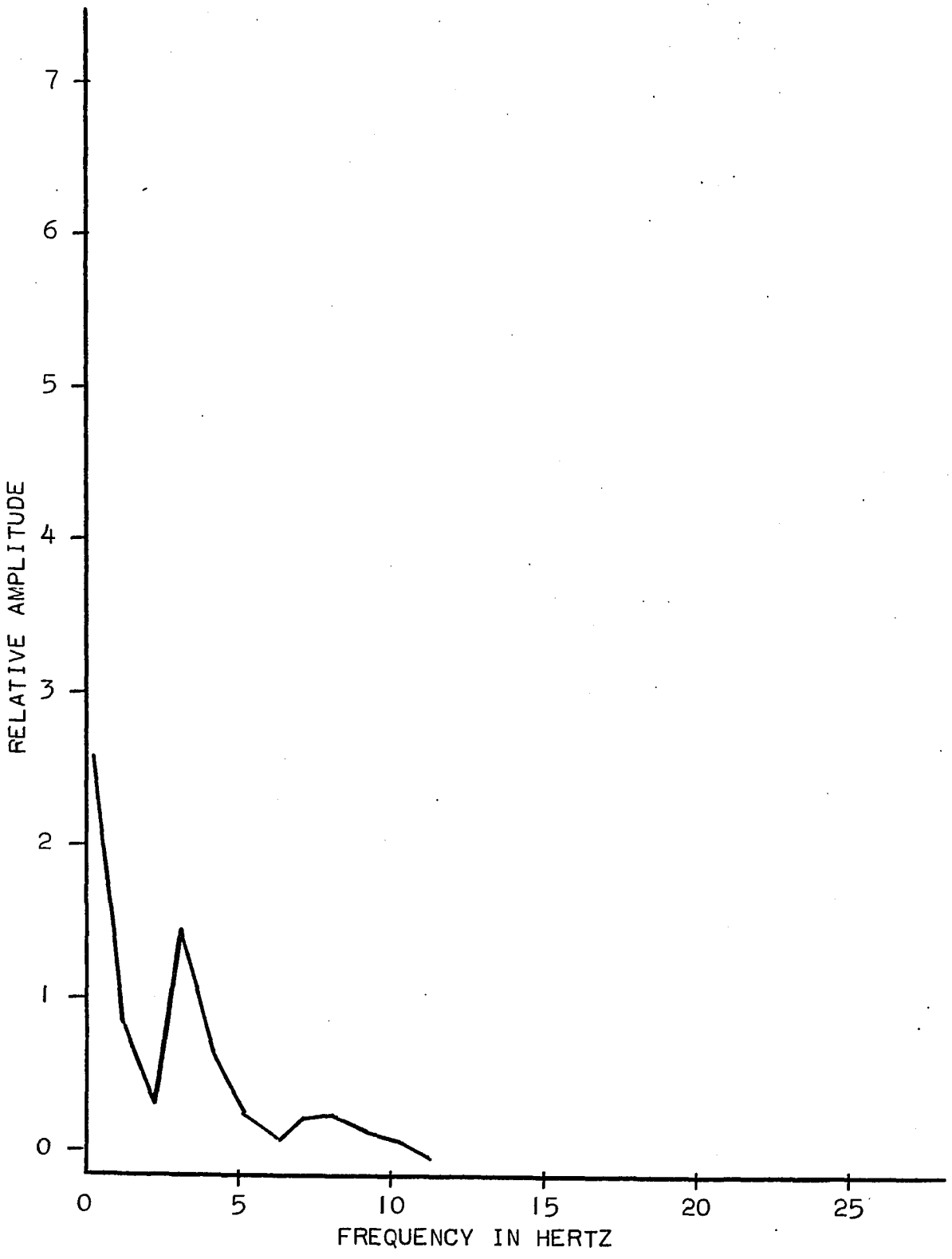

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 66. Animal 337. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz. One day pre-exposure.

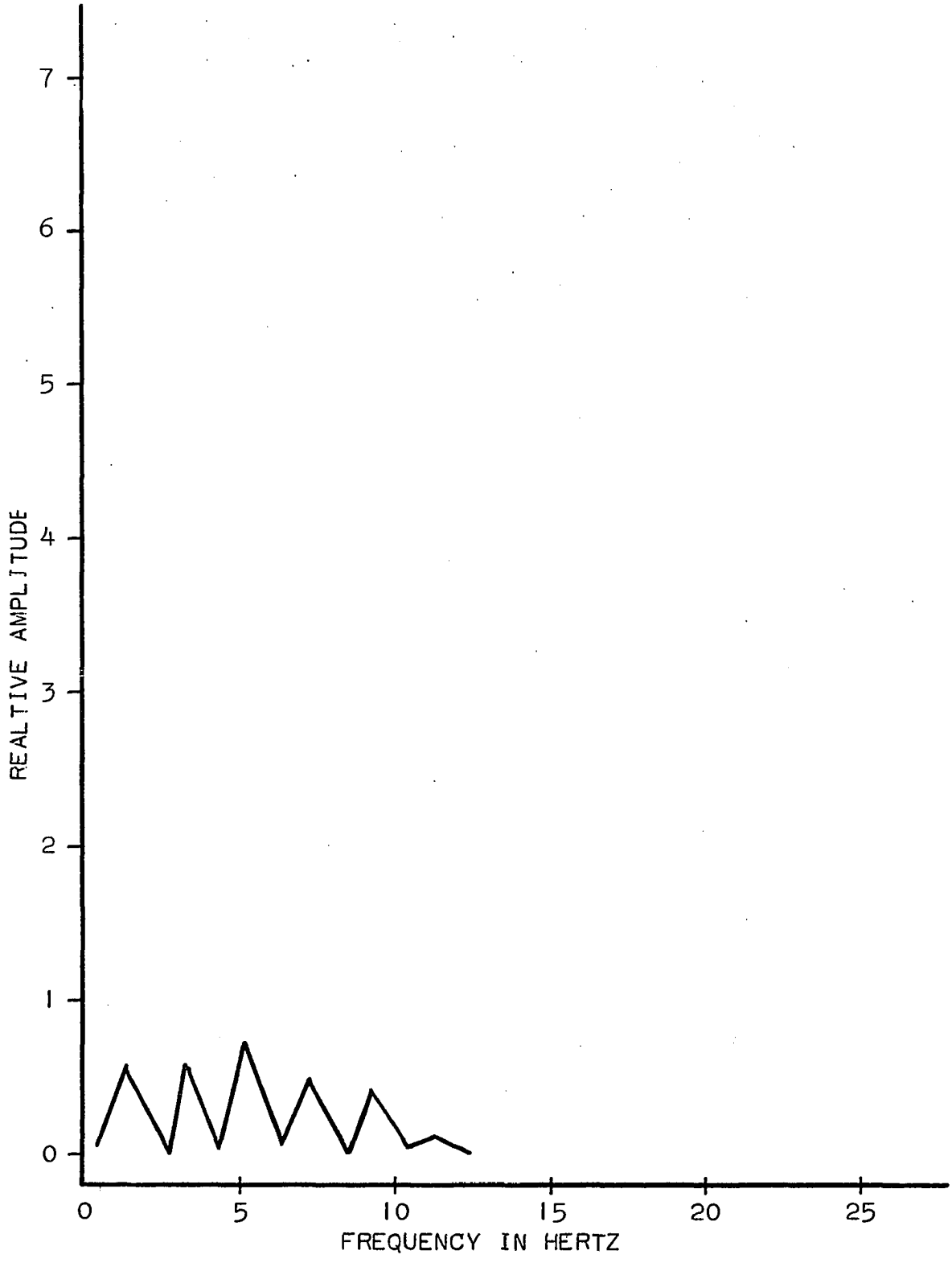

7
6
5
4
3
2
1
0
REALTIVE AMPLITUDE
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 67. Animal 337. Second day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz.

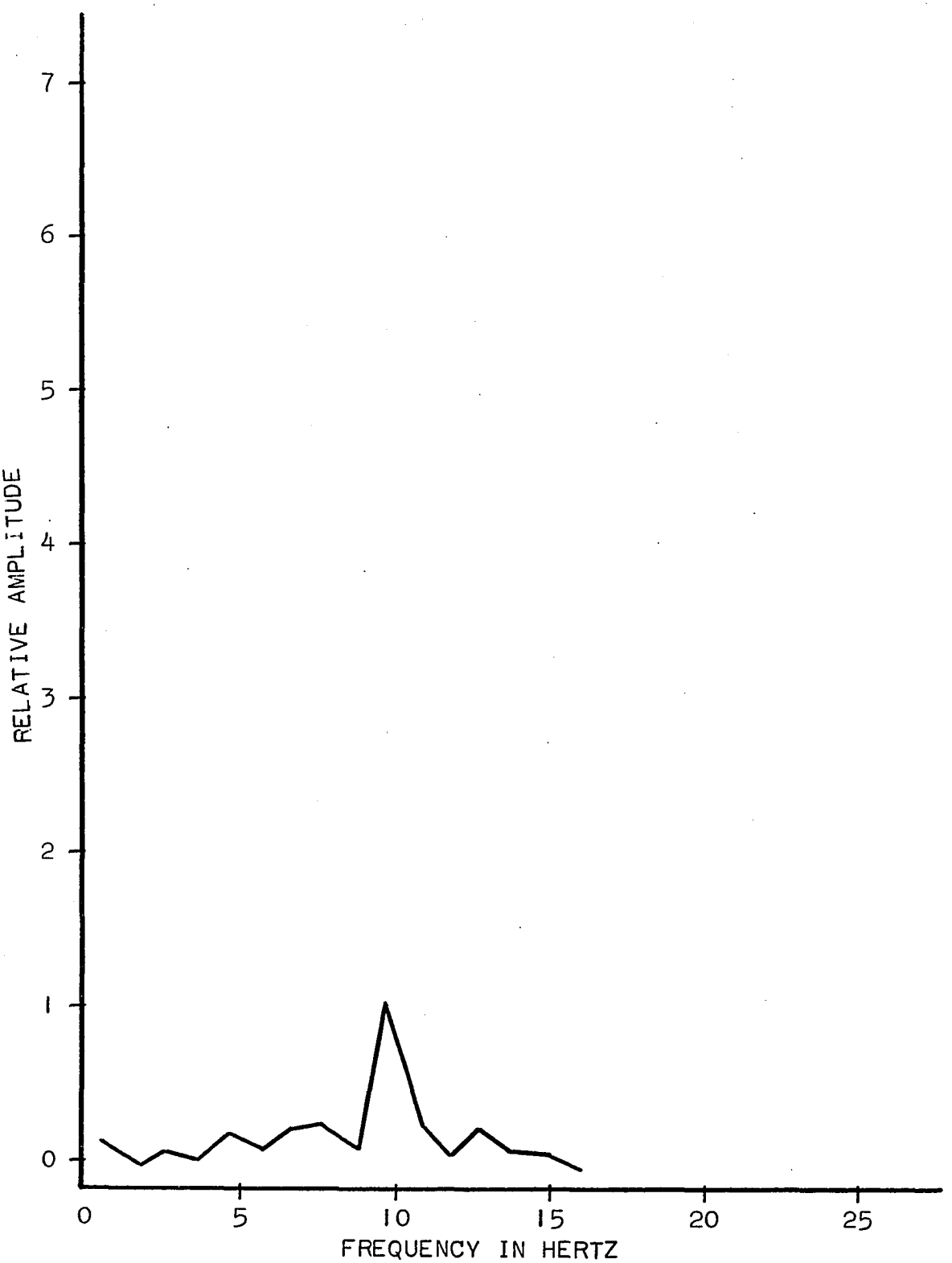

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 68. Animal 337. Third day of Rulene® exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 10 Hz.

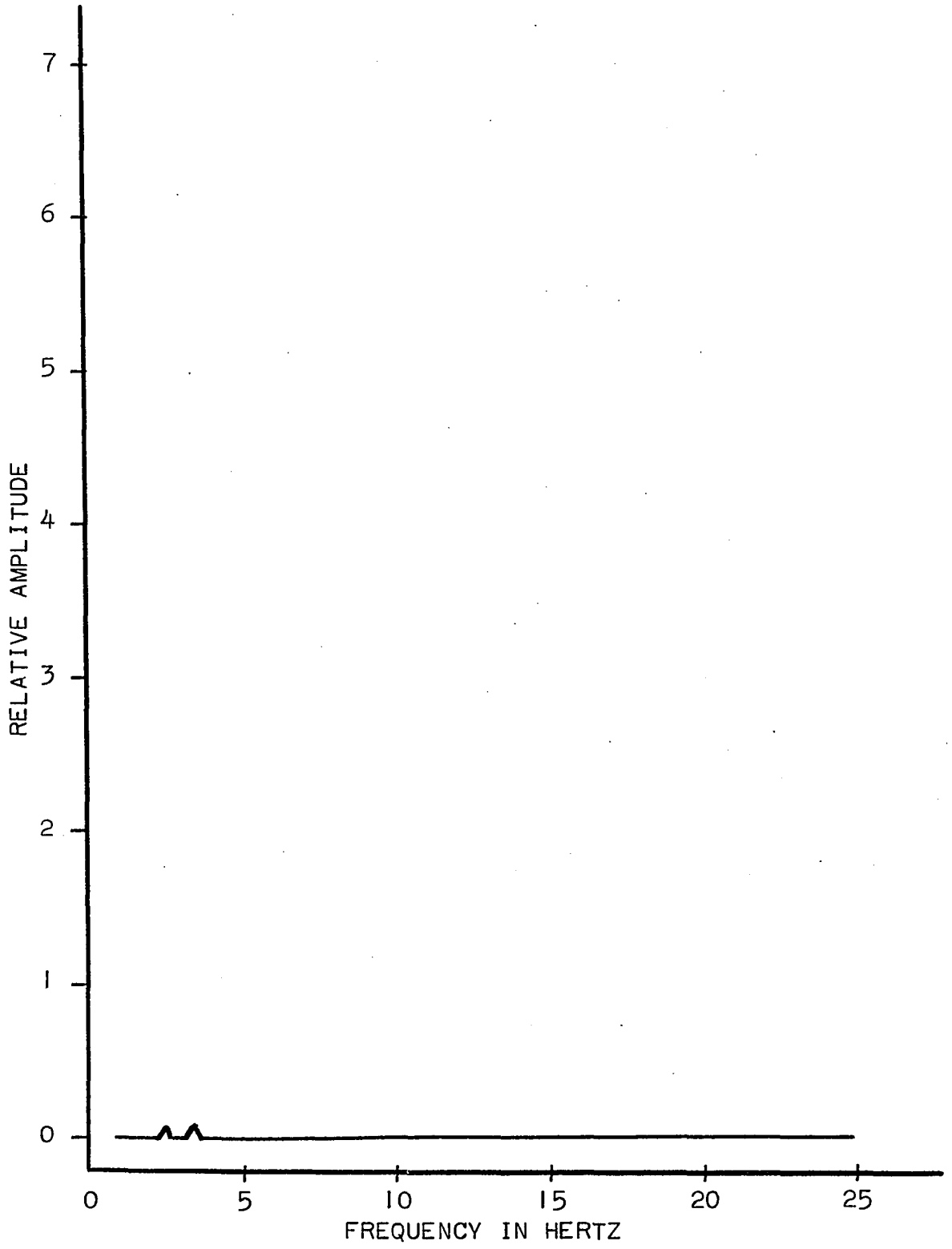

RELATIVE AMPLITUDE
7
6
5
4
3
2
1
0
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 69. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 2 Hz. Two days pre-exposure.

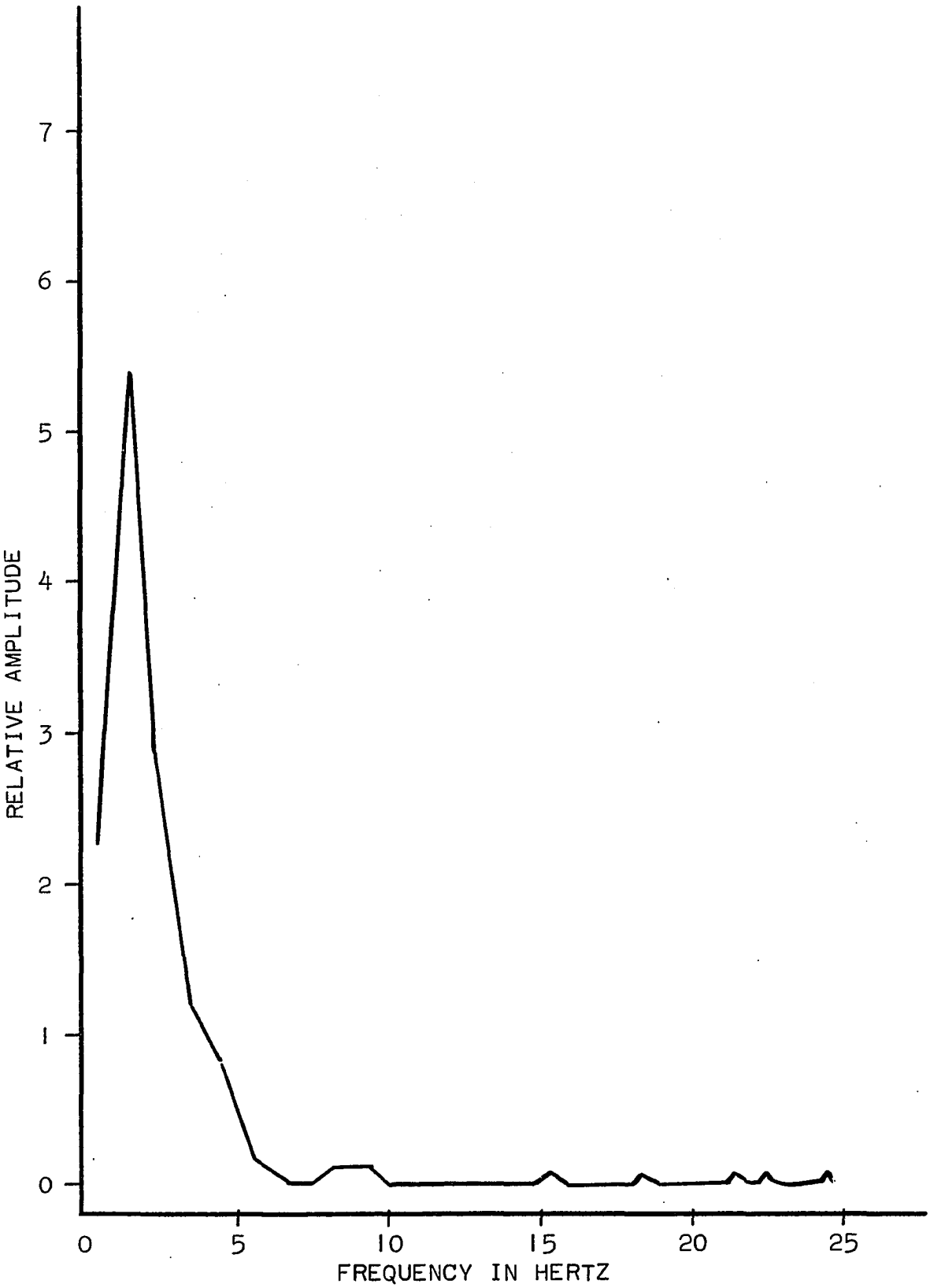

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 70. Animal 111. Control Data. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 2 Hz. One day pre-exposure.

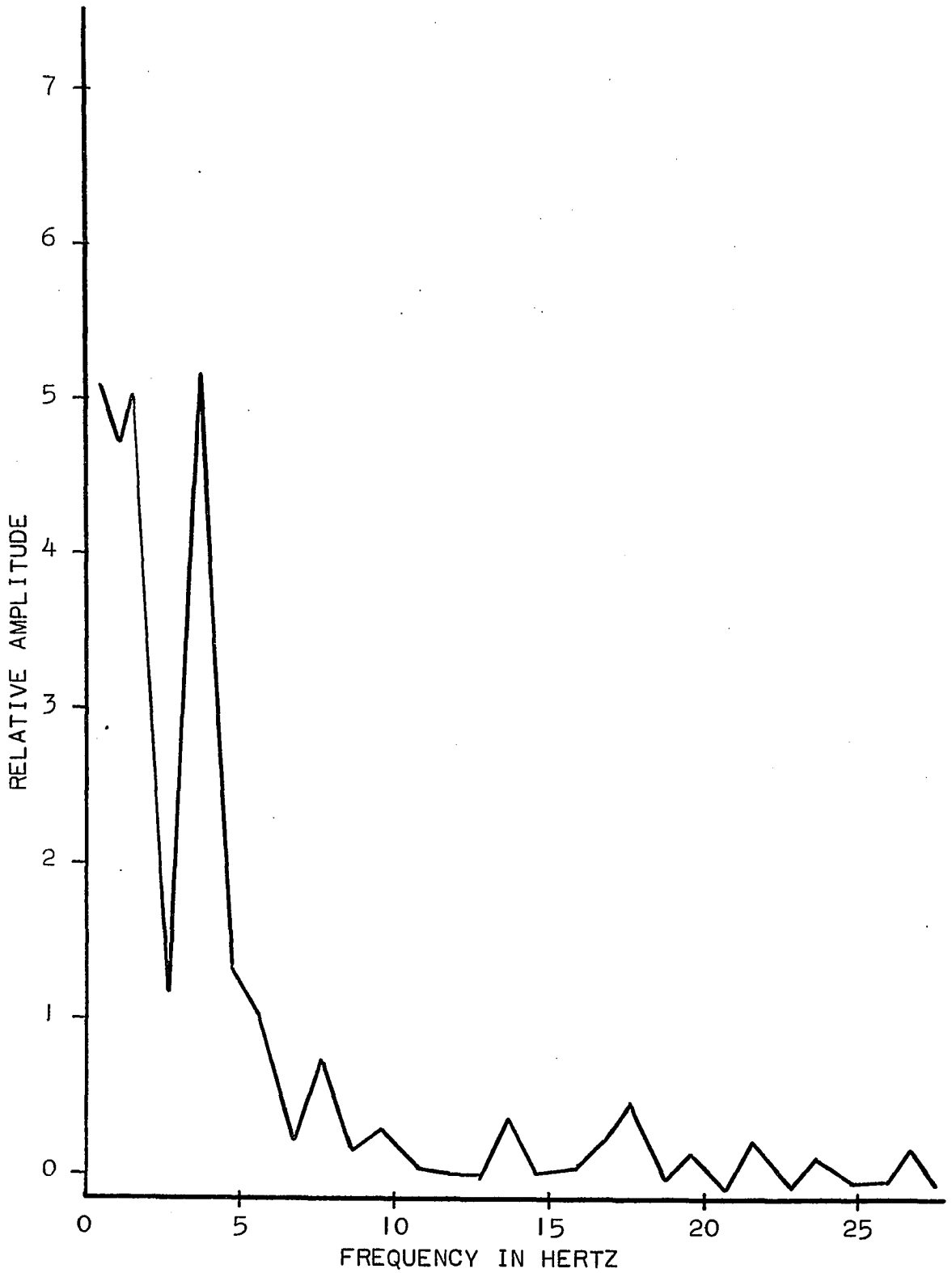

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 71. Animal 111. Fourth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 2 Hz.

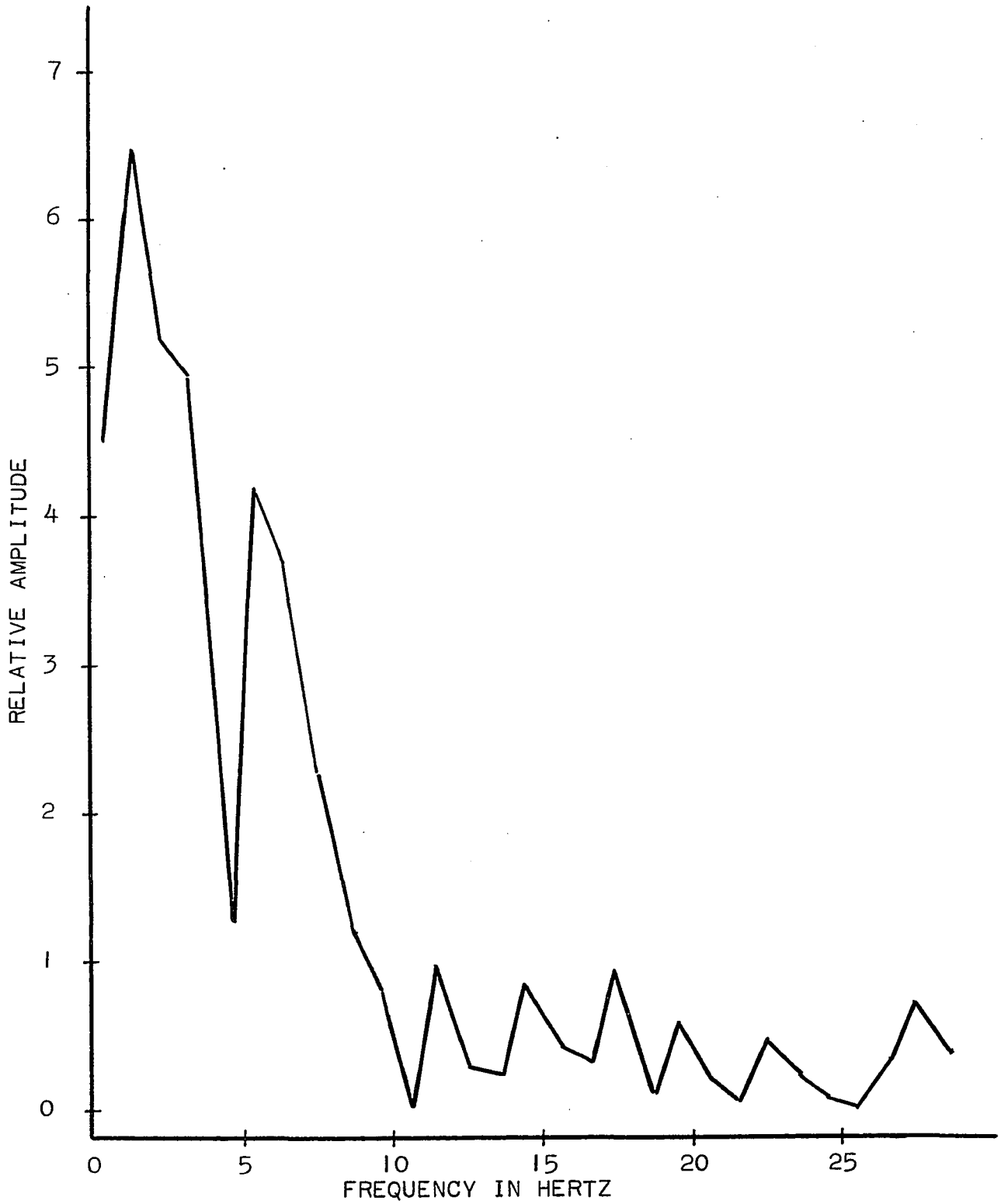

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 72. Animal 111. Fifth day of DDT exposure. Average power spectral density for both occipital and temporal electrodes. Stimulus was modulated sound at 2 Hz.

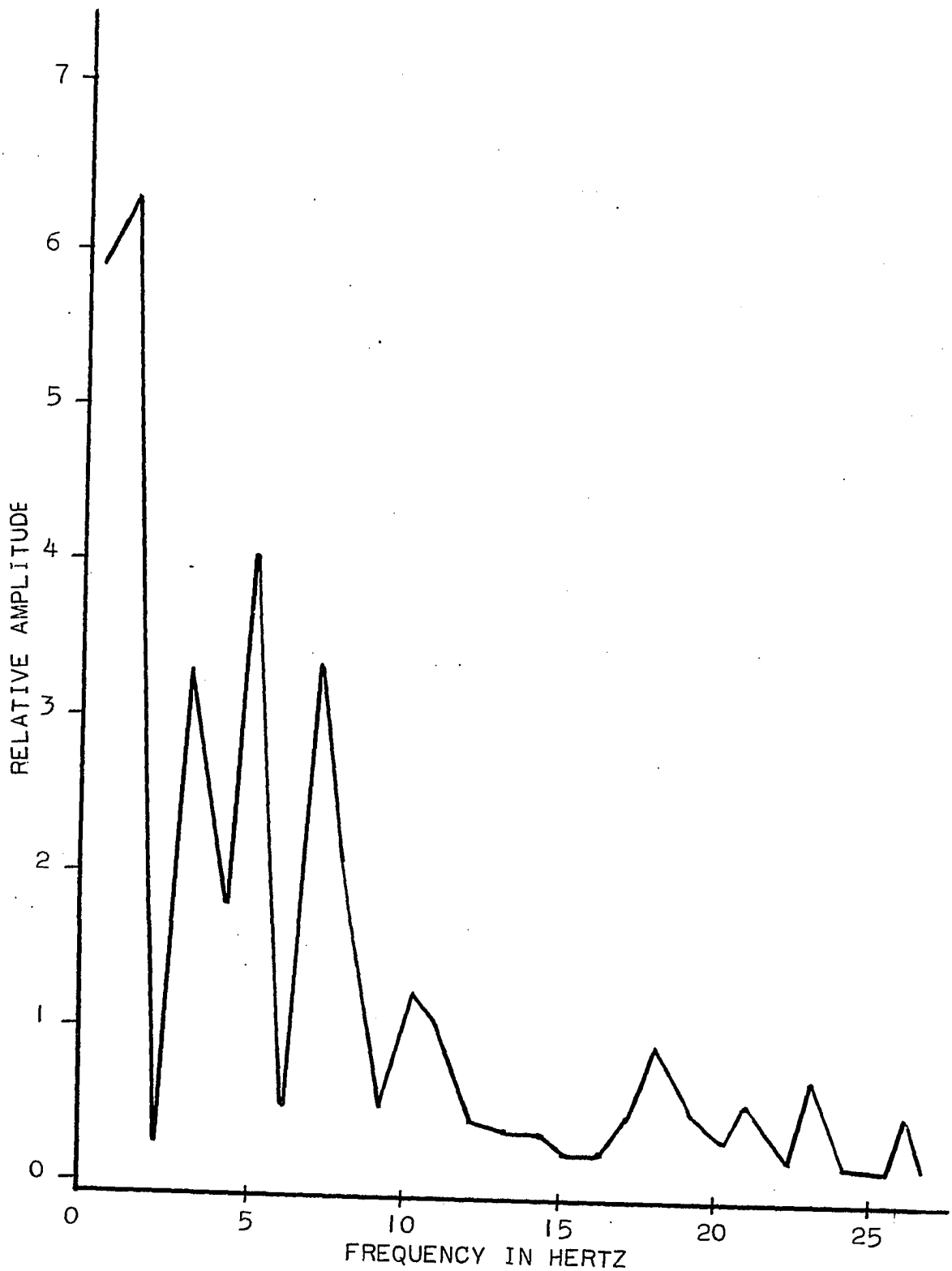
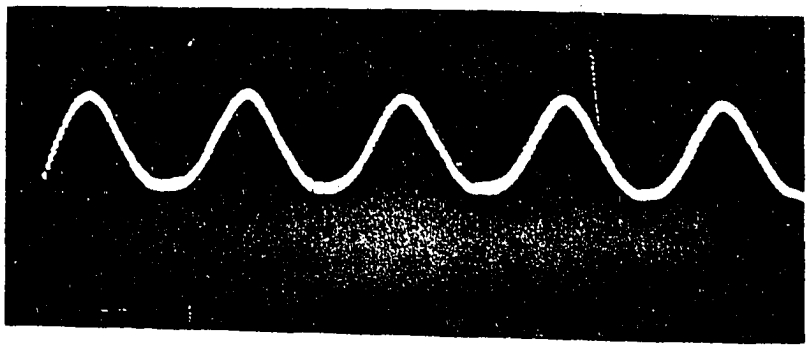

RELATIVE AMPLITUDE
0
1
2
3
4
5
6
7
0
5
10
15
20
25
FREQUENCY IN HERTZ

Figure 73. Animal 498. Summated evoked cortical responses.

(a) Trace of a 5 Hz. modulated light stimulus.

(b) Summated evoked cortical response recorded from an occipital electrode during the control period.

(c) Summated evoked cortical response recorded from an occipital electrode five days after exposure to dieldrin.



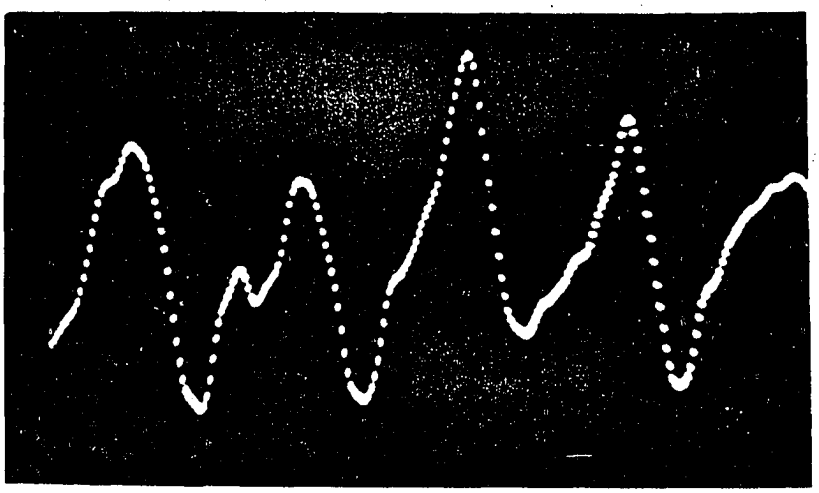
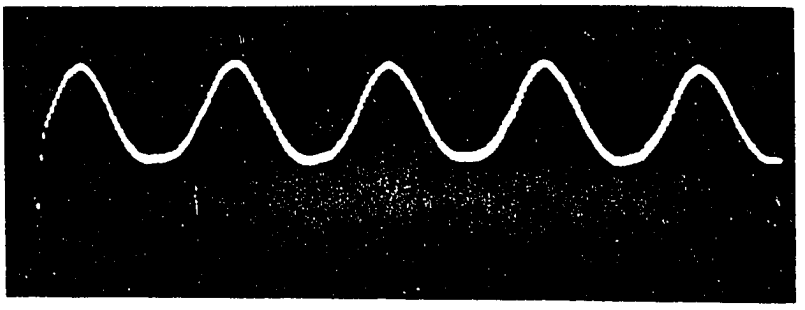


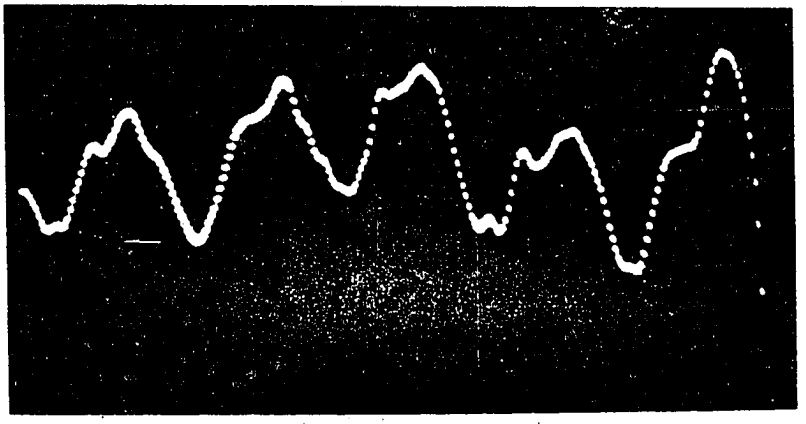
Figure 74. Animal 111. Summated evoked cortical responses.

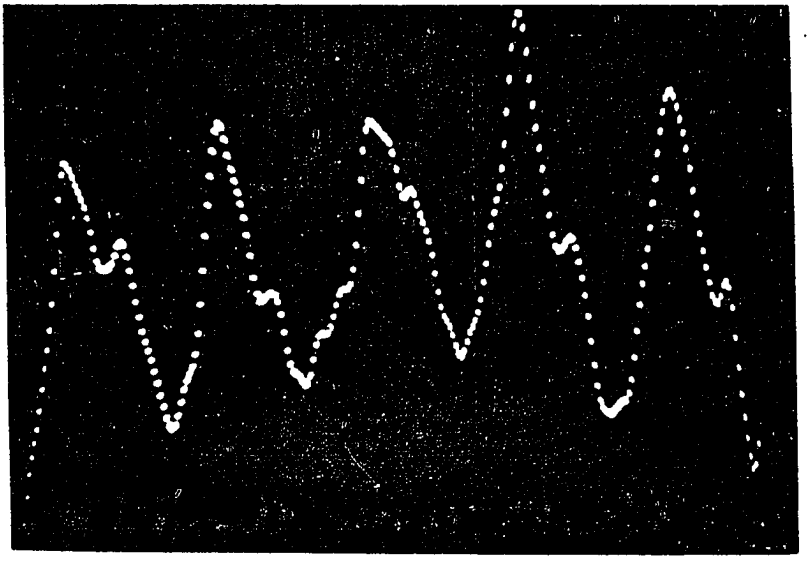
(a) Trace of a 5 Hz. modulated light stimulus.

(b) Summated evoked cortical response recorded from an occipital electrode during the control period.

(c) Summated evoked cortical response recorded from an occipital electrode four days after exposure to DDT.







SUMMARY AND CONSIDERATIONS FOR FURTHER INVESTIGATION

Correlation between clinical changes due to pesticide toxicity and changes in the evoked cortical potential due to pulsed light was not found. Little response to pulsed sound stimuli was recorded.

During exposure to the modulated light stimuli, changes were seen in plots of the total average power spectral density for all electrodes for the evoked cortical response. Dieldrin exposure was followed by higher frequency activity in the spectrum. An evoked response at the driving frequency was constant for the control period but variable following dieldrin exposure.

Loss of higher frequency activity was noted following exposure to Rulene® with some depression in amplitude of the spectrum. A recruiting response was also seen following Rulene® exposure as temporal activity became more evident. DDT administration was followed by a higher amplitude, predominately low frequency response to stimulation by modulated light.

Temporal recruitment was a feature following exposure to dieldrin, DDT and to some extent Rulene®. Variability in the evoked response at the fundamental driving frequency was seen following dieldrin exposure and in one animal exposed to DDT. Activity at the higher frequencies was also noted in animals

exposed to dieldrin and DDT.

Response from the temporal electrodes following stimulation by modulated sound was not pronounced. A greater temporal response occurred following exposure to DDT and dieldrin. Modulated sound as a stimulus produced no changes in the evoked cortical potentials which were related to pesticide exposure. Using the modulated light as a stimulus a frequency shift in activity toward the higher frequencies was noted.

Several considerations based on experience derived from this study perhaps would be of some assistance to any who choose to follow similar lines of investigation.

Initially the sensory projection areas should be verified for the experimental animal so that electrode placement will be on a known physiological basis.

Implanting depth electrodes would provide a breakdown of a particular sensory system so that the effects of pesticides might be more nearly isolated. Utilizing a group of animals as a long term control should be considered in conjunction with using an animal as its own control.

Cross correlation of the undriven EEG should be considered as a possible means of examining the pesticide effect on the EEG activity of an animal.

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APPENDIX A. SIGNAL AVERAGING

When an electrical signal of primary interest is carried along with other electrical signals of the same or greater "size" or amplitude, the problem arises as to how best to separate the signal of interest. These unwanted signals or interference are given the term "noise."

A classical problem is presented in the detection of an evoked response in the electroencephalogram. Because of the low voltage of the signal it is especially difficult to record in the conscious animal using conventional techniques.

A technique of signal averaging or signal summation may be used to recover a repetitive signal from a noisy background. This requires the use of electronic equipment designed for this purpose. For signal averaging to be effective it is necessary for the signal to be repetitive and to be uncorrelated with the noise. An evoked response is just a repetitive signal (Flynn, 1969).

Often the terms "signal averaging" and "signal summation" are used interchangeably. They are actually two techniques used to attempt to recover a signal buried in noise. In the work presented here the technique utilized was an electronic signal summation.

Sampling is done on the entire complex of signal and noise. The sampling must be begun at the beginning of the repetitive event. Information from the first sampling is

gathered and stored. In each successive sampling procedure a new sample is taken from the noise-signal complex and added to the sum of previous samples. Thus, the signal is the stored sum multiplied by the number of repetitions while the noise has not been time-locked to the signal and has made both positive and negative contributions at any one sample point (Trimble, 1968).

This may be expressed by representing the composite as a function of time, f(t), constructed of a noise portion, n(t), and a signal portion, s(t):

$$f(t) = n(t) + s(t).$$

Let the x^{th} repetition of s(t) start at time t_x where t_1 will be zero. The entire sampling will take place over a time span of T seconds.

For this signal the sample values will be:

$$f(t_x + iT) = s(t_x + iT) + n(t_x + iT)$$

$$f(t_x + iT) = s(iT) + n(t_x + iT).$$

At any given i and x the quantity $n(t_x + iT)$ will be a random variable and will be presumed to have a mean value of zero. The root mean square (rms) value for any i and x will be independent and can be expressed as some δ.

At any particular i^{th} sample the measure of the signal-to-noise ratio will be $S/N = s(iT)\delta$.

The sum after m repetitions stored in the i^{th} memory location will be

$$\sum_{k=1}^{m} f(t_x + iT) = \sum_{k=1}^{m} s(iT) + \sum_{k=1}^{m} n(t_x + iT) =$$

$$ms(iT) + \sum_{k=1}^{m} n(t_x + iT).$$

After m samples the mean square value of the noise samples will be $m\delta^2$, and the root mean square value will be $\sqrt{m}\delta$. Summation has the following effect on the signal-to-noise ratio:

$$(S/N)_m = ms(iT)/\sqrt{m}\delta = \sqrt{m}(S/N),$$

where $(S/N)_m$ is the signal-to-noise ratio of the m^{th} summation. Thus, the summation has improved the signal-to-noise ratio by a factor of $\sqrt{m}$.

APPENDIX B. COMPUTER PROGRAMS

Evoked Potentials

The programs to collect the summated cortical evoked responses are essentially the same. Subroutines to detect the synchronizing pulse vary.

Initially these programs establish a two channel display on the cathode ray tube of the computer. This display may be used to display analog channels 10 and 11 or 12 and 13 by the use of console sense switch one.

The collection routine is entered by activating sense switch 0. After twenty-five responses have been summed, the sampling stops. A 'save tape routine' allows the operator to place in the left switches the number of a block of tape. Beginning with this number, the routine accepts an index from the teletype and then stores the index and the data from analog channels 10, 11, 12, and 13 in consecutive blocks on the data storage tape.

Synchronization was obtained for the modulated sound by including a subroutine which examined the modulating wave for negative and positive values. When a change from negative to positive was detected, the program began to summate evoked responses. The modulated light program was begun by the closure of a microswitch. This switch was located so that an eccentric on the motor shaft activated the shaft with each revolution. The activation of the strobe light provided the

synchronizing pulse for the pulsed light program. A relay closure was the source of the synchronizing pulse for the pulsed sound program.

Console operation

1. Place program tape on tape drive 0.
2. Place data storage tape on tape drive 1.
3. Set switches for LAP-6 mode.
4. Call in the appropriate program by using a meta command and the LO instruction:

   →LO XX

   where XX may be

   PL- pulsed light

   PS- pulsed sound

   ML- modulated light

   MS- modulated sound
5. Activate the 'start 20' switch. This will enter the two channel display portion of the program.
6. Data collection is begun by raising 0.
7. Following the data collection an index may be typed from the teletype keyboard to provide animal identification, date, and stimulus type.
8. Raise sense switch 2.
9. Place in the left switches the block number for the first block of data to be stored. The first block will be the storage location on tape of the index. The next five

blocks will be used to store data from analog channels 9, 10, 11, 12, and 13.

10. Activate the 'save tape routine' by striking the '#' sign on the teletype keyboard.

Pulsed light

```
      LDA &
      2\4
      STC 5E
      LDA&
      3\1
      STC 5F
      LDA&
      4\2
      STC 5G
      LDA&
      5\3
      STC 5H
      LDA&
      6\4
      STC 5I
      LDA&
      7\5
      STC 5J
      LDA&
      4
      STC 5D
      STC 5K
#7A   SET&7
      3377
      SET&3
      1377
      SET&5
      2377
      SET&6
      2777
      SET&4
      3777
      CLR
      ATR
#7CSTA&3
      STA&4
      STA&5
      STA&6
      STA&7
      XSK 3
      JMP 7C
      JMP 1F
[2 CH DISPAY
#1F   SET&2
      4
      CLR
      STC 2A
#1HSNS&4
      JMP 4M
      JMP 4B
#4B   XSK &2
      JMP 1T
      JMP 1F
[CH 10,11
[EVR COLLECT
[OR EEG DISPLAY
#1TSNS& 1
      JMP 4A
      JMP 2T
#2T   SAM 10
      SCR 1R
      ADD 2M
      DIS 2
      SAM 11
      SCR 1R
      ADD 3M
      DIS 2
#7G   SAM 0
      APO&
      JMP 7G
      STC 2C
#7H   LDA&
      1
      ADM
      2C
      LDA
      2C
      AZE
      JMP 7H
      JMP 1H
#2M   175
#3M   -175
#2C   NOP
[CH 12,13
#4A   SAM 12
      SCR 1R
      ADD 2M
      DIS 2
      SAM 13
      SCR 1R
      ADD 3M
      DIS 2
#1G   SAM 0
      APO&
      JMP 1G
      STC 2C
#2G   LDA&
      1
      ADM
      2C
      LDA
      2C
```

```
     AZE
     JMP 2G
     JMP 1H
[START EVR,DISPLAY
#4D JMP 4M
[INPUT PULSE
#4N SAM 17
     SCR 1M
     AZE
     JMP 4E
     JMP 4N
#7DNOP
     CLR
     LDA
     2A
     ATR
     KST
     JMP 4D
     JMP 1N
#4D SNS & 1
     JMP 4S
     SNS&2
     JMP 4U
     SNS & 3
     JMP 4W
     SNS & 4
     JMP 4Y
#4X LDA & 7
     SCR 3
     DIS&2
     DIS &2
     XSK2
     JMP 4X
     JMP 4D
#4S LDA&3
     DIS&2
     DIS&2
     XSK 2
     JMP 4S
     JMP 4D
#4U LDA&4
     SCR 3
     DIS&2
     DIS&2
     XSK 2
     JMP 4U
     JMP 4D
#4W LDA&5
     SCR 3
     DIS&2
     DIS&2
     XSK 2
     JMP 4W
     JMP 4D
#4Y LDA & 6
     SCR 3
     DIS & 2
     DIS & 2
     XSK 2
     JMP 4Y
     JMP 4D
#4C SAM14
     APO&
     JMP 4E
     JMP 4C
#2D SAM 14
     APO&
     JMP 2D
     JMP 4C
[SET INITIAL ADDRESS
#4M NOP
     SET &2
     777
     SET&3
     1377
     SET&4
     3777
     SET&5
     2377
     SET&6
     2777
     SET&7
     3377
     LDA
     2A
     ADD 3A
     AZE
     JMP 3H
     JMP 7D
#3H SNS &5
     JMP 7D
     JMP 4N
#4R JMP 4D
#4E SAM 14
     SCR 1N
     ADM&4
     SAM 11
     SCR 1N
     ADM&5
     SAM 12
     SCR 1N
     ADM &6
```

```
        SAM 13
        SCR 1N
        ADM &7
        SAM 15
        SCR 2N
        ADM &3
        XSK 3
        JMP 7B
        CLR
        LDA&
        1
        ADM
        2A
        LDA
        2A
        ADD 3A
        AZE
        JMP 4M
        JMP 7D
        JMP 4M
#7B     SNS & 1
        JMP 4F
        SNS & 2
        JMP 4H
        SNS & 3
        JMP 4J
        SNS & 4
        JMP 4G
        LDA 7
        SCR 3
        DIS&2
        DIS&2
        JMP 2D
#4F     LDA3
        DIS&2
        DIS&2
        JMP 2D
#4H     LDA4
        SCR 3
        DIS&2
        DIS&2
        JMP2D
#4J     LDA 5
        SCR 3
        DIS&2
        DIS & 2
        JMP 2D
#4G     LDA 6
        SCR 3
        DIS & 2
        DIS & 2
        JMP 2D
[SAVE TAPE ROUTINE
#1W     LDA
        0
        STC 5D
        SET & 16
        -12
        SET& 15
        2L-1
#5M     LDA & 15
        OPR 14
        XSK & 16
        JMP 5M
        HLT
        LSW
        STA
        5K
        ADM
        5E
        LDA
        5K
        ADM
        5F
        LDA
        5K
        ADM
        5G
        LDA
        5K
        ADM
        5H
        LDA
        5K
        ADM
        5I
        LDA
        5K
        ADM
        5J
        SET & 7
        -376
        SET & 5
        777
        SET & 16
        -12
        SET & 15
        5N-1
#2D     LDA & 15
        OPR 14
        XSK & 16
```

```
      JMP  20
#5A   KBD  &
      SHD  &
      2244
      JMP  5B
      STA  & 5
      XSK  & 7
      JMP  5A
#5B   STA  & 5
      WRC  %
#5E   2\0
      WRC  %
#5F   3\1
      WRC  %
#5G   4\2
      WRC  %
#5H   5\3
      WRC  %
#5I   6\4
      WRC  %
#5J   7\5
#5D   0
#5K   0
#2L   212
      215
      315
      323
      307
      240
      260
      263
      212
      215
#5N   212
      215
      315
      323
      307
      240
      260
      264
      212
      215
 #2A  0001
 #3A  -31
      1R=1
      1N=1
      1M=6
      2N=6
```

Pulsed sound

```
PS,1  LN=1


     $20
     LDA &
     2\0
     STC 5E
     LDA&
     3\1
     STC 5F
     LDA&
     4\2
     STC 5G
     LDA&
     5\3
     STC 5H
     LDA&
     6\4
     STC 5I
     LDA&
     7\5
     STC 5J
     LDA&
     0
     STC 5D
     STC 5K
#7A  SET&7
     3377
     SET&3
     1377
     SET&5
     2377
     SET&6
     2777
     SET&4
     3777
     CLR
     ATR
#7CSTA&3
     STA&4
     STA&5
     STA&6
     STA&7
     XSK 3
     JMP 7C
     JMP 1F
[2 CH DISPAY
#1F  SET&2
     0
     CLR
     STC 2A
#1HSNS&0
     JMP 4M
     JMP 4B
#4B  XSK &2
     JMP 1T
     JMP 1F
[CH 10,11
[EVR COLLECT



[OR EEG DISPLAY
#1TSNS& 1
     JMP 4A
     JMP 2T
#2T  SAM 10
     SCR 1R
     ADD 2M
     DIS 2
     SAM 11
     SCR 1R
     ADD 3M
     DIS 2
#7G  SAM 0
     APD&
     JMP 7G
     STC 2C
#7H  LDA&
     1
     ADM
     2C
     LDA
     2C
     AZE
     JMP 7H
     JMP 1H
#2M  175
#3M  -175
#2C  NOP
[CH 12,13
#4A  SAM 12
     SCR 1R
     ADD 2M
     DIS 2
     SAM 13
     SCR 1R
     ADD 3M
     DIS 2
```

```
#1G SAM 4
    APO&
    JMP 1G
    STC 2C
#2G LDA&
    1
    ADM
    2C
    LDA
    2C
    AZE
    JMP 2G
    JMP 1H
[START EVR,DISPLAY
#4D JMP 4M
[INPUT PULSE
#4N NOP
    NOP
    SXL & 1

    JMP 4N
    JMP 4E
#7DNOP
    CLR
    LDA
    2A
    ATR
    KST
    JMP 4Q
    JMP 1W
#4Q SNS & 1
    JMP 4S
    SNS&2
    JMP 4U
    SNS & 3
    JMP 4W
    SNS & 4
    JMP 4Y
#4X LDA & 7
    SCR 3
    DIS&2
    DIS &2
    XSK2
    JMP 4X
    JMP 4D
#4S LDA&3
    SCR 3
    DIS&2
    DIS&2
    XSK 2
    JMP 4S
    JMP 4D
#4U LDA&4
    SCR 3
    DIS&2
    DIS&2
    XSK 2
    JMP 4U
    JMP 4D
#4W LDA&5
    SCR 3
    DIS&2
    DIS&2
    XSK 2
    JMP 4W
    JMP 4D
#4Y LDA & 6
    SCR 3
    DIS & 2
    DIS & 2
    XSK 2
    JMP 4Y
    JMP 4D
#4C SAM14
    APO&
    JMP 4E

    JMP 4C
#2D SAM 14
    APO&
    JMP 2D
    JMP 4C
[SET INITIAL ADDRESS
#4M NOP
    SET &2
    777
    SET&3
    1377
    SET&4
    3777
    SET&5
    2377
    SET&6
    2777
    SET&7
    3377
    LDA
    2A
    ADD 3A
    AZE
    JMP 3B
    JMP 7D
```

```
#3B SNS &5
    JMP 7D
    JMP 4N
#4R JMP 4D
#4E SAM 14
    SCR 1N
    ADM&4
    SAM 11
    SCR 1N
    ADM&5
    SAM 12
    SCR 1N
    ADM &6
    SAM 13
    SCR 1N
    ADM &7
    SAM 15
    SCR 2N
    ADM &3
    XSK 3
    JMP 7B
    CLR
    LDA&
    1
    ADM
    2A
    LDA
    2A
    ADD 3A
    AZE
    JMP 4M

      JMP 7D
      JMP 4M
  #7B SNS & 1
      JMP 4F
      SNS & 2
      JMP 4H
      SNS & 3
      JMP 4J
      SNS & 4
      JMP 4G
      LDA 7
      SCR 3
      DIS&2
      DIS&2
      JMP 2D
  #4F LDA3
      DIS&2
      DIS&2
      JMP 2D

#4H LDA4
    SCR 3
    DIS&2
    DIS&2
    JMP2D
#4J LDA 5
    SCR 3
    DIS&2
    DIS & 2
    JMP 2D
#4G LDA 6
    SCR 3
    DIS & 2
    DIS & 2
    JMP 2D
#2A 4401
#3A -31
[SAVE TAPE ROUTINE
#1W LDA
    0
    STC 5D
    SET & 16
    -12
    SET& 15
    2L-1
#5M LDA & 15
    OPR 14
    XSK & 16
    JMP 5M
    HLT
    LSW
    STA
    5K
    ADM
    5E
    LDA
    5K

    ADM
    5F
    LDA
    5K
    ADM
    5G
    LDA
    5K
    ADM
    5H
    LDA
    5K
    ADM
```

```
      ST                                215
      LDA                               315
      SK                                323
      ADM                               347
      SJ                                240
      SET & 7                           260
      -376                              264
      SET & 5                           212
      777                               215
      SET & 16                          1R=1
      -12                               1N=4
      SET & 15                          1M=6
      5N-1                              2N=6
#20   LDA & 15
      OPR 14
      XSK & 16
      JMP 20
#5A   KBD &
      SHD &
      2244
      JMP 5B
      STA & 5
      XSK & 7
      JMP 5A
#5B   STA & 5
      %RC %
#5E   2\0
      %RC %
#5F   3\1
      %RC %
#5G   4\2
      %RC %
#5H   5\3
      %RC %
#5I   6\4
      %RC %
#5J   7\5
#5D   0
#5K   0
#2L   212
      215
      315
      323
      347
      244
      264
      263
      212
      215
#5N   212
```

Modulated sound

```
      $24
      LDA &
      2\0
      STC 5E
      LDA &
      3\1
      STC 5F
      LDA &
      4\2
      STC 5G
      LDA&
      6\4
      STC 5I
      LDA &
      5\3
      STC 5H
      LDA &
      7\5
      STC 5J
      LDA &
      0
      STC 5D
      STC 5K
#7A SET&7
      3377
      SET&3
      1377
      SET&5
      2377
      SET&6
      2777
      SET&4
      3777
      CLR
      ATR
#7CSTA&3
      STA&4
      STA&5
      STA&6
      STA&7
      XSK 3
      JMP 7C
      JMP 1F
[2 CH DISLPAY
#1F SET&2
      0
      CLR
      STC 2A
#1HSNS&0
      JMP 4M
      JMP 4B
 #4B XSK &2
      JMP 1T
      JMP 1F
 [CH 10,11
 [EVR COLLECT

[OR EEG DISPLAY
#1TSNS& 1
      JMP 4A
      JMP 2T
#2T SAM 10
      SCR 1R
      ADD 2M
      DIS 2
      SAM 11
      SCR 1R
      ADD 3M
      DIS 2
#7G SAM 0
      APO&
      JMP 7G
      STC 2C
#7H LDA&
      1
      ADM
      2C
      LDA
      2C
      AZE
      JMP 7H
      JMP 1H
#2M 175
#3M -175
#2C NOP
[CH 12,13
#4A SAM 12
      SCR 1R
      ADD 2M
      DIS 2
      SAM 13
      SCR 1R
      ADD 3M
      DIS 2
#1G SAM 0
      APO&
      JMP 1G
      STC 2C
#2G LDA&
      1
      ADM
```

```
      2C
      LDA
      2C
      AZE
      JMP 2G
      JMP 1H
[START EVR,DISPLAY
#4D JMP 4M
[INPUT PULSE
#4N NOP
      SAM 16
      ADA&

      5A
      APO
      JMP 1K
      JMP 4N
#1K SAM 16
      APO&
      JMP 4E
      JMP 1K
#7DNOP
      CLR
      LDA
      2A
      ATR
      KST
      JMP 4Q
      JMP 1W
#4Q SNS & 1
      JMP 4S
      SNS&2
      JMP 4U
      SNS & 3
      JMP 4W
      SNS & 4
      JMP 4Y
#4X LDA & 7
      SCR 3
      DIS&2
      DIS &2
      XSK2
      JMP 4X
      JMP 4D
#4S LDA&3
      DIS&2
      DIS&2
      XSK 2
      JMP 4S
      JMP 4D
#4U LDA&4
      SCR 3
      DIS&2
      DIS&2
      XSK 2
      JMP 4U
      JMP 4D
#4W LDA&5
      SCR 3
      DIS&2
      DIS&2
      XSK 2
      JMP 4W
      JMP 4D
#4Y LDA & 6
      SCR 3
      DIS & 2
      DIS & 2
      XSK 2
      JMP 4Y
      JMP 4D
#4C SAM14
      APO&
      JMP 4E
      JMP 4C
#2D SAM 14
      APO&
      JMP 2D
      JMP 4C
[SET INITIAL ADDRESS
#4M NOP
      SET &2
      777
      SET&3
      1377
      SET&4
      3777
      SET&5
      2377
      SET&6
      2777
      SET&7
      3377
      LDA
      2A
      ADD 3A
      AZE
      JMP 3B
      JMP 7D
#3B SNS &5
      JMP 7D
      JMP 4N
```

```
#4R JMP 4D
#4E SAM 10
    SCR 1N
    ADM&4
    SAM 11
    SCR 1N
    ADM&5
    SAM 12
    SCR 1N
    ADM &6
    SAM 13
    SCR 1N
    ADM &7
    LDA
    2A
    ADA&
    -1
    APO
    JMP 6C
    JMP 6D
#6C SAM 16
    SCR 2N
    ADM&3

#6D XSK 7
    JMP 7B
    CLR
    LDA&
    1
    ADM
    2A
    LDA
    2A
    ADD 3A
    AZE
    JMP 4M
    JMP 7D
    JMP 4M
#7B SNS & 1
    JMP 4F
    SNS & 2
    JMP 4H
    SNS & 3
    JMP 4J
    SNS & 4
    JMP 4G
    LDA /
    SCR 3
    DIS&2
    DIS&2
    JMP 2D
```

```
#4F LDA3
    DIS&2
    DIS&2
    JMP 2D
#4H LDA4
    SCR 3
    DIS&2
    DIS&2
    JMP2D
#4J LDA 5
    DIS&2
    DIS & 2
    JMP 2D
#4G LDA 6
    SCR 3
    DIS & 2
    DIS & 2
    JMP 2D
#2A 4001
#3A -31
[SAVE TAPE ROUTINE
#1# LDA
    0
    STC 5D
    SET & 16
    -12
    SET& 15
    2L-1
#5M LDA & 15

    OPR 14
    XSK & 16
    JMP 5M
    HLT
    LSW
    STA
    5K
    ADM
    5E
    LDA
    5K
    ADM
    5F
    LDA
    5K
    ADM
    5G
    LDA
    5K
    ADM
    5H
```

```
      LDA
      5K
      ADM
      5I
      LDA
      5K
      ADM
      5J
      SET & 7
      -376
      SET & 5
      777
      SET & 16
      -12
      SET & 15
      5N-1
#20   LDA & 15
      OPR 14
      XSK & 16
      JMP 20
#5A   KBD &
      SHD &
      2240
      JMP 5B
      STA & 5
      XSK & 7
      JMP 5A
#5B   STA & 5
      WRC %
#5E   2\0
      WRC %
#5F   3\1
      WRC %
#5G   4\2
      WRC %
#5H   5\3
      WRC %
#5I   6\4
      WRC %
#5J   7\5
#5D   0
#5K   0
#2L   212
      215
      315
      323
      347
      244
      264
      263
      212
      215
#5N   212
      215
      315
      323
      347
      240
      260
      264
      212
      215
      1R=1
      1N=0
      1M=6
      2N=1
      3N=5
      6A=100
```

Modulated light

```
      $29
      LDA &
      2\0
      STC 5E
      LDA&
      3\1
      STC 5F
      LDA&
      4\2
      STC 5G
      LDA&
      5\3
      STC 5H
      LDA&
      6\4
      STC 5I
      LDA&
      7\5
      STC 5J
      LDA&
      0
      STC 5D
      STC 5K
#7A   SET&7
      3377
      SET&3
      1377
      SET&5
      2377
      SET&6
      2777
      SET&4
      3777
      CLR
      ATR
#7CSTA&3
      STA&4
      STA&5
      STA&6
      STA&7
      XSK 3
      JMP 7C
      JMP 1F
[2 CH DISLPAY
#1F   SET&2
      0
      CLR
      STC 2A
#1HSNS&0
      JMP 4M
      JMP 4B
#4B   XSK &2
      JMP 1T
      JMP 1F
[CH 10,11
[EVR COLLECT

[OR EEG DISPLAY
#1TSNS& 1
      JMP 4A
      JMP 2T
#2T   SAM 10
      SCR 1R
      ADD 2M
      DIS 2
      SAM 11
      SCR 1R
      ADD 3M
      DIS 2
#7G   SAM 0
      APO&
      JMP 7G
      STC 2C
#7H   LDA&
      1
      ADM
      2C
      LDA
      2C
      AZE
      JMP 7H
      JMP 1H
#2M   175
#3M   -175
#2C   NOP
[CH 12,13
#4A   SAM 12
      SCR 1R
      ADD 2M
      DIS 2
      SAM 13
      SCR 1R
      ADD 3M
      DIS 2
#1G   SAM 0
      APO&
      JMP 1G
      STC 2C
#2G   LDA&
      1
      ADM
```

```
     2C
     LDA
     2C
     AZE
     JMP 2G
     JMP 1H
[START EVR,DISPLAY
#4D JMP 4M
[INPUT PULSE
#4N NOP
     NOP
     SXL & 5

     JMP 4N
     JMP 4E
#7DNOP
     CLR
     LDA
     2A
     ATR
     KST
     JMP 4Q
     JMP 1W
#4Q SNS & 1
     JMP 4S
     SNS&2
     JMP 4U
     SNS & 3
     JMP 4W
     SNS & 4
     JMP 4Y
#4X LDA & 7
     SCR 3
     DIS&2
     DIS &2
     XSK2
     JMP 4X
     JMP 4D
#4S LDA&3
     DIS&2
     DIS&2
     XSK 2
     JMP 4S
     JMP 4D
#4U LDA&4
     SCR 3
     DIS&2
     DIS&2
     XSK 2
     JMP 4U
     JMP 4D
#4W LDA&5
     SCR 3
     DIS&2
     DIS&2
     XSK 2
     JMP 4W
     JMP 4D
#4Y LDA & 6
     SCR 3
     DIS & 2
     DIS & 2
     XSK 2
     JMP 4Y
     JMP 4D
#4C SAM14
     APO&
     JMP 4E
     JMP 4C

#2D SAM 14
     APO&
     JMP 2D
     JMP 4C
[SET INITIAL ADDRESS
#4M NOP
     SET &2
     777
     SET&3
     1377
     SET&4
     3777
     SET&5
     2377
     SET&6
     2777
     SET&7
     3377
     LDA
     2A
     ADD 3A
     AZE
     JMP 3B
     JMP 7D
#3B SNS &5
     JMP 7D
     JMP 4N
#4R JMP 4D
#4E SAM 10
     SCR 1N
     ADM&4
     SAM 11
```

```
      SCR 1N
      ADM&5
      SAM 12
      SCR 1N
      ADM &6
      SAM 13
      SCR 1N
      ADM &7
      SAM 15
      SCR 2N
      ADM &3
      XSK 3
      JMP 7B
      CLR
      LDA&
      1
      ADM
      2A
      LDA
      2A
      ADD 3A
      AZE
      JMP 4M
      JMP 7D

      JMP 4M
#7B   SNS & 1
      JMP 4F
      SNS & 2
      JMP 4H
      SNS & 3
      JMP 4J
      SNS & 4
      JMP 4G
      LDA 7
      SCR 3
      DIS&2
      DIS&2
      JMP 2D
#4F   LDA3
      DIS&2
      DIS&2
      JMP 2D
#4H   LDA4
      SCR 3
      DIS&2
      DIS&2
      JMP2D
#4J   LDA 5
      SCR 3
      DIS&2
      DIS & 2
      JMP 2D
#4G   LDA 6
      SCR 3
      DIS & 2
      DIS & 2
      JMP 2D
#2A   0001
#3A   -31
[SAVE TAPE ROUTINE
#1W   LDA
      0
      STC 5D
      SET & 16
      -12
      SET& 15
      2L-1
#5M   LDA & 15
      OPR 14
      XSK & 16
      JMP 5M
      HLT
      LSW
      STA
      5K
      ADM
      5E
      LDA
      5K
      ADM

      5F
      LDA
      5K
      ADM
      5G
      LDA
      5K
      ADM
      5H
      LDA
      5K
      ADM
      5I
      LDA
      5K
      ADM
      5J
      SET & 7
      -376
      SET & 5
```

```
     777
     SET & 16
     -12
     SET & 15
     5N-1
#20  LDA & 15
     OPR 14
     XSK & 16
     JMP 20
#5A  KBD &
     SHD &
     2200
     JMP 5B
     STA & 5
     XSK & 7
     JMP 5A
#5B  STA & 5
     WRC %
#5E  2\0
     WRC %
#5F  3\1
     WRC %
#5G  4\2
     WRC %
#5H  5\3
     WRC %
#5I  6\4
     WRC %
#5J  7\5
#5D  0
#5K  0
#2L  212
     215
     315
     323
     307

     240
     260
     263
     212
     215
 #5N 212
     215
     315
     323
     307
     240
     260
     264
     212
```

```
215
1R=1
1N=0
1M=6
2N=0
```

Evoked Response Analysis Program

This is a series of three programs[1] which will analyze pulse type waveforms stored on specified blocks of tape. The analysis gives the peak values, peak latencies and zero latencies of the waveform. See Figure 75.

Wave criteria is based on a difference of $\pm 30_8$ between the zero or average and peak values. This criteria may be altered by changing statements at the end of the RUN program where 7B = -30, #7C 30, and #7G -30. The beginning of the analysis is controlled by the 7A = 1407 statement. Quarter 3 (1400-1777) is the data location for the analysis.

The RUN program is the analysis routine. INPUT and OUTPUT are the input and output routines respectively.

Console operation

1. Place the data tape on Unit 1 of the tape drives.
2. Place the program tape on Unit 0 of the tape drives.
3. Use the LAP-6 mode of operation.
4. Load the program by using the meta command (→) and the following symbols, →LO EVRANA, O.
5. All sense switches must be in the down position.
6. Raise the console toggle switch toward the instructions

---

[1]This program was specifically written for this study by Dr. Norman Hutton and Dr. Gary Van Gelder. A wave analysis program of this nature is not at this time available in the Digitial Equipment Corporation Library. It is the intention of the authors to submit this program as an addition to the available programs.

"Start 400."

7. Wait for "TAPE" to be displayed on the oscilloscope.
8. Momentarily raise SNS-0 then return to the down position.
9. Type in 2 numbers (0-9); use a leading zero if only 1 digit I.D. If the number is correct (the I.D. you want) hit EOL (return) on the teletype keyboard, if the incorrect key is struck strike the "rubout" key and "Tape" will be displayed and you may begin again at step 7.
10. The word "BLOCK" should be displayed.
11. Lift SNS-1
12. Enter block numbers; leading zeros are not necessary but can be used. Terminate each block number by striking the EOL (return) key. The block number 000 cannot be used. Requesting this block will cause the program to halt. All other BLKS (1-777) are acceptable. A maximum of 251 BLKS can be requested at one time. Block input is terminated by striking the letter "D," (i.e. for done). The program begins at this point.
13. The program will HALT when the last block has been analyzed.
14. To analyze more data it is necessary to go back to step 3.

Figure 75. Definition of terms used with the evoked response analysis program.

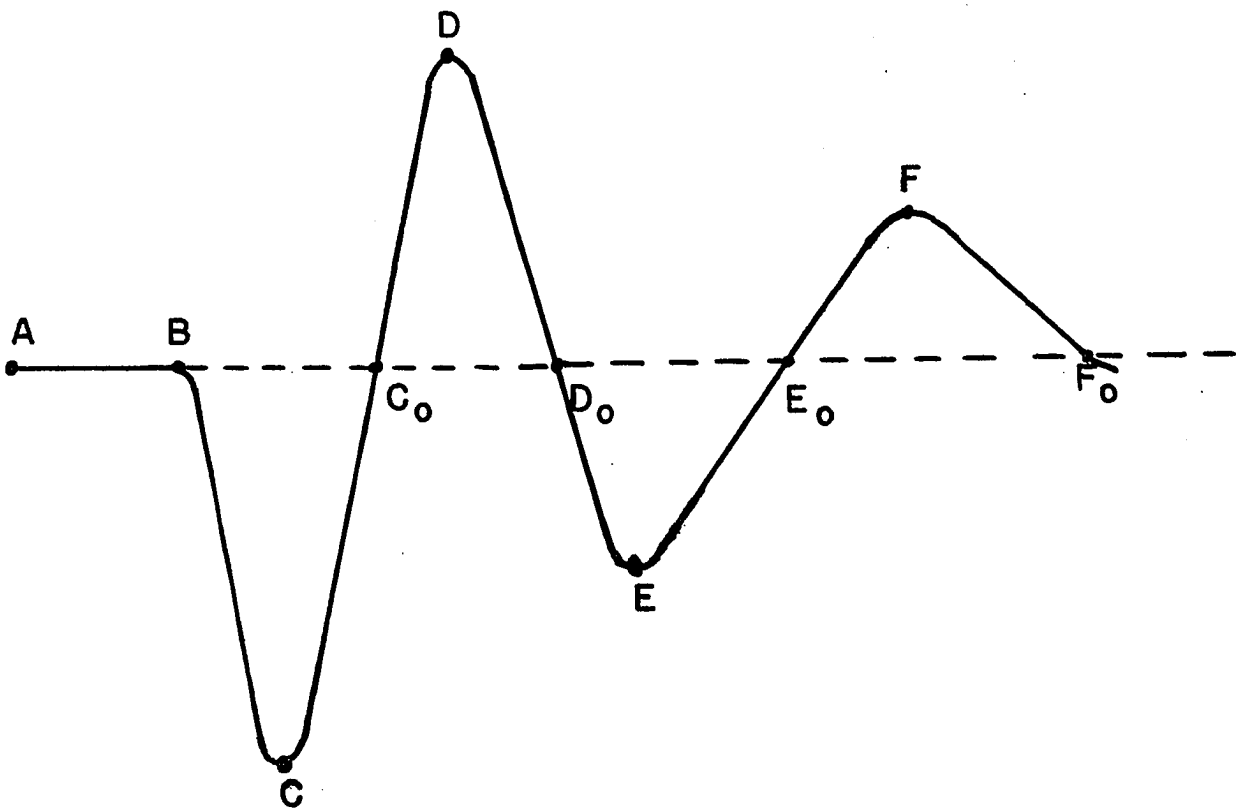
Latency: time from A-B.

Zero: relative position of A-B.

Peak Value: relative amplitude from A-B to C, D, E, F.

Peak Latency: time from A to peak.
Ex: A-C, A-D, A-E, A-F.

Zero Latency: time from A to 'zero' crossing. Ex: A to C_0, A to D_0, A to E_0, A to F_0.


D
F
A
B
C_o
D_o
E_o
F_o
E
C

```
     S20
     NOP
     NOP
     NOP
     NOP
     SET & 5
     1450
     SET & 2
     3777
     SET & 3
     1377
#1B  CLR
     SET & 4
     1773
     SET & 1
     0300
     SET & 7
     1377
#1A  CLR
     DSC&7
     DSC&7
     LDA &
     4
     ADM
     1
     SNS&0
     JMP 1C
     XSK & 4
     JMP 1A
     JMP 1B
#1C  CLR
     STA& 2
     XSK & 3
     JMP 1C
     SET & 2
     2000
#1D  KBD&
     OPR 14
     ADA&
     260
     STC 1E
     CLR
     ADD 1E
     STA& 2
     KBD&
     OPR 14
     ADA&
     260
     STC 1E
     CLR
     ADD 1E
     STA&2
     KBD&
     OPR 14
     STC 1E
     ADD 1E

     ADA&
     -13
     AZE
     JMP 1F
     JMP 20
#1I  NOP
#1E  NOP
#1F  CLR
     SET & 4
     1772
     SET & 1
     0300
     SET & 7
     1407
#1G  CLR
     DSC&7
     DSC & 7
     LDA &
     4
     ADM 1
     SNS& 1
     JMP 1H
     XSK & 4
     JMP 1G
     JMP 1F
#1H  CLR
     STC 1I
     STC 1E
#1M  KBD&
     OPR 14
     STC1I
     CLR
     ADD 1I
     ADA&
     -13
     AZE
     JMP 1J
     JMP 1H
#1J  CLR
     ADD 1I
     ADA&
     -27
     AZE
     JMP 1N
```

```
     JMP 1P          2651
#1N  CLR             0177
     ADD 1I          0301
     ADA&            4177
     -12             7741
     AZE             4136
     JMP 1K          2241
     JMP 1L          1077
#1L  CLR             4324
     ADD 1E
     STA& 2
     LDA&
     215
     OPR 14
     CLR
     CLR
     LDA&
     212
     OPR 14
     XSK & 5
     JMP 1H
     JMP 1P
#1K  CLR
     ADD 1E
     ROL 3
     ADD 1I
     STC 1E
     JMP 1M
#1P  OPR 14
     WRC
     4\151
     JMP 1001
     $1000
     NOP
     NOP
     NOP
     RDC
     0\144
     JMP 22
     HLT
     $1400
     4040
     4077
     4477
     7744
     4477
     3044
     4577
     4145
     5177
```

```
[EVOKED RESPONSE ANALYSIS
     $20
     NOP
     NOP
     NOP
     RDC
     1\145
     RDC
     2\146
     RDC
     4\151
     SET &2
     3777
     LDA&2
     ADA&
     2003
     STC 2R
     LDA&
     1
     ADM 2
     WRC
     4\151
     SET 2
     2R
     LDA2
     AZE
     JMP *+2
     HLT
     STC 2R
     ADD 2R
     ADA&
     3400
     STC *+2
     RDC&
     3400
     SET & 2
     2000
     LDA&2
     STC 2S
     LDA&2
     STC 2T
#1B  SET&2
     777
     SET&3
     1377
#1A  LDA&3
     DIS2
     DIS&2
[ LIFT SNS 0 TO GO TO ANALYSIS
     SNS& 0
     JMP1C
     XSK3
     JMP1A
     JMP1B
#1C  NOP
[BEGIN ANALYSIS

     SET & 14
     2777
     SET & 5
     1377
     CLR
     STC 5T
     STC 2K
#2Z  STA & 14
     XSK & 5
     JMP 2Z
     SET&5
     777
     SET&6
     3377
     SET&4
     7A
     CLR
     SET & 14
     2777
     SET & 15
     3077
     SET & 16
     3177
     SET & 17
     1770
     CLR
     STC 1400
#2A  LDA& 4
     ADD 1400
     STC 1400
     XSK & 17
     JMP 2A
     ADD 1400
     STC 20
     STC 10
     ADD 20
     APO&
     JMP *+4
     LDA&
     7777
     STC 10
     LDA&
     7
     STC 40
```

```
      JMP 3Q
      JMP 2B
#2B LDA
      2Q
      APO
      COM
      STC 2Q
      SET & 4
      7A
#2HLDA& 4
      XSK 4
      JMP '+2

      JMP 7Z
      APO&
      COM
      ADD 2Q
      APO&
      COM
      ADD 7C
      APO&
      JMP 2H
      NOP
      LDA&
      -1
      ADD4
      STC 7D
      SET&4
      7A
      CLR
      STC 2Q
      STC 1Q
#2G LDA&4
      ADD 2Q
      STC 2Q
      ADD 7D
      COM
      ADD4
      AZE
      JMP 2G
      NOP
      LDA&
      7A
      COM
      ADA
      4
      STC 4Q
      ADD 2Q
      APO&
      JMP'+4
      LDA&
      7777
      STC 1Q
      CLR
      ADD 4Q
      AZE
      JMP '+4
      LDA &
      2
      STC 4Q
      JMP 3Q
      JMP 6Z
[ DIVIDE SUBROUTINE
#3Q CLR
      ADDØ
      STC6Q
      ADD1Q
      BCO
      4Q

      STC5Q
      ADD4Q
      AZE&
      HLT
      APO
      JMP'+2
      COM
      ADA&
      1
      STA
      6Q+6
      STC4Q
      ADD1Q
      APO&
      JMP'+6
      COM
      STC1Q
      ADD2Q
      COM
      STC2Q
      SET&1
      1763
      CLR
      ADD2Q
      ROL&1
      STC2Q
      ADD1Q
      ROL&1
      STC1Q
      LDA
      5Q
      ROL&1
```

```
#7Q LDA
    2Q
    ROL&1
    STC2Q
    XSK&1
    JMP6Q+1
    ADD2Q
    APO&
    JMP'+5
    COM
    ADA&
    4ØØØ
    STC2Q
#6Q EXCIT
    ADD1Q
    ROL&1
    STA
    1Q
    LAM&
    Ø
    452
    STC1Q
    LDA
    4Q

        STC'-5
        JMP7Q
    #4Q Ø
    #1Q Ø
    #2Q Ø
    #5Q Ø
    #6Z CLR
        ADD2Q
        STC7E
    [PEAK VALUE
        SET&3
        1377
        SET&4
        3377
    [CONVERT POSITIVE
        SET&5
        1377
    #3A LDA&3
        ADA&
        377
        STA&4
        XSK3
        JMP3A
        JMP3B
    [WAVE ANALYSIS
    [ FIRST ADDR IN 7D
#3B NOP
    CLR
    STC 4T
    ADD7D
    ADA&
    -1400
    ADA&
    3400
    STC7F
#5K SET4
    7F
    XSK 4
    JMP5L
    JMP7Z
#5L LDA4
    STC4C
    LDA
    4
    STC4D
#3G XSK4
    JMP5M
    JMP7Z
#5M LDA&4
    COM
    STC4E
    LDA
    4
    STC4F
    ADD4C
    ADD4E

    AZE
    JMP3H
    JMP3G
#4C NOP
#4D NOP
#4E NOP
#4F NOP
#4G NOP
#4H NOP
#4I NOP
#4J NOP
#4K NOP
#4L NOP
#4M NOP
#4R NOP
#4S NOP
#4T NOP
#3H APO
    JMP3J
    JMP3I
```

```
#3I ADD7G
    APO
    JMP3G
    JMP3K
#3J COM
    JMP3I
#3K NOP
[ HAVE FOUND VALUE
[ ADDR IN 4F,4D
[ VALUE IN 4C,4E
    CLR
    ADD4C
    ROL1
    COM
    STC4G
    ADD 4E
    COM
    ADD 4C
    ADD 4G
    APO
    JMP3L
[ NEG WAVE
    JMP3M
[POS WAVE
[ ANALYSIS OF POSITIVE WAVE
#3M SET4
    7F
    SET&10
    3777
    SET&11
    2377
    SET&12
    1377
#6A CLR
    STA&10
    STA&11
    XSK&12
    JMP6A
    SET & 10
    3777
    SET & 11
    2377
    XSK4
    JMP5N
    JMP7Z
#5N LDA4
    STA&10
    COM
    STC4C
    LDA
    4
    STA&11
    STC4D
#3P XSK4
    JMP5P
    JMP7Z
#5P LDA&4
    STA&10
    STC4E
    LDA
    4
    STA&11
    STC4F
    ADD4E
    ADD4C
    AZE
    JMP 3N
    JMP3P
#3N APO
    JMP3P
    JMP3R
#3R STC4H
#3S XSK4
    JMP5R
    JMP7Z
#5R LDA&4
    STA&10
    STC4E
    LDA
    4
    STA&11
    STC4F
    ADD4E
    ADD4C
    AZE
    JMP3T
    JMP3S
#3T STC4I
    ADD4H
    COM
    ADD4I
    APO
    JMP 3U
    CLR
    ADD4I
    STC4H
    JMP3S
#3U NOP
[ DECIDE IF MAJOR WAVE
    LDA
```

```
     4
     ADA&
     -1
     STC4
     LDA
     4
     STC7H
[CORRECTED ADDR
     LDA4
     STC4J
     LDA
     4
     STC4K
#3W XSK4
     JMP5S
     JMP7Z
#5S LDA&4
     STA&10
     COM
     STC4L
     LDA
     4
     STA&11
     STC4K
     ADD4J
     ADD4L
     AZE&
     JMP3W
     JMP3X
#3X APO
     JMP3Y
     JMP3Z
#3Y CLR
     SET4
     4K
     JMP3S
#3Z NOP
     STC4M
     ADD4M
     ADD7G
     APO
     JMP3W
     JMP5A
[CRITERIA MET
[SEARCH TABLE
[POS WAVE TABLE SEARCH
#5A NOP
[DETERMINE NO. OF DATA POINTS
[FIRST ADDR IN 7F
[ LAST ADDR IN 4K
     CLR
     STC 4T
     ADD4K
     COM
     ADD7F
     ADA&
     1777
     STC4N
     SET13
     4N
     SET&10
     3777
     SET&11
     2377
     LDA&10
     STC4C
     LDA10
     STC4R
     LDA & 11
     LDA 11
     STC4D
     LDA 11
     STC4S
#5B LDA&10
     STC4E
     LDA & 11
     LDA 11
     STC4F
[GENERATE POS DIFF
     ADD4C
     COM
     STC4H
     ADD4H
     ADD4E
     APO
     JMP5B
     COM
     STC4G
[FIND MAX DIFF
#5D LDA&10
     STC4E
     LDA & 11
     LDA 11
     STC4F
[ZERO CROSSING
     ADD4T
     AZE
     JMP5I
     JMP5H
#5H ADD7E
     ADA&
     377
```

```
     COM
     ADD4E

     APO
     JMP5I
     CLR
     ADD4F
     STC4T
     JMP5I
#5I  CLR
     ADD 4R
     COM
     ADD 4E
     APO
     JMP 5C
     JMP 5G
#5C  XSK & 13
     JMP5D
     JMP5J
#5T  NOP
#4N  NOP
#5F  XSK&13
     JMP5D
     JMP5J
#5G  CLR
     ADD4E
     STC4R
     ADD4F
     STC4S
     XSK&13
     JMP5D
     JMP5J
[TO OUTPUT TABLE
[NEG WAVE ANALYSIS
#3L  NOP
     SET4
     7F
     SET&10
     3777
     SET&11
     2377
     SET&12
     1377
#1D  CLR
     STA&10
     STA&11
     XSK&12
     JMP1D
     SET & 10
     3777
     SET & 11
     2377
     XSK4
     JMP1E
     JMP7Z
#1E  LDA4
     STA&10
     STC4C
     LDA

     4
     STA&11
     STC4D
#1G  XSK4
     JMP1F
     JMP7Z
#1F  LDA&4
     STA&10
     COM
     STC4E
     LDA
     4
     STA&11
     STC4F
     ADD4E
     ADD4C
     AZE
     JMP1H
     JMP1G
#1H  APO
     JMP1G
     JMP1I
#1I  STC4H
#1K  XSK4
     JMP1J
     JMP7Z
#1J  LDA&4
     STA&10
     COM
     STC4E
     LDA
     4
     STA&11
     STC4F
     ADD4E
     ADD4C
     AZE
     JMP1L
     JMP1K
#1L  STC4I
     ADD4H
     COM
```

```
    ADD4I
    AZE
    JMP1M
    JMP1K
#1M APO
    JMP1N
[MIGHT BE NEW WAVE
    CLR
[RIGHT DIRECTION
    ADD4I
    STC4H
    JMP1K
#1N NOP
[DECIDE IF MAJOR WAVE

 [CORRECT ADDR
     LDA
     4
     ADA&
     -1
     STC4
     LDA
     4
     STC7H
     LDA4
     COM
     STC4J
     LDA
     4
     STC4K
 #1P XSK4
     JMP1R
     JMP7Z
 #1R LDA&4
     STA&10
     STC4L
     LDA
     4
     STA&11
     STC4K
     ADD4J
     ADD4L
     AZE
     JMP 1Z
     JMP 1P
 #1Z APO
     JMP1T
     JMP1U
 #1T CLR
     SET4
     4K
     JMP1K
#1U NOP
[NEW WAVE CRITERIA
    STC4M
    ADD4M
    ADD7G
    APO
    JMP1R
[CRITERIA NOT MET
    JMP1S
[TO TABLE SEARCH
#1S NOP
[NEG WAVE TABLE SEARCH
[FIRST ADDR IN 7F
[LAST ADDR IN 4K
    CLR
    STC 4T
    ADD4K
    COM
    ADD7F
    ADA&
    1777
    STC4N
    SET13
    4N
    SET&10
    3777
    SET & 11
    2377
    LDA&10
    STC4C
    LDA10
    STC4R
    LDA & 11
    LDA 11
    STC 4D
    LDA 11
    STC4S
#1V LDA&10
    STC4E
    LDA & 11
    LDA 11
    STC 4F
[ZERO CROSSING
    ADD4T
    AZE
    JMP1X
    ADD7E
    ADA&
    377
```

```
     COM
     ADD 4E
     APO&
     JMP1X
     CLR
     ADD 4F
     STC4T
     JMP1X
[FIND V-MIN
#1X CLR
     ADD 4E
     COM
     ADD 4R
     APO
     JMP1W
     CLR
     ADD4E
     STC4R
     LDA 11
     STC4S
     NOP
     XSK&13
     JMP1V
     JMP5J
#1W XSK&13
     JMP1V

     JMP5J
[GENERATE OUTPUT TABLE
#5J CLR
     LDA&
     1
     ADD 5T
     STC 5T
     ADD4R
     STA&15
     CLR
     ADD4S
     STA&14
     CLR
     ADD4T
     STA&16
     CLR
     ADD4S
     STC7F
     JMP5K
#7ZCLR
     SET & 3
     3777
     CLR
     ADD 2S
     STA&3
     CLR
     ADD 2T
     STA& 3
     CLR
     ADD 2R
     STA& 3
     CLR
     ADD 7D
     STA& 3
     CLR
     ADD 7E
     STA& 3
     CLR
     ADD 5T
     STA& 3
     CLR
     RDC
     0\153
     JMP 22
     7A=1407
     7B=-30
#7C 30
#7D NOP
#7E NOP
#7F NOP
#7G -30
#2K NOP
#2C NOP
#2D NOP
#2E NOP
#2F NOP
#7H NOP
#2R NOP
#2S NOP
#2T NOP
```

```
      $20
      NOP
      NOP
      NOP
      RDC
      1\154
      RDC
      2\155
      RDC
      3\156
      SET & 10
      1402
      SET & 6
      1501
      LDA &
      261
      STC 1N
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1401
      OPR 14
      OPR 14
      OPR 14
      OPR 14
[TAPE
      SET& 4
      1772
#1A LDA & 10
      OPR14
      XSK &4
      JMP 1A
      SET & 5
      3777
      LDA & 5
      OPR 14
      LDA & 5
      AZE
      OPR 14
      NOP
      NOP
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1401
      OPR 14
[BLOCK
      SET & 4
      1771
#1B LDA & 10
      OPR 14
      XSK &4
      JMP 1B
      LDA& 5
      SCR 6
      AZE&
      JMP *+4
      ADA&
      260
      OPR 14
      LDA 5
      BCL&
      7700
      SCR 3
      ADA&
      260
      OPR 14
      LDA5
      BCL&
      7770
      ADA&
      260
      OPR 14
      NOP
      NOP
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1401
      OPR 14
[LATENCY
      SET & 4
      1767
#1C LDA& 10
      OPR 14
      XSK &4
      JMP 1C
      LDA&5
```

```
     ADA&
     -1400
     MUL 6
     STC 9Z
     JMP 9S
     NOP
[SPACE
     SET &4
     1767
#1D  CLR
     ADD 1402
     OPR 14
     XSK &4
     JMP 1D
     NOP
     NOP
[ZERO
     SET & 4
     1772
#1E  LDA & 10
     OPR 14
     XSK &4
     JMP 1E
     LDA & 5
     STC 1L
     LDA 5
     STC 9Z
     JMP 9S
     NOP
     CLR
     ADD 1400
     OPR 14
     CLR
     ADD 1400
     OPR 14
     CLR
     ADD 1401
     OPR 14
[WAVE
     SET & 4
     1773
#1F  LDA& 10
     OPR 14
     XSK & 4
     JMP 1F
     LDA & 5
     STC 1K
     JMP '+4
#1K  NIP
#1L  NOP
#1N  NOP
     SET & 4
     1763
     LDA &
     240
     OPR 14
     XSK & 4
     JMP '-4
     CLR
     ADD 1K
     AZE
     JMP '+2
     JMP 2A
     CLR
     ADD 1K
     COM
     ADA&
     1777
     STC 1K
     ADD 1K
     ADA&
     -1766
     AZE
     JMP '+4
     SET 4
     1K
     JMP '+10
     APO
     JMP '+4
     SET 4
     1K
     JMP '+3
     SET & 4
     1764
     NOP
     NOP
     CLR
     ADD 4
     STC 1K
     CLR
     ADD 1N
     ADA&
     -272
     AZE&
     JMP '+16
     CLR
     ADD 1N
     OPR 14
     XSK &4
     JMP '+2
```

```
      JMP 1M
      LDA&
      1
      ADM
      1N
      JMP 1P
      NOP
      JMP '-22
      LDA&
      261
      OPR 14
      LDA&
      260
      OPR14
      XSK&4
      JMP '+2
      JMP 1M
      LDA&
      240
      OPR 14
      OPR 14
      LDA&
      261
      OPR 14
      OPR 14
      JMP 1M
#1R   NOP
#1P   CLR
      ADD 0
      STC 1R
      SET &11
      1773
      CLR
      LDA&
      240
      OPR 14
      XSK & 11
      JMP '-5
      JMP 1R
      NOP
 #1M  CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1401
      OPR 14
 [PEAK VALUE
      SET & 4
      1765
#1G   LDA& 10
      OPR 14
      XSK & 4
      JMP 1G
      SET 11
      1K
      SET & 12
      3077
      LDA &
      240
      OPR 14
      LDA &
      240
      OPR 14
      LDA &
      240
      OPR 14
      CLR
      ADD 1L
      COM
      STC 1L
      LDA & 12
      ADA &
      -377
      ADD 1L
      STC 9Z
      JMP 9S
      NOP
       XSK & 11
       JMP '-10
       NOP
       NOP
       CLR
       ADD 1400
       OPR 14
       CLR
       ADD 1401
       OPR 14
  [PEAK LATENCY
       SET & 4
       1763
  #1H  LDA & 10
       OPR 14
       XSK & 4
       JMP 1H
       SET 11
       1K
       SET &12
       2777
```

```
      LDA &
      240
      OPR 14
      LDA& 12
      ADA&
      -3400
      MUL 6
      STC 9Z
      JMP 9S
      NOP
      XSK & 11
      JMP '-10
      NOP
      CLR
      ADD 1401
      OPR 14
      CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
[ZERO LATENCY
      SET & 4
      1763
#1J   LDA& 10
      OPR 14
      XSK & 4
      JMP 1J
      SET 11
      1K
      SET &12
      3177
      LDA &
      240
      OPR 14
      LDA & 12
      AZE&
      JMP '+4
      ADA &
      -3400
      MUL 6
      STC 9Z
      JMP 9S
      NOP
      XSK & 11
      JMP '-12
      NOP
      NOP
#2A   CLR
      ADD 1400
      OPR 14
      CLR
      ADD 1400
      OPR 14
      RDC
      0\144
      JMP 22
      HLT
#8A   HLT
      LSW
      STC 9Z
      JMP 9S
      JMP 8A
#9S   LDA
      0
      STC 9V
      LDA &
      0
      STC 9W
      STC 9X
      STC 9Y
      SET & 1
      9W
      LDA
      9Z
      JMP 9J
      LDH
      4\9W
      STC 9A
      LDH
      9X
      STC 9B
      LDH
      4\9X
      STC 9C
      LDH
      9Y
      STC 9D
      LDH
      4\9Y
      STC 9E
      SET & 16
      -5
      SET & 1
      9A-1
#9F   LDA & 1
      STC 9I
      LDA
      9I
      ADA &
```

```
     -14
     AZE
     JMP 9R
     JMP 9H
#9R  LDA
     9I
     ADA &
     -17
     AZE
     JMP 9T
     ADA &
     255
     JMP 9G
#9H  ADA &
     240
     JMP 9G
#9T  LDA
     9I
     ADA &
     260
#9G  OPR 14
     XSK & 16
     JMP 9F
#9V  0
#9J  SCR & 1
     ROL & 1
     APO &
     COM
     STC 9N
     ADD 0
     STC 9P
     LDA &
#9K  ↑-;
     LZE
     ROR 6
     STH & 1
     SET & 2
     90-1
     JMP 9M
     AZE
     JMP 9L
     ADD9K
     STH 1
     LZE
     ROR 6
     STH & 1
     JMP '- 10
#9L  STH & 1
     JMP 9M
     JMP 9L
#9M  LDA
     0
     STC 9P-2
     SET & 3
     1777
     XSK & 2
     ADD 9N
     XSK & 3
     STA &
#9N
     ADA 2
     APO
     JMP '-5
     LDA
     3
     SRO &
     3567
     JMP
     STH & 1
#9P  JMP
#9Q  1750
     144
     12
     1
#9W  0
#9X  0
#9Y  0
#9Z  0
#9A  0
#9B  0
#9C  0
#9D  0
#9E  0
#9I  0
#8D  0
     $1400
     215
     212
     240
     324
     301
     320
     305
     275
     302
     314
     317
     303
     313
     275
```

```
314                                     331
301                                     0002
324
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316
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332
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APPENDIX C. SUMMARY OF POWER SPECTRAL FUNCTION

The power spectral density function is best introduced by considering two subjects which are its predecessors, the Fourier series and the Fourier integral.

A function f(t) is periodic if it is defined for all real t and if there is a positive number T such that

$$f(t + nT) = f(t). \qquad n = 1, 2, 3, \ldots$$

The number T is the period of f(t). The function must also possess a finite number of finite discontinuities.

Any periodic function may be synthesized as a sum of sines and cosines. This series representation of a periodic function is known as the Fourier series and may be expressed

$$(1) \qquad f(t) = a_0 + a_1 \cos \omega t + a_2 \cos 2\omega t + a_3 \cos 3\omega t + \ldots + b_1 \sin \omega t + b_2 \sin 2\omega t + b_3 \sin 3\omega t + \ldots$$

The first coefficient, a_0, is a coefficient of zero frequency and is often referred to as the 'D.C. component.' The value of the coefficients of the sine and cosine terms may be found by using the following expressions:

$$(2) \qquad a_n = 2/T \int_0^T f(t) \cos n\omega t dt$$

$$(3) \qquad b_n = 2/T \int_0^T f(t) \sin n\omega t dt$$

An example of the Fourier series representation of a waveform may be considered by examining a periodic square

square wave which may be expressed as

$+1$ when $\quad 0<t<\pi$

-1 when $\quad -\pi<t<\pi$

$f(t) = f(t + T) \qquad$ where $T = 2\pi$.

Evaluating the coefficients of a Fourier series with f(t) defined above, the a_0 and a_n terms are found to be zero. Thus, the square wave may be represented as a sum of sinusoidal waves:

$$(4) \qquad f(t) = \sin \omega t + \frac{1}{3} \sin 3\omega t + \frac{1}{5} \sin 5\omega t + \frac{1}{7} \sin 7\omega t + \ldots$$

$$\text{where } \omega = \frac{2\pi}{T}$$

Figure 76 shows the effect of adding the first four components of this series. The heavy line represents the sum of the waves depicted by the broken line. In Figure 76 (a) the first and third harmonics are added. The fifth and seventh harmonics are added in Figures 76 (b) and 76 (c) respectively. The resulting approximation can be seen to begin to synthesize a square wave. Hence, the Fourier series is equivalent to representing a periodic signal by its frequency components.

Using the identities $\cos x = \frac{1}{2}(e^{jx} + e^{-jx})$ and $\sin x = -\frac{j}{2}(e^{jx} - e^{-jx})$ Equation 4 may be written in the form of an exponential series.

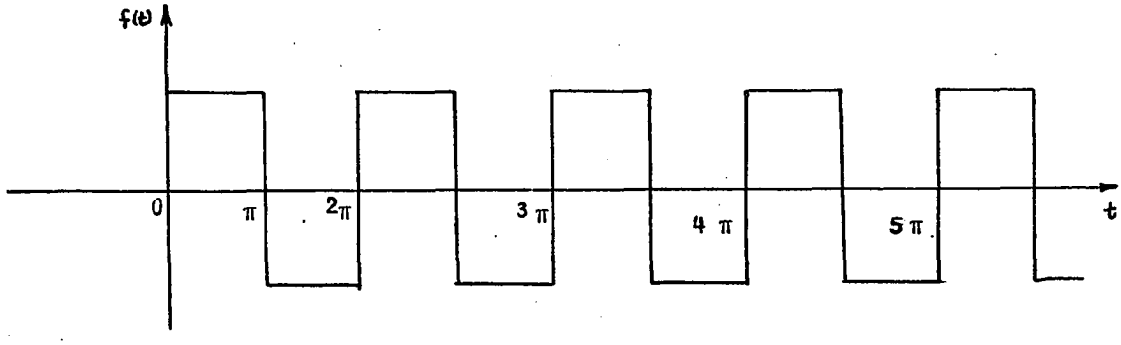
Figure 76. Approximation of a square wave by superposition of its components.

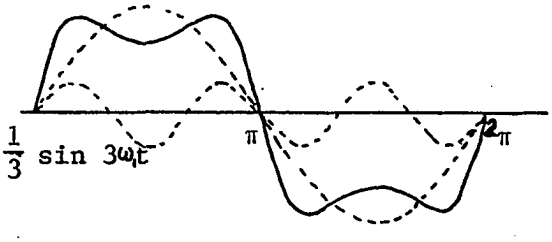
(a) Periodic square wave which can be synthesized by adding appropriate sinusoidal waveforms derived from a Fourier series expansion.

(b) Addition of the first and third harmonics. The resultant wave is shown by the solid line. The harmonics are denoted by the broken lines.

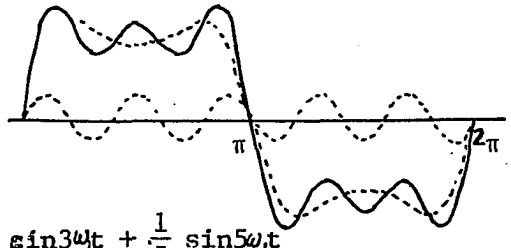
(c) Addition of the first, third, and fifth harmonics. The resultant wave is shown by the solid line. The harmonics are denoted by the broken line.

(d) Addition of the first, third, fifth and seventh harmonics. The resultant wave is shown by the solid line. The harmonics are denoted by the broken line.

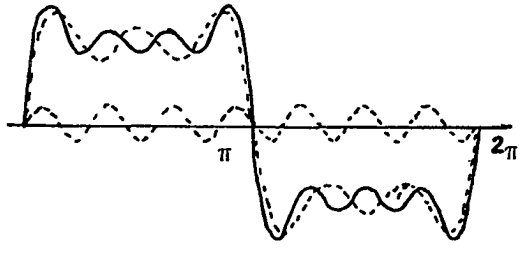




$$\sin\omega_1 t + \frac{1}{3}\sin 3\omega_1 t$$



$$\sin\omega_1 t + \frac{1}{3}\sin 3\omega_1 t + \frac{1}{5}\sin 5\omega_1 t$$



$$\sin\omega_1 t + \frac{1}{3}\sin 3\omega_1 t + \frac{1}{5}\sin 5\omega_1 t + \frac{1}{7}\sin 7\omega_1 t$$

(5) $$f(t) = A_0 + A_{-1}e^{-j\omega_1 t} + A_{-2}^{-j2\omega_1 t} +\ldots$$

$$+ A_1 e^{j\omega_1 t} + A_2 e^{j2\omega_1 t} +\ldots$$

The coefficients of this series may be found by evaluating the integral

(6) $$A_n = \frac{1}{2\pi}\int_0^{2\pi} f(t)e^{-jn\omega_1 t}\, d(\omega_1 t)$$

where n is any integer.

A more compact form of 5 may be expressed

(7) $$f(t) = \sum_{m=-\infty}^{\infty} Ame^{jm\omega_1 t}$$

where m is any integer. See Figure 77 (a).

If a train of rectangular pulses is considered with a pulse duration k the analysis will be

(8) $$A_n = \frac{1}{2\pi}\int_{-\pi/k}^{\pi/k} e^{-jnx}dx$$

(9) $$A_n = \frac{1}{-jn2\pi}\left(e^{-jnx}\right)_{-\pi/k}^{\pi/k} = \frac{1}{n\pi}\ \frac{e^{jn\pi/k} - e^{-jn\pi/k}}{2j}$$

(10) $$A_n = \frac{1}{k}\ \frac{\sin(n\pi/k)}{n\pi k}$$

Thus the rectangular pulse is the sum of the components

(11) $$f(t) = \sum_{n=-\infty}^{\infty}\frac{1}{k}\ \frac{\sin\, n\pi k}{n\pi k}\ e^{jn\omega t}$$

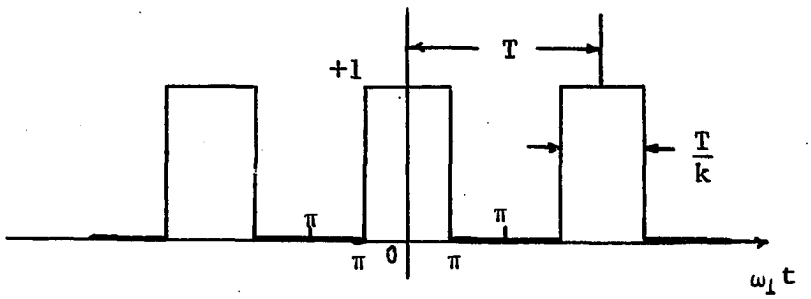
A spectrum of the frequency components may be drawn. See Figure 77 (b). In this example k=5 and the ratio n/k is

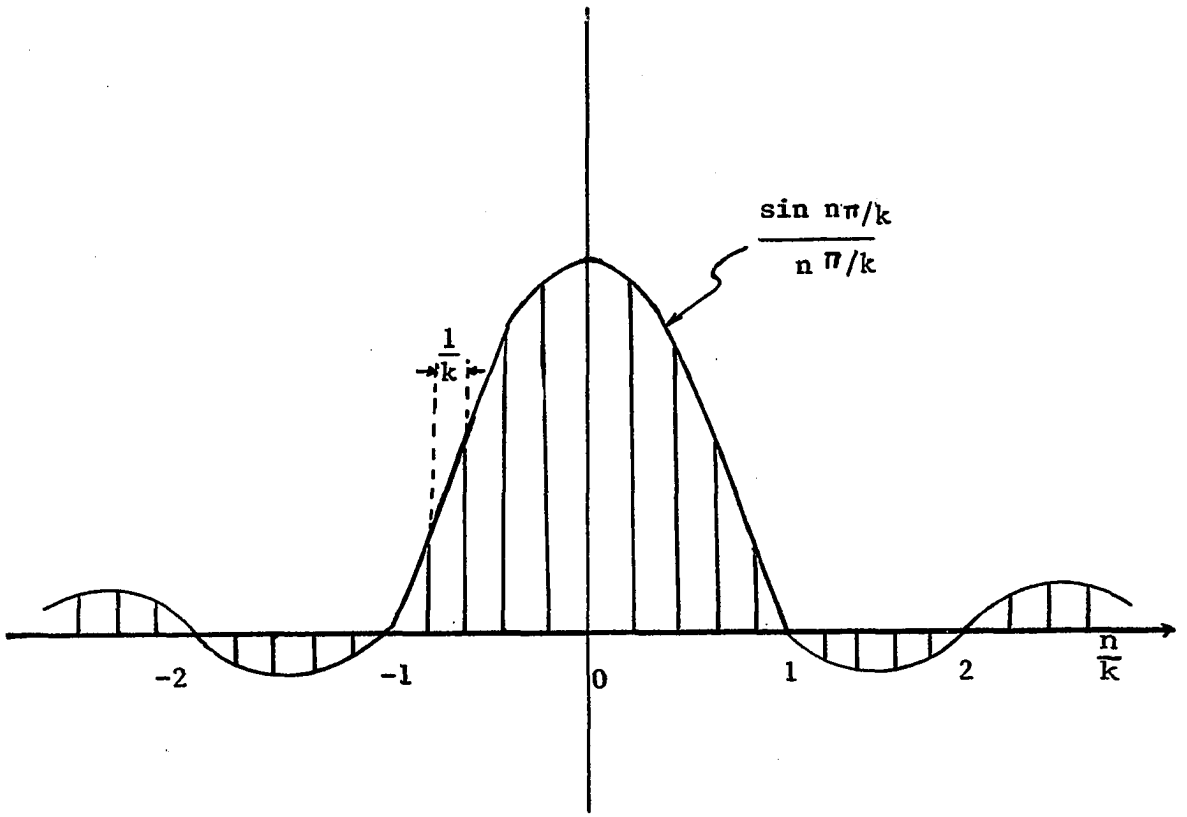
Figure 77. A train of rectangular pulses and its spectrum.

(a) A train of periodic square pulses.

(b) Discrete frequency spectrum derived from the pulses of Figure 77 (a). The envelope is

$$\frac{\sin n\pi/k}{n\pi/k}$$


T
+1
T/k
π
π
π
0
π
ω⊥t


sin nπ/k
n π/k
1/k
-2
-1
0
1
2
n/k

plotted along the horizontal axis. For any value of k the shape of the envelope,

$$\frac{\sin n\pi/k}{n\pi/k}$$

of the spectrum will remain the same, but the lines in the spectrum will be closer together or farther apart depending on whether k is large or small.

This synthesis is not limited to square waves but may be preformed with any periodic waveworm.

In contrast to the periodic train of rectangular pulses consider the case of a single pulse arrived at by letting the period of the periodic case become infinitely large. Equations 6 and 7 may be restated with the following changes. Since ω_1 is a constant it may be taken out of the integrand and placed in front of the integral sign; ω_n is written for $n\omega_1$ and the limits are stated in a different but equivalent form.

$$(12) \qquad A_n = \frac{\omega_1}{2\pi} \int_{-T/2}^{T/2} f(t)\ e^{-j\omega_n t}\ dt$$

$$(13) \qquad f(t) = \sum_{n=-\infty}^{\infty} A_n e^{j\omega_n t}$$

$$\text{where } \omega_n = n\omega_1 \qquad T = \frac{2\pi}{\omega_1}$$

Now the possibility of finding a series to represent a single pulse may be considered. This is done by letting the

time T between pulses become large. As this is done it can be seen from Equation 12 that ω_1 approaches zero and all values of A_n become infinitely small.

However, the function An/ω_1 will not be lost as T becomes infinitely large for as A_n becomes small so does ω_1 and the ratio does not approach zero. Let this ratio be defined

$$F_n = \frac{A_n}{\omega_1} \tag{14}$$

Equations 12 and 13 may be rewritten in terms of F_n.

$$F_n = \frac{1}{2\pi} \int_{-T/2}^{T/2} f(t)\ e^{-j\omega_n t}\ dt \tag{15}$$

$$f(t) = \sum_{n=-\infty}^{\infty} F_n e^{j\omega_n t} \omega_1 \tag{16}$$

If the time between pulses is now allowed to increase without limit only a single pulse will be left. See Figure 78.

As T approaches infinity ω_1 becomes small and may be called $d\omega$. In addition, one harmonic frequency becomes indistinguishable from the rest (the lines of Figure 77 (b) move increasingly close together). Consideration of a succession of discrete harmonics frequencies, ω_n, gives way to a consideration of all frequencies. Thus the variable ω_n may be replaced with the continuous variable ω which is permitted to have any value.

With these changes the equations for the Fourier series becomes the pair of equations for the Fourier integral.

$$F(\omega) = \int_{-\infty}^{\infty} f(t)\ e^{-j\omega t}\ dt$$

$$f(t) = \frac{1}{2\pi} \int_{-\infty}^{\infty} F(\omega)\ e^{j\omega t}\ d\omega$$

For a single pulse the Fourier integral may be thought of as performing the same function as the Fourier series in the case of the cyclic repetition of pulses; it finds the frequency components of the pulse. See Figure 78 (a).

To find the 'spectrum' of the rectangular pulse of Figure 78 (a) the Fourier integral is used.

$$F(\omega) = \frac{1}{2\pi} \int_{-\tau}^{\tau} (1) e^{-j\omega t}\ dt = -\frac{1}{2\pi j\omega} \left(e^{-j\omega t}\right)_{-\tau}^{\tau}$$

$$F(\omega) = \frac{1}{\pi\omega}\ \frac{e^{j\omega\tau} - e^{-j\omega\tau}}{2j} = \frac{1}{\pi\omega} \sin\ \omega\tau = \frac{\tau}{\pi}\ \frac{\sin\ \omega\tau}{\omega\tau}$$

The result $F(\omega)$ gives F as a function of frequency, ω. See Figure 78 (b).

A random signal x(t) may be considered with respect to its frequency distribution. An attempt to take the Fourier transform of x(t) leads to difficulties for this signal represents a time stationary situation such that its random properties are invariant with time.

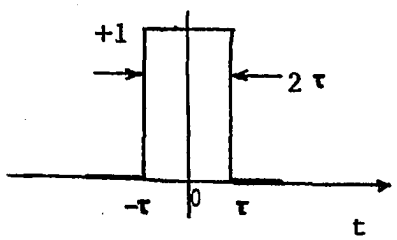
In this situation x(t) will possess no transform since

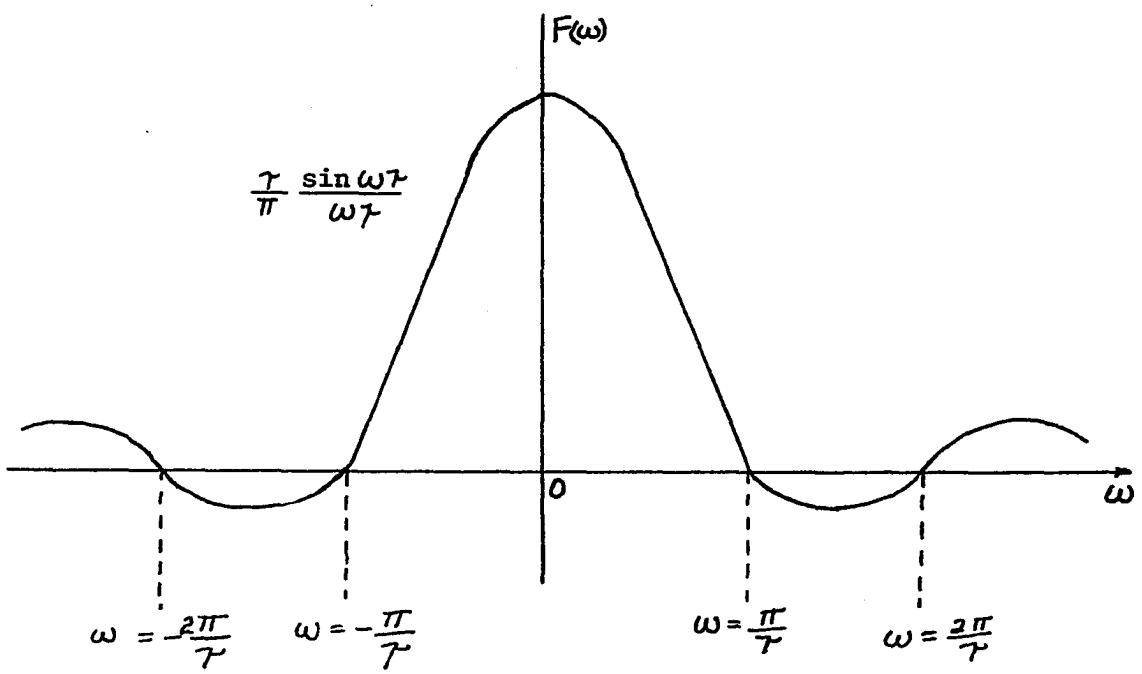
$$\int_{-\infty}^{\infty} x(t)\ e^{-j\omega t}\ dt$$

Figure 78. A single pulse and its spectrum.

(a) A single pulse which may be thought of as having come from a train of pulses {as shown in Figure 77 (a)} with a period T approaching infinity.

(b) Continuous frequency spectrum derived from the pulse shown in Figure 78 (a).


+1
2 τ
-τ
0
τ
t


F(ω)
$\frac{\tau}{\pi}\frac{\sin\omega\tau}{\omega\tau}$
0
ω
$\omega = -\frac{2\pi}{\tau}$
$\omega = -\frac{\pi}{\tau}$
$\omega = \frac{\pi}{\tau}$
$\omega = \frac{2\pi}{\tau}$

does not converge. The problem may be circumvented by defining a function called the power spectral density function. The power spectral density function for random data describes the general frequency composition of the data in terms of the spectral density of its mean square value. This average squared value will approach an exact mean square value as the observation time T approaches infinity.

The power spectral density function is defined where

$x(t)$ is the time-stationary random function

$$f(t) = \begin{cases} x(t) & -T/2 < t < T/2 \\ 0 & |t| > T/2 \end{cases}$$

Then $G(\omega)$, the power spectral density, is defined

$$G(\omega) = \lim_{T=\infty} \frac{1}{T} |F(\omega)|^2$$

The usefulness of the power spectral density in this study will now be examined by illustrating the results of taking a power spectral density of a sine wave. The discrete power spectrum for a sine wave is defined by

$$G(\omega) = \frac{|F(\omega)|^2}{2} \delta(\omega - \omega_0)$$

where $\delta(\omega - \omega_0)$ is defined as a delta function at $\omega = \omega_0$.

In actual practice when the integral of the power spectrum is taken over any frequency range which includes the frequency of

the sine wave the result will have a finite value equal to the mean square value of the sine wave.

For the purposes of this study the power spectral density was used since the results for a sinusoidal output would be known. If the output presented a power spectral density with the peak of activity at the frequency of the input one can then say that there is a correlation between the input and output.