FOREBRAIN MULTI-UNIT ACTIVITY AND FEEDING IN CATS

ABSTRACT

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FOREBRAIN MULTI-UNIT ACTIVITY CORRELATES OF ALIMENTARY BEHAVIOR IN THE CAT

Integrated multi-unit activity was recorded from 47 limbic, thalamic, and hypothalamic sites in 16 cats before, during, and after feeding behavior. Different patterns of activity level changes specific to food intake were seen at 10 loci in the amygdala, thalamus, lateral and ventrolateral hypothalamus, and other parts of the hypothalamus. Long-term activity levels at several other recording sites, however, in the lateral and ventromedial hypothalamus and in other structures implicated in the regulation of feeding behavior by electrical and chemical stimulation or lesion techniques were unaffected by food ingestion. It is concluded that the "feeding system" is located in several forebrain structures but is not uniformly distributed within those structures. The data also suggest that different aspects of food intake regulation are mediated by separate neural groups in the feeding system, and that general arousal effects are exerted independently of specific motivational effects on the feeding system.

FOREBRAIN MULTI-UNIT ACTIVITY CORRELATES OF ALIMENTARY BEHAVIOR IN THE CAT

by

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INTRODUCTION

The regulation of food intake presents two facets. It may be viewed as a purely physiological process in which feeding behavior is considered as one aspect of a complex homeostatic mechanism governing energy balance in the organism. On the other hand, the control of food intake is closely related to problems of drive and motivation and is therefore of considerable interest to psychologists. The problems and techniques involved in the study of feeding behavior have become increasingly common to psychology and physiology so that both approaches have become interwoven. The regulation of food intake has thus become a major field of research in physiological psychology.

At the turn of this century, the control of feeding behavior was studied by physiologists, who searched for a localized, peripheral regulatory mechanism responsive to a single aspect of food intake. The subsequent discovery of discrete hypothalamic brain areas which appeared to exert powerful regulatory influences on food intake shifted interest to the central nervous system and attracted neuropsychologists as well as physiologists to the field. The search for a single, essential regulatory factor which governs the hypothalamic mechanism ensued and has resulted in a variety of separate hypotheses favoring different

physical, chemical, or sensory processes. In addition, clinical and experimental studies of food intake in humans have indicated that cognitive factors may play an important part in the regulation of food intake. The increasing diversity of known regulatory influences on food intake has been accompanied by an increase in the number of brain areas implicated in the mediation of feeding behavior. The hypothalamus is now considered to be only a part of an anatomically dispersed "feeding system" which includes cortical, limbic, diencephalic, and midbrain structures.

The various hypotheses concerning the nature of regulatory factors influencing feeding behavior have been combined in a generally accepted multi-factor view of food intake regulation. Similarly, the variety of brain structures involved in the control of feeding behavior is acknowledged by most investigators. The individual functional contributions of these structures, however, remain obscure. Knowledge of the neuroanatomical basis of feeding behavior has advanced far beyond knowledge of the operational characteristics of the structures involved. Further investigation of the functional properties of the "feeding system" is clearly required before the regulation of food intake can be adequately understood.

Energy Requirements

All living organisms utilize energy from the environment in order to replace the energy dissipated, mainly as heat, in the maintenance of life processes (Brown & Brengelmann, 1965). The organization of matter into life forms--cells, tissues, organs, organisms--is opposed to the universal tendency of all matter toward equilibrium in accordance with the second law of thermodynamics. Energy is thus constantly required to maintain the structural integrity and high energy concentrations that are essential to life. Plants derive their external energy from solar radiation, and animals consume energy either directly from plants or indirectly through other animals which feed on plants. Since animals lack appropriate coupling mechanisms to obtain usable energy from other external sources, their only energy source lies in the molecular characteristics of ingested food. The chemical energy in food is converted to adenosine triphosphate (ATP), which can supply that energy to the metabolic processes that sustain life.

In animals, energy loss results in varying degrees from inefficiency of energy conversion, maintenance of high energy concentrations, structural synthesis and resynthesis, nerve impulse formation, blood flow and respiratory friction, muscular activity, and so on (Brown & Brengelmann, 1965). Although energy

loss is constantly occurring, it is not a constant. Variation in metabolic and locomotor activity and in the external environment alters the rate of energy loss. The organism's energy equation, which may be roughly expressed as $E_{in} = f(E_{out})$, demands that energy intake (food intake) be balanced against energy loss. Food intake, then, must be sufficient to provide for growth, metabolic maintenance, and locomotion, and it must be adjustable to compensate for changes in these variables. Starvation in the presence of food or failure to ingest sufficient food to meet energy requirements is obviously maladaptive, but it is also maladaptive for an animal to overeat. Excessive food intake can lead to a variety of pathologies, including obesity and consequent loss of agility, or may tend to confine the animal to a food source where he is vulnerable to predation (Kennedy, 1960; Mayer, 1953b; Rozin, 1964). Limitation of food intake is therefore particularly important to some predators and most herbivores, who are customarily surrounded by a bountiful food supply. Food intake limitation also becomes crucial to any animal faced with a scarcity of food over an extended period of time. Most animals must therefore regulate their food intake within relatively narrow limits, and the observed stability of the adult organism's body weight over long periods of time indicates the precision of this regulation

in practice.

Regulation

The general concept of physiological regulation has been traced to vague origins in classical Greece (Adolph, 1961; Cannon, 1929; Carlson, 1916; Rosenzweig, 1962). Hippocrates, Alcmaeon, and Aristotle contributed rudimentary ideas about the stability of organisms and the conditions under which it is maintained. Health was identified with a balance in the overall economy of the body, and a principle of self-renewal was roughly understood. Subsequent philosophers and physicians advanced these ideas with some embellishment. With the aid of hindsight and perhaps, in some cases, a selective skill in translating, it is possible to discern relevant statements about physiological regulations in the works of Galen, Paracelsus, Descartes, Spinoza, Lavoisier, Locke, Berkeley, Hume, and others (Adolph, 1961; Rosenzweig, 1962). A few 18th-century investigators, with the beginnings of an experimental approach, studied physiological regulations specifically. By the early 19th Century, physiological textbooks accepted the stability of vital phenomena in the face of various external influences as a criterion of life. As experimental sophistication increased, so did understanding of the nature of energy transformations occurring in living tissues. Concurrent progress in chemistry (e.g.

Berthollet, Gibbs), physics (e.g. Maxwell), and biology (e.g. Bichet, Hunter, Pfluger, Spencer) eventually culminated in the work of Claude Bernard (1878), who is commonly credited with the discovery of the importance and universality of physiological regulations in living systems. The term "homeostasis" was originated by Cannon (1929, 1932), who applied Bernard's concept to a wide range of physiological processes, such as oxygen flow, blood chemistry, food and water intake, body temperature, and so on.

Theories of hunger and its origin were advanced long before adequate experimental evidence was available (see Anand, 1961; Carlson, 1916; Larsson, 1954; Rosenzweig, 1962 for reviews). Near the turn of the 18th century, Haller and Erasmus Darwin proposed a local or peripheral theory of hunger in which the activity of the stomach exclusively controlled the desire for food intake. Magendie (1826), Milne-Edwards (1878), and others cited by Rosenzweig (1962), held that a portion of the brain, a "hunger center", was influenced by the nutritional state of the blood and stimulated higher neural levels to generate the urge to eat when necessary. A third view (Foster, 1891; Roux, 1897, 1907) proposed that the hunger center in the brain could be influenced as well by an approaching inanition in <u>all</u> parts of the body and received stimuli from many tissues, including

the blood. Thus, three broad ideas concerning the nature of hunger sensations--a local or peripheral theory, a central theory, and a general or multi-factor theory--were current at the time when modern experimental approaches to physiological processes began to be applied.

Local Theory

Cannon and Washburn (1912), taking advantage of Washburn's fortunate talent for swallowing balloons, obtained evidence favoring the stomach as the primary regulator of food intake. They found that the occurrence of phasic contractions of the stomach correlated very well with reports of hunger in the human subject deprived of food. This finding was reproduced with essentially the same technique in laboratory animals as well as humans (Carlson, 1912-13; Meschan & Quigley, 1938).

The role of blood sugar in the control of gastric motility and, therefore, as a possible regulatory mechanism was also investigated (Bulatao & Carlson, 1924a, 1924b). It was found that insulin-induced hypoglycemia caused reported hunger and, conversely, injections of glucose into the blood stopped gastric contractions (Bulatao & Carlson, 1924b; Luckhardt & Carlson, 1915). Subsequent investigation, however, failed to show a correlation between normal blood sugar variation and gastric contractions or reported hunger (Janowitz & Ivy, 1949; Quigley

& Halloran, 1932; Scott, Scott, & Luckhardt, 1938).

The peripheral theory received much attention at first, perhaps because the relevant experiments were obvious and relatively easy to perform, and the evidence initially seemed to support the theory. Gastric motility was commonly taken to be the regulatory mechanism of hunger, appearing as such in a psychology textbook of the time (Pillsbury, 1916). The intragastric balloon technique, however, has been criticized on the grounds that other methods of measuring gastric motility do not confirm Cannon's and Carlson's data and, in fact, indicate that the presence of the balloon in the stomach actually increases gastric motility (Gianturco, 1934; Martin & Morton, 1952). Furthermore, there was, at the time, an extensive body of clinical evidence indicating that partial or even total gastrectomy does not interfere with reported hunger. In the 19th Century, Milne-Edwards (1878) had noted that removal of the pneumogastric nerves in animals did not markedly affect food intake. Even earlier, Schiff (1867) had reported that patients with extensive lesions of the stomach still felt hunger, and he also cited experiments done by himself and others which showed that total denervation of the stomach does not interfere with food intake regulation. Sherrington (1900a), also reported evidence of the existence of hunger after gastrectomy. Muller (1915) confirmed

Schiff's clinical data, pointing out that patients with nearly complete removal of the stomach still reported normal hunger sensations.

Wangensteen and Carlson (1931) summarized the early evidence against a gastric mechanism of hunger regulation, and some investigators returned to this literature and set about verifying the earlier clinical and experimental findings. Once again, total removal of the stomach was shown to have no effect on the occurrence of reported hunger, and the possibility of small-intestinal contractions acting as a local cue in the absence of a gastric mechanism was eliminated (Ingelfinger, 1944; MacDonald, Ingelfinger & Belding, 1947; Wangensteen and Carlson, 1931). A similar lack of effect on feeding after total denervation of the stomach was demonstrated in dogs (Bash, 1939), and this result was confirmed in other animals (Harris, Ivy, & Searle, 1947; Morgan & Morgan, 1940), including humans (Grossman, Cummins, & Ivy, 1947; Grossman & Stein, 1948).

Although Cannon apparently never changed his view of gastric motility as the basis of hunger, other investigators began to look for other local regulatory mechanisms. In spite of the extant data concerning gastrectomized patients and gastric denervation, some interest centered on the role of gastric distension as an essential satiety cue. Two main methods of studying this

variable were employed. One method consisted of "diluting" the food of a subject with non-nutritive material to see if a compensatory increase in ad libitum intake would occur in spite of the abnormal increase in gastric distension. The other method utilized a gastric fistula through which food or non-nutritive bulk could be injected directly into the stomach before the regular meal time to see if this would inhibit or reduce normal food intake. It was found that, within limits, dilution of food does increase intake, and gastric preloading with inert material does not effectively reduce it. Preloading the stomach with nutritive material, on the other hand, was found to inhibit subsequent food intake, although not completely (Adolph, 1947; Cowgill, 1928; Harris et al., 1947; Janowitz & Grossman, 1949a, 1949b; Janowitz & Hollander, 1955; Morgan & Morgan, 1940; Share, Martyniuk, & Grossman, 1952; Tsang, 1938). Janowitz and Grossman (1949b) also artificially distended the stomachs of their subjects with balloons and found that only extreme distension caused any inhibition of food intake. Although there is some disagreement in the details of the studies cited, the general findings are consistent: gastric distension is not an indispensable factor in long-term food intake regulation.

In an attempt to assess the contribution of oropharyngeal stimulation to regulation, Hollinger, Kelly, & Ivy (1932) combined a jejunal fistula with a gastric fistula in a dog, so that food taken orally did not reach the stomach, while the subject was maintained through the gastric fistula. Oral intake gradually extinguished over the course of several months. Other workers confirmed this and showed that when the two fistulae were connected, so that ingested food entered the stomach, oral feeding was reinstated (Hull, Livingston, Rouse, & Barker, 1951). It has also been demonstrated that rats can regulate their food intake by performing operant responses which inject food directly into the stomach through a gastric fistula (Epstein & Teitelbaum, 1962). Thus, it is clear that, like gastric distension, oropharyngeal cues are not essential to food intake regulation over long periods of time. While it is true that no local or peripheral signals have been shown to be indispensable to regulation, it is also true that most studies have indicated that oropharyngeal and gastric factors do affect food intake to some degree, and they are clearly implicated in reinforcement (Berkun, Kessen, & Miller, 1952; Epstein, 1967; Hull et al., 1951; Kohn, 1951; Miller & Kessen, 1952; Pfaffman, 1960; Sheffield & Roby, 1950; Teitelbaum, 1967a, 1967b; Teitelbaum & Epstein, 1963).

The experiments relevant to peripheral regulatory hypotheses

have been reviewed several times (Anand, 1962; Grossman, 1955; 1958; 1960; Janowitz, 1958, 1962, 1967; Quigley, 1955; Smith & Duffy, 1957). It is now generally acknowledged that peripheral sensory mechanisms may participate in regulation but do not in themselves, individually or in concert, completely govern the pattern of food intake in the organism. The importance of oral factors in the control of food intake is, however, still controversial, and many investigators have argued strongly for the primacy of oral factors in the short-term regulation of feeding behavior (Jacobs, 1967; LeMagnen, 1969; Morgane & Jacobs, 1969; Nicolaidis, 1969; Wyrwicka, 1969).

Central Theory

While the peripheral theory of Cannon and Carlson was still in vogue, other investigators were gathering evidence that the central nervous system plays an essential role in the regulation of food intake. Frölich (1901) reviewed a number of cases of obesity in humans associated with damage to the base of the brain near the hypophysis. He attributed the obesity to pituitary dysfunction and a resulting endocrine disorder. Erdheim (1904), however, claimed that the obesity was due to hypothalamic damage, and for some years thereafter the nature of "Frölich's syndrome" was controversial. Bailey and Bremer (1921) furnished the initial data in support of Erdheim's position.

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cortical stimulation, however, has been shown to elicit feeding responses (Babkin & Van Buren, 1951; MacLean & Delgado, 1953). Although the cortex does not appear to be strictly essential to regulated food intake (Morgane & Kosman, 1959), it may participate in the fine control of motor adjustments associated with feeding and may underlie the variability of behavior patterns available for accomplishing regulation (Hess, 1957). Furthermore, it is likely that many cognitive factors influencing food intake (Bruch, 1969; Hamburger, 1960; Mendelson, 1964; Schacter, 1968) are mediated by the cortex.

Other Drives

The anatomical dispersion of brain areas implicated in feeding behavior has also been encountered with investigations of other drives. Chemical or electrical manipulation of a variety of diencephalic structures affects water regulation and drinking behavior (Andersson, 1953; Andersson & Wyrwicka, 1957; Coury, 1967; Fisher, 1969, Fisher & Coury, 1962, 1964; Fitzimons, 1966; Grossman, 1964a, 1964b, 1967a; Robinson, 1964; Robinson & Mishkin, 1968; Singer & Montgomery, 1970; Stevenson, 1967). A similar dispersion of central substrates of sexual behavior has become apparent (Beach, 1942; MacLean, 1962; MacLean & Ploog, 1962; Schreiner & Kling, 1953, 1956), and diffuse representation of elements of defensive and attack behavior (Brown & Hunsperger,

1963; Brown, Hunsperger, & Rosvold, 1969; deMolina & Hunsperger, 1962) and sleep (Hernandez-Peon & Chavez-Ibarra, 1963; Hernandez-Peon, Chavez-Ibarra, Morgane, & Timo-Jaria, 1963) has been found in the cat.

Clearly, the view that "primary" behaviors are controlled principally by "centers" or pairs of nuclei in the hypothalamus (Anand & Brobeck, 1951a, 1951b; Anand et al., 1955; Stellar, 1954, 1960) is untenable. This view has largely been replaced by a neuronal circuit theory of drive which stresses the importance of viewing the central control of food intake and other "primary" motivational behavior patterns as the result of activity in several cortical, limbic-diencephalic, and midbrain areas as well as in the various peripheral afferent systems interacting with hypothalamic structures in the intact, normal organism (deRuiter, 1963; Grossman, 1967a; MacKay, 1959; Morgane, 1964, 1969; Morgane & Jacobs, 1969).

Functional Organization

Generally speaking, current neurophysiological descriptions of motivational systems deal adequately with the anatomical dispersion of neural substrates of various drives. Recent attempts to organize the available information on motivational processes, however, have been almost exclusively devoted to the enumeration of the structures involved without regard to details

of function. Little attention has been paid to how these structures normally operate and interact to control the complex behavior patterns essential to regulation. The common view of the lateral-ventromedial hypothalamic relation that has emerged from lesion and stimulation techniques thus treats both areas as more or less functionally homogeneous neural populations with reciprocally related tonic firing rates.

Elaboration of the food intake regulatory system to include parts of the cortex, telencephalic limbic system, thalamus, and midbrain indicates a greater anatomical complexity in the feeding system but does not furnish detailed information about the functional correlates of this complexity. Somehow, the components of the feeding system must act together to monitor the nutritional state of the tissues, to initiate feeding when necessary and to maintain it in the presence of food without interference of inappropriate responses, to terminate feeding when sufficient food has been ingested, and to accomplish all these tasks in a co-ordinated manner so as to assure that the organism's energy balance is maintained over long periods of time. At present, however, there are no adequate hypotheses concerning the functional organization or individual functional characteristics of the structures involved. When functional relations are mentioned at all, they are usually stated in terms implying

tonic activity relations between entire structures, which were given anatomical identity by lesioning techniques and were then extensively investigated by electrical stimulation, EEG recording, and local chemical stimulation. Interpretation of lesion effects and electrical or chemical stimulation effects, however, is not straightforward. These methods do not selectively affect the structures to which they are applied; they may overlap anatomical boundaries and may involve functionally diverse fibers passing through the area of interest, and they affect "upstream" as well as "downstream" structures in unpredictable ways. Furthermore, these techniques do not readily furnish information about the normal functional characteristics of the structures under investigation. Interpretation of the effects of lesions within a complicated neural system that is perhaps multi-functional and capable of compensatory adjustments is extremely difficult (Gregory, 1961; Morrell, 1961). The detailed effects of electrical and chemical stimulation are also poorly understood, but it is likely that electrical stimulation effects involve more than a simple, general activation of cells near the electrode (e.g. Schlag & Villablanca, 1968; Valenstein, Cox, & Kakolewski, 1970), and chemical stimulation effects are controversial (Chiaraviglio & Teleisnik, 1969; Fisher & Levitt, 1967; Grossman, 1967b; Routtenberg, 1967).

Perhaps the most direct and convincing way to study the role

of a brain structure in a particular type of behavior is to examine neural activity in that structure while it is functioning normally in an unrestrained animal. Neverthless, there are few studies of neural activity associated with feeding in subjects with chronically implanted electrodes. The available information is largely based on EEG and single-unit records taken from acutely-prepared subjects under anesthetized or paralyzed conditions (Anand, Chhina, Sharma, Dua, & Singh, 1964; Anand, Chhina, & Singh, 1962; Brobeck, Larsson, & Reyes, 1956; Oomura, Ono, Ooyama, & Wayner, 1969; Sharma, Anand, Dua, & Singh, 1961; Wayner & Oomura, 1968). Some studies of EEG activity during alimentary behavior have been done with chronic preparations (Anand, Dua, & Singh, 1961; Clemente, Sterman, & Wyrwicka, 1964; Freeman, 1960; Grastyan, Karmos, Vereczkey, & Kellenyi, 1966; Morgane, 1961a; Morgane & Jacobs, 1969; Rabin, 1968; Roth, Sterman, & Clemente, 1967; Wyrwicka, 1964; Wyrwicka & Doty, 1966), and some similar observations of single units have recently been made (O'Keefe & Bouma, 1969; Oomura et al., 1967; Oomura, Ooyama, Naka, Yamamoto, Ono, & Kobayashi, 1969; Sawa & Delgado, 1963). There are, however, difficulties in the interpretation of EEG and unit data. Little is known about the neurophysiological events underlying the EEG, and a single EEG pattern may be associated with a variety of experimental effects (Brown &

Melzack, 1969; Feldman & Waller, 1962; Morell, 1961, 1967; Roth et al., 1967; Wikler, 1952). Single-unit studies indicate, moreover, that the relation between the form and amplitude of EEG waves and the discharge rates of neurons at the same recording site is a complex one (Creutzfeld, Watanabe, & Lux, 1966; Cross & Silver, 1966; Morrell, 1961, 1967). Furthermore, EEG recording does not provide reliable information about activity levels in discrete, localized subcortical brain areas, as indicated by multi-unit recordings (Alcarez, Guzman-Flores, Salas, & Beyer, 1969; Brown & Melzack, 1969; Buchwald, Halas, & Schramm, 1966a, 1966b). Individual unit data is better understood, but practical considerations limit the number of cells sampled in a given area, and it is difficult to generalize about an entire brain area on the basis of relatively few, possibly unrepresentative, components. Also, single-unit recording in freely-moving preparations is technically difficult, and such studies are rare. Finally, neither EEG nor single-unit data are appropriate for deriving an immediate, quantitative picture of ongoing changes in activity levels in subcortical brain areas during behavior.

Multi-unit activity recording has been shown to be a more reliable and sensitive method of observing neural activity than the EEG technique (Bambridge, 1968; Brown & Melzack, 1969;

Buchwald et al., 1966a, 1966b). In addition, it integrates or "summarizes" the activity of a population of cells at the recording site and therefore provides a more representative, immediate picture of neural activity in the area under investigation than does the single-cell approach. Since many theories of brain function in motivation and regulation are based implicitly on activity level relations between cell populations, the multi-unit technique seems most appropriate for obtaining information relevant to those theories. The neural populations in question are commonly identified with telencephalic-limbic, diencephalic, and other structures, and multi-unit records taken from these structures should reveal some of their functional attributes.

Purpose of this Study

Recordings of multi-unit activity in various telencephalic-limbic and diencephalic structures in freely-moving cats were taken before, during, and after eating and during other motivational situations. These records were taken in order to obtain an empirical view of normal activity level changes of cell populations in structures that have been implicated in the regulation of feeding behavior and feeding motivation. The directions and time courses of such activity level changes could suggest ways in which these brain areas participate in regulation and motivation with respect to feeding behavior. A further aim of this

study was to reveal some of the responses of structures involved in feeding behavior to other types of consummatory responses, such as drinking and sleeping. Comparison of the responses of telencephalic and diencephalic structures during feeding and during other types of motivated behavior may help to clarify some aspects of functional organization in neural substrates of motivation.

METHODS

Subjects

Sixteen male cats, weighing 2.75 - 4.2 kg., served as subjects. They were housed in individual cages and fed with canned commercial cat food (Puss'n Boots fish, chicken, or liver, Quaker Oats Co. of Canada, Ltd.). The same food was provided during recording sessions.

Surgical Procedure

Animals were placed in a Kopf stereotaxic instrument under pentobarbital anesthesia. The skull was exposed, and starting holes for self-tapping, stainless-steel skull screws were drilled into the skull. Separate burr holes were drilled through the skull for each electrode, and the dura was pierced beneath the holes just prior to electrode insertion. The bipolar electrodes were made of two 250-μ, formvar-insulated, stainless steel wires twisted together with bared tips separated by approximately

0.5 mm. The electrodes were positioned in limbic and diencephalic areas using the Jasper-Ajmone-Marsan (1954) stereotaxic atlas.

Two types of connector were used. A 10-pin Sheatz-type pedestal (Sheatz, 1961) bolted through the skull resulted in a very firm and durable preparation, but the shielding on the connecting cable was inadequate for use with unrestrained subjects, and records taken with the Sheatz assembly tended to be seriously flawed by movement artifact. A 9-pin female hexagonal Amphenol connector (126-122) combined with an 8-lead Microdot (#250-3804) connecting cable gave better results, and this assembly was used with most of the subjects reported here. Durability was achieved by fastening a stainless steel 2/56 X ½" bolt through a "keyhole" slot drilled through the skull close to the final Amphenol connector position. Additional security was provided by three or four skull screws placed around the electrode insertion points.

The electrode leads were soldered to the Amphenol connector, and a ground wire from one of the skull screws was soldered to the 9th pin. The connector was then secured to the skull with dental acrylic cement. Afterwards, the scalp incision was sutured firmly around the hardened cement crown, and topical antibiotic cream or powder was applied to the wound. Chloramphenicol

antibiotic was given intramuscularly for two or three days postoperatively.

Recording System

A block diagram of the recording system is shown in Figure 1. Signals were led via the connecting cable to a selector switchbox and then to four Tektronix differential amplifiers (Type 2A61) with the pass band (using the built-in filters) set at 600-6000 Hz (half-amplitude--20db/decade). The 600 Hz setting permitted transmission of signals within the action potential frequency range but blocked EEG and other slow electrical activity. The upper pass band limit reduced the possibility of contamination from extraneous radio frequency signals. The amplified signals were led to a four-channel CRT monitor and to integrating circuits (see Figure 2) modified from a design by Weber and Buchwald (1965). The d-c output of the integrator was proportional to the root-mean-square of a 1000 Hz sine wave input used to calibrate the circuit, and its time constant was approximately 5 seconds. This relatively long time constant was chosen to minimize the effects of short, transient fluctuations in activity levels, smoothing the record so that long-term changes could be more readily appreciated. Integrator outputs from the electrodes were recorded on the d-c channels of a Grass model 7 polygraph, with chart speeds ranging

from 9.0 mm/min to 900 mm/min. Most records were taken at chart speeds of 9.0 or 18.0 mm/min.

After the experiments were completed, the noise level of the system for each electrode, within the pass-band used, was determined by measuring the d-c output of the integrator with the electrode still in the brain of the sacrificed cat. Signals exceeded noise levels by 2/1 to 9/1. 2% changes in the d-c output were discriminable even at low signal levels. The peak-to-peak range of input signal levels displayed on the CRT monitor was about 5 to 25 μv.

Apparatus

For recording, subjects were placed in a 51 x 71 x 61 cm wooden enclosure with a 51 x 61 cm one-way glass window in the front door. Ventilation was provided by ten 1.25-cm holes at floor level and by a 12-cm ceiling fan. A 60-watt house light fixed to the ceiling illuminated the enclosure.

A 14 x 32 x 16 cm divided feeding box was placed within the enclosure. A pair of photocells was fixed to the divider panel of this box so that the subject shaded one photocell or the other when eating or drinking. The photocells were connected in series, with polarities opposed, to a d-c driver amplifier on the polygraph. Shading of one photocell therefore deflected the polygraph pen in one direction while shading of the other

deflected the pen in the opposite direction. The onset, duration, and termination of feeding and drinking episodes were thus recorded simultaneously with multi-unit activity from the subject's electrodes.

Recording Procedure

Recording sessions were begun 7-10 days after electrode implantation and were carried out over periods ranging from three weeks to five months. The subjects were deprived of food, water, or food and water for 12 to 24 hours, and occasionally for 36 hours, prior to recording sessions, which lasted for 2-8 hours. When stable baseline records were obtained from a deprived subject, whether during sleep or some other level of behavioral arousal, food or water or both were placed in the feeding box within the recording enclosure. Records were taken continuously during sleep, resting, eating, drinking, grooming, or locomotion. The subjects' states of behavioral arousal during recording sessions were categorized as sleeping, resting, sitting, standing, and moving. Shifts from one category to another were written on the polygraph chart. Typical postures associated with each classification of behavioral arousal are shown in Figure 3. Multi-unit activity levels during similar states of behavioral arousal before and after feeding (or drinking) were compared in order to avoid confusing activity

level changes due to feeding with changes due to variations in general arousal. Sleeping was preferred for activity level comparisons because it was accompanied by very characteristic records from almost every electrode and correlated with extremely stable activity levels between episodes of paradoxical sleep. Food deprivation for 24 hours or more, however, often resulted in the subjects' remaining awake and restless until food was provided, and some subjects rested quietly but never slept in the recording enclosure, regardless of their deprivation state and total amount of time spent in the enclosure. In these cases, comparisons were made of records obtained during the lowest stable behavioral arousal state attained by the subject in both deprived and satiated conditions during each recording session.

A stable baseline activity level of at least 5 and usually 15 minutes was required from all electrodes in deprived subjects before food or water was made available. In fact, baselines and stable post-ingestion comparison records of an hour or more in duration were often obtained.

Since the canned cat food provided during recording sessions and in the home cage contained water, records of activity levels before and after water ingestion alone were taken in order to separate food intake effects from water intake effects. When similar activity level changes were seen in both situations,

the effect was considered to be unrelated to food intake. To obtain drinking during recording sessions, prior deprivation of both food and water was often necessary, since the food contained sufficient water to satisfy the daily requirements of some subjects.

Several recording sessions were run with subjects in a satiated condition in the presence of food and water in order to estimate the range of spontaneous long-term activity level changes and to observe changes associated with normal, ad libitum food intake. A few prolonged (12-15 hour) recording sessions were run with some subjects for similar reasons.

Histology

After noise level determinations, the subjects were placed in the stereotaxic instrument, and a 1-ma d-c current was passed through each electrode for 10 seconds. The brain was then blocked at the same angle as the electrode penetrations, and the block was stored in a formal-saline solution containing 2-3% potassium ferricyanide to obtain a Prussian-blue reaction. 40- or 80-u sections were cut from the frozen block and stained with neutral red, and 20 x 25 cm photographic enlargements were made directly from the covered slides to aid identification of recording sites.

RESULTS

Out of 64 implanted electrodes, 47 provided useful records of multi-unit activity levels for as long as recording sessions were continued. The distribution of these electrode placements is shown in Figure 4. Of the 47 functioning electrodes, only 10 consistently showed long-term activity level changes specifically related to feeding, and several electrodes placed in the lateral and ventromedial hypothalamic areas did not show such changes. One of the surprising results of this study, then, was the relative scarcity of subcortical loci affected on a long-term basis by food intake. A further interesting finding was that several of the recording sites which yielded positive results were not confined to the lateral and ventromedial hypothalamic regions but were located also in other parts of the hypothalamus and in the thalamus and amygdala. The food intake regulatory system thus appears to be widely distributed in the brain, but it cannot be described adequately by identification with entire anatomical structures. In the case of the feeding system, functional differentiation apparently does not always coincide with structural differentiation in the brain.

Typically, activity levels from all electrodes were relatively high at the beginning of a recording session. These

levels then gradually subsided, roughly in parallel, to stable resting or sleeping levels (Figure 3). Stable baseline activity levels were usually obtained within 20-40 minutes, even when subjects failed to fall asleep but rested quietly in the enclosure. The very stable baseline activity levels between episodes of paradoxical sleep at most recording sites facilitated comparisons of activity levels before and after eating or drinking. Comparisons could thus be made under unmistakably similar conditions of general arousal. When differences in activity levels before and after eating were noted in the sleeping animal, activity levels in the resting, but awake, animal during deprivation and satiation were also compared. In all cases, if differences in activity levels were visible when sleeping activity levels were compared, similar differences were also seen when resting levels were compared. The activity changes reported here occurred reliably as long as activity was recorded from the site. The magnitudes of feeding-related changes were consistent from one recording session to another; they did not appear to vary systematically with length of deprivation or amount of food ingested. The slight variations in magnitude which did occur could reflect genuine motivational variation but could also be due to slightly different populations of cells, at different average distances from the electrode, responding to food ingestion in successive

recording sessions.

Hypothalamic Activity Levels after Feeding

Reliable changes in multi-unit activity levels after food ingestion were observed in several hypothalamic areas. These changes were of two sorts. Activity levels (1) changed gradually, beginning soon after termination of food intake and reaching a maximum value in 15-45 minutes, or (2) changed abruptly during feeding and remained altered but relatively stable after feeding was terminated.

Gradual activity decrements were the most commonly observed of all changes specific to food intake. They were obtained from one electrode out of 10 situated in the lateral hypothalamic area (Figure 5a) and from 3 other electrodes, one in the periventricular area near the ventromedial hypothalamic nucleus, one in the zona incerta, and one just posterior to the mammillary bodies at the medial edge of the cerebral peduncle (Figure 6). After feeding, activity at these sites fell below baseline levels within 5-10 minutes and continued to fall until stable lower levels were reached. Gradual activity level increments were seen only in the medial mammillary body (Figure 7). These increments appeared to be reciprocally related to the gradual decrements seen at more rostral hypothalamic sites, and they had about the same latency. Relatively small long-term changes in activity

levels after feeding were noted occasionally at a few other hypothalamic recording sites (Electrodes 1, 4, 16, 18), but these changes were unrepeatable or inconsistent and were therefore disregarded.

Abrupt activity level changes related to feeding were seen at fewer recording sites. They were, however, reliably obtained from one electrode in the ventrolateral hypothalamus, where activity increased during and after food ingestion (Figure 8a), and from one electrode in the perifornical lateral hypothalamus, where activity decreased with food intake (Figure 5b). Activity level changes at these sites were stable after the termination of feeding; once the rapid transition in activity level occurred, further gradual activity level changes were not observed.

The majority of lateral and ventromedial hypothalamic recording sites showed no changes in activity levels after food intake, even when electrodes were placed in areas where lesions and electrical or chemical stimulation are known to alter patterns of food intake dramatically (Figure 9). It is certain that these electrodes were functional, since the appearance of multi-unit activity on the CRT monitor was normal in these areas, and changes related to general arousal were evident in the records. The structural boundaries of the lateral and ventromedial hypothalamic areas thus do not appear to reflect accurately the

functional diversity encountered in these areas.

The alterations in activity levels following food ingestion, whether gradual or abrupt, usually persisted for the duration of a recording session. Subjects often returned to the feeding dish and ate again after the initial feeding episode, taking their food in two or three installments during the session. Activity level changes occurring after the first intake of food continued without modification through subsequent feeding episodes (see Figures 5a, 7). That is, ongoing activity level changes were not enhanced by subsequent food intake, and feeding commonly occurred when changed activity levels had stabilized.

During very long recording sessions (up to 15 hours), when considerable time elapsed between feeding episodes, there was no evidence of cyclic variation of activity levels, between feeding episodes, at any recording site. Occasionally, at some positive sites, activity returned abruptly to pre-eating baseline levels for varying lengths of time when the subject awoke or was disturbed from its resting position. In areas where activity decrements had occurred, for example, a brief arousal-related activity increment might subside to a higher stable level than was recorded just previously. Although feeding was not usually observed immediately after this happened, such events could be the way in which motivational baselines are "reset".

Thalamic and Subthalamic Activity Levels after Feeding

Of 5 active recording sites in thalamic and subthalamic areas, 2 electrodes, in the prothalamic and subthalamic nuclei, showed gradual activity level decrements after food intake (Figure 10). These activity level changes resembled the gradual hypothalamic changes in magnitude and time course, and they, too, did not appear to recycle before each feeding episode, even during prolonged recording sessions. At the recording site in the subthalamic nucleus, the activity decrement was partially diminished approximately 20-25 minutes after a feeding episode, but baseline levels were never equalled. No other thalamic recording sites showed either abrupt or gradual long-term activity level changes specific to feeding.

Telencephalic Activity Levels after Feeding

One recording site in the amygdala showed abrupt, sustained activity level increments after feeding (Figure 8b). These changes resembled those observed in the ventrolateral hypothalamic site mentioned above. Two other recording sites in the amygdaloid complex, however, did not show any lasting activity level changes associated with food intake (Figures 11b, 12b). Multi-unit activity in at least one part of the amygdaloid region, then, responds selectively to food intake while activity in other parts does not.

Activity levels at all recording sites in the hippocampus and fornix were unchanged, on a long-term basis, by feeding. In these areas, a characteristic pattern of irregular, 2-10 second fluctuations of activity levels was seen during quiet resting and sleep. These fluctuations appeared to reflect the general arousal state of the subject, gradually increasing in amplitude and decreasing in frequency as arousal decreased, and were largely eliminated during the emission of feeding and drinking responses. Neither food nor water intake, however, appreciably altered long-term average activity levels in these structures. Activity usually returned to baseline levels almost immediately after ingestion, and the fluctuation pattern reappeared shortly thereafter, when the animal resumed resting or sleeping. Recovery of the fluctuation pattern was gradual following consummatory behavior, but its appearance was unchanged.

Other Areas

Activity levels at recording sites within and outside of limbic, thalamic, or hypothalamic areas, including the caudate nucleus, internal capsule, and cerebral peduncle, exhibited no long-term changes specific to either feeding or drinking (Figures 11, 12). Short-term activity in these structures tended to be covariant with hypothalamic and thalamic activity in the resting cat, and during general arousal or paradoxical sleep (although

the caudate area appeared to show slight decrements in activity during paradoxical sleep episodes).

Activity Levels during Consummatory Behavior

The long time-constant of the integrator circuit used in these experiments prevented the recording of details of brief or rapid multi-unit activity level changes. Furthermore, mechanical artifacts associated with sudden movements of the animal's head were a continuing problem. Nevertheless, several eating and drinking episodes were of sufficient duration to provide a view of activity levels during ongoing consummatory responses, and reasonably artifact-free records were obtained from some subjects on such occasions.

At most recording sites in the thalamus and hypothalamus, activity levels increased during both feeding and drinking by approximately equal amounts. There was no indication that such increments were differential to either type of consummatory response, and no striking regularities in the activity level changes appeared over successive feeding or drinking episodes. These changes were therefore considered to result nonspecifically from motor activity or arousal. Some recording sites showed no activity level changes during either feeding or drinking (Figure 13), and most of these areas were also among those which did not show long-term activity level changes after feeding. Apparently

reduced activity levels during drinking occurred in several areas (Figure 14), but it is difficult to determine in these cases whether the activity levels were actively depressed or merely "set" during ingestion at a given value which happened to be lower than the usual preceding activity levels. Repeated recording did not elucidate the matter, since animals were normally aroused and moving just prior to feeding, and their activity levels therefore tended to be relatively high. These reductions in ongoing activity levels could reflect either a rapid decay of previously high, arousal-related activity or an active inhibition of activity in the area during performance of a particular kind of consummatory response.

Comparisons of activity levels at a given locus during eating and drinking in the same recording session were possible in a few animals. Activity levels during feeding were consistently higher than during drinking in parts of the hypothalamus (Figure 15). It cannot be safely inferred, however, that a lower activity level during drinking than during eating signifies that an area is more concerned with mediating food intake (see Schlag & Balvin, 1963). As noted above, an activity level decrement at a recording site may result from either active inhibition (which would suggest that the reduction in activity is crucial to the performance of the response) or passive decay of general arousal.

Nevertheless, activity level differences during different consummatory responses suggest that an area is differentially involved in these responses.

In contrast to the differential activity levels during feeding and drinking observed in some thalamic and hypothalamic areas, recording sites throughout the trajectory of the fornix showed apparently uniform reductions in activity levels during both types of consummatory response (Figures 16b, c, 17b, c, d, e). At hippocampal sites, on the other hand, approximately equal increments in activity levels were observed during feeding and drinking (Figures 16a, 17a). Some discrepancy in activity levels during feeding and drinking was occasionally seen in the fornix, but the majority of intrasession comparisons revealed no consistent activity level differences. The multi-unit activity level fluctuations often failed to disappear during feeding, however, while they were always absent during drinking.

At least one recording site in the dorsomedial thalamus showed consistent, graded increments in multi-unit activity during drinking in contrast to the usual stable activity level changes seen in other areas (Figure 18). These graded activity changes in the dorsomedial thalamus occurred at about the same absolute levels during successive drinking episodes. Activity levels from other recording sites during consummatory behavior

were either occluded by mechanical artifact or were recorded at such slow chart speeds that the relatively brief periods of changed activity levels during ingestion were not clearly visible.

Activity Levels after Drinking

No long-term differences between activity levels before and after water ingestion were observed at any recording site in this study. Changes in activity levels were noted occasionally at some sites after water intake (electrodes 11, 34, 35), but they were not reliable and could not be consistently produced by water deprivation and subsequent drinking. The absence of long-term activity level responses to drinking at all recording sites was remarkable, since the regulation of water intake is thought to be mediated by some of the structures sampled in this study. Drinking episodes were generally very brief, however, and for reasons mentioned above, activity level changes during drinking were not often visible. It is possible that short-term activity changes during ingestion, rather than long-term, post-consummatory changes, are important to water intake regulation at these sites. Long-term regulatory variables in the control of water intake may be mediated by other areas or may be reflected by neural activity not measured by the multi-unit technique.

Incidental Observations

Absolute levels of resting or sleeping baseline multi-unit activity at any given recording site showed little day-to-day variation. The normal intersession range of activity level variation was approximately 10% during sleep and 15-20% during resting in both deprived and satiated subjects. There was no apparent correlation between baseline activity levels and the duration of food or water deprivation at any recording site. Severely deprived subjects, however, were often restless and did not fall asleep, which tended to prevent the occurrence of normally low baseline activity levels at many recording sites.

Electrodes implanted in telencephalic limbic and hypothalamic sites in the same subject were convenient for making comparisons of activity levels in these areas. When the electrodes had similar characteristics, the amplitudes of unintegrated activity, observed on the CRT monitor, tended to be higher in the limbic telencephalon and thalamus than in the hypothalamus by a factor of two or three. This was reflected by higher integrated baseline activity levels from former areas.

Resting activity levels in the amygdala, hippocampus, and fornix, recorded simultaneously with hypothalamic activity levels at high gain and fast chart speeds, showed a generally reciprocal relation with activity levels in some hypothalamic areas

(Figure 19). This reciprocity disappeared when subjects were highly aroused or engaged in consummatory behavior but was reinstated when resting positions were resumed and when subjects were in nonparadoxical sleep. Simultaneous recordings from the hippocampus and fornix were not obtained, and it is therefore not possible to assess the nature of activity level relations between these structures. Activity fluctuations in both areas, however, appeared to be similar except during consummatory behavior, and therefore resting activity in these structures is probably either covariant in parallel or reciprocal.

If the sleeping or resting subject was disturbed by the experimenter calling out, tapping on the enclosure, or opening the door and touching the subject, activity levels from most electrodes changed abruptly, usually increasing, and then returned slowly to previous levels. The magnitude and duration of this general arousal effect seemed to depend roughly on the intensity and duration of stimulation. The effect was prolonged if the subject oriented to the stimulus, more prolonged if the resting position was changed in the course of orientation, and still more prolonged if the subject actively investigated the stimulus or interacted with the experimenter. These activity level increments were also non-specifically associated with "spontaneous" locomotion, small movements of the head or limbs, or grooming

activity. In most cases, activity returned to baseline levels within 10 minutes, even when the subject was aroused from sleep and stroked for several seconds by the experimenter.

Changes in multi-unit activity during the transition between waking and sleeping states were usually smooth and gradual at all recording sites. Occasionally, very small, abrupt decrements in activity levels were seen when a resting subject lowered his head just before falling asleep. Activity levels in the thalamus, hypothalamus, and amygdala normally fell slowly during the next several minutes until reaching a stable sleeping baseline. The average decrement was about 5%. Activity levels in the hippocampus and fornix showed an increasingly high-amplitude, irregular fluctuation pattern during resting and non-paradoxical sleep (Figures 3, 16, 20). This activity pattern appeared on the CRT monitor as irregular, repetitive bursts of high-amplitude spikes, the bursts varying in duration from about 2 to 10 seconds. These bursts became more prolonged as the subjects fell asleep (Figure 21). They were much reduced or absent when the subject awoke and became alert.

In the sleeping subject, transient increments in activity levels were noted at most recording sites during episodes of paradoxical sleep (Figures 22, 23). During these episodes, activity levels were often higher than levels normally seen in

the awake, moving animal. The activity increments were accompanied by accelarated respiration, ear twitching, slight movements by the paws and limbs, and occasional small rolling movements of the head. The onset of paradoxical-sleep activity increments and their decline to the stable sleeping baseline levels were relatively gradual (e.g. Figure 23a), except when a subject awoke during a paradoxical sleep episode. Then the activity levels fell abruptly to normal waking levels (e.g. Figure 22c, f). Slight activity level decrements were recorded from the caudate area, and no changes in activity levels were seen in the basomedial amygdala, periventricular hypothalamus, preoptic area, or parts of the lateral hypothalamus during paradoxical sleep (Figures 22, 23). During long periods of uninterrupted sleep, paradoxical activity increments were observed approximately every 30-40 minutes. They occurred at irregular intervals and were also irregular in magnitude and duration. The appearance of these increments was nevertheless unmistakeable at most recording sites and provided an excellent criterion for discriminating between sleeping and waking states of a subject. The high-amplitude fluctuation pattern characteristic of multiunit activity levels in the hippocampus and fornix during nonparadoxical sleep was also useful in determining the general arousal state of a subject lying motionless in the recording enclosure.

DISCUSSION

An important feature of the data is the widespread distribution of recording sites showing multi-unit activity changes specifically related to food intake. Changes in activity levels after feeding were recorded from discrete portions of the amygdala, thalamus, and hypothalamus. This finding is in general agreement with the results of chemical and electrical stimulation studies (Booth, 1967; Coury, 1967; Fisher, 1969; Grossman, 1967a, 1967b; Morgane, 1969; Robinson & Mishkin, 1962, 1968; Wagner & deGroot, 1963) and lesion studies (see Anand, 1961; Brobeck, 1960; deGroot, 1967; Morgane, 1964, 1969 for reviews), which have indicated widespread central representation of alimentary behavior.

Areas implicated in feeding behavior in this study were not as ubiquitous as electrical or chemical stimulation points yielding alimentary reactions in other experiments (Booth, 1967; Fisher, 1969; Robinson, 1964; Robinson & Mishkin, 1962, 1968). A smaller number of loci, however, were sampled in the present study. Furthermore, the multi-unit recording technique is not necessarily an exact complementary analogue of the electrical or chemical stimulation techniques, and it is possible that the positive effects of stimulation at some points in the brain are due to convergence on the relatively fewer areas shown to be affected

by food intake in the present study. It should also be noted that the brain areas sampled in this study do not constitute an exhaustive survey of subcortical structures implicated in feeding behavior. Although the recording sites were widely distributed in the thalamus, hypothalamus, and limbic areas, they were not necessarily located optimally in the feeding system.

The data clearly show, however, that a given anatomical structure, previously considered to be a functional unit in the feeding system, may be functionally differentiated with respect to feeding. Closely adjacent electrodes, or electrodes in the same anatomical region, often showed different patterns of multi-unit activity variation after food ingestion. This was particularly noticeable at recording sites in the hypothalamus. A significant result of these experiments, then, is the finding that multi-unit records from the hypothalamus conflict with previous observations of the hypothalamic components of the feeding system. The majority of lateral and ventromedial hypothalamic recording sites in the present study showed no long-term activity level changes related to feeding. While some lateral hypothalamic sites did show gradual or abrupt activity decrements after food ingestion, many did not, and records taken from the ventromedial nucleus did not reveal any corresponding activity increments after feeding. The only reciprocally-related lateral and ventral hypotha-

lamic activity level changes that occurred were recorded from only one site in each region.

A number of single-unit recording studies and neuroanatomical investigations have indicated a close, reciprocal relation between cells in the lateral and ventromedial hypothalamus (e.g. Anand, et al., 1962; Arees & Mayer, 1969; Morgane, 1961b, 1964; Oomura et al., 1962, 1964, 1967; Tsubokawa & Sutin, 1963). These results have been taken to support the concept of a lateral-ventromedial hypothalamic mechanism dominating the control of food intake. This interpretation of the single-unit data, however, assumes that relatively small samples of individual cells accurately represent an entire anatomical structure. The present data show that such an assumption is unwarranted. Moreover, the details of the single-unit studies reveal that only a certain proportion of the cells sampled in the lateral and ventromedial hypothalamus respond reciprocally. It is important to bear in mind that integrated multi-unit activity records from a brain area do not necessarily furnish a complete discription of the activity of individual cells in that area. The records obtained in this study show net changes of activity at recording sites. Some units within the area of tissue around an electrode tip may fire in ways not indicated by the records. For example, an activity increment in some cells and a simultaneous, balanced activity decrement in

others would not be reflected in the recorded multi-unit activity level. It should be understood, then, that integrated multi-unit activity can provide only a summary of neural activity at a recording site. The disagreement between multi-unit records and single-unit data is therefore not altogether surprising, although it is important. Evidently, further direct observations of the feeding system would best be undertaken at the single-unit level as well as at the multi-unit level in order to define further the location and functional attributes of feeding system components within subcortical structures.

The disagreement between multi-unit recording results and electrical stimulation or lesion results is more significant. The latter techniques have strongly encouraged the view that the lateral and ventromedial hypothalamic areas function reciprocally as homogeneous entities in the control of food intake. The results of this study contradict that view. There is little indication that the traditional lateral-ventromedial hypothalamic reciprocal relation is valid if the two areas are considered as a whole.

There is, in fact, some experimental precedent for this contradiction in the stimulation and lesion literature (see Reynolds, 1965). In an extensive study of the effects of hypothalamic lesions on food intake in rats, Kennedy (1950) found no

evidence of a "satiety center" in the ventromedial nucleus. The most effective lesions for producing hyperphagia were located slightly ventrolateral to the ventromedial nucleus. It has also been reported that, while lesions in the ventromedial nucleus produce hyperphagia in female rats, destruction of this area in male rats may have little or no effect on food intake (Cox, Kakolewski, & Valenstein, 1969; Singh, 1969; Valenstein, Cox, & Kakolewski, 1969). In one recent study (Cox et al., 1969), lesions restricted to the arcuate nucleus in one female rat clearly produced hyperphagia. In an early study by Anand & Brobeck (1951a), some lesions lateral to the ventromedial nucleus, between it and the lateral hypothalamic "feeding center", produced hyperphagia. Graff & Stellar (1962) also produced hyperphagia in rats with lesions outside and just posterior to the ventromedial nucleus. On the basis of their electrical stimulation studies with monkeys, Robinson & Mishkin (1968) concluded that the ventromedial nucleus does not apparently play a critical role in satiety in that species. There is also some evidence that electrical or chemical stimulation of the ventromedial hypothalamus in rats and cats has a general disruptive effect on behavior rather than a specific inhibitory effect on food intake (Grossman, 1966, 1967b; Krasne, 1962; Margules & Stein, 1969; Morgane, 1961; Morgane & Jacobs, 1969).

A similar functional differentiation of the lateral hypothalamus has been indicated by other electrical and chemical stimulation or lesion studies. Small lesions at separate sites within the lateral hypothalamus may affect food intake differentially, presumably by involving different parts of the feeding system within the lateral hypothalamic area (Morgane, 1961b). Electrical stimulation studies have suggested that a variety of separate neural elements mediating different types of primary behavior may be found in the lateral hypothalamus (Morgane, 1969; Stevenson, 1964; Valenstein et al., 1968, 1970). Chemical stimulation studies indicate that the functional discretion of some of these behavior substrates is based upon differential sensitivity to different synaptic transmitter substances (Blundell & Herberg, 1969; Grossman, 1962a, 1962b, 1967b; Herberg & Blundell, 1969; Miller, 1965).

The arrangement of feeding system components within the lateral and ventromedial hypothalamus may render the system particularly vulnerable to disruption at these points. Indiscriminate destruction or activation of tissue in either region may therefore be more effective than elsewhere in the feeding system, where cells mediating feeding behavior are more diffuse or redundant. Thus, the dramatic and apparently specific effects of lateral and ventromedial hypothalamic stimulation or lesions

on food intake do not necessarily imply that those structures are primarily involved in food intake regulation or even that the part of the feeding system located within these structures is more important to regulation than other parts (see Gregory, 1961).

The participation of the ventromedial nucleus and lateral hypothalamic area as units in the control of food intake is controversial, then, even in rats. It seems likely, moreover, that the arrangement of hypothalamic tissue mediating food intake regulation varies to some extent between species (Booth, 1968; Grossman, 1966). In the cat, the present data indicate that the involvement of the ventromedial nucleus, as a whole, in food intake regulation may be less important than previously believed. Similar considerations apply to the lateral hypothalamic area. The multi-unit records show that the lateral region is functionally differentiated, since food ingestion influences activity levels in different parts of the region in different ways. The observations of feeding-related activity changes on both lateral and ventral hypothalamic regions, however, characterize only restricted areas of tissue, and the data do not justify consideration of the lateral and ventromedial areas, in their entirety, as homogeneous, reciprocally-related structures exercising dominant control over feeding behavior.

Thus, the overall picture of the feeding system which emerges

from the multi-unit activity records indicates a dispersal of its components in the brain. The present data suggest, however, a more restricted anatomical distribution of the system within brain structures than stimulation or lesion techniques have implied. In particular, while several hypothalamic loci in this study were implicated in the control of food intake, the records clearly demonstrate that neither the lateral nor the ventromedial hypothalamic area functions as a homogeneous component of the feeding system. There was, in fact, no evidence that the ventromedial nucleus itself participates in long-term food intake regulation. Instead, restricted areas of tissue in the hypothalamus, thalamus, and amygdala show different kinds of activity changes after food intake, and closely adjacent portions of the same structures may show no effects. The boundaries of the feeding system thus do not appear to coincide in a simple way with presently known anatomical boundaries, and descriptions of the feeding system which refer to entire subcortical structures may be misleading.

The results of this study also extend current notions of the feeding system by suggesting that different aspects of food intake regulation may be mediated at separate brain loci. No single recording site showed a pattern of activity level changes during and after feeding which could reasonably account for all

of the requirements of food intake regulation. Activity changes specific to feeding which occurred at various thalamic, amygdaloid, and hypothalamic recording sites were not uniform among these areas, and presumably they reflect different aspects of food intake regulation. In addition to gradual activity decrements and increments following ingestion, abrupt and sustained activity level changes were observed, and variation in activity level changes during ongoing consummatory behavior was also seen. These observations do not correspond to a simple notion of paired, antagonistic neural populations controlling all aspects of regulation, even if such groups are postulated to exist in parallel at different levels of the neuraxis. Instead, the multi-unit records suggest that the requirements for regulation -- such as monitoring of intake leading to inhibition of consummatory responses, short-term maintainence of consummatory response inhibition, and long-term monitoring of nutritional status -- may be mediated by separate neural populations. Brief changes in multi-unit activity levels during consummatory behavior, particularly the graded changes seen in the dorsomedial thalamus, for example, might monitor the amount of food or water ingested, serving to signal or control the termination of responses when sufficient food or water has been ingested. Abrupt but sustained activity level changes after feeding could

maintain consummatory response inhibition until absorption of nutriments is complete. The gradual changes in activity levels observed after food intake might reflect the nutritional state of the tissues as digestion and absorption proceed, could maintain consummatory response inhibition for long periods of time, and could conceivably "reset" regulatory activity levels when energy stores are again depleted.

These notions are speculative, but they are testable. For example, feeding an immobilized animal through a gastric fistula would bypass the consummatory response controls and should result in abnormal activity level changes or no changes at all in any structures mediating short-term, pre-absorptive consummatory response regulation. If the gradual long-term activity level changes actually reflect the organism's nutritional state, those levels should not be affected abnormally by intragastric feeding, and it should be possible to manipulate them by controlling the amount of food placed in the stomach.

The failure of long-term feeding-related changes in activity levels to reflect precisely the amount of food ingested (i.e. to recycle before each feeding episode) in these experiments is understandable if the areas involved are primarily concerned with monitoring the energy requirements of the organism as distinct from feeding-motivational status in general. The small

size of the recording enclosure prohibited any great expenditure of energy by the subjects, who spent most of their time resting or sleeping. Thus, repeated episodes of eating in the absence of activity level recycling could perhaps be attributed to such non-regulatory motivational processes as displacement behavior or, more likely, an acquired habit of excessive food intake caused by previous deprivation experience. These factors would not necessarily be reflected in the activity of areas more specifically concerned with homeostatic regulatory processes.

In general, long-term activity patterns were more informative than activity levels in the hippocampus and fornix, and the data encourage the view that the hippocampus is more concerned with general arousal, response-readiness, or response lability than with long-term mediation of specific regulatory motivational variables. Although the hippocampus may participate in short-term control of feeding responses, long-term activity level differences specific to particular motivational situations seem to be confined to the amygdaloid, thalamic, and hypothalamic areas sampled in this study.

There was little evidence of selective or differential activity level changes during different types of consummatory behavior in either the fornix or the hippocampus. Activity levels in the hippocampus increased during both eating and

drinking while consummatory behavior was always associated with activity level decrements in the fornix. The decrements in fornix activity are surprising, since the hippocampus is a major contributor of fibers to that structure, but is is possible that the transformation from the ventral hippocampal activity pattern to the fornix activity pattern occurs in the dorsal hippocampus. There is some anatomical and neurophysiological evidence for dorsal-ventral functional differentiation of the hippocampus (Douglas, 1967; Elul, 1964; Raisman, Cowan, & Powell, 1966). It is also possible that the activity differences are due to extra-hippocampal inputs to the fornix, which are numerous (Nauta, 1958).

The details of records taken from the fornix (Figures 16, 17) do show some differences in activity patterns during feeding and drinking, although the average activity levels are about the same. During feeding, fluctuations in activity levels are not entirely eliminated, but during drinking the activity levels appear to be quite stable. It is not clear whether these differences are significant. A finer analysis of neural activity, such as microelectrode recording can provide, might reveal important differences in individual cellular discharge patterns during different types of consummatory response.

The striking feature of multi-unit activity at recording

sites in the hippocampus and its main efferent bundle, the fornix, was the appearance of irregular, high-amplitude activity level fluctuations when the animal was at rest. The frequencies of these fluctuations were well below electroencephalographic theta rhythm frequencies that have been recorded from the hippocampus (Grastyan et al., 1966; Routtenberg, 1968; Vanderwolf, 1969). Orientation to stimuli, changes in the resting position, or locomotion were associated with the disappearance of this pattern and, usually, concomitant increments in activity levels. It was not possible to determine whether these changes in activity were primarily sensory-related or response-related, but it is noteworthy that such changes persisted in some cases for several minutes after termination of the original disturbing stimulus, during which time overt behavioral responses were often absent. Here, too, an immobilized preparation could probably provide useful information about the nature of these changes.

A simple expression of the relation between hippocampal-fornix activity and the behavior of the subjects is that the fluctuating pattern of multi-unit activity appears whenever arousing stimuli or overt responses are absent. The disappearance of the pattern coincides with any motor activity or disturbance of the animal. Within these limits, multi-unit activity

in the fornix and hippocampus furnished a sensitive, graded indication of the arousal state of the animal.

If the fluctuation pattern is considered alone, changes in multi-unit activity at hippocampal and fornix sites are largely nonspecific; the pattern is reduced or disappears whenever the animal is behaviorally aroused. This nonspecificity of activity changes corresponds fairly well with the view that the hippocampus plays a role in general response inhibition (Daland, 1970; McCleary, 1966). In addition to the previously mentioned effects on food intake, hippocampal lesions have been shown to cause response perseveration in a variety of behavioral situations. Reported alterations in food intake following hippocampal damage might be attributable, therefore, to a failure of consummatory response inhibition normally mediated by the hippocampus. Elimination of the fluctuation pattern in the hippocampus and fornix during consummatory behavior may thus coincide with consummatory response disinhibition. Activity level increments in both structures in the absence of the fluctuation pattern during general arousal might coincide with inhibition of consummatory behavior as the organism orients to new stimuli or prepares for other responses. The extensive projections of the fornix to hypothalamic areas (Nauta, 1958; Raisman, 1966) could transmit such hippocampal and other limbic influences.

The results of this study indicate that general arousal effects are exerted independently of regulatory motivational influences (see Bambridge, 1968; Podvoll & Goodman, 1967). Activity level changes associated with arousing stimulation or motor activity are identical in the deprived and satiated subject. In the hippocampus and fornix, no differences in the appearance of the activity fluctuation pattern were noted during deprivation and satiation in the same subject. Long-term changes in multi-unit activity levels in hypothalamic areas after feeding involved lower or higher sustained activity levels during sleep in the satiated animal than in the deprived animal. Thus, the range of activity level variation between sleeping and waking states in such areas is shifted as a whole by the change in motivational state, but the general covariance of activity in all areas and the appearance of phasic activity level changes during arousal remain unchanged.

In summary, then, arousal-related changes in multi-unit activity levels in parts of the amygdala, thalamus, and hypothalamus appear to be superimposed upon long-term activity levels determined by the motivational or nutritional state of the organism. Specific motivational regulatory function appears to be largely restricted to these areas, where general arousal effects are exerted nonspecifically. Conversely, long-term specific

motivational variables do not appear to be mediated at sites in the hippocampus or in the fornix, but general arousal was sensitively reflected by multi-unit activity patterns in those structures.

Multi-unit activity recording has provided a useful picture of activity level changes related to food intake in neural populations at various brain loci. Some suggestions for extensions of the present experiments have already been made. Perhaps the most fruitful experimental approach to neural function underlying feeding behavior would involve a combination of techniques allowing simultaneous manipulation and recording of neural activity at separate brain loci. The application of indiscriminate lesioning and stimulation techniques in isolation, while useful in the early stages of investigation, appears to have limited utility at this time for detailed analysis of the normal functional characteristics of the feeding system. Further investigation of the feeding system, involving refinement of the multi-unit recording technique (e.g. Buchwald, Weber, Holstein, Grover, & Schwafel, 1969), more control over motivational variables, more extensive sampling of brain areas at the single-unit and multi-unit levels, and a wider variety of behavioral situations, should result in a better understanding of the operating principles of the feeding system and its components.

SUMMARY

Integrated multi-unit activity before, during, and after food and water ingestion was recorded from 47 electrodes chronically implanted in 16 cats. Activity level changes specifically related to food intake occurred reliably at only 10 sites, which were located in amygdaloid, thalamic, and hypothalamic structures. Records from several electrodes placed in the lateral and ventromedial hypothalamic areas and in telencephalic limbic structures which have been implicated in the control of food intake did not show long-term changes related to feeding. It is concluded that components of the feeding system are widely distributed in the brain but are not uniformly distributed within subcortical structures. Descriptions of the food intake regulatory system which refer to entire brain structures therefore do not adequately specify the anatomical localization of the system. The implications of the data are discussed with respect to the traditional view of the feeding system. The data also suggest that separate aspects of food intake regulation are mediated by different components of the feeding system and that hippocampal contributions to regulation, if any, are of a short-term nature. General arousal effects appear to be exerted independently of regulatory motivational effects and influence

short-term activity fluctuations at some loci and long-term activity levels at others. Some suggestions are made for further research to extend the present work.

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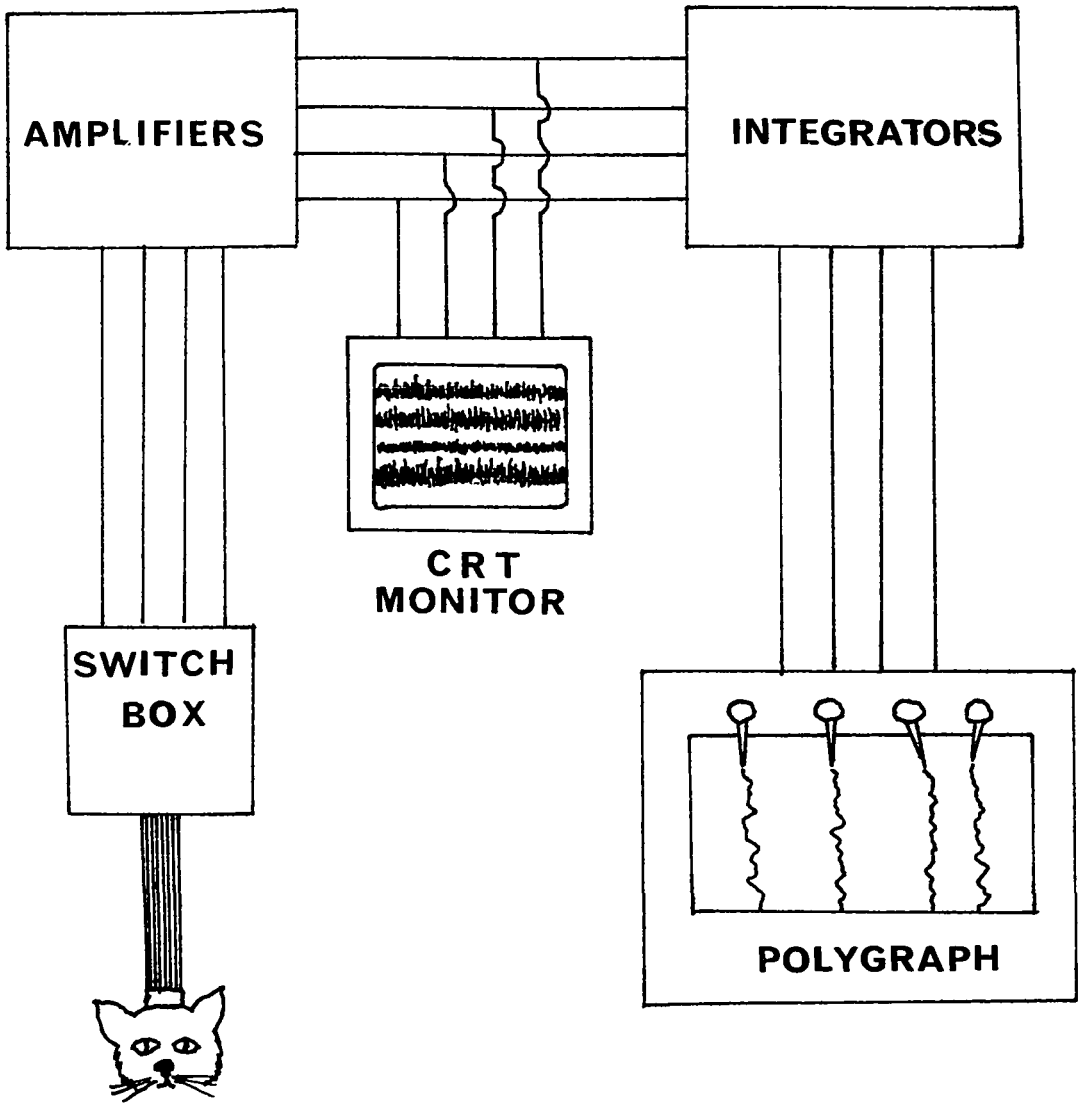


Figure 1. Block diagram of recording system.

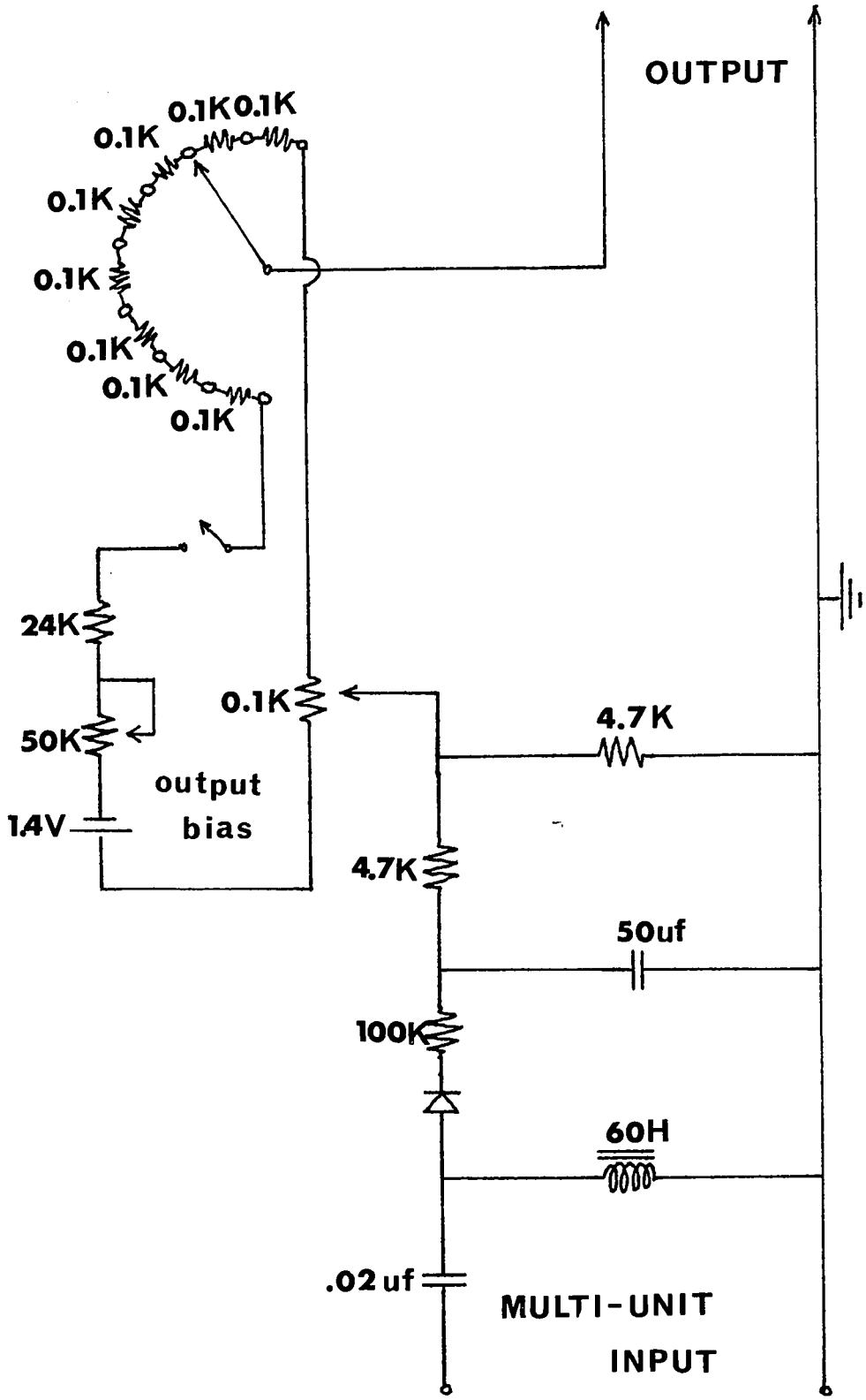


Figure 2. Integrator circuit.

Figure 3. Typical postures and multi-unit activity records associated with various categories of behavioral arousal referred to in text and figures. Fornix: Electrode 29. Lateral hypothalamus: Electrode 30. Horizontal calibration: 1 minute. Vertical calibrations: 10% of signal.

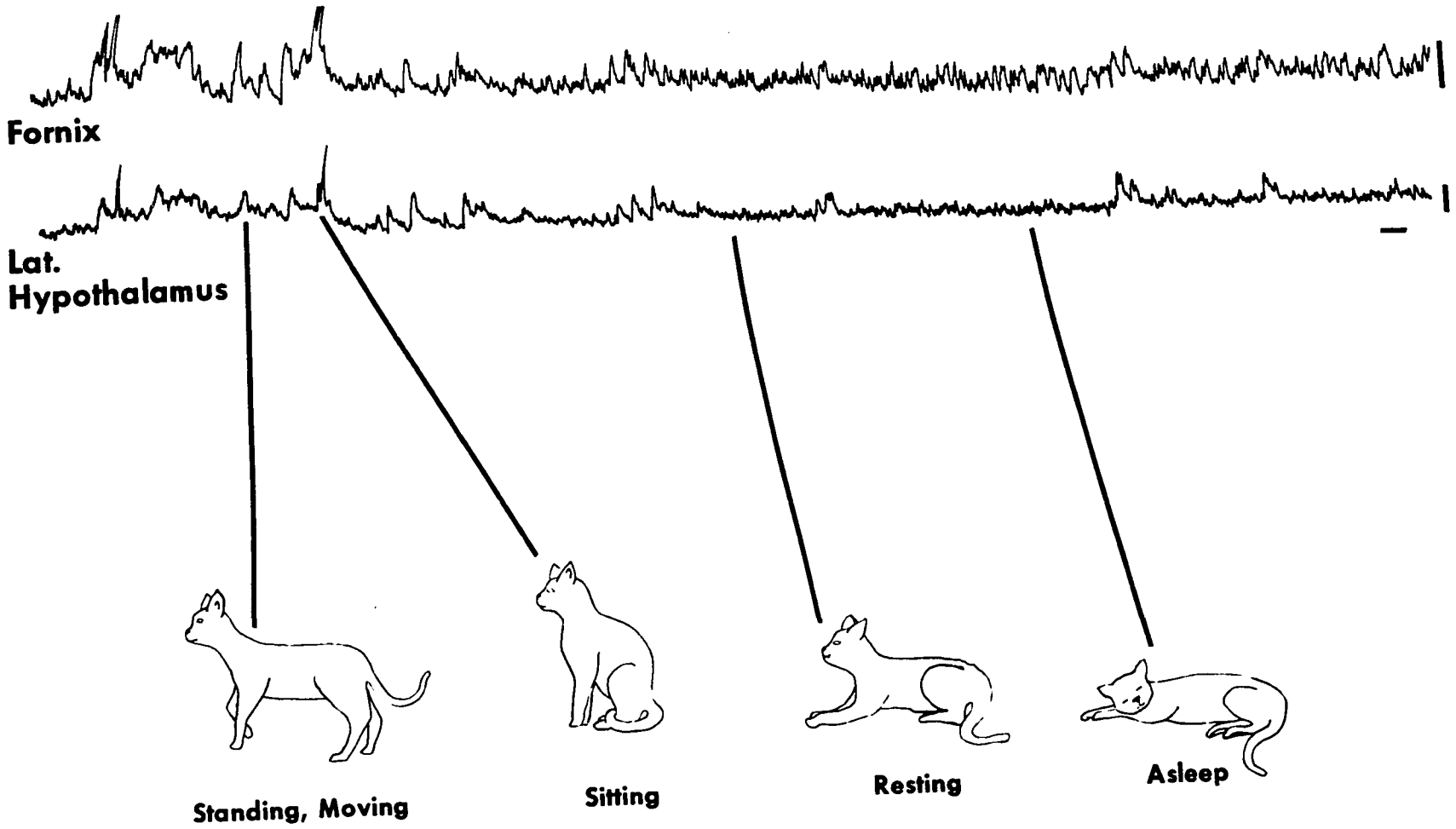
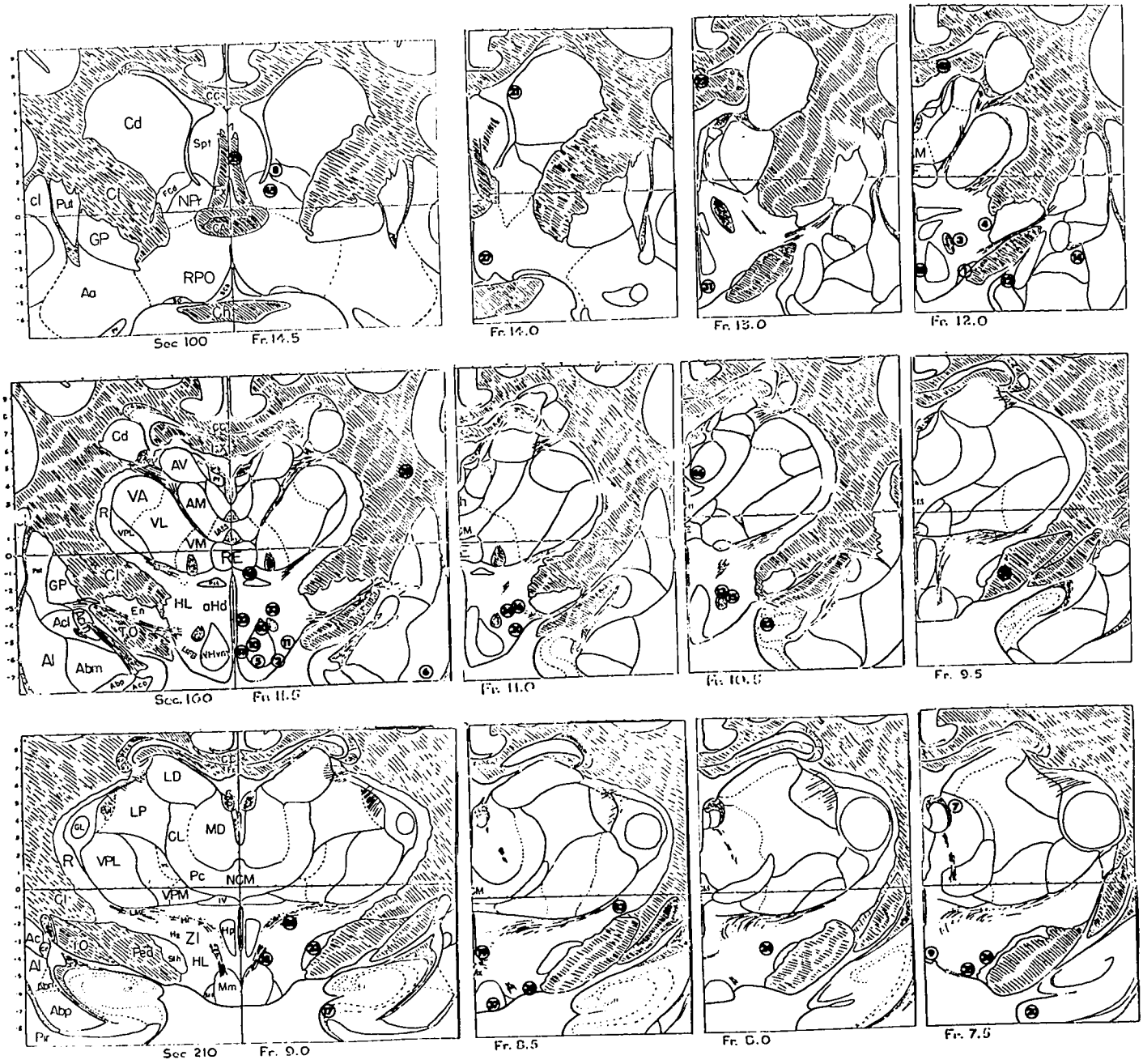

Fornix
Lat.
Hypothalamus
Standing, Moving
Sitting
Resting
Asleep

Figure 4. Distribution of the 47 electrode placements from which records were obtained. Atlas pages taken from the Jasper--Ajmone-Marsan (1954) stereotaxic atlas of the cat brain. Aco = cortical amygdaloid nucleus, Abm = Basal amygdaloid nucleus (pars magnocellularis), aHd = dorsal hypothalamic area, Al = lateral amygdaloid nucleus, Cd = caudate nucleus, Ch = optic chiasm, Fx = fornix, HL = lateral hypothalamus, MD = dorsomedial nucleus, MFB = medial forebrain bundle, Mm = medial mammillary body, NHvm = ventromedial hypothalamic nucleus, NPr = prothalamic nucleus, Sth = subthalamic nucleus, TO = optic tract, ZI = zona incerta.


Cd
Spt
cl
Put
C
NPr
GP
RPO
Aa
CPi
Sec 100
Fr. 14.5
Fr. 14.0
Fr. 13.0
M
Fr. 12.0
Cd
AV
VA
AM
R
VL
VPL
VM
RE
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C
HL
aHd
En
Acl
TO
Al
Abm
Sec. 100
Fr. 11.5
Fr. 11.0
Fr. 10.5
Fr. 9.5
LD
LP
CL
MD
R
VPL
Pc
NCM
VPM
Acl
TO
ZI
Al
Pea
HL
Mm
Abp
Pir
Sec 210
Fr. 9.0
Fr. 8.5
Fr. 8.0
Fr. 7.5

Figure 5. Examples of gradual and abrupt activity decrements at different lateral hypothalamic loci after food intake. Dark bars: food intake. Striped bar: water intake. Horizontal calibration: 1 minute. Vertical calibration: 10% of signal.

A. Electrode 30. Continuous record.

B. Electrode 33. The sudden, brief deflection of the pen after water intake is due to mechanical artifact.

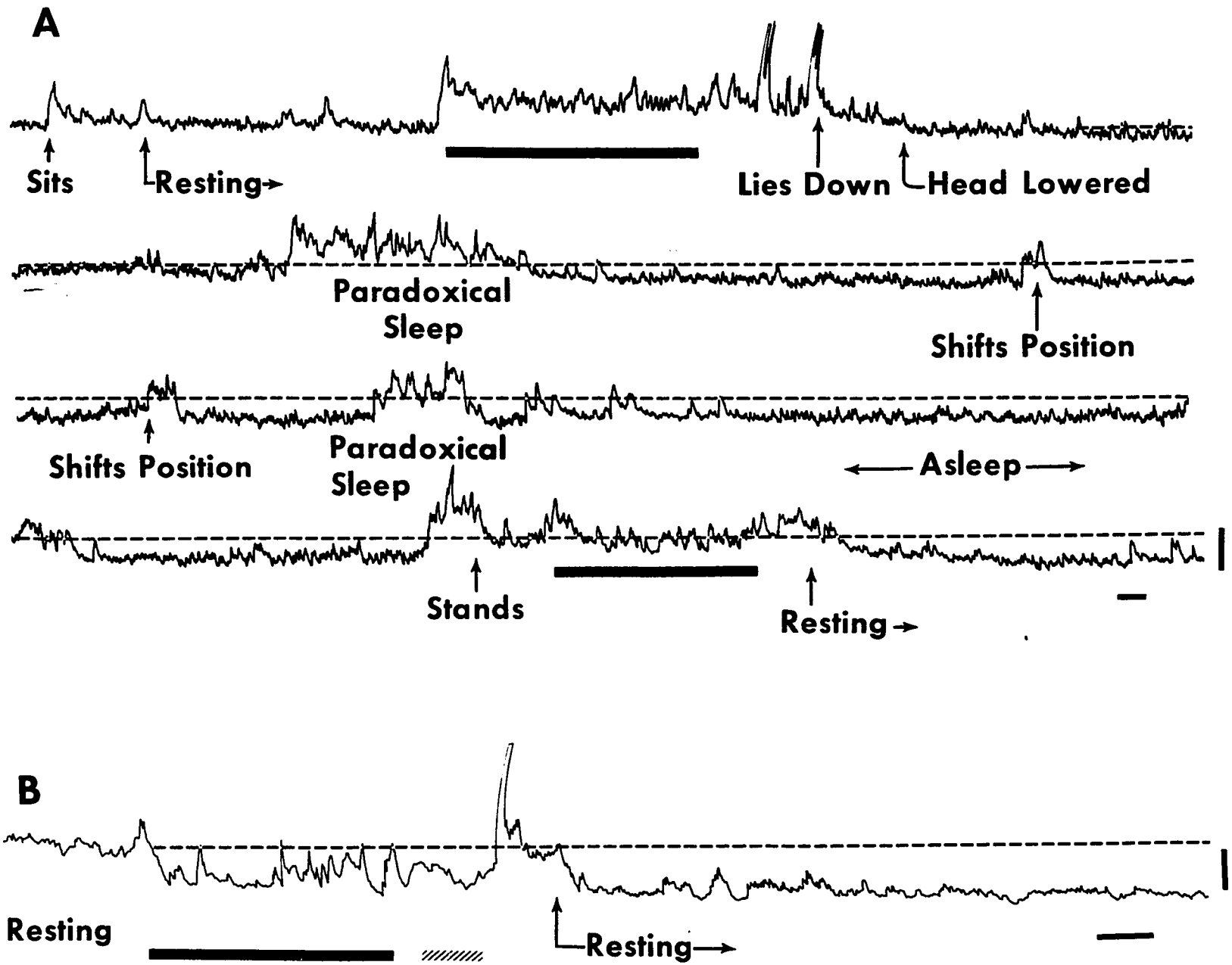

A
Sits
Resting
Lies Down
Head Lowered
Paradoxical
Sleep
Shifts Position
Shifts Position
Paradoxical
Sleep
Asleep
Stands
Resting
B
Resting
Resting

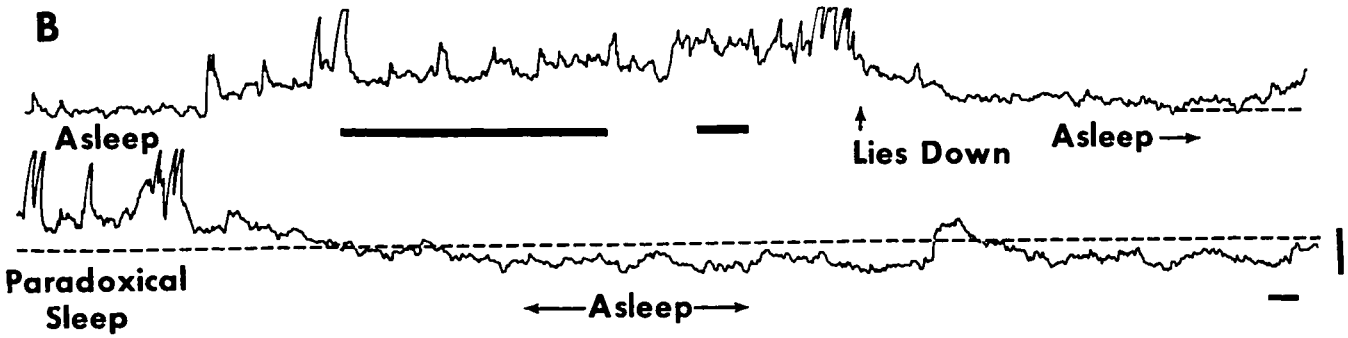
Figure 6. Continuous records of gradual multi-unit activity decrements at hypothalamic loci after food intake. Dark bars: food intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 32. Periventricular hypothalamus.

B. Electrode 36. Zona incerta.

C. Electrode 38. Posteroventral hypothalamic region.


A
Asleep
Grooming
Grooming
Lies Down
←Asleep→


B
Asleep
Lies Down
Asleep→
Paradoxical
Sleep
←Asleep→

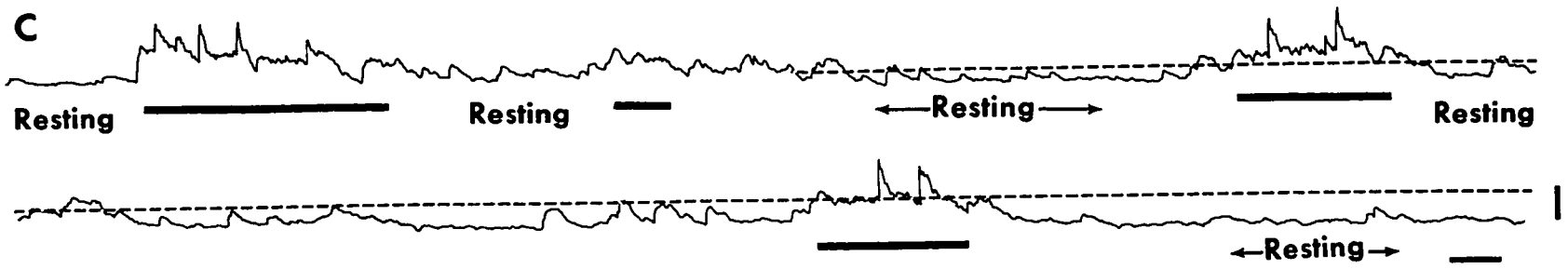

C
Resting
Resting
←Resting→
Resting
←Resting→

Figure 7. Electrode 37. Continuous record of gradual multi-unit activity increment in medial mammillary body after food intake. Activity level change continues through successive feeding episodes. Full deflections of pen during moving and grooming are due to mechanical artifacts. Dark bars: food intake. Horizontal calibration: 1 minute. Vertical calibration: 10% of signal.

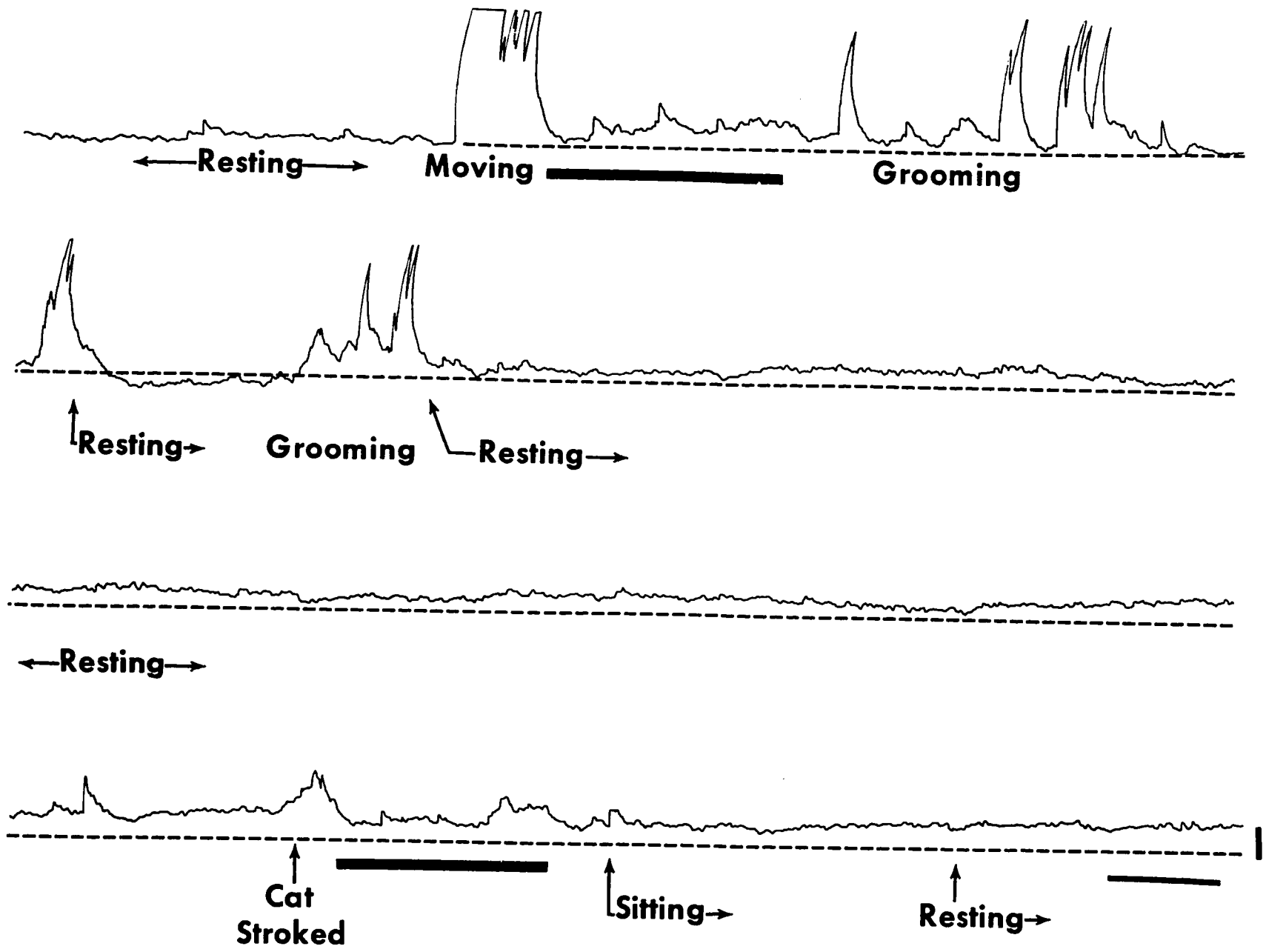
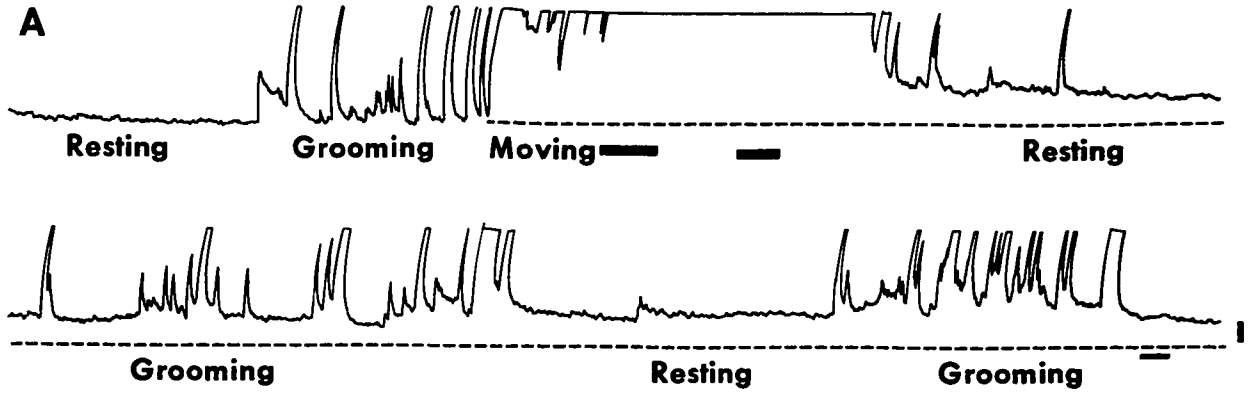

Resting
Moving
Grooming
Resting
Grooming
Resting
Resting
Cat
Stroked
Sitting
Resting

Figure 8. Continuous records of abrupt multi-unit activity increments in ventrolateral hypothalamus and amygdala after food intake. Successive feeding episodes do not alter changed activity levels after initial food intake at either locus. Full deflections of pen during moving, eating, and grooming are due to mechanical artifacts. Dark bars: food intake. Horizontal calibration: 1 minute. Vertical calibration: 10% of signal.

A. Electrode 2. Ventrolateral hypothalamus.

B. Electrode 12. Cortical amygdaloid nucleus.


A
Resting
Grooming
Moving
Resting
Grooming
Resting
Grooming

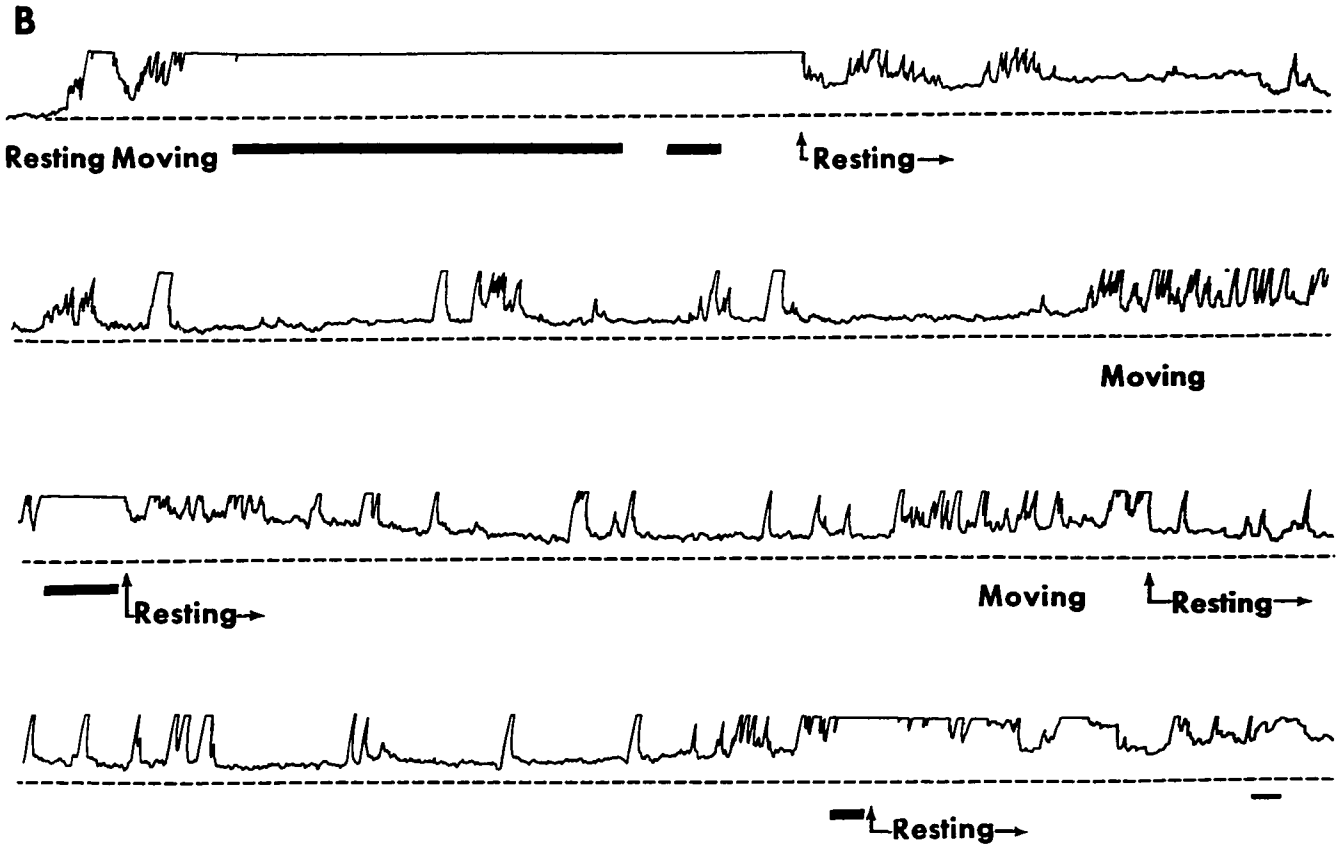
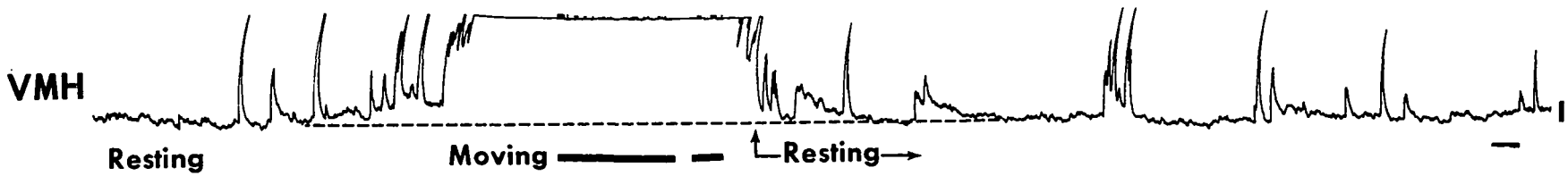
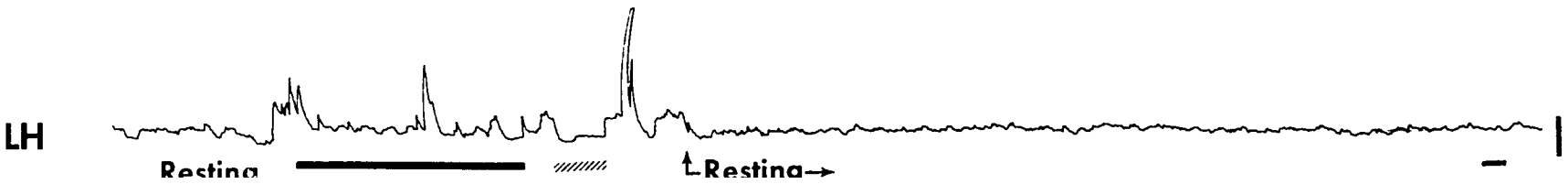
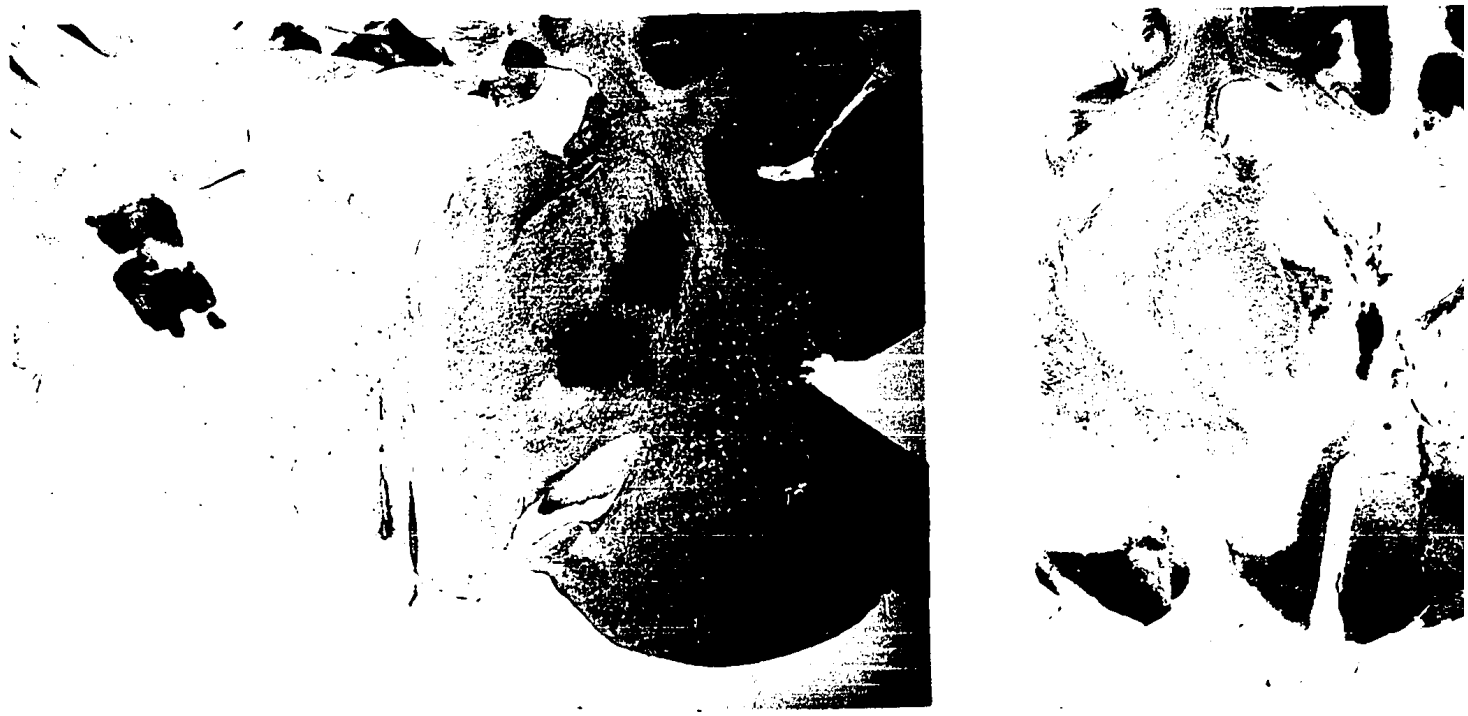

B
Resting Moving
Resting
Moving
Resting
Moving
Resting
Resting

Figure 9. Lack of effect of food intake on activity levels in lateral and ventromedial hypothalamic sites. The records shown are also typical of those obtained from several other sites in the lateral and ventromedial hypothalamic areas (electrodes 4, 5, 11, 13, 15, 16, 18, 34, 40, 41). LH: Electrode 3, lateral hypothalamus. VMH: Electrode 10, ventromedial hypothalamic nucleus. The activity level from the VMH electrode during food intake is occluded by mechanical artifact. Dark bars: food intake. Striped bar: water intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.


VMH
LH

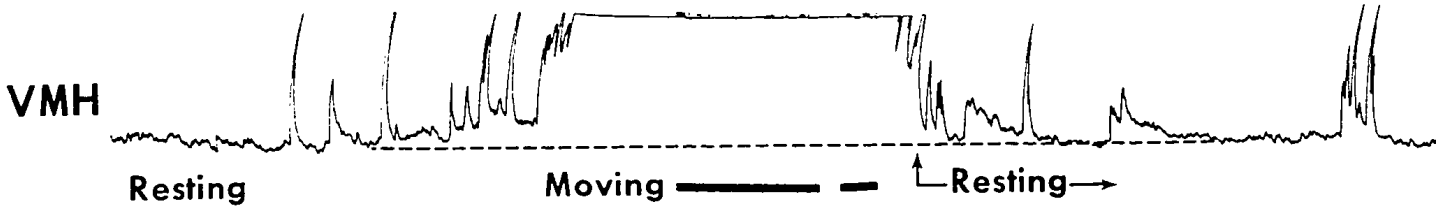

VMH
Resting
Moving
Resting

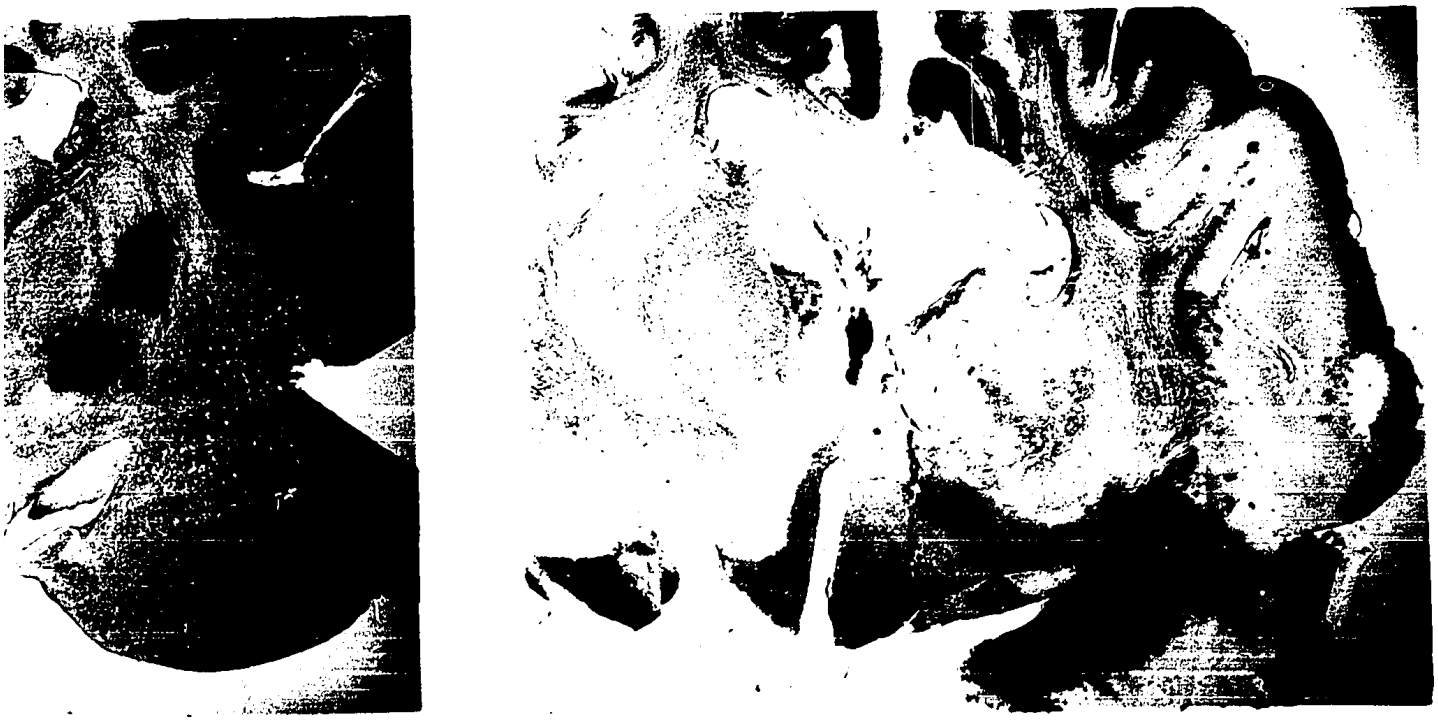

LH
Resting
Resting



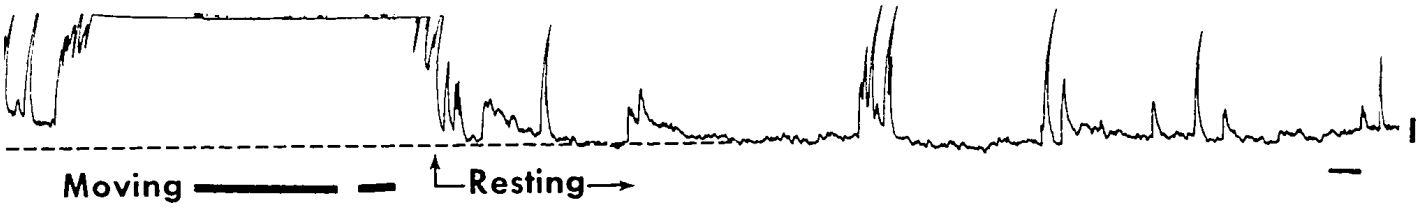
VMH

L





LH



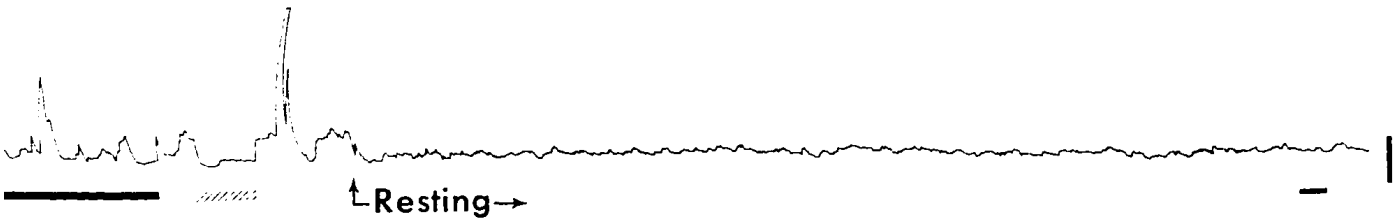
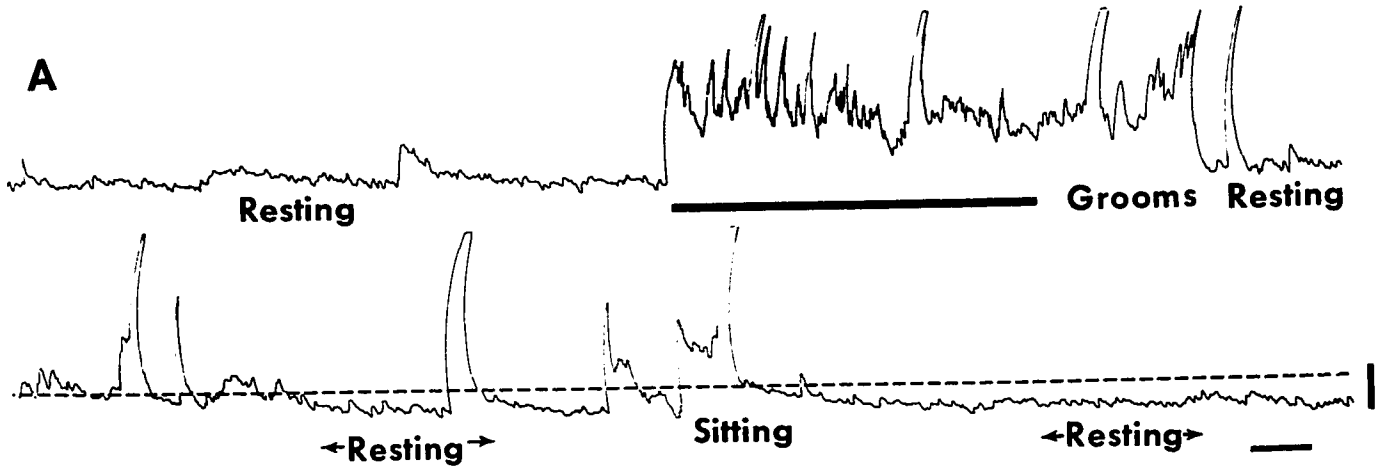


Figure 10. Continuous records of gradual multi-unit activity decrements at thalamic and subthalamic loci after feeding. Dark bars: food intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 45. Prothalamic nucleus.

B. Electrode 23. Subthalamic nucleus. Note partial reversal of activity level decrement, which consistently occurred approximately 20 - 25 minutes after food ingestion.


A
Resting
Grooms
Resting
Resting
Sitting
Resting

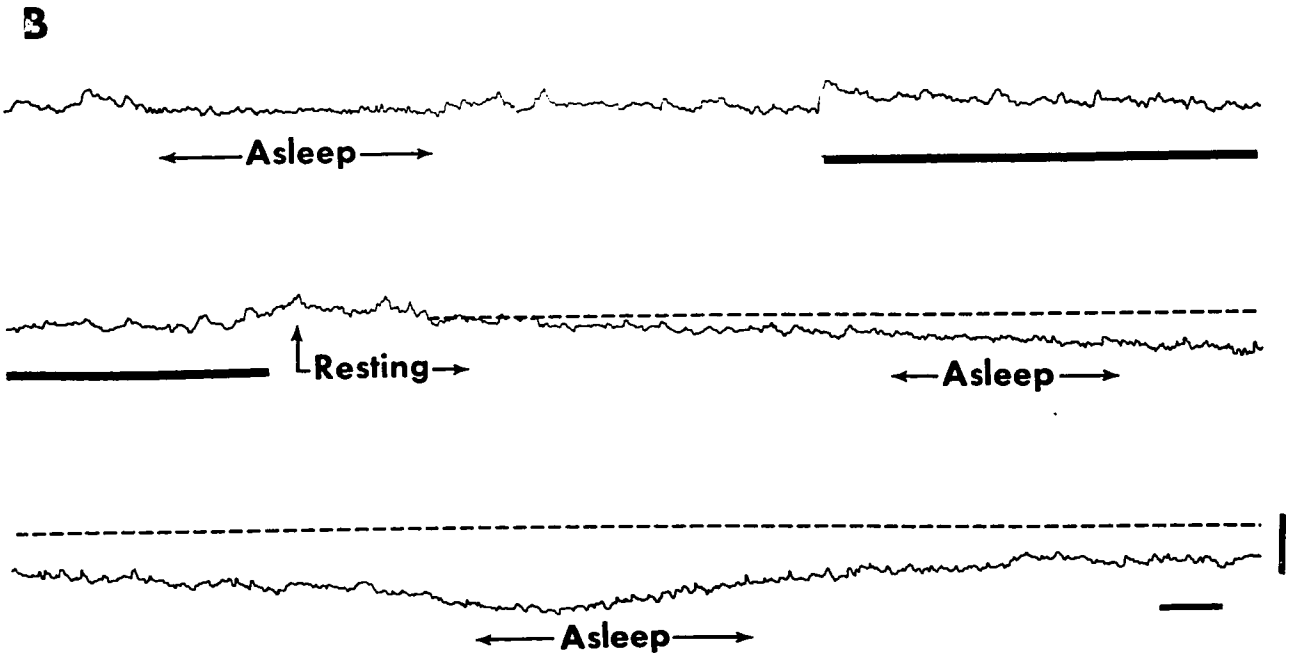

B
Asleep
Resting
Asleep
Asleep

Figure 11. Lack of long-term effect of food intake on activity levels at various telencephalic recording sites, many of which have been implicated in food intake regulation by electrical and chemical stimulation or lesion techniques. Dark bars: food intake. Striped bars: water intake. Horizontal calibration: 1 minute. Vertical calibration: 10% of signal.

A. Electrode 42. Ventral hippocampus. Activity levels during eating and moving are occluded by artifact.

B. Electrode 14. Basomedial amygdala.

C. Electrode 29. Fornix.

D. Electrode 27. Preoptic area.

E. Electrode 21. Caudate nucleus.

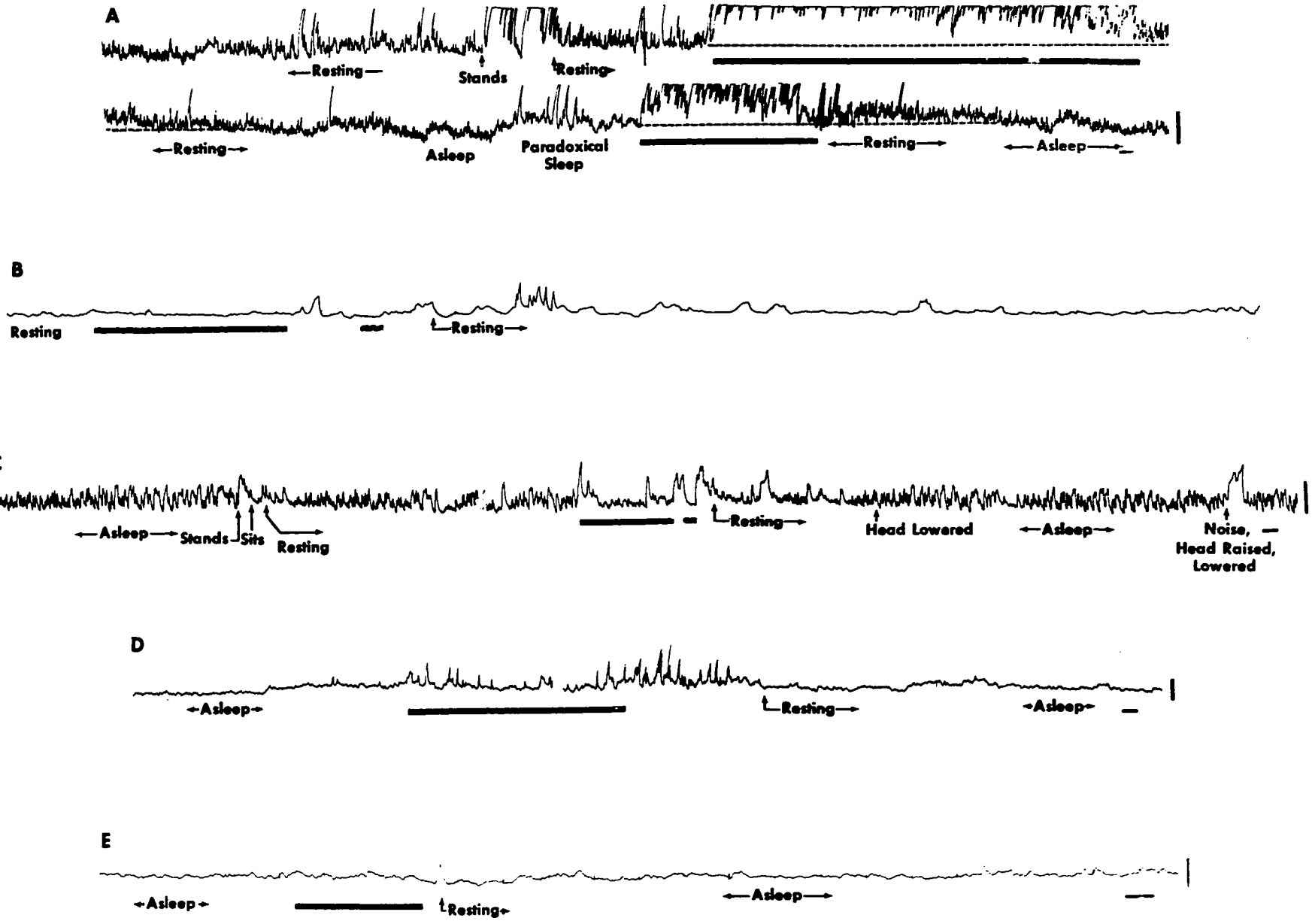

A
Resting
Stands
Resting
Resting
Asleep
Paradoxical Sleep
Resting
Asleep
B
Resting
Resting
C
Asleep
Stands
Sits
Resting
Resting
Head Lowered
Asleep
Noise, Head Raised, Lowered
D
Asleep
Resting
Asleep
E
Asleep
Resting
Asleep

Figure 12. Lack of long-term effect of food intake on activity levels at various telencephalic and diencephalic recording sites. Dark bars: food intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 46. Dorsomedial thalamus. Continuous record, occluded by mechanical artifact during eating and grooming.

B. Electrode 6. Lateral amygdala. Full pen deflections are due to artifact.

C. Electrode 18. Lateral hypothalamus near mammillothalamic tract.

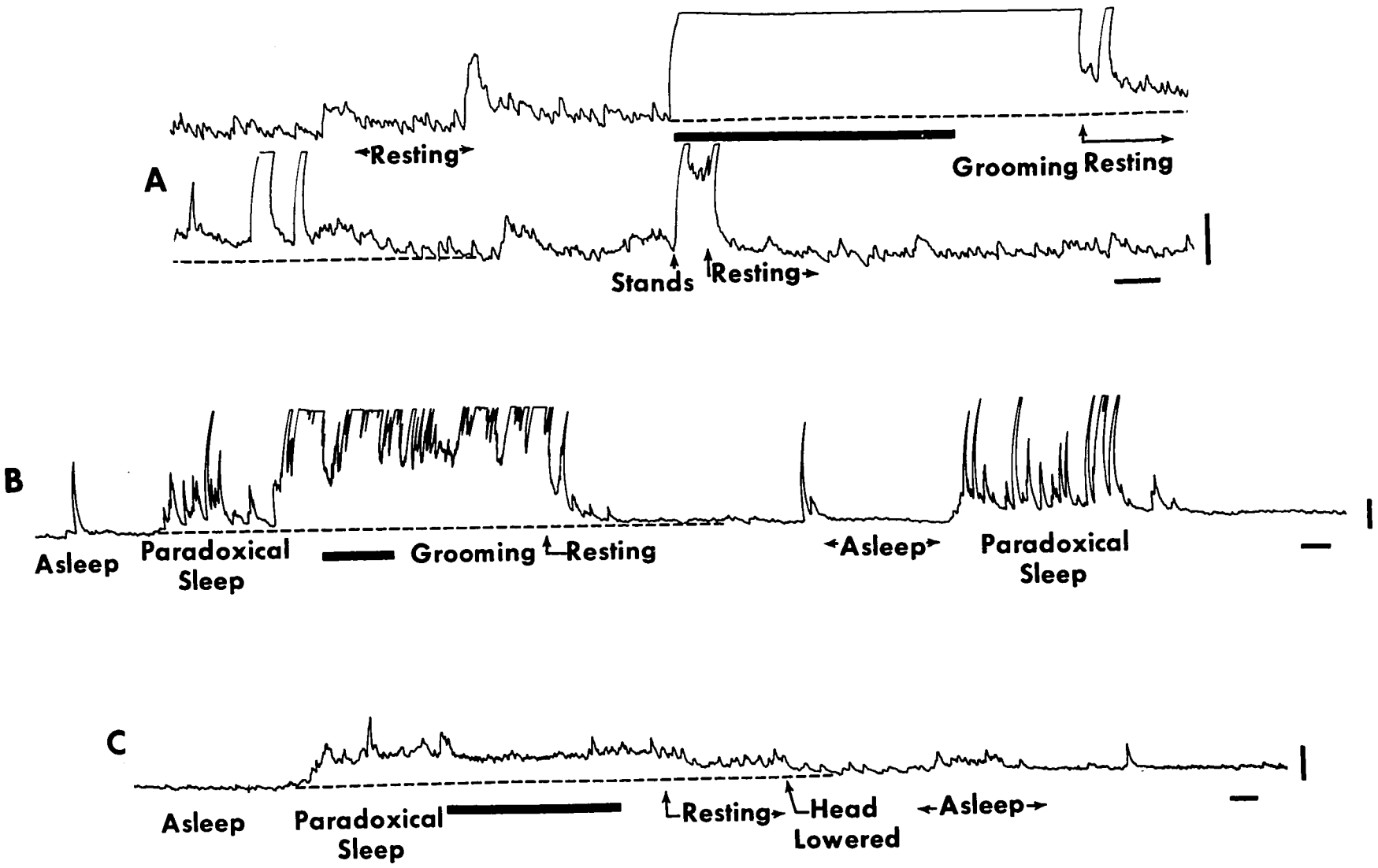

A
Resting
Grooming
Resting
Stands
Resting
B
Asleep
Paradoxical Sleep
Grooming
Resting
Asleep
Paradoxical Sleep
C
Asleep
Paradoxical Sleep
Resting
Head Lowered
Asleep

Figure 13. Examples of lack of activity level changes during consummatory responses. All records in this figure were taken from resting animals. Dark bars: food intake. Striped bars: water intake. Vertical calibrations: 10% of signal.

A. Electrode 32. Periventricular hypothalamus.

B. Electrode 34. Lateral hypothalamus

C. Electrode 27. Preoptic area.

D. Electrode 28. Periventricular hypothalamus.

E. Electrode 19. Lateral hypothalamus near supramammillary chiasm.

F. Electrode 18. Lateral hypothalamus near mammillothalamic tract.

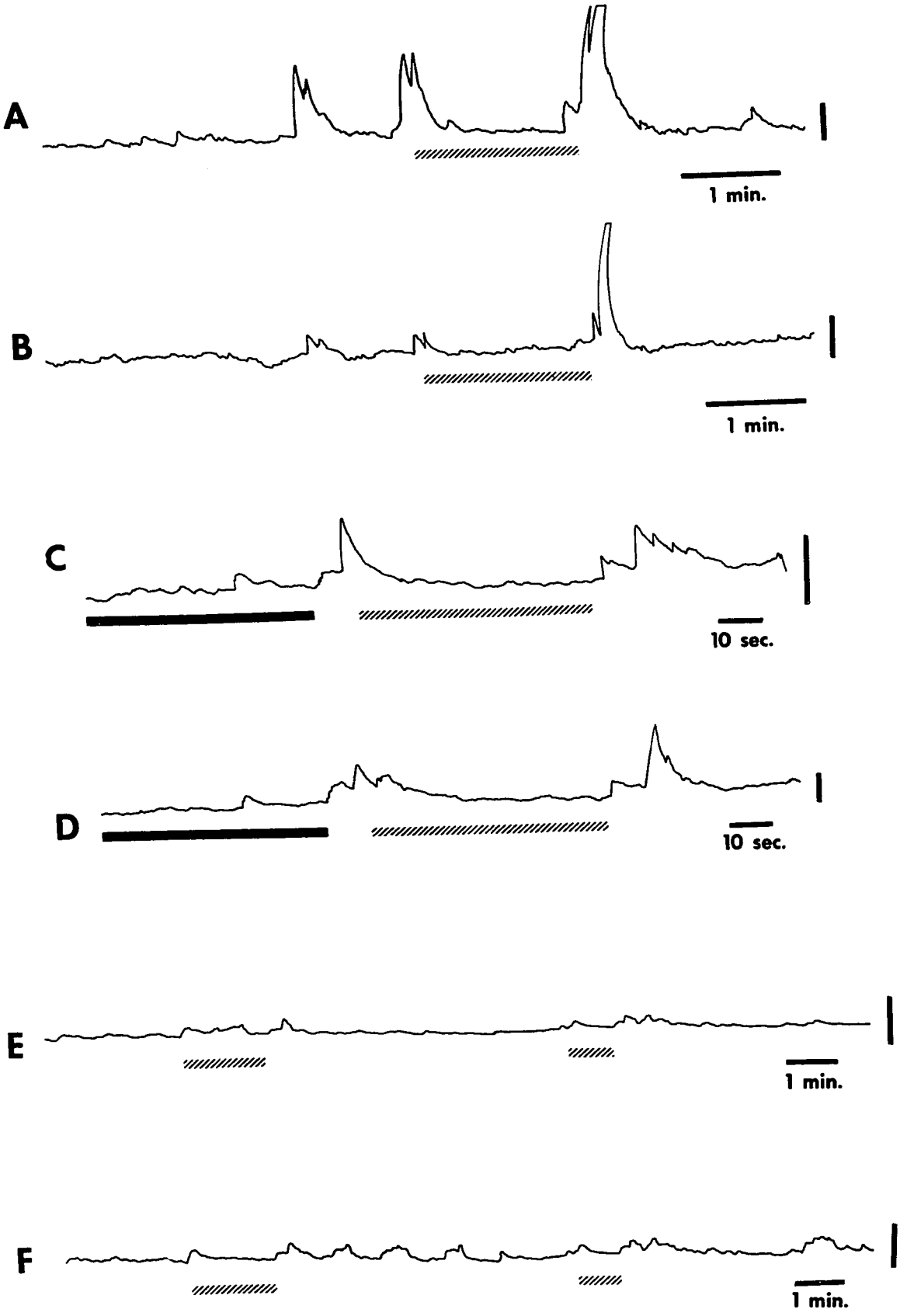

A
1 min.
B
1 min.
C
10 sec.
D
10 sec.
E
1 min.
F
1 min.

Figure 14. Examples of apparently reduced activity levels during drinking. The effect was reliable at these sites but was more noticeable with high activity levels previous to water intake. Full pen deflections are due to mechanical artifact. Dark bars: food intake. Striped bars: water intake. Horizontal calibrations: 1 minute (except as noted). Vertical calibrations: 10% of signal.

A. Electrode 30. Lateral hypothalamus.

B. Electrode 26. Zona incerta.

C. Electrode 36. Ventral zona incerta.

D. Electrode 37. Medial mammillary body.

E. Electrode 38. Posteroventral hypothalamic region.

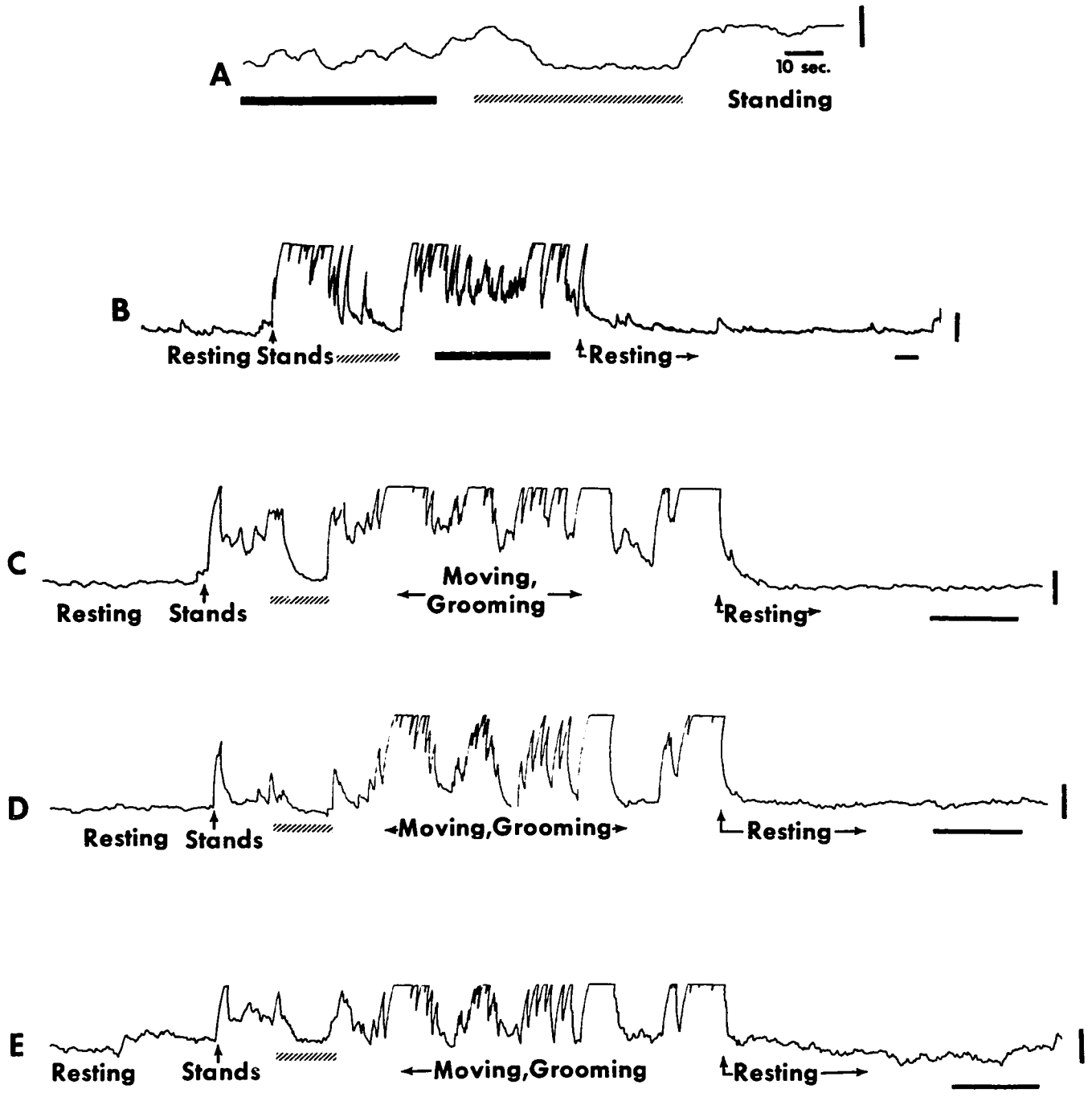

A
10 sec.
Standing
B
Resting
Stands
Resting
C
Resting
Stands
Moving,
Grooming
Resting
D
Resting
Stands
Moving,Grooming
Resting
E
Resting
Stands
Moving,Grooming
Resting

Figure 15. Discrepancies between activity levels during food intake and during water intake. Dark bars: food intake. Striped bars: water intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 31. Anteroventral hypothalamus.

B. Electrode 30. Lateral hypothalamus.

C. Electrode 15. Lateral hypothalamus. Note that activity level during drinking is lower than during eating.

D. Electrode 13. Lateral hypothalamus. Activity level during drinking is higher than during eating. Note the close juxtaposition of electrodes 13 and 15 (in the same cat) and the different activity level relations recorded from them simultaneously during consummatory behavior.

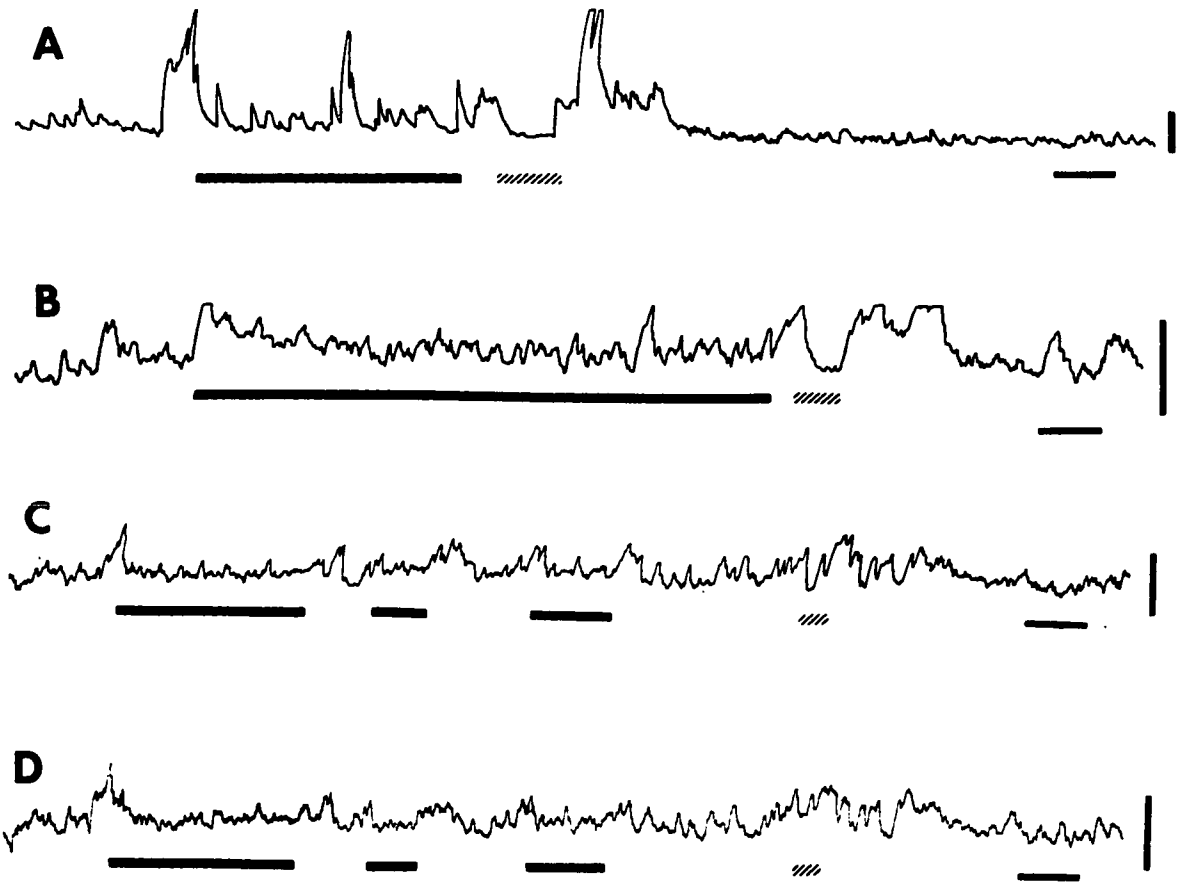

A
B
C
D

Figure 16. Activity levels in ventral hippocampus and fornix during feeding. Records also illustrate characteristic activity level fluctuation pattern in these areas and its relation to general arousal. Dark bars: food intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 17. Ventral hippocampus.

B. Electrode 29. Anterior fornix.

C. Electrode 47. Dorsal fornix.

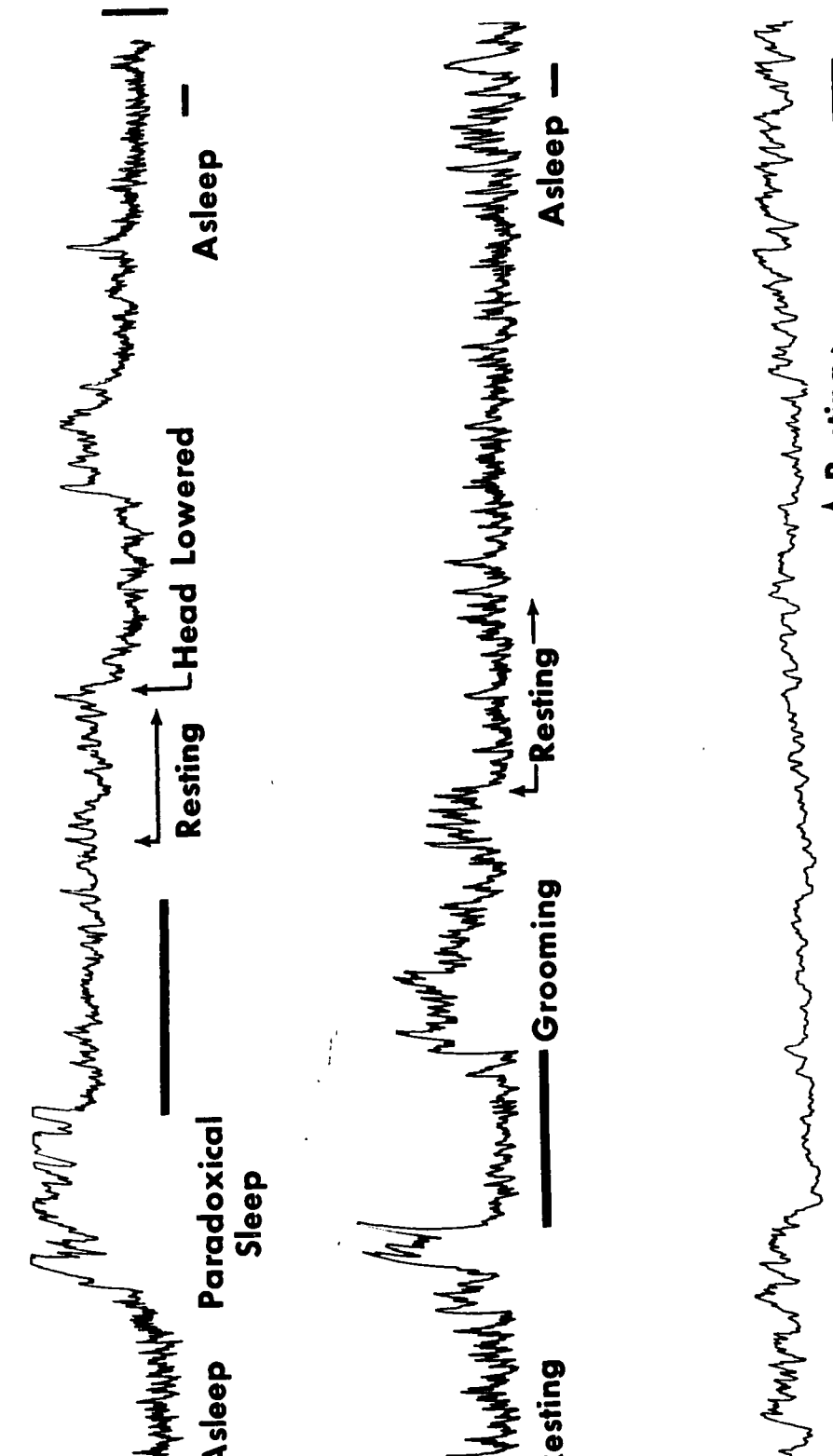

A
Asleep
Paradoxical Sleep
Resting
Head Lowered
Asleep
B
Resting
Grooming
Resting
Asleep
C
Resting
Resting

Figure 17. Activity levels in ventral hippocampus and fornix during drinking. Striped bars: water intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 17. Ventral hippocampus.

B. Electrode 29. Anterior fornix.

C. Electrode 47. Dorsal fornix.

D. Electrode 22. Dorsal fornix.

E. Electrode 33. Perifornical lateral hypothalamus. Full pen deflections are due to mechanical artifact.

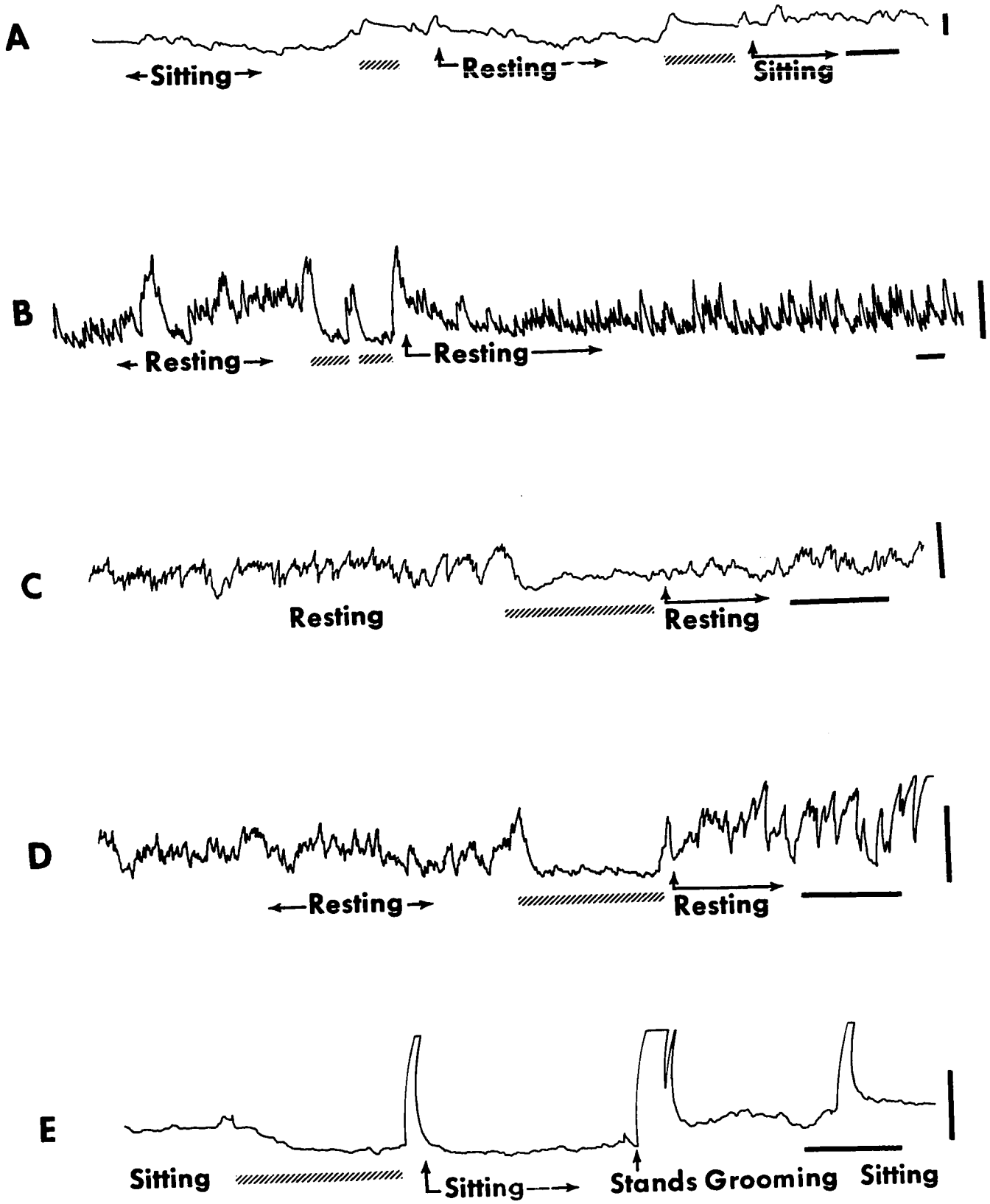

A
Sitting
Resting
Sitting
B
Resting
Resting
C
Resting
Resting
D
Resting
Resting
E
Sitting
Sitting
Stands
Grooming
Sitting

Figure 18. Stable and graded multi-unit activity increments at different loci during drinking. Dark bar: food intake. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 23. Subthalamic nucleus.

B. Electrode 24. Lateral hypothalamus, vicinity of zona incerta.

C. Electrode 46. Dorsomedial thalamus. Continuous record. During eating and grooming, activity levels are largely occluded by mechanical artifact. Graded activity increments during drinking appear to begin and to terminate at approximately the same absolute levels in successive drinking episodes. Full pen deflections are due to mechanical artifact.

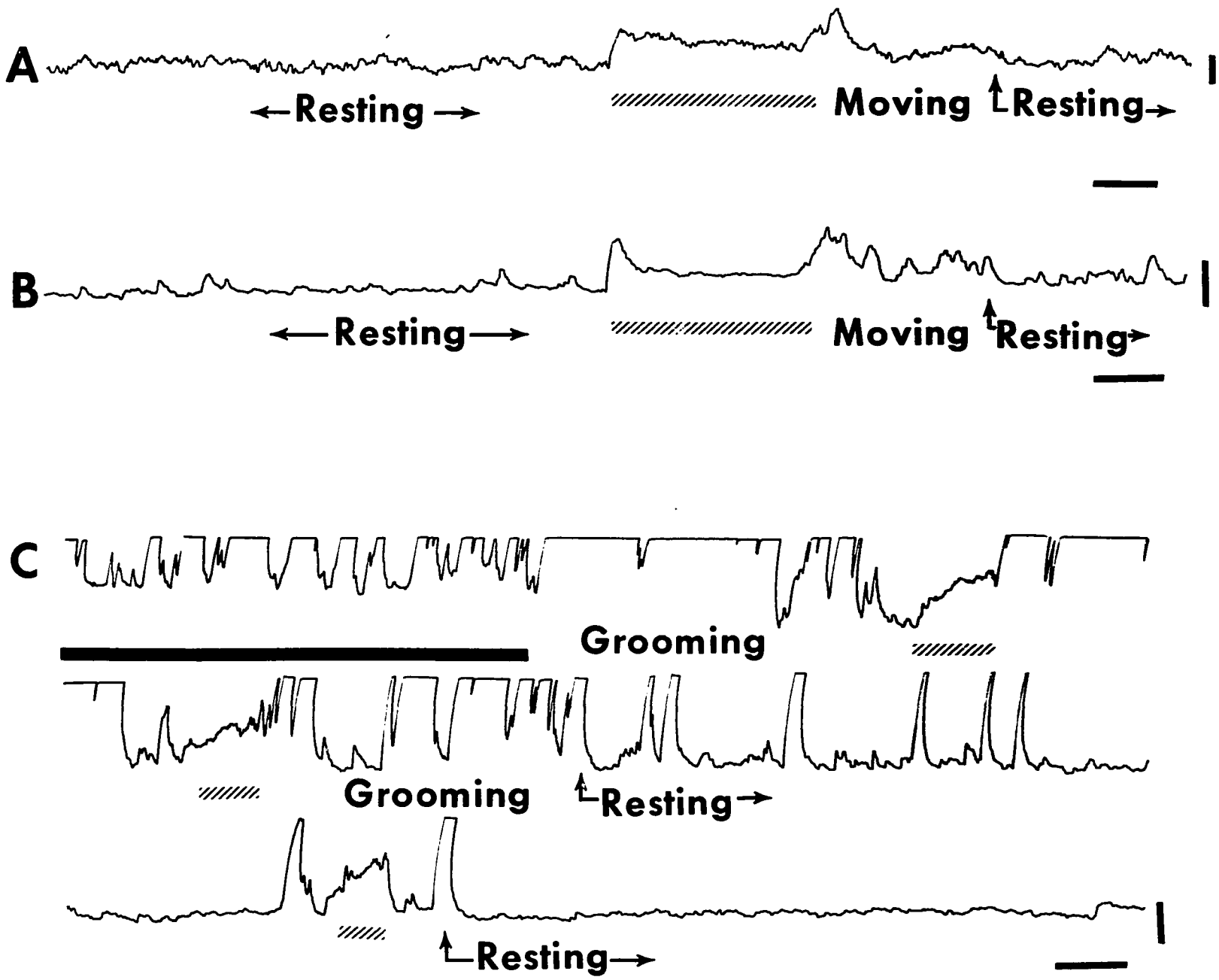

A
Resting
Moving
Resting
B
Resting
Moving
Resting
C
Grooming
Grooming
Resting
Resting

Figure 19. Reciprocal resting activity level relations between talencephalic and diencephalic sites in two subjects. Vertical calibrations: 10% of signal.

A. (1) Electrode 28. Periventricular hypothalamus.

(2) Electrode 29. Fornix.

These records, taken simultaneously from one subject, are roughly reciprocal in fine detail, but long-term, sustained activity levels were not reciprocally related.

B. (1) Electrode 14. Basomedial amygdala.

(2) Electrode 15. Perifornical lateral hypothalamus.

(3) Electrode 16. Perifornical lateral hypothalamus.

Activity levels in amygdalar and hypothalamic sites in this subject are generally reciprocal over a longer time base than in A. Fine details of these records, however, tend to show parallel variation.

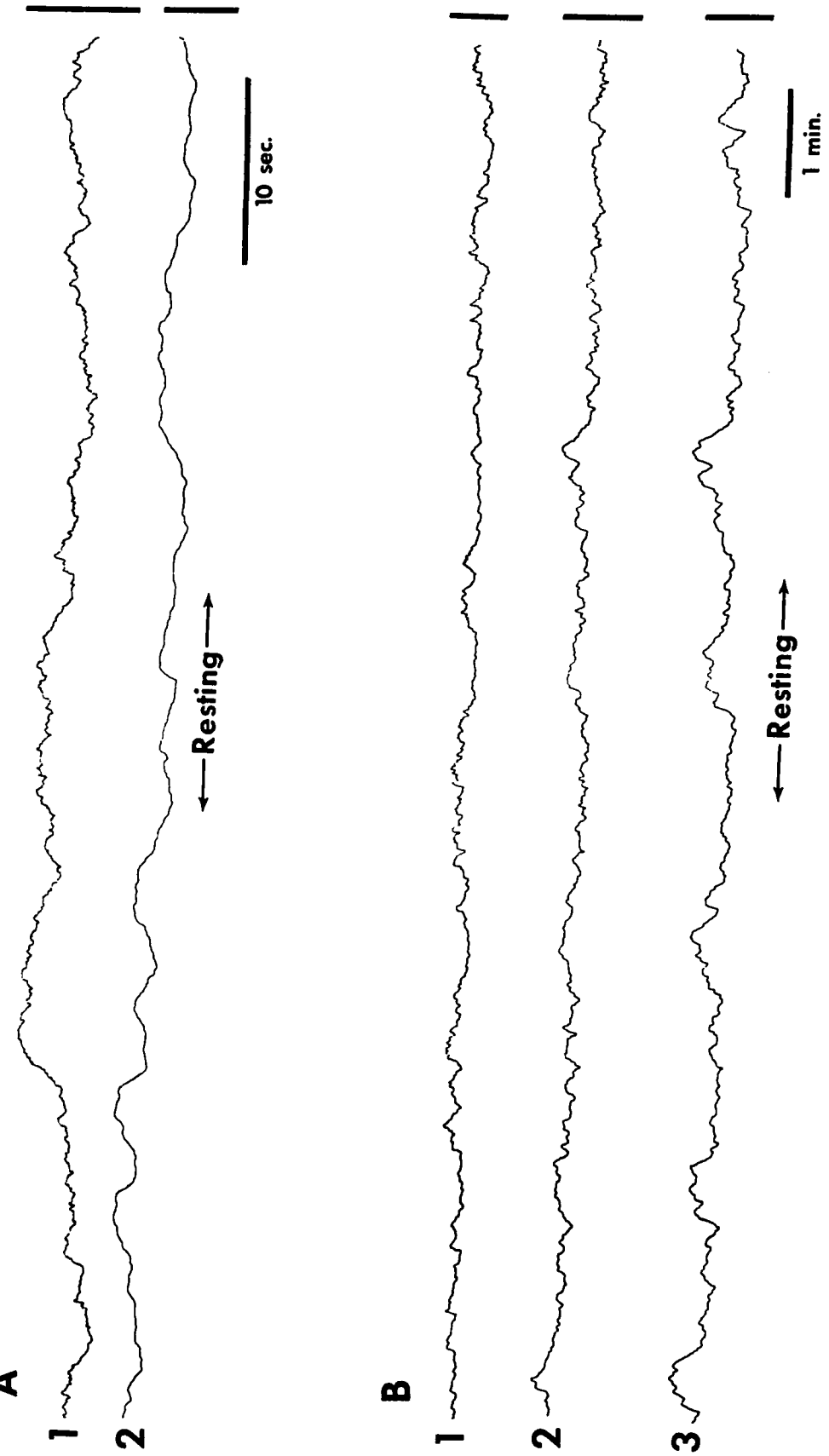

A
1
2
Resting
10 sec.
B
1
2
3
Resting
1 min.

Figure 20. Multi-unit activity level fluctuation and general arousal effects in hippocampus and fornix. Note increasing amplitude and decreasing frequency of fluctuations with decreasing behavioral arousal. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 42. Ventral hippocampus.

B. Electrode 17. Ventral hippocampus.

C. Electrode 29. Fornix.

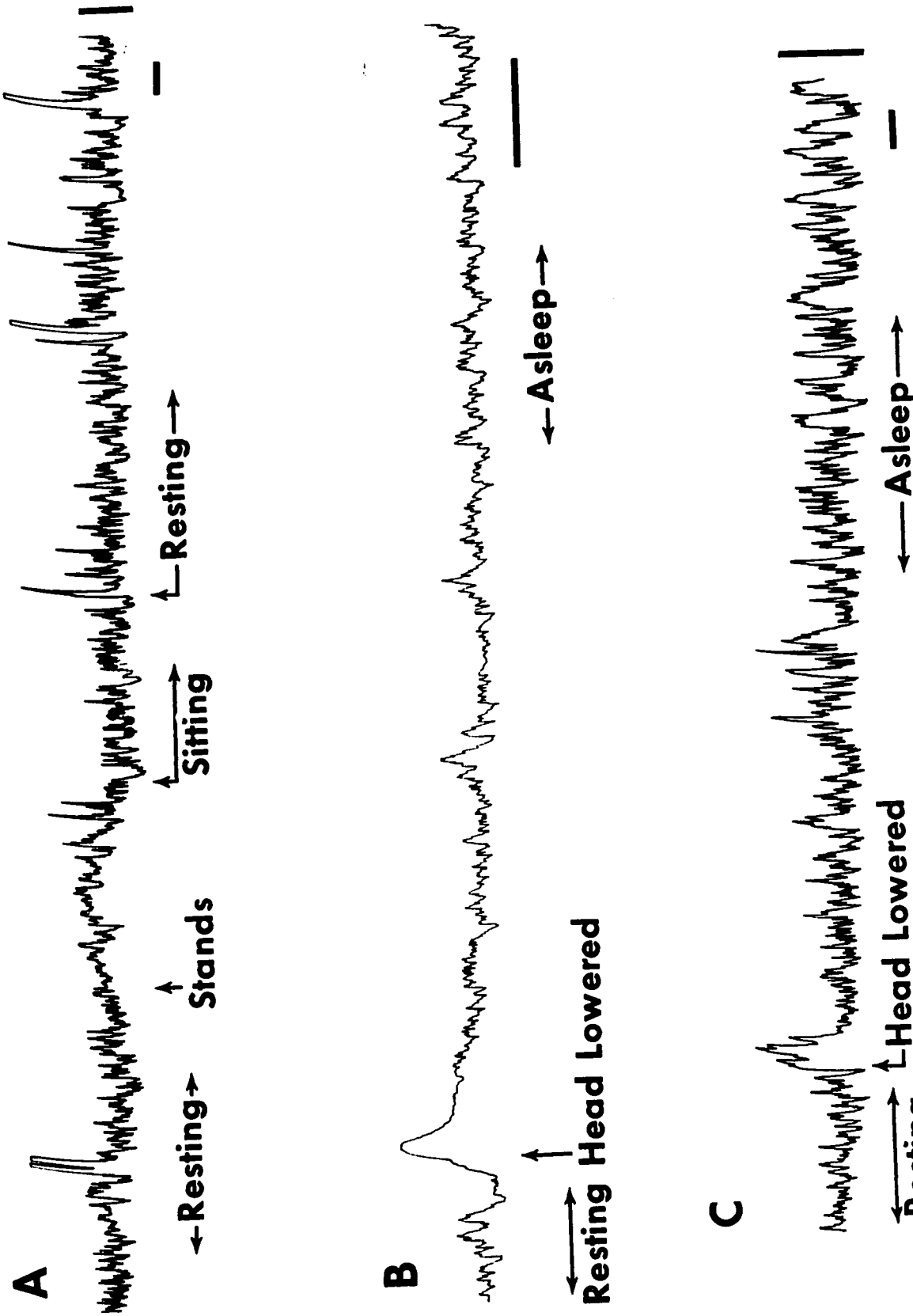

A
Resting
Stands
Sitting
Resting
B
Resting
Head Lowered
Asleep
C
Resting
Head Lowered
Asleep

Figure 21. Electrode 29. Anterior fornix. Continuous record, taken at fast chart speed as subject falls asleep, showing gradual amplitude increments and frequency decrements in fluctuation pattern. Subject's head was lowered just prior to beginning of record. A paradoxical sleep episode began approximately 30 seconds after the record terminates in the figure. Vertical calibration: 10% of signal.

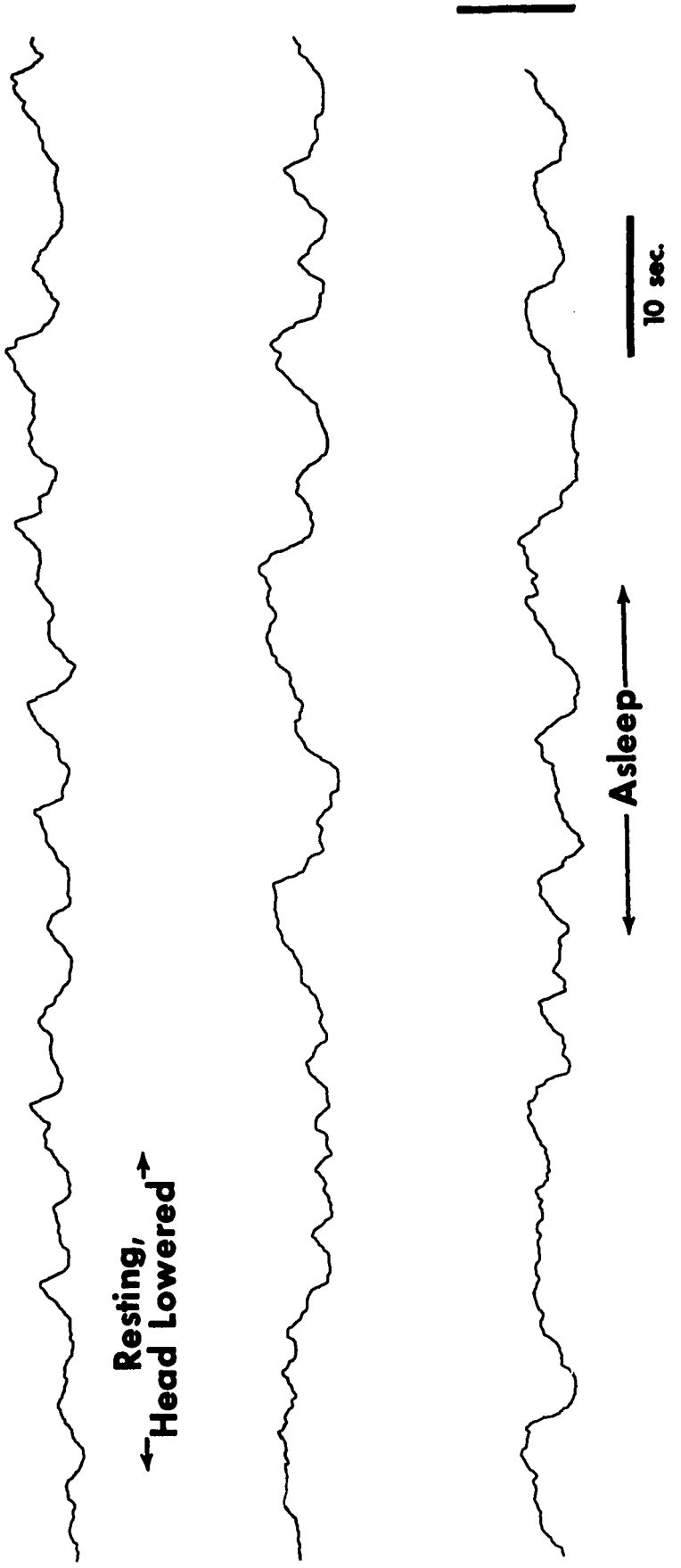

Resting,
Head Lowered
Asleep
10 sec.

Figure 22. Examples of multi-unit activity at various recording sites during paradoxical sleep. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal.

A. Electrode 26. Zona incerta.

B. Electrode 16. Lateral hypothalamus.

C. Electrode 33. Lateral hypothalamus.

D. Electrode 25. Cerebral peduncle.

E. Electrode 46. Dorsomedial thalamus.

F. Electrode 29. Anterior fornix.

G. Electrode 17. Ventral hippocampus.

H. Electrode 27. Preoptic area. No activity increment during paradoxical sleep, which occurred during interval marked by arrows. Compare with record F taken simultaneously from the same subject.

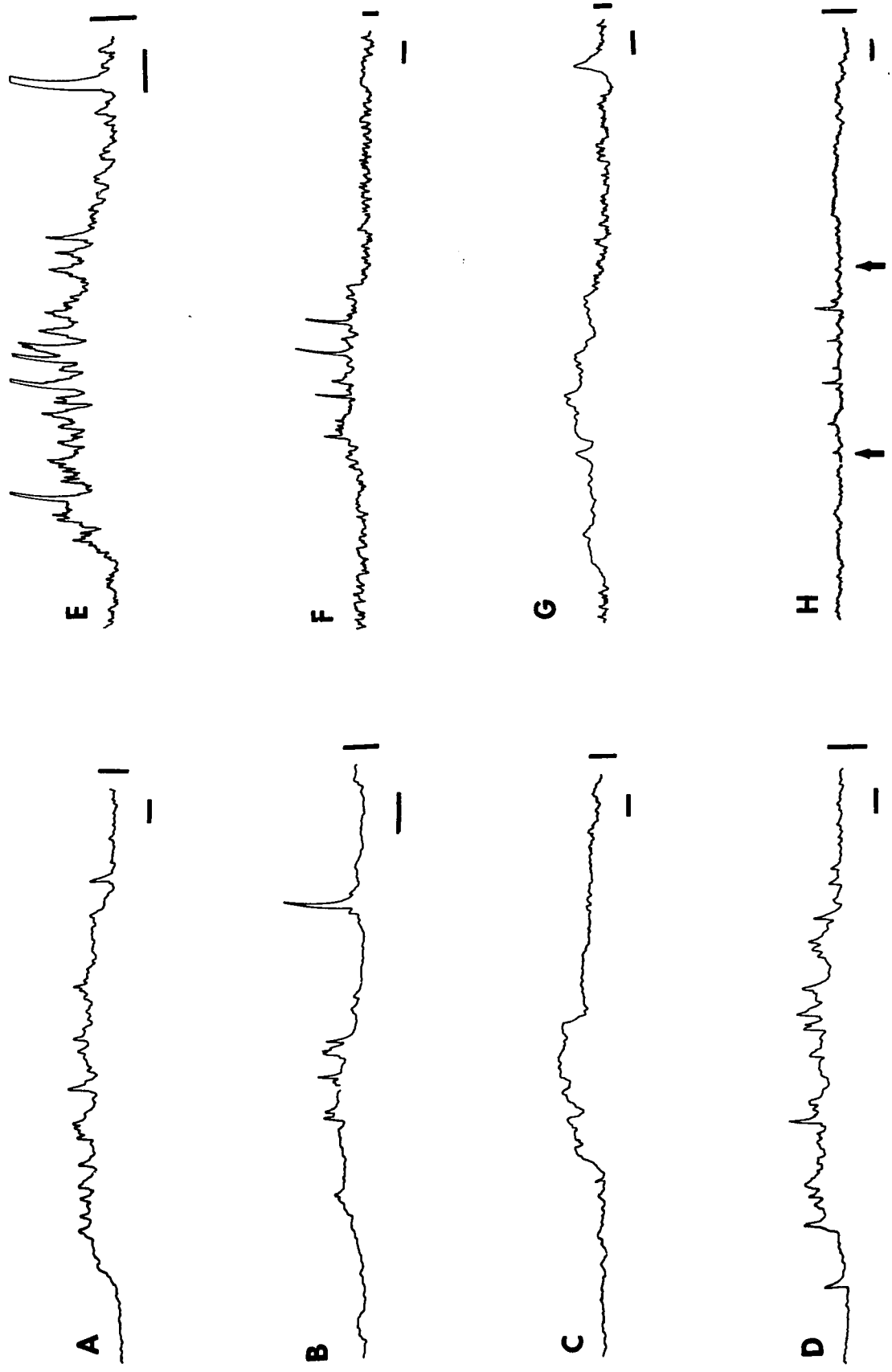

A
B
C
D
E
F
G
H

Figure 23. Examples of multi-unit activity at various recording sites during paradoxical sleep. Horizontal calibrations: 1 minute. Vertical calibrations: 10% of signal. In D, E, F, and G, paradoxical sleep occurred during intervals marked by arrows.

A. Electrode 39. Internal capsule.

B. Electrode 13. Perifornical lateral hypothalamus.

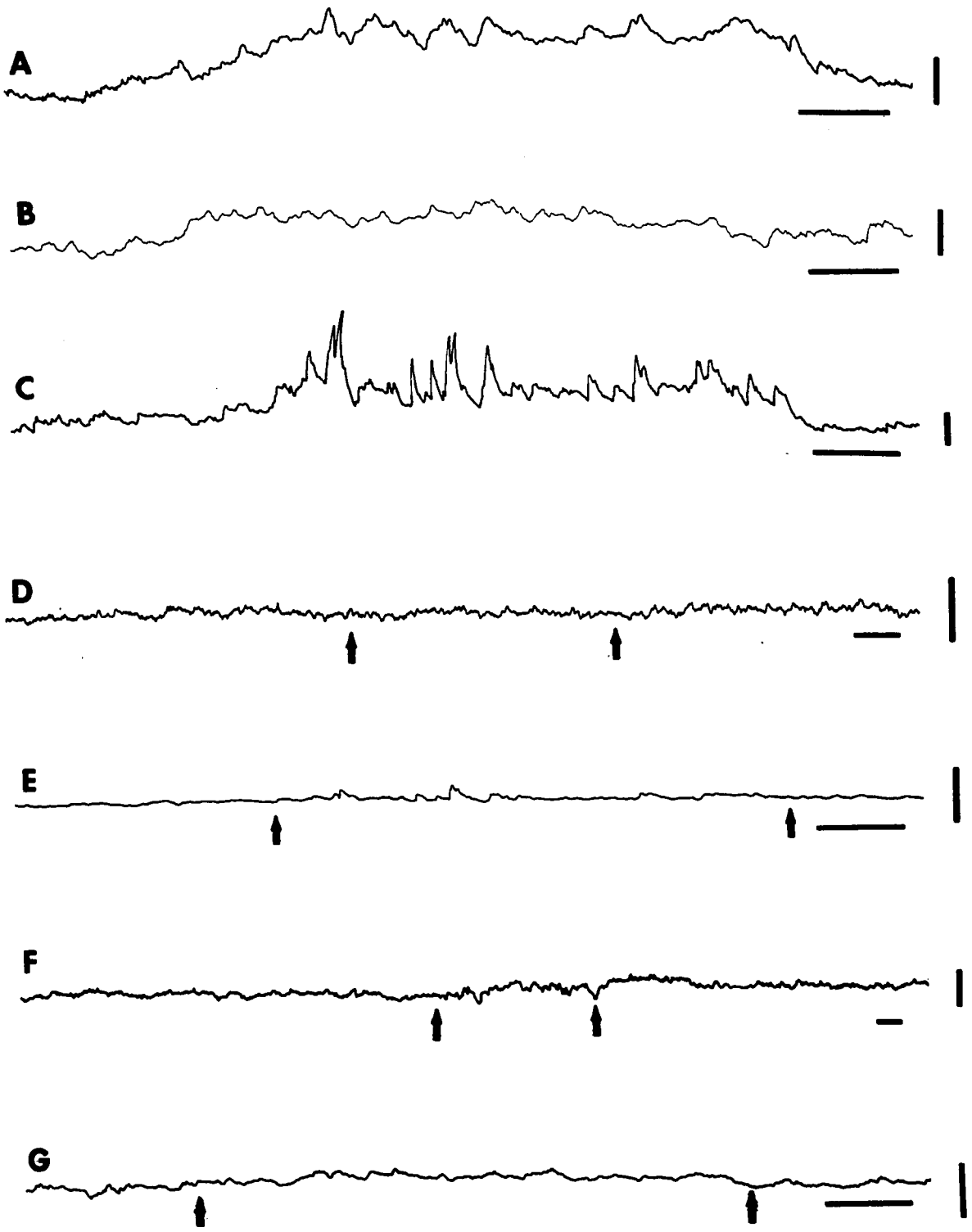
C. Electrode 40. Ventromedial hypothalamic nucleus.

D. Electrode 21. Caudate nucleus.

E. Electrode 41. Periventricular hypothalamus. Compare with record C taken simultaneously from the same subject.

F. Electrode 34. Lateral hypothalamus.

G. Electrode 14. Basomedial amygdala.


A
B
C
D
E
F
G