STUDIES OF EVOKED ACTIVITY IN THE ASSOCIATION CORTEX OF THE UNANESTHETIZED CAT

by

Jon Angus Shaw, B.A.

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(Professor in Charge of Thesis)

[redacted]

(Chairman, Graduate Council)

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INTRODUCTION

I

The "association cortex" was described by Fleshsig (15) to indicate a cortical area distinguished by certain morphological characteristics. Von Bonin and Bailey (50) refer to these cortical areas as being homotypical with all six layers usually being easily recognized with the possible exception of the fifth and sixth. Cell size varies widely within each strata and there is usually a lack of preponderance of any one layer.

With the revolutionary techniques of electrophysiology an alternative definition of the association cortex in terms of evoked activity has been developed. Initially, cortex which was not primary sensory or motor was considered to be association. However, the discovery of the secondary sensory areas and other specific areas by oscilloscopic methods has narrowed the classical definition of the association cortex. (51)

The term "association" appears to have been adopted from the nineteenth century associonistic psychologists. William James (24), in particular, found it natural to assign the function of forming associations to those cortical areas between the primary sensory and motor cortex. He identified sensation with sensory cortex and perception with association cortex. A lesion separating these two areas was interpreted as a loss of association between a sensation and what it signified.

Pavlov, elaborating upon a hypothesis presented by Sechenov in

his monograph Reflexes of the Brain (1886) developed the model of the transcortical reflex. Pavlov, as reported by Diamond and Chow (11), described the association cortex as a switchboard with the incoming sensory impulses to the sensory cortex being transmitted via the association cortex to the motor cortex. The process of conditioning was seen as a shifting of synaptic connections in the association centers due to changes in synaptic resistance. If the pathways from the sensory to the motor cortex were interrupted then it was speculated the conditioned reflex would be lost.

Several investigators have severed these pathways. (13, 26, 42) Sperry (42) cross-hatched the sensori-motor arm cortex and found no incoordination in arm and hand movements, reflex or voluntary. Nor did brief testing indicate any deficiency in capacity for motor learning. Lashley (26) found that rats with a lesion separating the visual area from the motor cortex were able to learn a complex visual conditioning reaction. (Rats were taught to jump to a white triangle and to avoid a white cross when both figures were presented on a black background. If the background was striped the animals were taught to avoid the white triangle and to select the white cross. No differences were found between the normal and operated group.)

Spontaneous electrical rhythms have been recorded from the association areas for many years. However, inability to record evoked responses in these areas under barbiturates resulted in these fields being referred to as the "silent areas" of the cortex. In recent years it has become possible to record evoked activity in these areas under other conditions such as chloralose anesthetic (1, 2, 6, 46, 48),

the "encephale isole" preparation (5), the unanesthetized cat immobilized with Flaxedil (7), and in the waking animal with chronic implanted electrodes. (3)

Amassian (4) was the first to describe "association" evoked responses using chloralose anesthetic on the anterior lateral gyrus of a cat. The evoked responses were seen to occur with auditory and somatic-sensory stimulation to any one of the four limbs. These responses were differentiated from primary sensory evoked responses utilizing oscilloscopic methods by their characteristics of longer latency (15-30 msec.), greater duration of both positive and negative components, smaller amplitude (usually less than 1 mv.), and by their variability of occurrence. Amassian believed evoked activity represented relay both directly and indirectly from the primary sensory areas.

Albe-Fessard (1) found similar cortical evoked responses having a latency of 60-100 msec. on the suprasylvian gyrus, the anterior lateral gyrus, and the pericruciate area of the cat upon stimulation of the sciatic nerve.

Buser, Borenstein, and Brunner (6) observed cortical evoked responses in cats deeply anesthetized with chloralose to visual and auditory stimulation on the suprasylvian and anterior lateral gyri having longer latency, longer duration and greater lability than primary evoked potentials.

Thompson and Sindberg (46) using click stimulation observed four distinct areas bilaterally on the cat cortex which gave the characteristic evoked responses as described above. These fields were seen on

the anterior lateral gyrus, pericruciate cortex, and two foci on the middle suprasylvian gyrus, one anterior and the other posterior. Electrical stimulation of the apical and basal turns of the ipsilateral cochlear nerve produced identical cortical fields on the suprasylvian gyrus.

Thompson, Johnson, and Hoopes (48) in a later study recorded the evoked activity of these four distinct fields described in the cat to auditory, tactile, and visual stimulation. The evoked response recorded upon stimulation with any one of these modalities was identical in organization and duration in all four association areas. The association areas thus appeared to represent convergent areas for auditory, tactile, and visual stimuli.

Thompson, Smith, and Bliss (47) performed a correlational analysis between response amplitudes in the association fields and between association and primary responses to peripheral stimulation. Correlations between responses of primary and association areas for any specific modality were approximately zero. Intercorrelations of responses occurring in any two association fields with any modality of stimulation recorded simultaneously demonstrated a Pearson product-moment varying from .89 to .97. The authors also observed interaction effects between cortical association responses to stimuli of different modalities. Interactions between any two sensory stimuli separated temporally produced decreasing amplitude of the second response as the two stimuli approached each other suggesting usage of the same neurophysiological system by all impulses arriving at the association areas. In contrast to interactions between two presentations of the

same stimuli recorded in the primary areas, the relative refractoriness begins at one second and does not become absolutely refractory until approximately 0.2 seconds.

Thompson et al (46), Buser, et al, (7), and Albe-Fessard, et al (2), in separate investigations, noted that association responses to a specific stimulus persisted even with ablation of the respective primary sensory area. The implication was that impulses arriving at the association areas were being transmitted from subcortical structures.

Thompson (45), Prescott (37), Albe-Fessard, et al (2), and Buser, et al (6), have investigated subcortical areas in order to demonstrate association-like responses.

Albe-Fessard (2) found responses similar to association evoked responses in the centromedian nucleus using peripheral tactile stimulation. Upon stimulation of the centromedian nucleus, "association responses" were observed on the cortex.

Buser, et al. (6), recorded association-like responses to either visual or auditory stimulation in the lateral posterior nuclear group of the thalamus. Visual evoked responses were observed in the nucleus posterior and the dorsal part of the nucleus lateralis posterior. Auditory evoked responses were observed in the inferior part of the nucleus lateral posterior and the nucleus suprageniculatus. Stimulation of these areas was reported to evoke suprasylvian evoked activity.

Prescott (37) recorded association-like responses to auditory, tactile, and visual stimuli in the central median nucleus, the suprageniculate nucleus, the ventral anterior nucleus, the rostral pole of

the reticular nucleus, and the central gray area using peripheral stimulation. The thalamic distribution of association responses was identical for all three modalities. Extrathalamic areas which gave similar responses included the mesencephalic reticular formation, the hypothalamus, the cerebral pedundle, the hippocampus, the dorsal subthalamus and the anterior limb of the internal capsule. Diencephalic "association" responses were found to correlate with cortical association responses in occurrence with Pearson product-moment coefficients ranging above 0.80.

Thompson (45) has concluded "a peripheral stimulus of any modality activates one and the same central association system which projects to the diffuse thalamic recruiting nuclei and thence to the four association fields in an equivalent and undifferentiated fashion."

There is much indirect evidence suggesting that the association cortical foci are electrophysiologically related to the Diffuse Thalamic Projection System (43, 44) and to the Ascending Reticular Activating System (48). It is believed that the ARAS is responsible for both initiating prolonged tonic activation of the cortex and maintaining a long-lasting, generalized state of arousal in the waking animal. A lesion in the mid-brain tegmentum will result in profound somnolence (28). Stimulation of this area in the sleeping cat will result in awakeness, alertness, and arousal (35). The ARAS arises in the medulla, extends through the central core of the brain stem, the pons, midbrain, hypothalamus and subthalamus. At the level of the subthalamus, the ARAS divides into a thalamic and extrathalamic projection to the cortex. The extrathalamic projection passes through the internal

capsule and impinges upon widespread cortical areas. The thalamic projection passes from the subthalamus to the non-specific nuclei of the thalamus (the Diffuse Thalamic Projection System) and continues on to project predominantly to the association cortical areas. (43, 44) The activity of the DTPS appears to be more variable and of shorter duration. Lindsley (27) has speculated that this latter system may function as a specific alerting mechanism capable of modifying the focusing of attention.

II

Most of the studies concerned with association evoked activity have been conducted with cats under chloralose anesthetic. It is known that chloralose exerts a dramatic, if somewhat unknown, effect upon the quality of electrophysiological responses evoked from neural tissue. Ammassian (4) believes chloralose is the most productive due to its effect upon cerebral excitation and enhancement of cortical relays. Buser and Imbert (8) describe the effect of deep chloralose narcosis as producing an increase in the amplitude of association responses and restricting their superficial extent to limited foci. Meulders, et al (34), have demonstrated the ability of chloralose to enhance the amplitude of evoked responses in the centromedian nucleus with somatic sensory stimulation. They reported the maximum amplitude in the centromedian to be 290 mv. in locally anesthetized cats. One half hour after injection of chloralose (80 mg./kg.) the maximum amplitude at the same locus was 550 mv.

Because of the effect of chloralose upon neural tissue, it remains

to be demonstrated that the cortical and central association systems operate in an identical and equivalent fashion in the unanesthetized animal. D. Albe-Fessard (3) in a brief communication stated she was able to obtain responses in the unanesthetized and unrestrained cat to stimulation of the superficial radial nerve with chronic electrodes from the suprasylvian and anterior marginal gyri.

III

A number of studies have been concerned with attempts to correlate the electrical activity of various loci in the brain with behavioral states of "attention".

Hernandez-Peon and Scherrer (19) reported that when a new and novel stimulus, such as two white rats in a jar, was presented to an unanesthetized and unrestrained cat the evoked activity to an acoustic stimulus recorded from the cochlear nucleus appeared to be blocked. A similar blocking effect was seen when an olfactory stimulus (fish odors) and a tactile stimulus (a nociceptive shock delivered to the forepaw) were utilized as the attention acquiring stimulus in later studies. (20)

Hernandez-Peon, et al (21), noted that when an animal's attention is directed and attracted to a non-visual stimulus, photically evoked responses in the visual cortex, lateral geniculate body, and the optic tract were reduced in size. The author suggested that when an animal's attention is attracted to a novel stimulus the mesencephalic reticular formation is able to control the sensory input from stimuli which it judges to be "insignificant" in order to focus its attention on the new stimulus.

Horn (22) took exception to this theoretical explanation and stated that reduction in amplitude of an evoked potential does not necessarily signify that signals are being blocked. If the units composing the response were dispersed in time, the amplitude of the evoked potential would appear to be reduced but the total input need not be diminished. So that when a cat observes a mouse, perhaps it also listens.

In order to verify this hypothesis, Horn implanted monopolar electrodes on the lateral gyrus of six unanesthetized and unrestrained cats. The evoked response to flash was recorded when the cat was resting and when it was watching a mouse. While observing the mouse the evoked response decreased significantly in amplitude. The cats were then conditioned to receive a shock after a series of tones. It was found that the evoked response to the flash was reduced only if there was a visual searching component to the cat's response to the auditory stimulus. If there was no visual searching there was no noticeable change in the amplitude of the visually evoked response. In one cat an electrode was placed on the auditory cortex. When a mouse was presented to obtain the cat's attention the auditory evoked response was noticably smaller in amplitude during the first few trials. Later, even though the cat observed the mouse intently, the amplitude of the evoked response was seen to increase. It is possible to conceive in the earlier stage the cat was listening as well as looking, while in the later instance it was possible the cat was no longer searching for auditory cues related to the mouse. Horn concludes that depression of an evoked response occurs in the modality

actually being used for examining the sensory field.

Buser and Borenstein (7) have shown there is some variation of the association evoked response with changes in the alertness of the animal. Using the "curare preparation" the authors observed changes in the amplitude of the association evoked responses which could be correlated with changes in the E.E. G. pattern. During cortical activation by electrical stimulation of the reticular formation, the responses were reduced in size. At a lower degree of alertness, responses with higher amplitudes were noted; but when the animal was deeply asleep these responses seemed to disappear or to be greatly reduced in size.

D. Albe-Fessard, et al (3), has stated that when chronic monopolar electrodes are implanted in the anterior marginal and suprasylvian association areas, the amplitude of the evoked response to stimulation of the superficial radial nerve varies with the level of "attention". The amplitude of responses occurring during "non-attention" was greater than those occurring during E.E.G. arousal.

While attempts have been made to relate electrical activity of the brain to "attention", the exact behavioral meaning of this term has continued to be loosely defined. It now seems likely that the generalized E.E.G. arousal reaction which has been considered to be the cortical electrical equivalent to "attention" forms a part of what Pavlov described as the orienting or investigatory reflex. Pavlov, as reported by Magoun (29), stated, "the appearance of any new stimulus immediately evokes the investigatory reflex and the animal fixes all its appropriate receptor organs upon the source of disturbance, prick-

ing up its ears, fastening its gaze upon the disturbing agency and sniffing the air." The orientation of head, eyes and body toward a novel stimulus appears to be a reactive attempt to gain information about the stimulus and has been described as pre-adaptive in nature. The orienting reflex is not specific for any modality of stimulation but seems rather to be predominantly related to the "novelty" of the stimulus (40). Although the reflex habituates rapidly upon repetition of the stimulus, usually after three or four trials, its value as an operational definition of the behavioral state of attention appears unique.

It is known that the domestic cat will exhibit simple and accurate head orienting responses to a brief novel auditory stimulus. Thompson and Welker (49) have developed a rating scale whereby they attempted to measure the degree of orienting behavior. The orienting reflex tends to habituate rapidly upon stereotyped repetition of the stimulus. The rapidity with which habituation occurs appears to be a function of stimulus duration, the time interval between sessions, and the time interval between trials in a given session.

IV

Habituation of behavioral responses to a repetitively occurring
ch was originally arousing is one of the most uniformly
cribed by psychologists. Numerous attempts to
correlates of habituation in the central
en undertaken. Habituatory changes have been
ctrophysiologically in both the sensory specific

and non-specific sensory systems of the central nervous system.

Artemiev, as reported by Hernandez-Peon (17), observed that auditory evoked potentials recorded from the auditory cortex of awake cats disappeared rapidly if an unreinforced acoustic stimulus was continuously presented.

Hernandez-Peon and Scherrer (19) reported that repetition of single clicks at intervals of no less than two seconds resulted in the action potential recorded from the cochlear nucleus to diminish or disappear after a variable number of trials. Persistence of this blocking effect continued on one occassion for as long as fifteen hours.

Galambos, Sheatz, and Vernier (16) recording from the cochlear nucleus noted the evoked response to an auditory stimulus presented every three seconds gradually diminished in size. They implied similar changes took place in the auditory cortex, hippocampus, caudate nucleus, septal area, and amygdala.

Sharpless and Jasper (39) found that upon presentation of a train of clicks, twelve/six seconds repeated at varying intervals, the arousal reaction or activation pattern gradually disappeared. The evoked potential recorded from the auditory cortex during this period of time changed significantly. But, rather than decreasing, it became greater in amplitude. The potentials increased from a mean size of 98 microvolts before habituation to 108 microvolts after habituation of the activation pattern had taken place. Transitory periods when the evoked auditory potentials appeared to diminish were noted but these were related to extreme activation of the animals.

Huttenlocher (23) studied click evoked responses in the mesen-

cephalic reticular formation, the cochlear nucleus and the primary auditory cortex during sleep and wakefulness in unanesthetized and unrestrained cats. Habituation of the late slow component of the evoked response in the auditory cortex occurred sometimes after several hundred successive clicks were presented. Occassionally there was spontaneous recovery of the late evoked response during the same series of clicks. No evidence of habituation of cochlear nucleus responses were obtained after several hours or days of clicks. A transient decrease in the amplitude of the cochlear nucleus response was seen with body movement, vocalizing and licking activity.

Marsh, McCarthy, Sheatz, and Galambos (31) presented a click stimulus every ten seconds for five to seven days to unanesthetized and unrestrained cats. They observed a reduction in the auditory evoked responses in the cochlear nucleus. The superior olive and the auditory cortex showed at various times no change, an increase, or a decrease in amplitude. The amplitude of the responses in the intermediary centers (inferior colliculus, MG body) either revealed no change or was increased.

Marsh, Worden, and Hicks (30) recorded auditory evoked responses to both click and tone from the cochlear nuclei of four cats. They found that changes in the position of the cat within the sound field or even minimal movements of the cat's head would result in significant changes in the amplitude of the evoked response. Decrements up to thirty-seven percent were seen in click evoked responses.

Worden and Marsh (52) implanted bipolar electrodes bilaterally in the cochlear nuclei of six cats. Two of these cats were presented with

a click stimulus every ten seconds for five days, the others were given six hours of training. They concluded that while statistically significant changes in amplitude occurred, these were in either direction. Amplitude changes were inconsistent between the right and left cochlear nucleus as well as between two adjacent areas in the same CN. They observed that alertness was associated with higher mean amplitudes than the sleep samples. They believed these latter differences were probably secondary to position differences between the alerted and the sleeping samples. There was noticeable waxing and waning during the five days; but, at the end, the average amplitude equaled or was greater than the initial recording.

If one accepts the apparent superior methodological approach utilized by Huttenlocher (23), Worden, et al (52), Sharpless and Jasper (39), and the remarkable effects of head position (30), bodily movement and vocalization (23) on the amplitude of evoked response, it becomes evident that habituation of evoked responses to click has not been demonstrated satisfactorily in the specific auditory sensory pathways.

Habituation to visual stimulation has been reported by Hernandez-Peon (17, 21) in the optic tract, LG body, and the visual cortex to repeated flashes of light every eight to ten seconds at irregular intervals and also by John and Killam (25) using ten flicks per second in the reticular formation, superior colliculus, visual cortex, and thalamic relay nuclei.

Recent evidence indicates habituation of visual evoked responses in the optic tract and lateral geniculate body is dependent upon pupil-

lary motility (14). If the eye is atropinized and an artificial pupil used, habituation of evoked responses will not take place in these areas to light flash although some suggestion of habituation is observed in the visual cortex.

Hernandez-Peon, Davidovich, and Miranda (17) noted that potentials recorded from the face area of the primary sensory cortex and the spinal fifth sensory nucleus which were evoked by weak electrical stimulation or puffs of air to the face diminished with regular repetition of the tactile stimulus at intervals of one to three seconds.

Santibanez, et al (38), failed to find habituation of evoked responses in the VPL nucleus of the thalamus with somatic sensory stimulation.

In general, it appears that habituation of evoked activity in various loci of the specific sensory pathways has not been consistently demonstrated under the various conditions of repeated stimulation.

Habituation of evoked activity has been stressed by numerous investigators as a phenomenon which occurs readily not only in the sensory specific pathways but also in the non-specific sensory pathways. Several authors have indicated that habituation of evoked activity in the non-specific sensory areas occurs faster than in the primary specific areas.

Hernandez-Peon, Davidovich, and Miranda (17) reported that reticular potentials evoked by tactile stimulation disappear faster than those from the spinal fifth sensory nucleus.

Huttenlocher (23), as previously mentioned, recorded click evoked responses from the mesencephalic reticular formation. The author noted that the amplitude of evoked responses recorded during the quiet waking

state persisted undiminished after more than one thousand successive clicks had been presented. However, during slow wave sleep the amplitude of the evoked response diminished to about 50 percent of the original response size within five to ten clicks.

Hernandez-Peon, et al (17), recorded auditory evoked potentials from the sensorimotor cortex. He stated, "very often after two or three presentations of the stimulus the cortical evoked responses disappear completely. This is one of the fastest examples of habituation." (17)

Palestini (36), John, and Killam (25) have also observed faster rates of habituation in the non-specific sensory pathways than in the specific sensory pathways. The latter authors in their study indicated that rapidity of habituation to repeated presentations of a flash stimulus occurred in the following order: rhinencephalon, reticular formation, superior colliculi, visual cortex, and the thalamic relay nuclei. However, the pupil was not controlled in these studies.

The present experiments were undertaken to obtain a clearer understanding of evoked responses recorded from the posterior association areas in the unanesthetized and unrestrained cat and their possible relationship to behavioral variables.

The first phase will be concerned with attempts to record evoked responses in these areas to peripheral auditory, somatic sensory, and visual stimuli. Characteristics of these responses will be compared with those described using chloralose anesthetic.

The second phase will attempt to relate changes in the evoked activity of the association cortex to changes in the "behavioral state"

of the unanesthetized and unrestrained cat as modified by variable situations of peripheral stimulation. Two different definitions of "behavioral state" were used: 1) bodily activity measured by a simple nominal rating scale (i.e., sitting, walking, etc.) and 2) presentation of "novel" stimuli, the latter being defined simply as stimuli not otherwise present in the experimental situation.

The third phase consists of an experiment attempting to relate degrees of behavioral orientation to click using the method of Thompson and Welker (49) with amplitudes of the click evoked association response. The behavioral orientation performance will be taken as a simple operational definition of behavioral attention.

The final phase of the study will investigate what changes, if any, occur in the amplitude of evoked responses to click in the association areas if the stimulus is continually presented at regular intervals over an extended period of time (i.e., habituation).

All experiments in this study were based on a rather general and inexact set of hypotheses. If it is assumed that cortical evoked association responses represent focalized projections of the Ascending Reticular Activating System (ARAS) and the Diffuse Thalamic Projection System (DTPS), a number of predictions could be entertained. First, evoked responses should be obtained to auditory, somatic sensory and visual peripheral stimulation. Second, evoked association response amplitudes may be related to behavioral "attention". If the further assumption is made that this system is "utilized" or desynchronized when the animal is active or attending, then during such behavioral conditions evoked responses should be less easily obtainable and of

smaller amplitude. Thus, evoked association responses to all modalities of stimulation should be reduced during heightened bodily activity. Similarly, they should be reduced for all modalities when a "novel" stimulus of any modality is presented. In the orientation experiment, there should be an inverse relationship between degree of orientation and evoked association response amplitude, attention being defined by degree of orientation. Since behavioral orientation or attention habituates rapidly within a few trials, we would expect a concomitant increase in the click evoked association response. In a habituation experiment in which a discrete and brief auditory stimulus is continuously presented in a monotonous fashion within a non-changing environment we would expect little activation of "attention" mechanisms, consequently, evoked responses to an auditory click should not exhibit any consistent alterations over time. Thus, habituation, per se, of the evoked response would not be expected to occur, although waxing and waning might occur due to changes in bodily activity and changes in the intrinsic alertness of the cat. All of these predictions were verified.

MATERIALS AND METHODS

Electrodes

In an attempt to record the electrical activity of the cortical association areas to peripheral stimuli in the unanesthetized and unrestrained cat, chronic electrodes were surgically placed using aseptic techniques.

Most recording electrodes were coaxial bipolar in design. Surface monopolar electrodes were used in initial pilot studies and were found to be less satisfactory. The inner lead of the bipolar electrode was designed to penetrate the cortex 1.8 mm. while the external cylindrical lead was to come in contact with the cortical surface. The potential difference between the penetrating lead (the indifferent pole) and the surface lead (the active pole) was recorded. The inner lead consisted of type 316 stainless steel (0.010 inch) wire which had been insulated with enamel. The cylindrical lead consisted of a one cm. length of nineteen guage stainless steel tubing. The stainless steel tubing was connected to a 126-013 Amphenol plug with nine pins by soldering an insulated stainless steel wire from the tubing. The inner lead was also soldered to the Amphenol plug. Consequently, it was possible to make four coaxial bipolar electrodes for each plug. Once the leads had been established, a foundation for the Amphenol plug was created out of Acralite to conform to the skull of an average size cat. This was possible by trephining a previously sacrificed cat's skull over the designated association cortical area and expanding as nec-

essary with rongeurs. The coaxial leads were made to conform in an orderly manner by passing them through Tefalon which had been placed over the opening in the skull. This was fixed to the skull by adhesive tape and thereafter layered with bone wax to prevent cementing of the plug to the skull. The plug itself was designed to overlay the midline and thus pressure exerted upon the plug would be exerted against intact bone. This arrangement was structured by generous amounts of Acralite to fix the appropriate design to the model skull. The creation "en masse" was then lifted off the skull, and the Tefalon was lifted over the recording leads. Once the Tefalon had been removed, the plug was then replaced upon the model skull. Bone wax was then applied to the inner table of the skull and Acralite was carefully applied to confrom to the margins of the opening and to be continuous with the inner surface of the inner table of the skull. When this was completed, the cylindrical leads would project about 0.5 mm. to 1.0 mm. beyond the confines of the Acralite and, consequently, the inner table of the skull.

Operations

A total of 42 cats was studied. Satisfactory evoked responses were recorded from 20 of these. The cats were furnished by the University of Oregon Medical School animal supply. The only requirements for selection were that the cats weighed at least two kilograms and appeared healthy.

All recording electrode systems were implanted under aseptic conditions. The cats were anesthetized with Nembutal (pentobarbital)

40 mg./kg. administered intraperitoneally. After anesthesia was obtained, atropine 0.08 mg. was injected intramuscularly to reduce tracheal secretions during the procedure. The animal was then placed in a head holder.

Under sterile conditions the animal was draped. The initial incision extended from the nasion to about one cm. beyond the occipital protuberance. The skin was retracted and the temporalis muscle was freed from its attachments to the skull. The periosteum was scraped off and the skull was entered by means of a trephine over the designated association area. The opening was then expanded, as indicated, with rongeurs. The area of brain exposed was contingent upon the design of the recording electrode. Once the area of exposure was complete the dura mater was penetrated and an area consistent with the exposed area was excised. Saline was administered periodically to prevent drying of the cortex.

At this time the surrounding intact skull was thoroughly dried with sponges and a stainless steel screw was placed in the frontal bone overlying the frontal sinus. The recording electrode system was then applied over the skull which had been layered with wet Acralite in the prospective areas of contact. The coaxial electrodes impinged upon the cortex and the inner surface of the Acralite was continuous with the inner table of the skull. The recording apparatus was further fixed to the skull with subsequent applications of Acralite to the surrounding skull and over the exposed heads of the jeweler screws in the frontal area.

When the Acralite had solidified, the temporalis muscle was

approximated and sutured with 3-o chromic. The skin was closed with single interrupted subcutaneous sutures when possible. The skin around the protruding plug was drawn up to its lateral surfaces by a purse stitch.

Following closure of the surgical wound, two silver wire sutures were taken one cm. apart on the dorsal aspect of the left forepaw. This was done to provide a means of stimulating the tactile receptors by a weak electrical current during subsequent experiments.

At the close of the above procedures, 300,000 units of Penicillin G was administered I.M. and the animal was allowed to recover during a period varying from six to eighteen hours under an infra-red heat lamp. After at least four days of recovery the animal was taken to the lab for the recording of evoked activity under varying conditions of stimulation.

Apparatus

Upon recovery the cat was placed within a test box, measuring 22 inches long, 16 inches wide, 18 inches deep, and enclosed on all sides by wire mesh, which was designed specifically for recording from the unanesthetized and unrestrained cat. The male counterpart of the Amphenol plug was connected to the indwelling female plug. There was a longitudinal opening the length of the cage to allow the cable freedom of movement. The separate leads of the cable were connected to a switch box where it was possible to manipulate the leads in order to measure the potential difference between the surface lead (the active pole) and the penetrating lead (the indifferent pole) of the four coaxial electrodes. It was possible to establish recording

connections for eight bipolar electrodes in the switch box. By selecting the proper cable from the switch box and connecting it to a separate Tektronix-Type 122 Low Level Pre-Amplifier it was possible to choose from which point on the cortex we wanted to record the electrical activity. The preamplifier in turn was connected to a Tektronix-Type 502 Dual Beam Oscilloscope. Two Tektronix-Type 162 Waveform Generators were used. One of these triggered the oscilloscope every two seconds, the other produced a 100 msec. sawtooth corresponding to sweep duration. Pulse output delay by the 161 was set for 10 msec. after the sweep began. The 502 was synchronized with a similar dual beam oscilloscope for photographic purposes. A Grass Model C4G Kymograph Camera was connected through an external electronic shutter (built by the University of Oregon Medical School instrument shop) to the slave scope. It was possible to set the camera in such a way that it would expose only once per sweep; or, if desired, any number of tracings could be superimposed before the shutter was closed and the film advanced.

Stimuli were produced by a Tektronix-Type 161 pulse generator, powered by a Tektronix-Type 160 A Power Supply. For visual stimulation the pulses from the 161 triggered a Grass Instrument Co. Model PS-2 Photo-Stimulator and noiseless flash gun. For the production of either auditory or tactile stimulation the 161 was connected to a Model HF-20 Eico audio amplifier. The auditory click was emitted from an eight-ohm speaker three feet from the side of the cage. The tactile stimulus was delivered by the 161 and modified by the Eico amplifier. The shock terminals were applied to the two silver wires

sutures on the dorsal aspect of the left forepaw and taped in place by masking tape.

A further elaboration of the apparatus was necessary in order to carry out the experiment concerned with recording evoked potentials during head orientation to a brief discrete auditory click. In this instant a push button switch powered by a forty-five volt battery was utilized to trigger the Tektronix-Type 162 waveform generator which in turn triggered the oscilloscope and the 161. Two eight inch speakers were placed symmetrically 18 inches from the lateral sides of the test box. Sound stimuli could be produced in either one or the other speakers by a double throw switch controlling the output of the Eico amplifier. The front of the test box faced a one way viewing window in the sound shielded room.

Procedures

The spontaneous occurrence of irregular deflections in the brain activity of unanesthetized and unrestrained cats makes it difficult to attempt to extrapolate meaning from a single oscilloscopic tracing in response to a stimulus. Dawson (10) found that if he superimposed fifty or more successive sweeps of a cathode-ray oscilloscope and photographed them on a single record it was possible to discriminate the signal from the noise. He was able to record the evoked response to stimulation of the ulnar nerve at the elbow from the contralateral sensory area in human subjects using silver cup electrodes fixed on the scalp with collodion. Exact synchrony of events was insured by a trigger circuit locked to the sweep of the oscilloscope. In this

way a deflection would consistently follow a timed impulse at regular intervals. The superimposition of twenty to forty consecutive tracings were commonly used in this experiment to differentiate the variably occurring association evoked responses from the spontaneously occurring waves. Series of individual tracings were also recorded in some experiments and various statistical measures computed.

In an attempt to determine if association evoked responses could be elicited in the unanesthetized and unrestrained cats to auditory, tactile, and visual stimulation, the cat was placed in the test box which was located within a shielded room. A cable was attached to the indwelling Amphenol plug. The animal was allowed sufficient time to become adapted to his new environment and to make himself comfortable. Auditory stimulation was produced by an eight inch speaker located approximately eighteen inches from the side of the box. Tactile stimulation was delivered by taping the shock terminals to the two silver wire sutures located on the dorsal aspect of his left forepaw. Visual stimulation was provided by a photo-stimulator with a noiseless flash gun directed at the lateral side of the test box from about twelve inches away. All the surfaces of the test box were covered with aluminum foil except the side receiving the stimulus in order to maximize reflection if the animal was not looking directly at the visual stimulus. The presentation of the stimulus was so arranged that it would occur ten msec. after the onset of the oscilloscopic sweep. Total duration of the sweep was 100 msec. and the interstimulus interval was two seconds. The cortical evoked responses were transmitted by a bipolar coaxial electrode, preamplified and visualized on

an oscilloscope. Twenty to forty tracings were superimposed on a single record. The responses were permanently recorded by a camera directed toward a "slave" scope.

An attempt was made to qualitatively measure the behavioral state of the animal by using the following rating scale:

A. The cat was lying down, head resting on the floor of the box.

B. The cat was sitting on forelimbs, head erect.

C. The cat was sitting, forelimbs extended.

D. The cat was washing himself.

E. The cat was pacing back and forth in the box.

F. The cat was scratching at the side of the cage.

This was done in order to relate the amplitude of the response with different behavioral states.

To determine if a new and novel stimulus might influence the amplitude of the evoked response to either a continuously presented auditory, tactile, or visual stimulus, two records of superimposed tracings were followed with presentation of a novel stimulus for twenty or more tracings and then two or more records were taken after the removal of the stimulus. The novel stimuli on different occassions consisted of a white rat housed in a glass jar, cat food placed in a petri dish, the experimenter entering the sound shielded room, tactile stimulation with an air hose and "barking" sounds emitted by the experimenter.

Several control procedures were employed in this portion of the study. Changes in head position within the sound field and in response to novel stimuli were noted when this was thought to be of

crucial significance, and no relationship was found between amplitude of response and change in head position. One cat was anesthetized with chloralose anesthetic and evoked responses recorded when the animal's head was placed in several different positions in the sound field. A ninety degree difference in head position relative to the speaker failed to show any significant difference in the mean amplitudes recorded under these conditions. To exclude changes in the intensity of the auditory stimulus to the cat during head orientation as a possible mechanism for response amplitude reduction, a small microspeaker (a 9C receiver designed by the Baltimore Instrument Co., Inc.) which had been molded with a gel-like substance to the external auditory canal of a previously sacrificed cat was inserted and evoked responses recorded before and during the presentation of a novel stimulus.

The habituation experiments were carried out using the above recording methods. The repetitive stimulus was an auditory click which was presented every two seconds for sixty to seventy-four hours. The cat was placed in the test box within the soundproof room. Records of the evoked response were taken initially at the commencing of habituation and every twelve hours or less. Usually after recording evoked cortical responses the experimenter would enter the recording chamber to feed and water the cat.

The procedure used in the orienting responses experiment consisted of giving four test sessions, ten trials per session, to the cats implanted with chronic bipolar coaxial electrodes. The electrodes were implanted along the left suprasylvian gyrus. The time interval

separating the successive test sessions was a twenty-four hour period. On each trial an auditory click was presented from one or the other speaker in a random manner when the cat was facing at a right angle to a line joining the two speakers. During a given session, five of the stimuli were presented through the left speaker and five through the right speaker. The stimulus remained the same throughout and consisted of a click. The interval varied from thirty seconds to five minutes. The presentations of stimuli during any one session were made constant for each cat but varied between sessions. A rating scale to measure the quality of the orienting response was adopted from Thompson and Welker (49). "Rapid, immediate, and accurate orientation in one movement received a score of 4. Accurate head orientation requiring several head movements was scored as 3. Immediate but incomplete orientation in the correct direction was scored as 2. Delayed and/or incomplete head orientation in the correct direction was scored as 1. No head movement, or orientation in the incorrect direction was scored as 0." Individual oscilloscope tracings of evoked click responses were recorded in this experiment.

Usually three to four weeks following surgery the electrical resistance between the bipolar leads would gradually begin to increase. This, apparently, was due to the rapid growth and extension of the dura mater over the exposed cortex. The cats were then sacrificed and perfused with formalin, the brain removed and placed in a jar of formalin. The points where the inner lead penetrated the cortex were easily observed. Electrode locations were measured in relationship to the fissures for each brain using a pointer mounted on an electrode

manipulator calibrated in millimeters. For composite mapping the right angle bend of the middle and posterior suprasylvian fissures and a line extending up from the posterior suprasylvian fissure and the junction of the anterior lateral and ansate fissures were used as reference points.

Various statistical methods were applied to the different catagories of information derived from the experimental procedures. Mean amplitudes and differences between means of superimposed evoked responses to a repetitive stimulus during states of bodily activity and before and after presentation of novel stimuli were estimated using the methods of Dixon and Massey (12). In these methods the estimated arithmetic means and ranges are used for calculating approximate differences and the probability of differences were obtained from a respective table. Evoked association response amplitudes and behavioral orientation were compared using chi-square. A chi-square analysis of changes in head orientation over all days and over trials for day one and all days was completed. An analysis of variance was completed on the evoked association response data in the orientation experiment evaluating days, trials, subjects, and the interaction of trials and days. Two separate analyses were calculated using raw and percentage scores. For habituation trials the 99 percent confidence interval around the initial superimposed mean was estimated and used to compare subsequent response amplitudes (12).

RESULTS

Evoked Responses

Characteristics of the mean amplitude and latency of evoked responses recorded from the posterior suprasylvian gyrus of the unanesthetized and unrestrained cat were determined by measuring the amplitudes of a hundred consecutive single tracings to auditory, tactile, and visual peripheral stimulation and the latencies of representative responses. These are demonstrated in Figures 1 and 2. Latency differences are observed for the three modalities of stimulation. Evoked responses to click have the shortest latency, those to visual stimuli have the longest, and somatic sensory evoked responses have a latency of intermediate length. While the differences in latency were noted consistently among the majority of tested cats, there were exceptions where the latency of evoked responses to tactile stimulation appeared to be longer than the latency of the visual response. Although the differences in latency are similar to those described using chloralose anesthetic (48), they appear to be more variable in the waking state. Tactile and visual evoked response amplitudes were remarkably similar in their amplitude frequency distributions, while auditory evoked responses had a somewhat less broad frequency distribution. The mean amplitudes of evoked responses to tactile and visual stimuli were similar in magnitude while the mean amplitude of the auditory evoked responses was lower relative to the other two modalities. Uniformity of mean response amplitudes to the three modalities of stimulation was relatively constant in the majority

of tested cats.

Single and superimposed tracings of evoked responses to peripheral auditory, tactile, and visual stimuli recorded from the suprasylvian gyri of three cats in both the unanesthetized and anesthetized (chloralose 70 mg./kg.) state are seen in Figures 3,4,5, and 6. All cortical leads were responsive to the three modalities of peripheral stimulation. The association response waveform characteristics are essentially identical from all recording sites regardless of the modality of stimulation. The predominant wave pattern is one having an onset latency of 15-30 msec. with an initial positivity (deflection in an upward direction) of 25-45 msec., followed by a variable negative component.

Evoked tracings to visual stimuli from cortical electrodes in the unanesthetized cats displayed an additional waveform to the one described above. This wave pattern is characterized by a short latency (less than 10 msec.), initial positivity of marked amplitude and of brief duration. These visually evoked, early appearing responses of brief duration probably reflect activity from the small visual field located in the suprasylvian sulcus (9, 32) with two possible exceptions. The visual evoked response in lead one, Figure 4, appears to be activity from the secondary visual area on the posterior lateral gyrus, and that of lead four, Figure 3, may be the anterior portion of the secondary visual area on the posterior suprasylvian gyrus (32).

Short latency responses to click stimulation of very low amplitude are seen at electrodes one and two, Figure 5. This is well

demonstrated in the single tracings, and a suggestion of the response is seen in the superimposed tracings. This may reflect activity from adjacent auditory fields.

A comparison of evoked responses to auditory, tactile, and visual stimuli under the two conditions of chloralose anesthetic and the unanesthetized state for cat 64-13 is seen in Figure 3. Similar waveforms are observed under both conditions. There was less variability and greater response amplitude using chloralose anesthetic. With few exceptions, the early visual evoked response was not seen with chloralose anesthetic. Evoked responses to auditory and tactile stimulation correlated well in all leads. The visual association responses were best observed in leads one and two and were barely perceptable in leads three and four in the unanesthetized state, while association evoked responses recorded using chloralose were represented maximally in leads one, three, and four with only a slight reduction in lead two.

Comparison of evoked responses recorded under chloralose anesthetic and in the unanesthetized state for cats 63-97 and 63-88 can be seen by comparing Figure 4 with Figure 6 and Figure 5 with Figure 6. In both comparisons association evoked responses in the waking state are best seen in electrodes one, two, and three with a marked reduction in the amplitude of the evoked response noted in the fourth electrode. This suggests that in both instances the electrode was placed on the margin of the association area posteriorly. In both cats the visual evoked responses under chloralose anesthetic are clearly evident in lead four, but there is little or no suggestion of responses to the other modalities of stimulation. The possibility exists that the visual

evoked responses in lead three and four of cat 63-88 reflect activity in the visual cortical areas because of their short latency. While association evoked responses are observed in all cortical leads in cats 63-97 and 63-88 in the unanesthetized state, the presence of evoked responses recorded using chloralose anesthetic appear to be more restricted in their manifestations with the possible exception of the late visual evoked response. With chloralose, the association evoked responses are best seen in cat 63-97 for electrodes two and three, and in cat 63-88 for electrodes one and two.

In summary, evoked responses have been recorded to auditory, tactile, and visual peripheral stimuli in the unanesthetized and unrestrained cat. These responses are similar in their latency of response and waveform pattern to those previously described using chloralose anesthetic (48), although of lower amplitude, and correlate well with evoked responses recorded from the same electrodes under chloralose. With the possible exception of the visual evoked responses, the responses appear to be more superficially restricted under chloralose than in the waking state.

Evoked responses recorded from the suprasylvian gyri of 14 additional unanesthetized animals verified the above described characteristics of the association responses. In almost all cases when a well defined evoked response occurred to one modality of stimulation, equivalent responses could be found to occur to the other two modalities of stimulation. Cortical areas responsive to the three modalities of stimulation appear evident and localized in the unanesthetized cat.

Bodily Activity

Table I illustrates the changes in the mean amplitude of evoked responses measured in microvolts to auditory, tactile, and visual stimulation for different levels of behavioral activity. Significance levels were determined using the method of Dixon and Massey (12).

A comparison between amplitudes of association evoked responses recorded during two different behavioral states (i.e., moving and sitting) to peripheral tactile stimulation is illustrated and the mean amplitudes plotted on a graph in Figure 5. Figure 7 illustrates the influence of behavioral state on association responses evoked by all modalities of stimulation. The difference in these illustrations were found to be statistically significant at the .05 level for all electrodes (Table I). Using the rating scale depicted in Figure 7, evoked responses to auditory, tactile, and visual stimuli were recorded during different behavioral states. The mean amplitudes of evoked responses recorded for the different degrees of bodily activity were found to be significantly different at the .05 level. In summary, amplitude of evoked responses recorded from the suprasylvian gyrus to the three modalities of stimulation is related to the level of bodily activity. With heightened activity, there is a reduction in the amplitude of the response relative to a lesser degree of activity.

Novel Stimuli

Tables II and III indicate the changes in the mean amplitude of the evoked responses to auditory, tactile, and visual stimulation when a novel stimulus of auditory, tactile, or visual modality is briefly

presented. Significance levels were calculated using the methods of Dixon and Massey (12).

The effects of novel stimuli upon association evoked responses elicited by a repetitive stimulus (auditory, tactile, or visual) are illustrated in Figures 8, 9, and 10. Three catagories of novel stimuli were employed to represent the three modalities of stimulation. A jet stream of air was used for the tactile stimulus, a rat for the visual stimulus, and barking sounds for the auditory novel stimulus. Figures 8, 9, and 10 indicate that presentation of any one of these novel stimuli results in a reduction of the evoked responses to either repetitive click, tactile, or flash stimulation and that upon removal of the novel stimulus, the amplitude of the evoked response approaches its original magnitude. A comparison of the mean amplitude before and during presentation of the novel stimulus is illustrated in table II for cats 64-17 and 64-18. Results obtained from a number of other cats are given in Table III. The differences between mean amplitudes are statistically significant at the .05 level for novel stimuli presented to cats 64-17 and 64-18 when stimulated repetitively with auditory and tactile stimulation. With repetitive visual stimulation, differences between mean amplitudes were significant at the .05 level for cat 64-18 for all novel stimuli and for cat 64-17 for auditory and visual novel stimuli. While there appears to be a reduction of the amplitude of the visual evoked response upon presentation of the tactile novel stimuli for cat 64-17, this was not significant. Evidence from other cats indicates this is an exception and that generally the differences are of a magnitude sufficient to be statistically significant.

In summary, mean amplitudes of evoked responses occurring to either repetitive auditory, tactile, or visual peripheral stimulation are reduced in magnitude when a novel stimulus which may be either auditory, tactile, or visual in character is presented for a brief interval. Upon removal of the novel stimulus, the amplitude of the evoked responses approaches its original magnitude.

Rate of recovery of the mean amplitude of click evoked association responses upon removal of a novel stimulus is demonstrated in Figure 11. The mean amplitude of the evoked response usually returns to its original value within a minute and a half depending upon the quality of the novel stimulus. When food was used as the novel stimulus, a period of two minutes was necessary before the differences between mean amplitudes before and after the novel stimulus were no longer statistically significant.

Reduction of evoked responses will occur with novel stimuli when the intensity of the repetitive click stimulus is held constant by the placement of a microspeaker within the external auditory canal of cat 64-18 as seen in Figure 8. A statistically significant reduction in the mean amplitude of the click evoked response upon presentation of the various novel stimuli is demonstrated in Table II.

Failure to elicit a significant difference in amplitude between click evoked association responses with changes in head position up to ninety degrees relative to the speaker in the chloralose anesthetized cat is shown in Table IV. This would imply that changes in head position within the sound field could not account for the changes in the amplitude of the click evoked responses which occurred with presentation

of a novel stimulus or changes in behavioral state.

Orientation Experiment

This experiment consisted of placing a cat in a test box with a speaker located an equal distance away on both sides. A single click was presented randomly from either one or the other speaker for ten trials each day for a period of four days. On any one day, five clicks were emitted from the right speaker and five from the left. The degree of head orientation was graded using the method of Thompson and Welker (49).

The purpose of this study was to attempt to define the relationship between the degree of head orientation and the amplitude of the click evoked responses recorded from the suprasylvian gyrus. Five cats were used.

The relationship between amplitude of click evoked association responses measured in percent and the degree of head orientation for day one and for all days is illustrated in Figure 12. An inverse relationship between head orientation and amplitude of evoked response is suggested. Changes in the mean orientation score and mean amplitude of evoked responses for all five subjects over trials for each day is seen in Figures 13 and 14. For each day, the mean orientation score appears to decrease in magnitude over trials as the mean amplitude of the evoked response appears to increase in magnitude. Changes in mean association evoked responses measured in microvolts and in percent collapsed over days and over trials are illustrated on graphs in Figures 15 and 16. When the mean orientation scores and mean evoked amplitudes are collapsed over days the inverse relationship of these parameters

becomes readily observable. Over trials the mean evoked amplitude progressively increases in magnitude while the mean orientation score decreases. When the mean orientation scores and the mean evoked amplitudes are collapsed over trials and plotted over days a decrease in the mean evoked response is suggested over the four day period. Mean orientation score decreases more abruptly over the four days with the greatest decrease being evident between the first and second day.

A summary of the analysis of variance of association evoked responses measured both in absolute amplitude and in percent is given in Table V. Both subjects and trials were found to be significant at the .001 level when responses were measured in absolute values. However, when responses were measured in percent of maximum responses for each animal, between subjects was no longer significant, while between trials remained significant at the .01 level. Since subjects were significant with absolute values but not with percentage values, the differences between subjects were probably only in absolute level, not in the way different subjects reacted to the other variables (i.e., trials and days). A statistically significant effect for trials would be expected if the relationship between head orientation and amplitude of evoked response is an inverse one. As habituation of the orienting reflex takes place the amplitude of the evoked response would become greater. In order to determine the degree of relationship between head orientation and amplitude of click evoked responses a chi-square analysis was completed. Evoked responses measured in percent were segregated into four catagories, those less and those greater than 49.99 percent, and those associated with slight (number one as determined by

the Thompson and Welker rating scale) or no head orientation and those with a rating of two, three, or four. The chi-square was significant at the .05 level. The contingency coefficient was calculated to be .30 using the method of McNemar (33). Distribution of observed amplitudes for the different catagories are seen in Table VI. Further analyses were completed to evaluate changes in head orientation ratings over all days, over trials for all days, and for day one. In the first analysis, orientation ratings were segregated into two catagories, those occurring on either the first and second days; those occurring on the third and fourth days. These ratings were in turn distributed into two more catagories, those with a rating of zero or one, and those with ratings of two, three, and four. The chi-square was found to be significant at the .05 level. Orientation ratings over trials were segregated into those with ratings of zero or one, and those with ratings of two, three, and four. These ratings were then distributed into three catagories, those occurring on trials one to three, those on trials four to six and those on trials seven to ten. The chi-squares for day one and for all days were found to be significant at the .001 level. Distribution of observed ratings for these analyses are given in Table VII.

Habituation

The evoked electrical activity of the middle marginal and posterior suprasylvian gyri of cat 63-97 to repetitive presentation of a click stimulus every two seconds for 74 hours is illustrated in Figure 17. Changes in the mean amplitudes of evoked responses measured in micro-

volts from eight electrodes implanted along the suprasylvian gyri of this and two other cats are demonstrated in Figures 18 through 21. The 99 percent confidence interval for each electrode is illustrated with a band of dots. The changes in the mean amplitude over the 74 hour time interval for all four electrodes in cat 63-97 are seen in Figures 18 and 19. The graphs fail to indicate any consistent reduction in the amplitude of the evoked responses. For the first 23 hours there is a gradual diminution of the amplitude of the responses. Beyond this point there seems to be a gradual increase in the mean amplitude of the responses. The mean amplitude of evoked click responses recorded in cat 64-17 over a 69 hour interval are plotted in Figures 20 and 21. The graphs do not indicate any consistent change in the amplitude of the evoked responses in either direction during the time course. Similarly evoked responses recorded from cat 63-109 and plotted along the time course in Figure 21 fail to reveal any consistent pattern of change. A fourth cat (data not shown) did demonstrate progressive diminution of click evoked responses over a 72 hour interval. However, attempts to record evoked responses 24 and 72 hours after cessation of continuous stimulation failed to show recovery. It seems likely that the reduction of the mean amplitudes of evoked responses was the result of irreversible changes at the cortical site of the electrodes rather than a manifestation of habituation, per se, of the evoked response.

In summary, habituation of evoked responses recorded from the suprasylvian gyri of unanesthetized cats has not been demonstrated to repetitive click stimulation every two seconds for varying intervals of time. Waxing and waning of the response amplitudes over the time intervals were observed.

FIGURE 1

Characteristic waveforms of evoked responses from the posterior suprasylvian gyrus to peripheral auditory, tactile, and visual stimulation in the unanesthetized cat are demonstrated. Auditory evoked responses have the shortest latency followed by tactile and visual responses. Mean amplitudes of responses to tactile and visual stimuli are of similar magnitude, while auditory responses are slightly smaller in mean amplitude. Mean values were derived from one hundred consecutive evoked responses to the three modalities of stimulation. Mean latency values were calculated on the findings in ten of these responses for each modality.

In this, and all subsequent Figures, upward deflections indicate positivity in the surface lead relative to the depth lead.

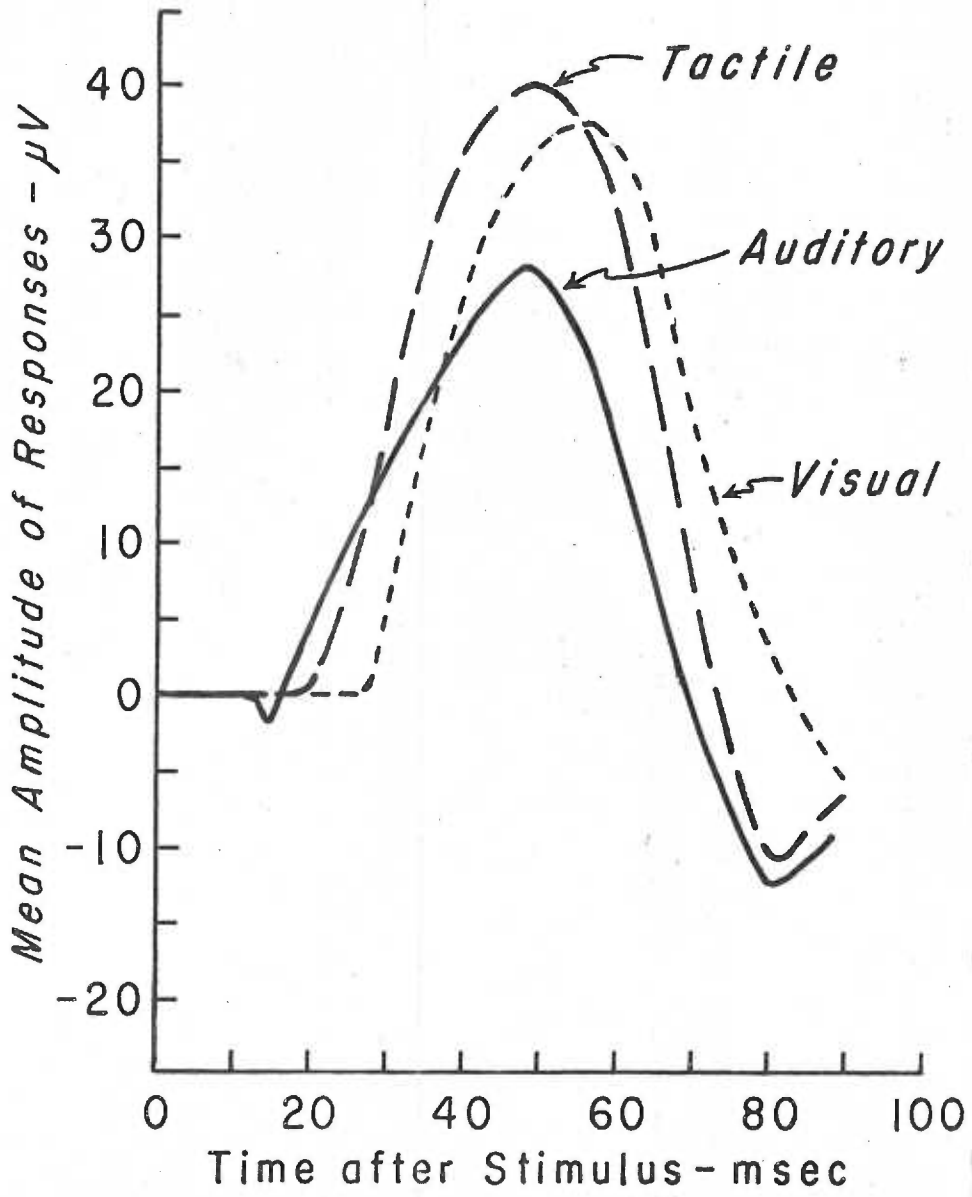

Tactile
Auditory
Visual
Mean Amplitude of Responses - μV
40
30
20
10
0
-10
-20
0
20
40
60
80
100
Time after Stimulus - msec

FIGURE 2

The amplitudes of one hundred consecutive evoked responses to peripheral auditory, tactile, and visual stimulation were measured and histograms of frequency distributions for each modality were constructed.

Tactile and visual evoked response amplitudes were similar in their distributions while auditory evoked responses had a somewhat less broad frequency distribution.

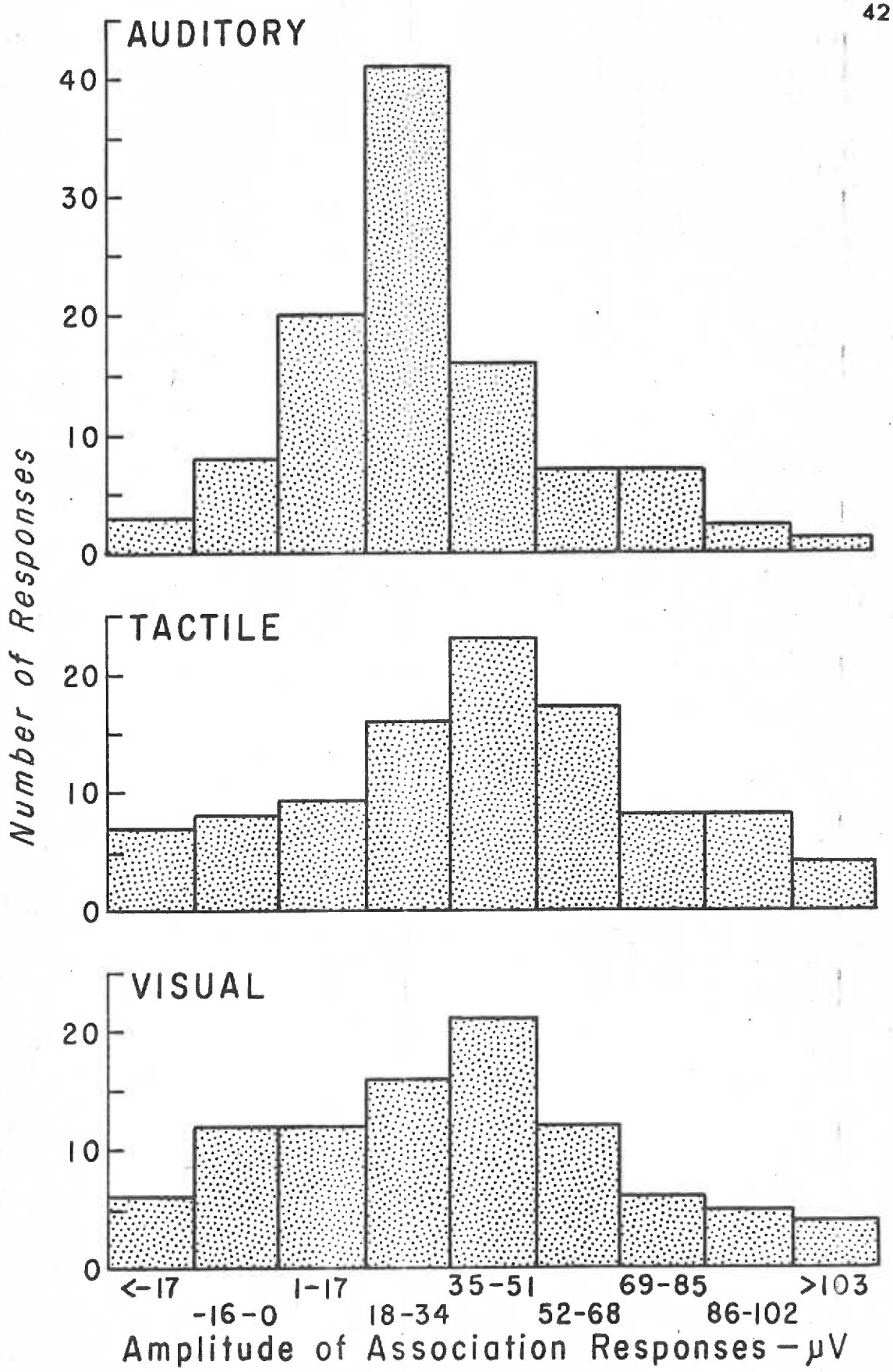

AUDITORY
TACTILE
VISUAL
Number of Responses
0
10
20
30
40
<-17
-16-0
1-17
18-34
35-51
52-68
69-85
86-102
>103
Amplitude of Association Responses – μV

FIGURE 3

Superimposed tracings of evoked responses to auditory, tactile, and visual stimulation recorded under conditions of chloralose anesthetic and in the unanesthetized state are illustrated.

The predominant waveform is one having an onset latency of 15-30 msec., with an initial positivity (deflection in an upward direction) of 25-45 msec. followed by a variably occurring negative component. An earlier appearing visual evoked waveform preceding the association response is seen in the waking state but is absent when recorded using chloralose anesthetic. Evoked responses recorded from the chloralose preparation demonstrated greater amplitude and less variability of waveform. Evoked responses under both conditions were similar in their characteristics and occurrence to tactile and auditory stimuli. The visual association responses were best observed in leads one and two and barely perceptable in leads three and four in the unanesthetized state, while evoked responses recorded from the chloralose preparation were represented maximally in leads one, three, and four with only a slight reduction evident in lead two.

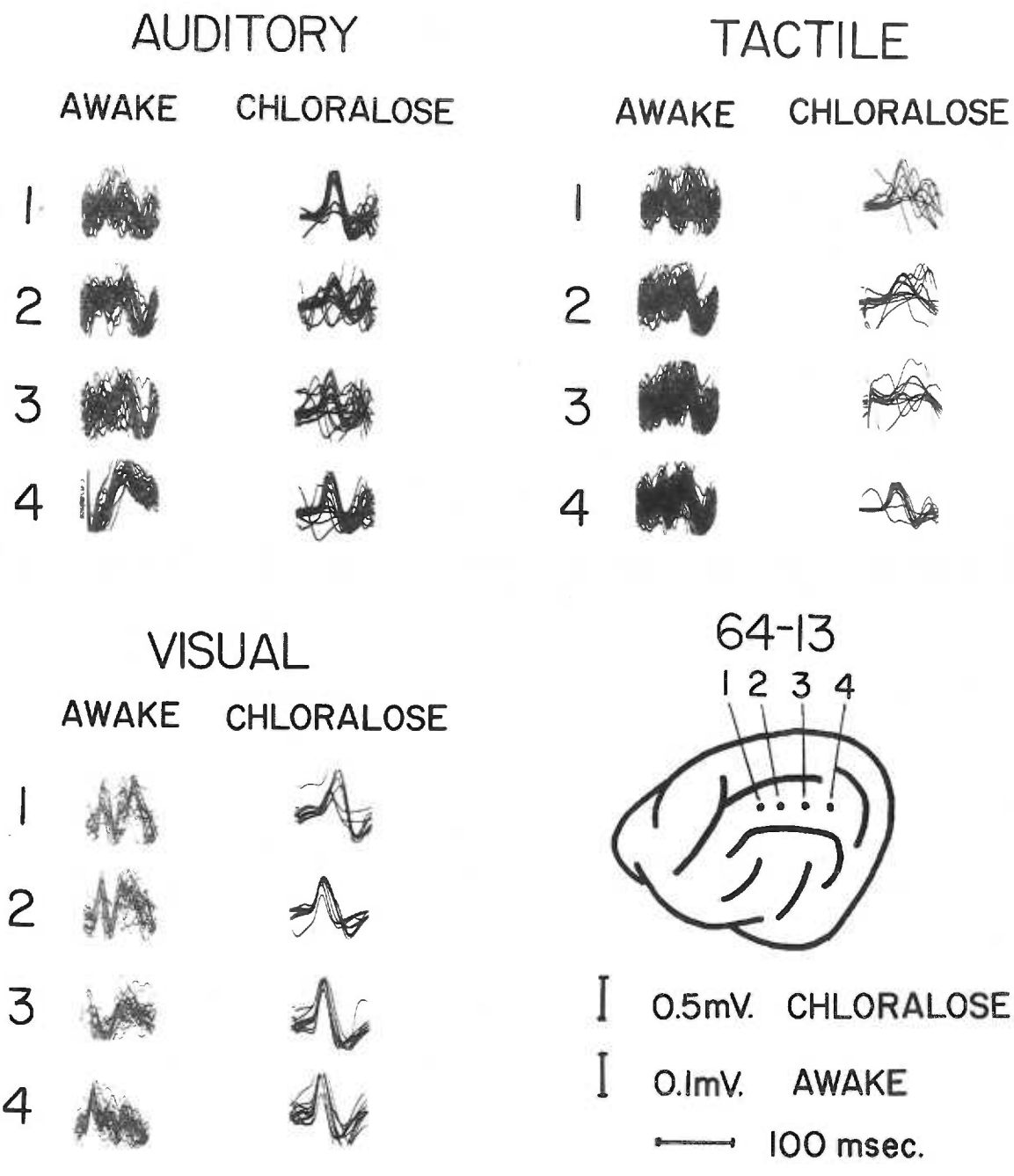
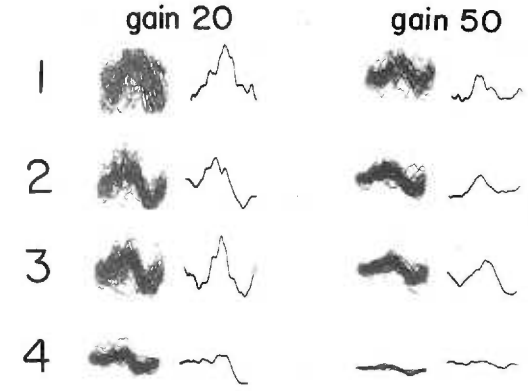

AUDITORY
AWAKE
CHLORALOSE
1
2
3
4
TACTILE
AWAKE
CHLORALOSE
1
2
3
4
VISUAL
AWAKE
CHLORALOSE
1
2
3
4
64-13
1 2 3 4
0.5mV. CHLORALOSE
0.1mV. AWAKE
100 msec.

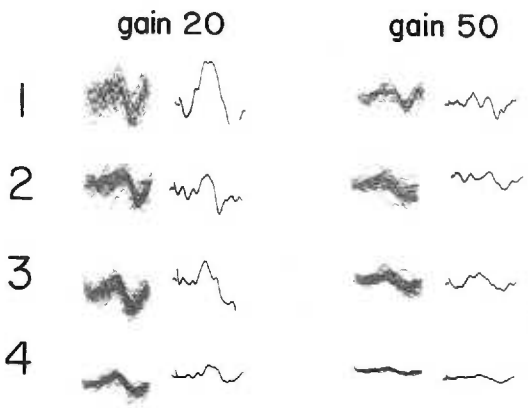
FIGURE 4

Single and superimposed tracings to auditory, tactile, and visual peripheral stimulation are demonstrated for the normal waking state. The predominant waveform is one having an onset latency of 15-30 msec. followed by an initial positivity (deflection in an upward direction) of 25-45 msec. The evoked responses are seen best in electrodes one, two, and three. There is a marked reduction of the mean evoked response amplitude in lead four which might indicate its position is on the posterior margin of the active field. An earlier evoked waveform is seen preceding the late response to visual stimuli in all electrodes. In lead one this probably reflects activity in the secondary sensory visual area while the early waveform in leads two, three, and four may indicate activity in the visual field located in the suprasylvian sulcus.

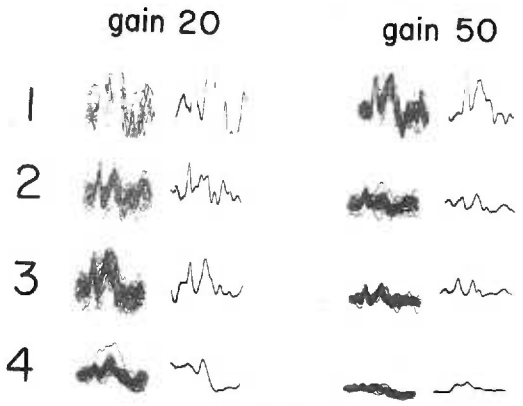
AUDITORY



TACTILE



VISUAL



63-97

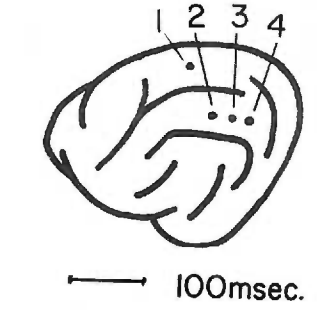
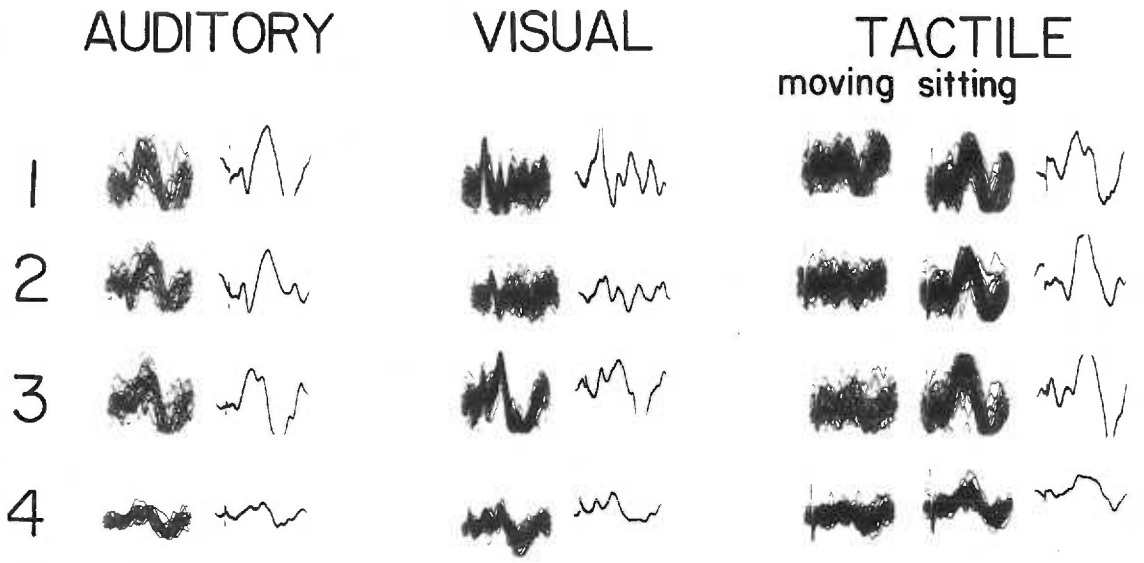


FIGURE 5

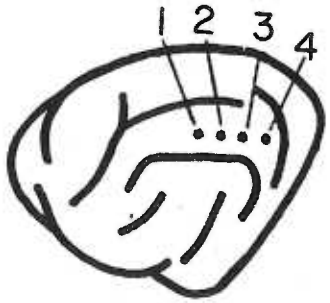
Single and superimposed tracings to auditory, tactile, and visual peripheral stimulation are demonstrated for the normal waking state. The predominant waveform is one having an onset latency of 15-30 msec. followed by an initial positivity (deflection in an upward direction) of 25-50 msec. The evoked responses are demonstrated maximally in leads one, two, and three. There is a significant reduction in the size of the response in lead four which might indicate its location on the posterior margin of the association field. An earlier waveform is seen preceding the late response to visual stimulation. This may represent activity from the small visual field located in the suprasylvian sulcus.

A graph demonstrating the mean amplitudes of tactile evoked responses recorded during two different behavioral states (i.e., moving and sitting) is shown. The amplitude of the evoked responses is greater in a state of lesser activity than in the more active state for all electrodes.



63-88

100msec 0.1mV



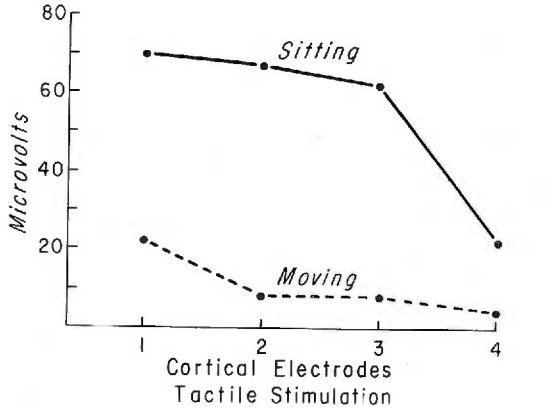


FIGURE 6

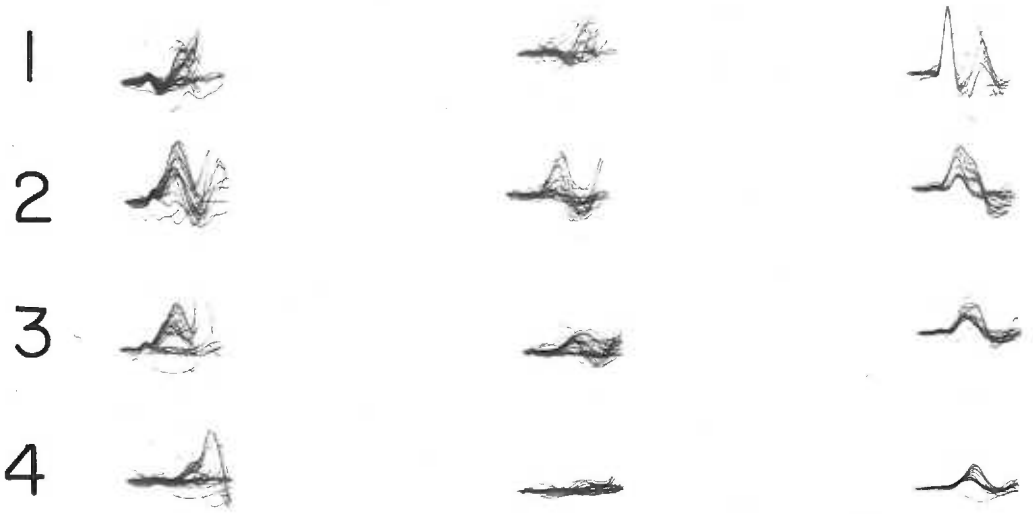
Superimposed tracings to auditory, tactile, and visual stimulation are recorded using chloralose anesthetic in cats 63-97 and 63-88. Pictorial illustrations of the cortical locations of the electrodes are seen in Figures 4 and 5 respectively. Association responses are best seen in leads two and three to all modalities in cat 63-97 and in leads one and two in cat 63-88. The visual evoked responses are present in all leads in both cats. The possibility exists that the visual evoked responses in leads three and four of cat 63-88 reflect activity in the secondary visual area on the posterior suprasylvian gyrus or in the visual field located in the suprasylvian sulcus because of their short latency of response.

63-97

CHLORALOSE

0.25mV. 100msec.

AUDITORY TACTILE VISUAL



63-88

CHLORALOSE

0.1mV. 100msec.

AUDITORY TACTILE VISUAL

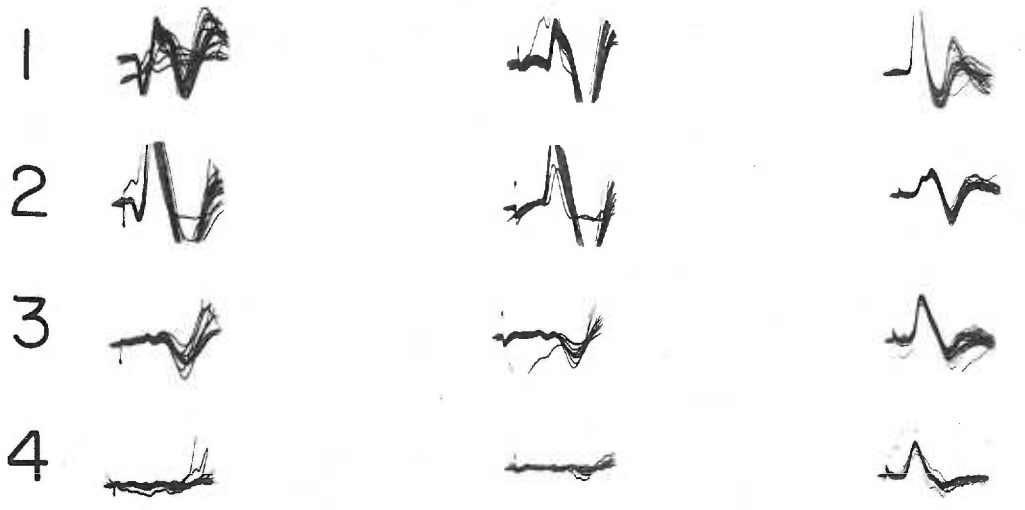


TABLE I

Association Evoked Response Changes With Bodily Activity

STIMULUS	CAT	ELECTRODE	N	MEAN AMPLITUDE-μV LEVEL "B"	MEAN AMPLITUDE-μV LEVEL "E"
Auditory	63-97	1	40	67	0*
Auditory	63-97	2	40	67	8*
Auditory	63-97	3	40	46	0*
Auditory	63-97	4	40	25	4*
				LEVEL "A"	LEVEL "C"
Tactile	63-97	1	40	25	8*
Tactile	63-97	2	40	17	2*
Tactile	63-97	3	40	21	4*
Tactile	63-97	4	40	19	8*
				LEVEL "B"	LEVEL "E"
Tactile	63-88	1	40	71	21*
Tactile	63-88	2	40	67	8*
Tactile	63-88	3	40	63	8*
Tactile	63-88	4	40	21	4*
				LEVEL "B"	LEVEL "E"
Visual	64-17	1	25	83	21*
Visual	64-17	2	25	79	13*
Visual	64-17	3	25	42	0*

* Decrease significant at p. < .05 level

Rating Scale Of Behavioral State

A. The cat was lying down, head on floor.
B. The cat was sitting on forelimbs, head erect.
C. The cat was sitting, forelimbs extended.
D. The cat was washing himself.
E. The cat was pacing back and forth.

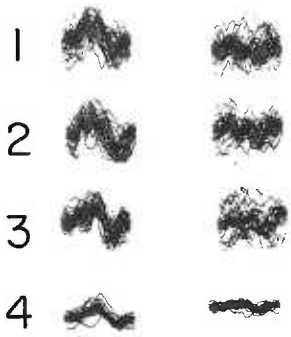
FIGURE 7

Evoked association responses to auditory, tactile, and visual stimulation were recorded during different levels of bodily activity as determined by the rating scale depicted.

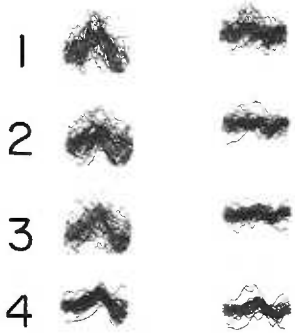
It was found that with heightened activity there is reduction of the mean amplitude of the evoked responses relative to a lesser degree of activity.

63-97

AUDITORY
gain 20

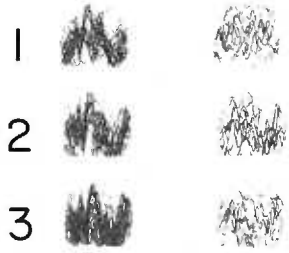


TACTILE
gain 10



64-17

VISUAL
gain 20



BEHAVIORAL STATE

A laying down, head on floor.

B sitting on forelimbs, head erect.

C sitting, forelimbs extended.

D washing himself.

E pacing back and forth.

64-17

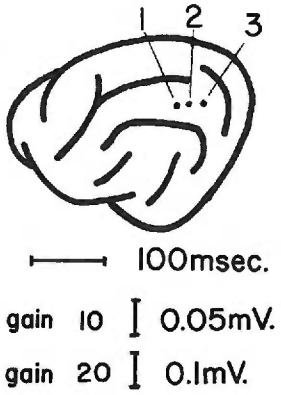


TABLE II

Association Evoked Response Changes With Novel Stimuli

STIMULUS	CAT	N	AMPLITUDE BEFORE STIMULUS-μV	NOVEL STIMULUS	AMPLITUDE DURING STIMULUS-μV
Auditory	64-17	20	66	air (T)	17*
Auditory	64-17	20	54	barking (A)	0*
Auditory	64-17	20	66	rat (V)	21*
Auditory	64-18	25	146	air (T)	21*
Auditory	64-18	25	94	barking (A)	0*
Auditory	64-18	25	146	rat (V)	63*
Tactile	64-17	25	54	air (T)	0*
Tactile	64-17	25	54	barking (A)	29*
Tactile	64-17	25	33	rat (V)	13*
Tactile	64-18	20	96	air (T)	25*
Tactile	64-18	20	60	barking (A)	0*
Tactile	64-18	20	63	rat (V)	0*
Visual	64-17	25	94	air (T)	83
Visual	64-17	25	125	barking (A)	73*
Visual	64-17	25	125	rat (V)	73*
Visual	64-18	25	75	air (T)	21*
Visual	64-18	25	83	barking (A)	46*
Visual	64-18	25	88	rat (V)	46*

* Decrease significant at $p. < .05$ level

TABLE III

Association Evoked Response Changes With Novel Stimuli

STIMULUS	CAT	N	AMPLITUDE BEFORE STIMULUS-μV	NOVEL STIMULUS	AMPLITUDE DURING STIMULUS-μV
Auditory	63-109	40	22	rat (V)	6*
Auditory	64-2	20	79	exp. (V)	29*
Auditory	64-2	20	100	food (V)	17*
Auditory	64-2	20	92	rat (V)	29*
Auditory	64-2	20	125	exp. (V)	10*
Auditory	64-2	20	135	food (V)	63*
Auditory	64-2	20	135	rat (V)	42*
Auditory	64-3	30	54	exp. (V)	0*
Auditory	64-3	30	46	food (V)	8*
Auditory	64-3	30	54	cat (V)	0*
Auditory	64-13	25	54	air (T)	25*
Auditory	64-13	25	42	rat (V)	20
Auditory	64-13	25	38	barking (A)	8
Auditory	64-13	25	54	rat (V)	13*
Auditory	64-13	25	33	air (T)	13*
Tactile	64-13	25	50	air (T)	33
Tactile	64-13	25	33	barking (A)	29
Tactile	64-13	25	50	rat (V)	17*
Tactile	64-13	25	52	air (T)	0*
Tactile	64-13	25	31	barking (A)	5*
Tactile	64-13	25	52	rat (V)	5*
Visual	64-2	20	33	exp. (V)	39
Visual	64-13	25	44	air (T)	29*
Visual	64-13	25	38	barking (A)	33
Visual	64-13	25	42	rat (V)	42
Visual	64-15	20	25	air (T)	8*
Visual	64-15	20	15	barking (A)	9*
Visual	64-15	20	10	rat (V)	8
Visual	64-17	25	75	barking (A)	38*
Visual	64-17	25	79	rat (V)	25*

* Decrease significant at $p. < .05$ level

FIGURE 8

Reduction of the auditory evoked responses upon presentation of novel visual (rat), auditory (barking sounds), and tactile (air stream) stimuli are observed in cats 64-17 and 64-18 in the unanesthetized state. The evoked responses in cat 64-18 occurred in response to click stimulation from a microspeaker which had been placed within the external auditory canal. Drawings of the approximate cortical locations of the electrodes on the suprasylvian gyrus are seen for cat 64-18 and may be seen for cat 64-17 in Figure 7.

A deflection of one cm. is equivalent to 83.3 microvolts at a gain of 20. At a gain of 50, a deflection of one cm. is equivalent to 208.3 microvolts.

AUDITORY

64-18

gain 50

BEFORE AIR AFTER

2

BARKING

2

RAT

2

64-17

gain 20

BEFORE AIR AFTER

2

BARKING

2

RAT

2

64-18

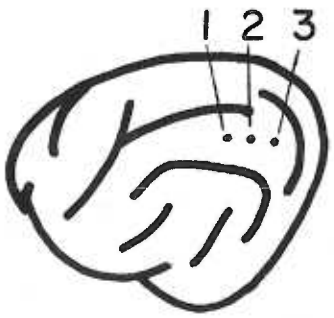


FIGURE 9

Reduction of the tactile evoked response upon presentation of novel visual (rat), auditory (barking sounds), and tactile (air stream) stimuli are observed in cats 64-17 and 64-18 in the unanesthetized state. Approximate location of cortical electrodes on the suprasylvian gyrus are demonstrated in Figures 7 and 8.

A deflection of one cm. is equivalent to 83.3 microvolts at a gain of 20.

TACTILE

64-17

gain 20

BEFORE AIR AFTER

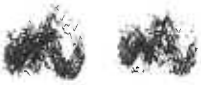
2

BARKING

2

RAT

2



64-18

gain 20

BEFORE AIR AFTER

2

BARKING

2

RAT

2

FIGURE 10

Reduction of the visual evoked response upon presentation of novel visual (rat), auditory (barking sounds), and tactile (air stream) stimuli are observed in cats 64-17 and 64-18 in the unanesthetized state. Drawings of the approximate cortical locations of the electrodes for cat 64-17 are seen in Figure 7 and for cat 64-18 in Figure 8.

A deflection of one cm. is equivalent to 83.3 microvolts at a gain of 20. At a gain of 50, a deflection of one cm. is equivalent to 208.3 microvolts.

VISUAL

64-18

gain 20

BEFORE AIR AFTER

2   

BARKING

2   

RAT

2   

64-17

gain 50

BEFORE AIR AFTER

2   

BARKING

2   

RAT

2   

FIGURE 11

Reduction of click evoked responses upon presentation of various novel stimuli such as a rat, food (the cat was allowed contact with the food), the experimenter walking into the soundproof chamber, a stream of air, and barking sounds emitted by the experimenter and the subsequent recovery rate of the amplitudes of the response are observed. Recovery usually takes place within a minute and a half, with the exception of food stimuli where two minutes were required for the amplitude to approach its original magnitude.

A deflection of one cm. is equivalent to 83.3 microvolts at a gain of 20. At a gain of 50, a deflection of one cm. is equivalent to 208.3 microvolts.

AUDITORY

64-13

gain 20

BEFORE AIR MINUTES AFTER

2

0.67 1.33

BARKING

2

0.67

64-2

gain 50

BEFORE EXP. MINUTES AFTER

4

0.67 1.33

gain 20

FOOD

4

0.67 1.33 2.0 2.67

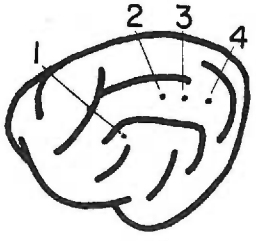
gain 50

RAT

4

0.67 1.33

64-2



64-13

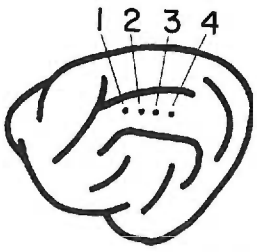


TABLE IV

Effect Of Head Position Upon Mean Amplitudes Of Evoked Responses In The Chloralose Preparation

STIMULUS	CAT	N	MEAN AMPLITUDE MICROVOLTS	ALTERATION IN POSITION	MEAN AMPLITUDE MICROVOLTS	LEADS
Auditory	64-13	20	563	Changes in head	500	2
Auditory	64-13	20	667	position 90 degrees away from speaker	625	4

FIGURE 12

The relationship between amplitude of association responses averaged over subjects measured in percent of maximum response for each animal and the mean orientation scores for the subjects is plotted for day one and all days. There is a suggestion of an inverse relationship.

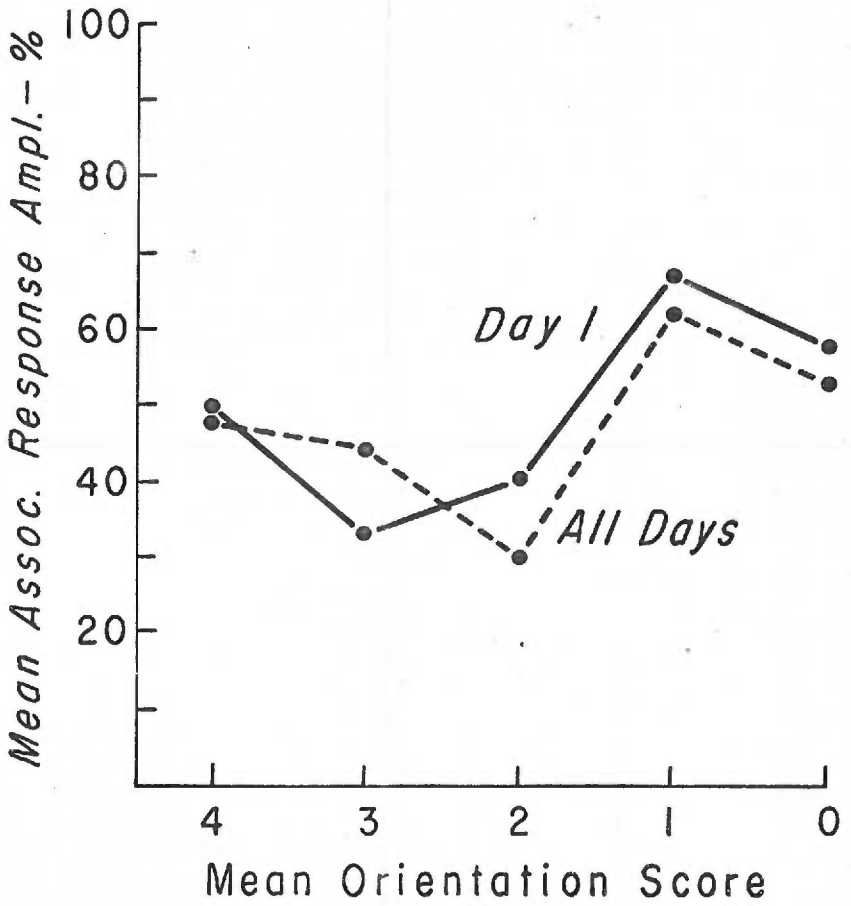

Mean Assoc. Response Ampl. - %
100
80
60
40
20
Day 1
All Days
4
3
2
1
0
Mean Orientation Score

FIGURE 13

Changes in the mean orientation score and the mean amplitude of click evoked responses measured in absolute amplitude are plotted over trials for days one and two. For both days the mean orientation score appears to decrease in magnitude as the mean amplitude of the evoked responses appears to increase in magnitude over trials, thus implying an inverse relationship between the two parameters.

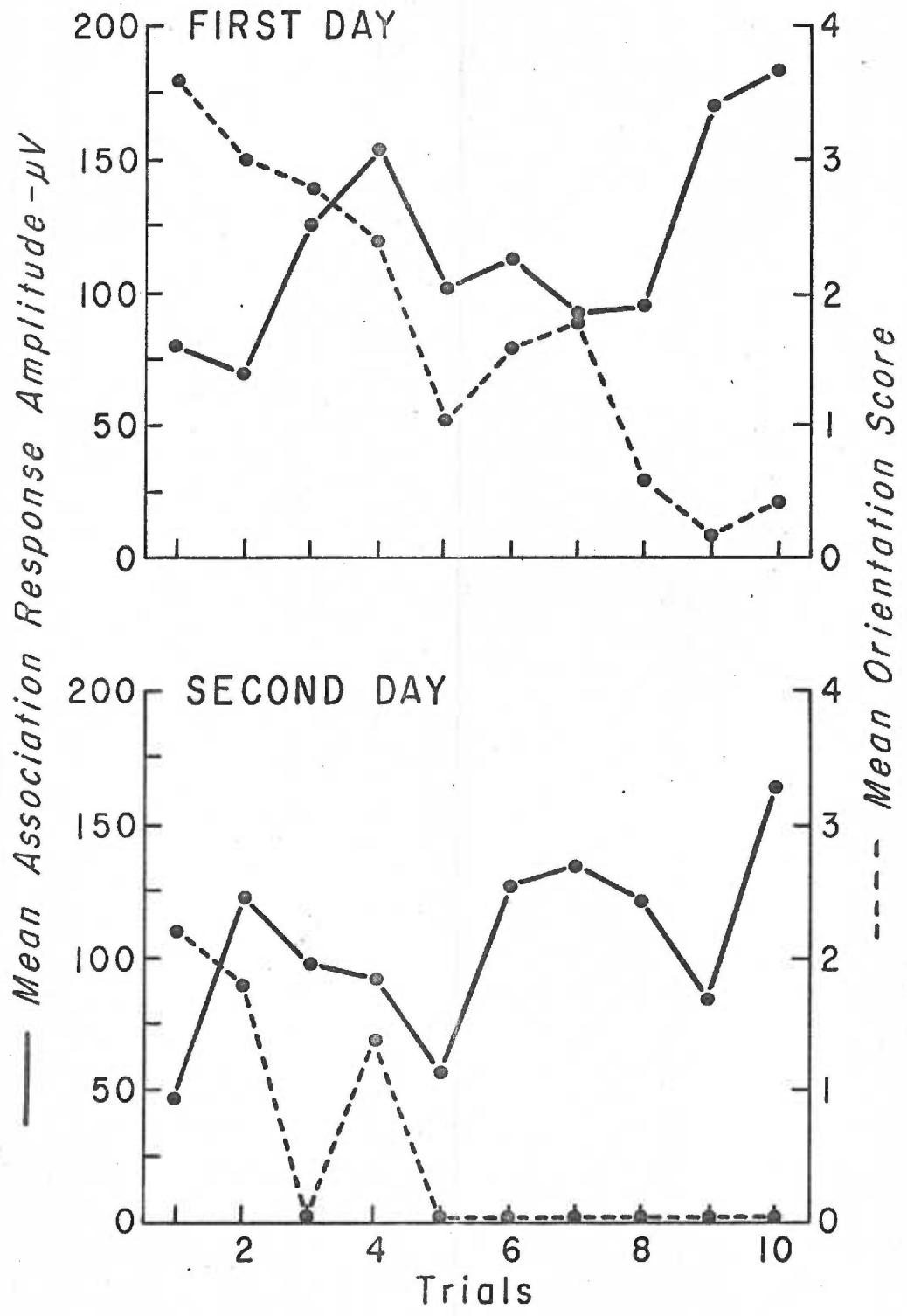

FIRST DAY
SECOND DAY
200
150
100
50
0
4
3
2
1
0
2
4
6
8
10
Trials
Mean Association Response Amplitude-μV
Mean Orientation Score

FIGURE 14

Changes in the mean orientation score and the mean amplitude of click evoked responses measured in absolute amplitude are plotted over trials for days three and four. For both days the mean orientation score appears to decrease in magnitude as the mean amplitude of the evoked responses appears to increase in magnitude over trials, thus implying an inverse relationship between the two parameters.

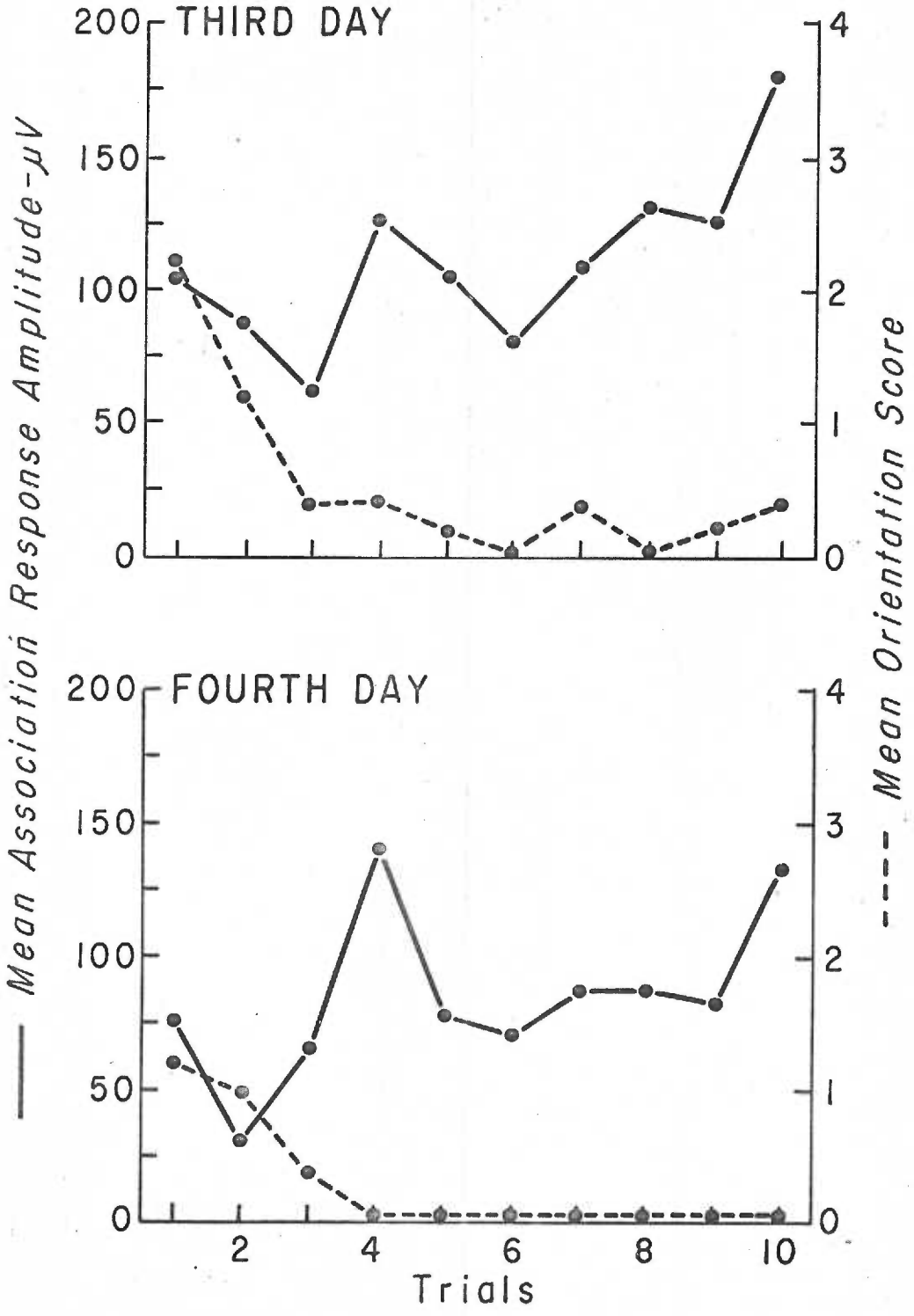

THIRD DAY
FOURTH DAY
200
150
100
50
0
4
3
2
1
0
2
4
6
8
10
Trials
Mean Association Response Amplitude-μV
Mean Orientation Score

FIGURE 15

Changes in the mean orientation score and the mean amplitude of click evoked responses for all five subjects measured in microvolts are plotted against trials (summed over all days) and against days (summed over all trials). When the mean orientation scores and mean evoked amplitudes are collapsed over days and plotted against trials the inverse relationship of these parameters becomes readily observed. When these values are summed over trials and plotted over days a decrease in the mean evoked response is suggested over the four day period. The mean orientation score decreases more abruptly over the four days with the greatest decrease being evident between the first and second day.

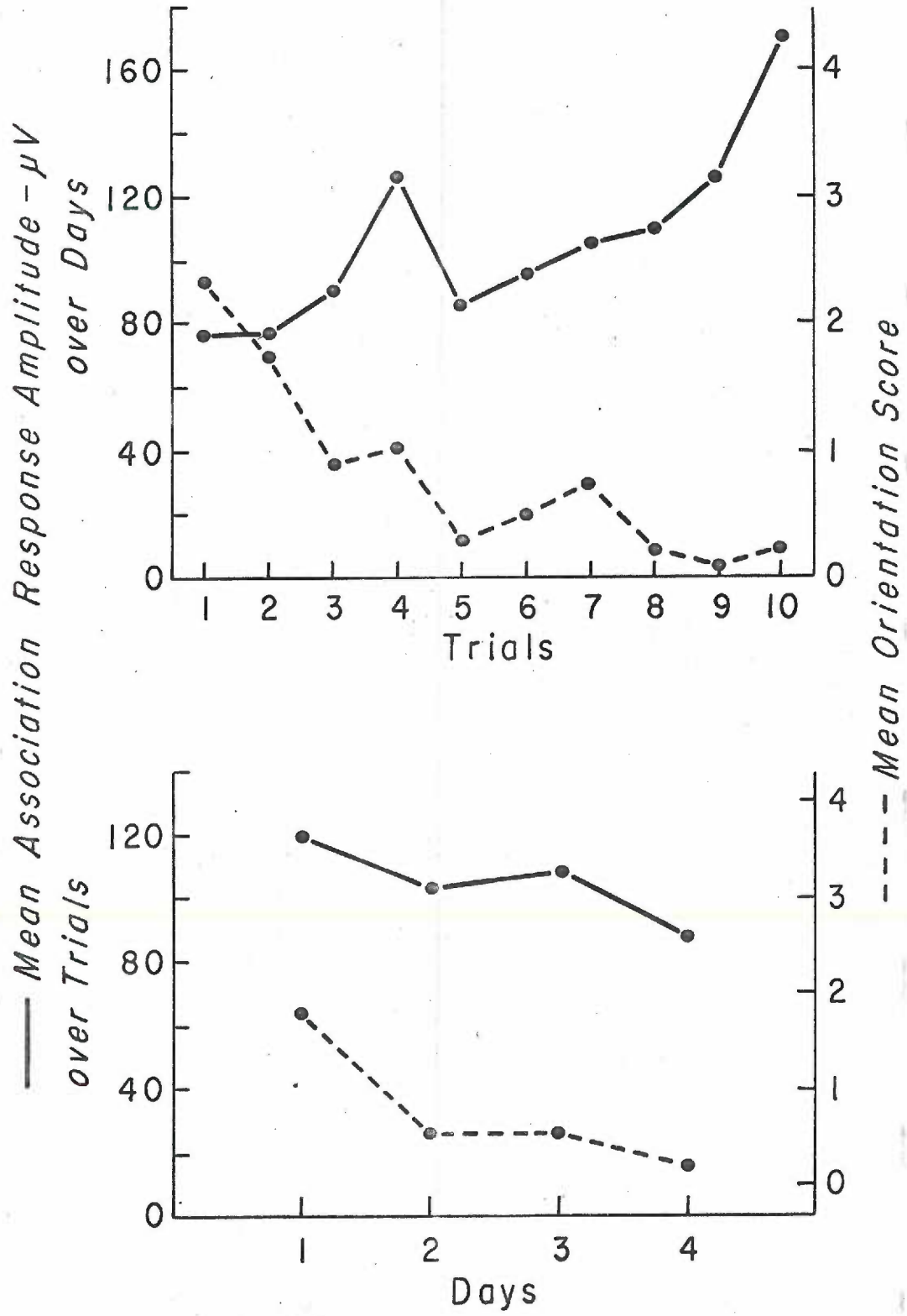

Mean Association Response Amplitude - μV over Days
Mean Orientation Score
160
120
80
40
0
4
3
2
1
0
1 2 3 4 5 6 7 8 9 10
Trials
Mean Association Response Amplitude - μV over Trials
Mean Orientation Score
120
80
40
0
4
3
2
1
0
1 2 3 4
Days

FIGURE 16

Changes in the mean orientation score and the mean amplitude of click evoked responses for all five subjects measured in percent of maximum response for each animal are plotted against trials (summed over all days) and against days (summed over all trials). When the mean orientation scores and the mean evoked amplitudes are collapsed over days and plotted against trials the inverse relationship of these parameters becomes readily observed. When these values are summed over trials and plotted over days a decrease in the mean evoked response is suggested over the four day period. The mean orientation score decreases more abruptly over the four days with the greatest decrease being evident between the first and second day.

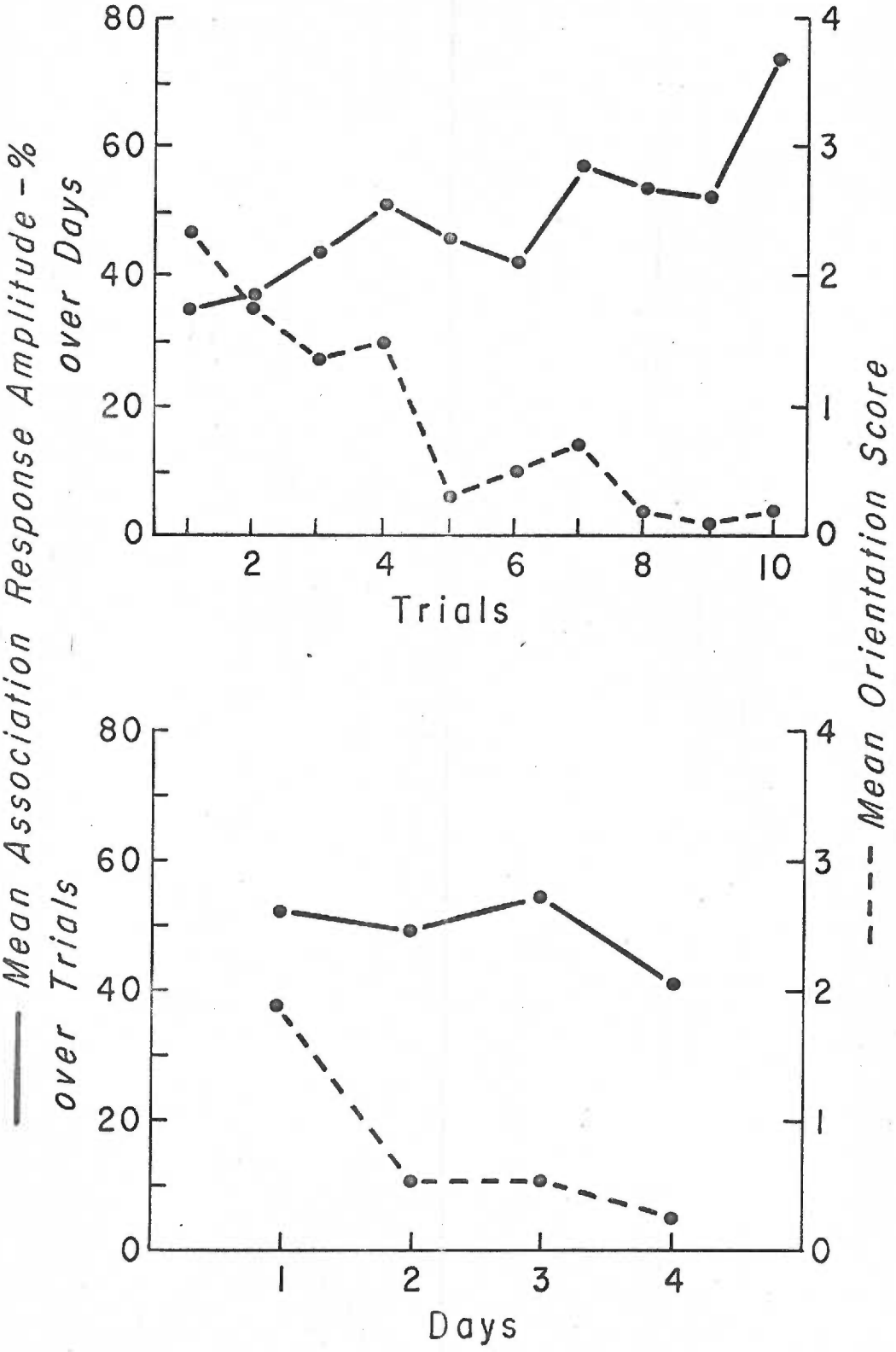

80
60
40
20
0
4
3
2
1
0
2
4
6
8
10
Trials
Mean Association Response Amplitude - % over Days
80
60
40
20
0
4
3
2
1
0
1
2
3
4
Days
Mean Association over Trials
Mean Orientation Score

TABLE V

Summary Of Analysis Of Variance

A

Association Evoked Responses-In Absolute Amplitude

SOURCE	df	SS	MS	F
Between Days	3	67.93	22.64	2.35
Between Subjects	4	291.11	72.77	7.55***
Between Trials	9	450.67	50.07	5.19***
Trials X Days	27	89.09	3.29	.34
Within (error)	156	1503.11	9.63	
Total	199			

B

Association Evoked Responses-In Percent

SOURCE	df	SS	MS	F
Between Days	3	5178.13	1726.04	1.99
Between Subjects	4	2693.05	673.26	.78
Between Trials	9	22916.64	2546.30	2.94**
Trials X Days	27	17497.28	648.05	.75
Within (error)	156	135004.12	865.41	
Total	199			

** Significant at F01

*** Significant at F001

TABLE VI

Distribution Of Association Response Amplitudes On The First Day

Orientation Ratings	Amplitude in Percent	
	0-49.99%	50-100%
4, 3, 2,	12	11
1, 0	6	21

$X^2=4.82$
$X^2.05=3.84$

TABLE VII

Distribution Of Orientation Ratings Over Days

Orientation Ratings	Days	
	Days 1 and 2	Days 3 and 4
4, 3, 2,	30	14
1, 0	70	86

$X^2=8.33$
$X^2.05=3.84$

Distribution Of Orientation Ratings Over Trials For Day One

Orientation Ratings	Trials		
	1-3	4-6	7-10
4, 3, 2,	13	7	3
1, 0	2	8	17

$X^2=17.70$
$X^2.001=13.82$

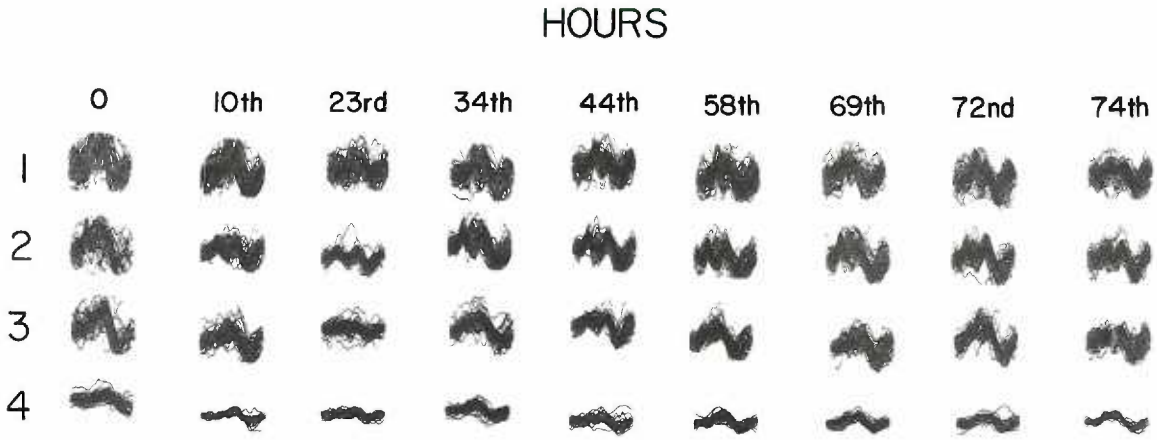
Distribution Of Orientation Ratings Over Trials For All Days

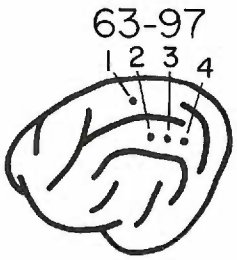
Orientation Ratings	Trials		
	1-3	4-6	7-10
4, 3, 2,	30	9	5
1, 0	30	51	75

$X^2=40.68$
$X^2.001=13.82$

FIGURE 17

The electrical activity of the middle lateral and posterior suprasylvian gyri of cat 63-97 recorded at varying intervals over a time course of 74 hours to repetitive click stimulation every two seconds is illustrated. No consistent change in the amplitude of the evoked responses over this time course is noted.





AUDITORY

I 0.1mV

100msec

FIGURE 18

Graphic illustrations of changes in the mean amplitude of click evoked responses in cat 63-97 for electrodes one and two over the 74 hour time course are observed. For the first 23 hours there is a progressive diminution of the mean amplitude of the evoked responses. Beyond this point there seems to be a gradual increase in the amplitude of the responses.

The 99 percent confidence interval is indicated by the band of dots.

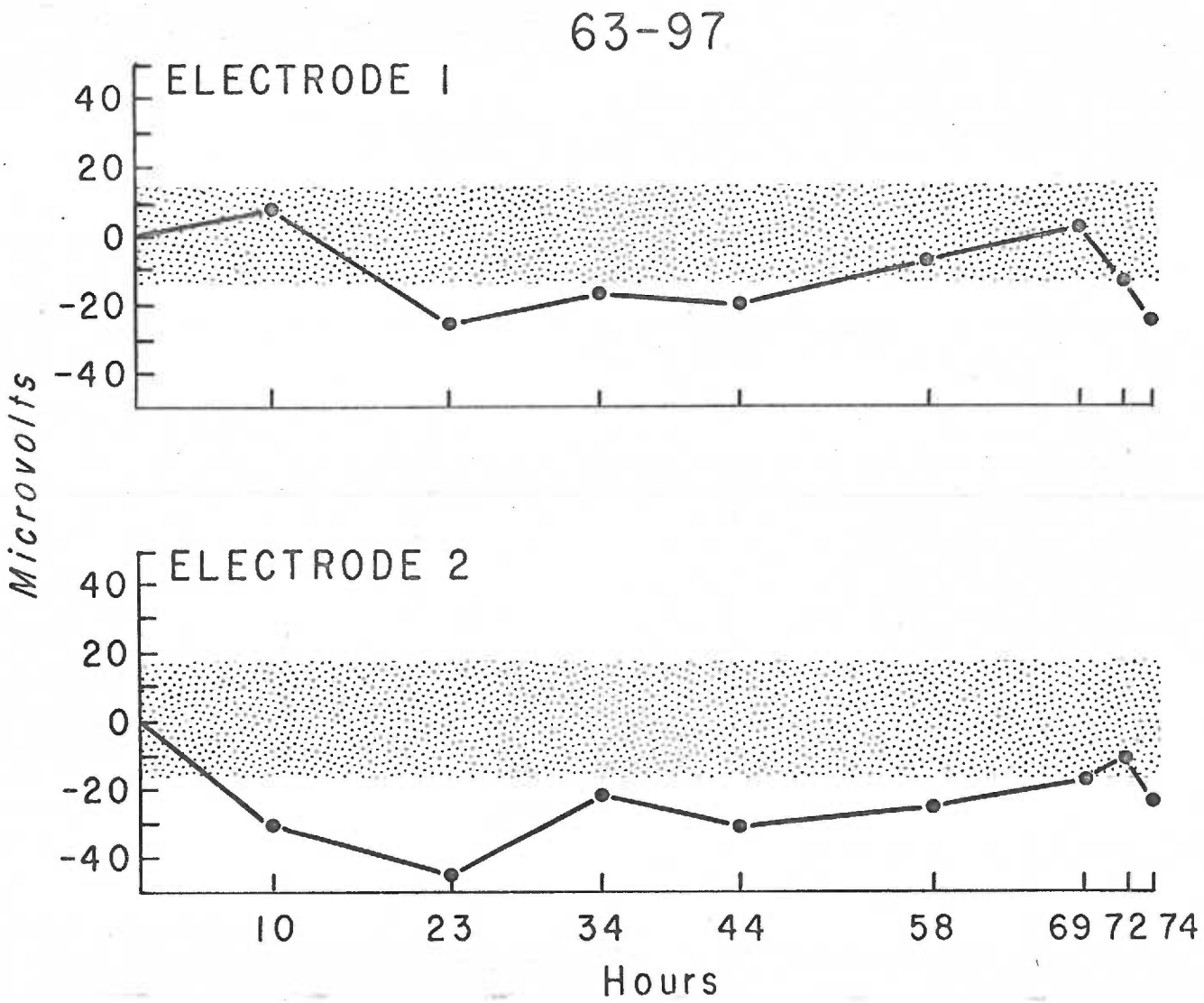

63-97
ELECTRODE 1
40
20
0
-20
-40
ELECTRODE 2
40
20
0
-20
-40
Microvolts
10
23
34
44
58
69
72
74
Hours

FIGURE 19

Graphic illustrations of changes in the mean amplitude of click evoked responses in cat 63-97 for electrodes three and four over the 74 hour time course are observed. For the first 23 hours there is a decrease in the mean amplitude of the evoked responses. Beyond this point there seems to be a progessive increase in the amplitude of the responses.

The 99 percent confidence interval is indicated by the band of dots.

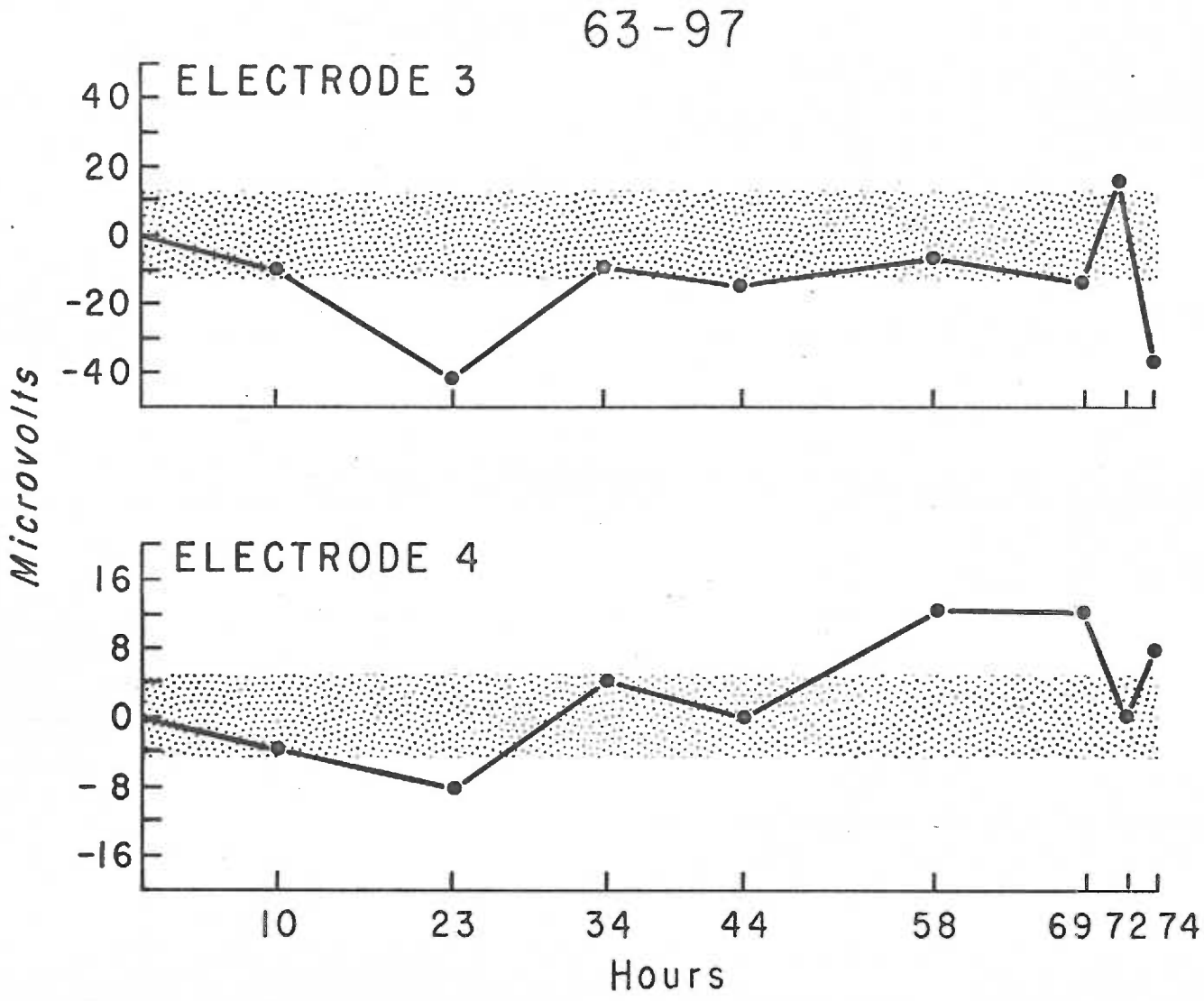

63-97
ELECTRODE 3
40
20
0
-20
-40
ELECTRODE 4
16
8
0
-8
-16
Microvolts
10
23
34
44
58
69
72
74
Hours

FIGURE 20

Graphic illustrations of changes in the mean amplitude of the click evoked responses in cat 64-17 for electrodes one and two over the 69 hour time course are observed. No consistent change in amplitude was noted, although waxing and waning of the amplitude was observed.

The 99 percent confidence interval is indicated by the band of dots.

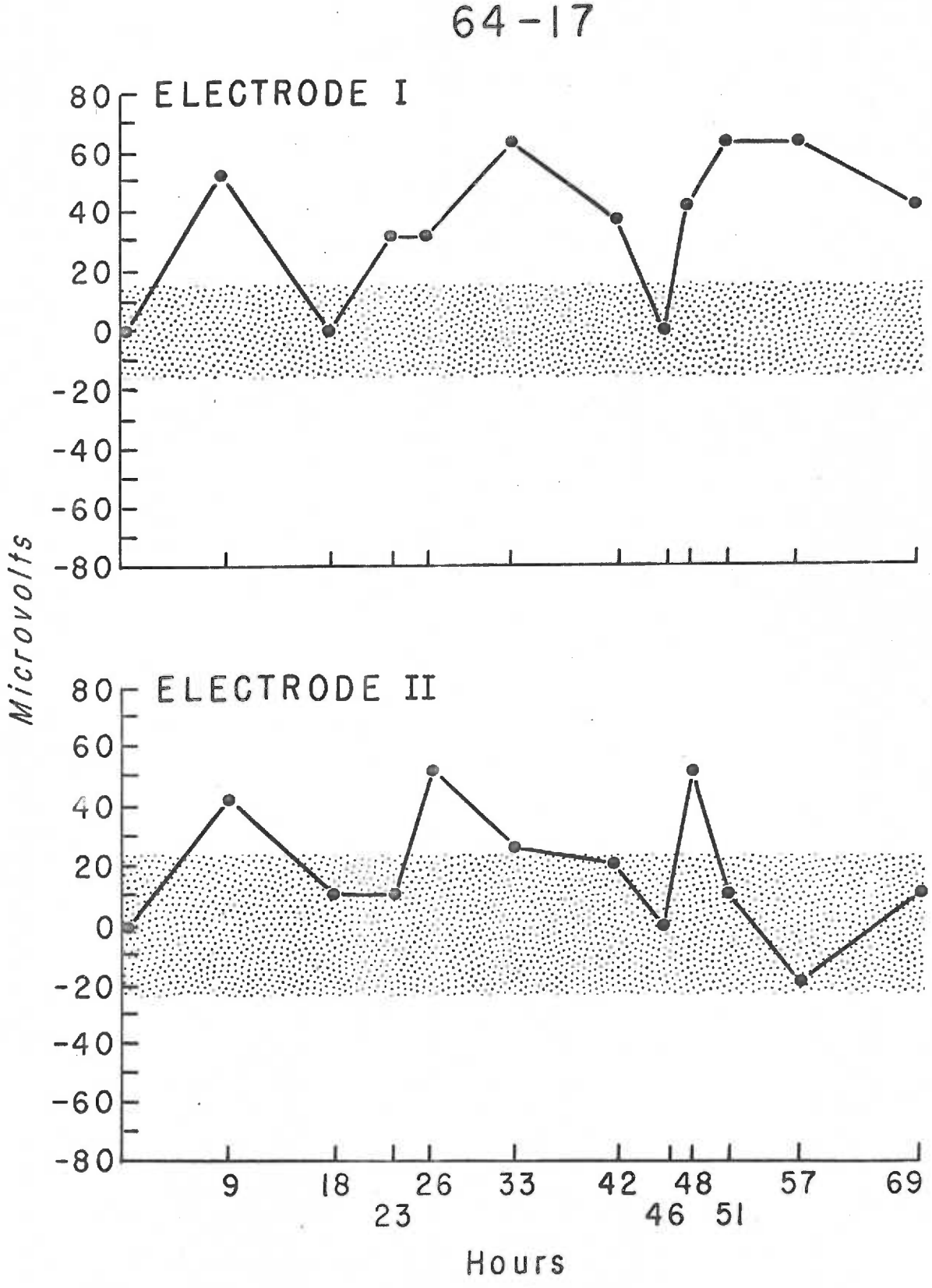
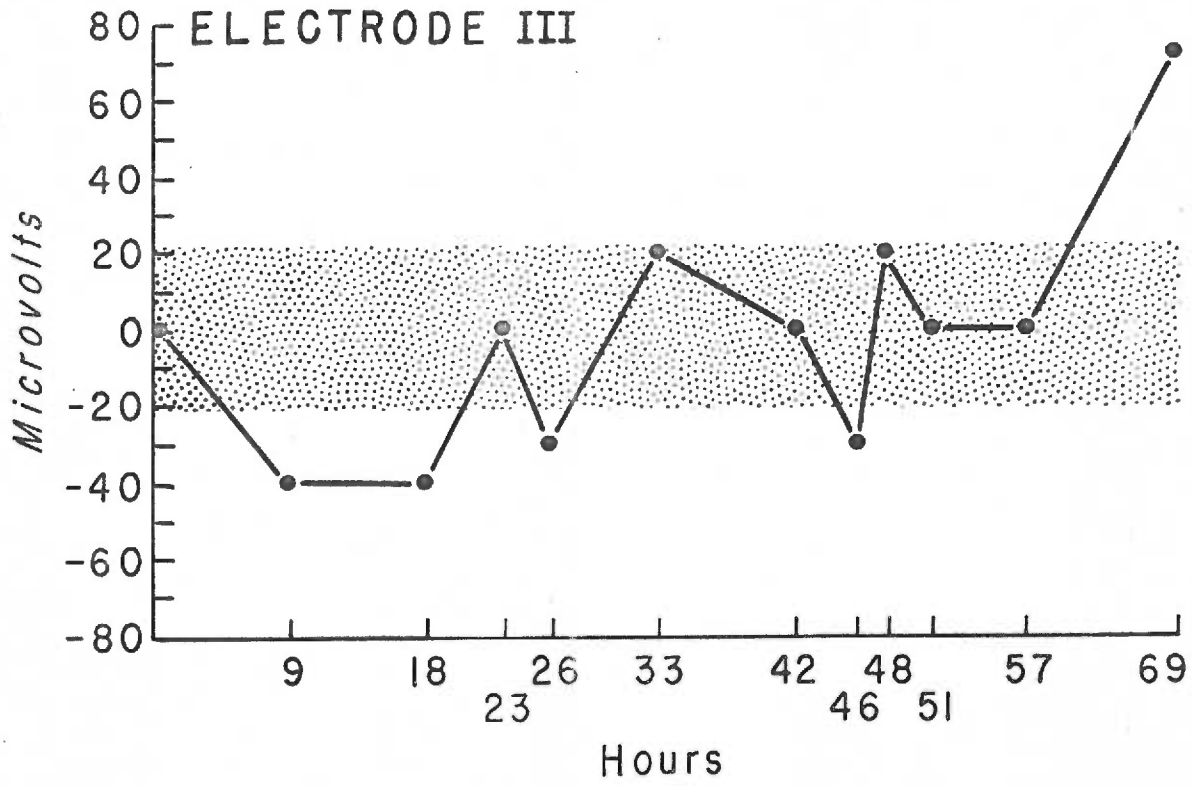

64-17
ELECTRODE I
80
60
40
20
0
-20
-40
-60
-80
ELECTRODE II
Microvolts
9
18
23
26
33
42
46
48
51
57
69
Hours

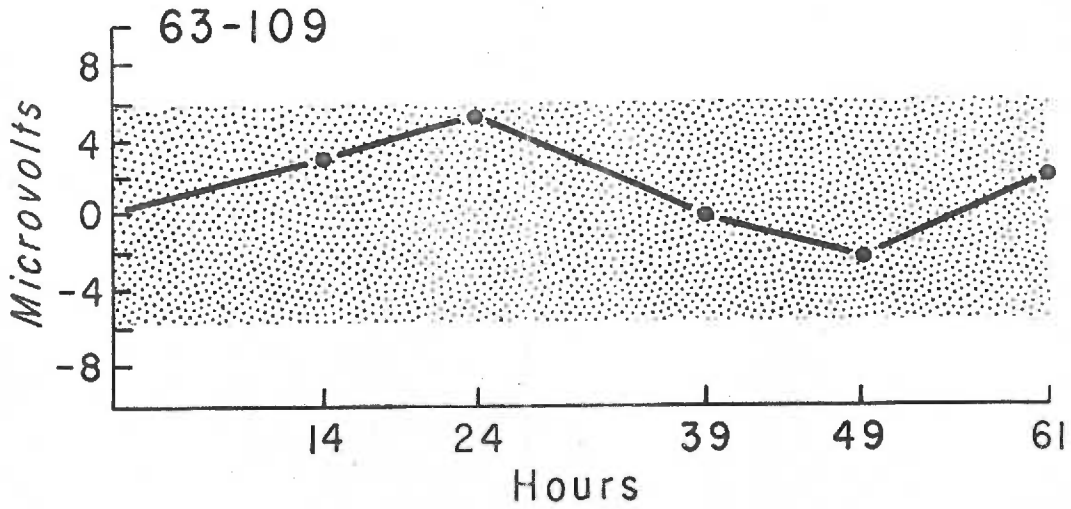
FIGURE 21

Graphic illustrations of changes in the mean amplitudes of click evoked responses in cats 64-17 and 63-109 for electrodes placed on the posterior suprasylvian gyrus over their respective time courses are demonstrated. No consistent change in amplitude was observed, although waxing and waning of the response amplitude was noted.

The 99 percent confidence interval is indicated by the band of dots.

64-17


ELECTRODE III
80
60
40
20
0
-20
-40
-60
-80
Microvolts
9
18
23
26
33
42
46
48
51
57
69
Hours


63-109
8
4
0
-4
-8
Microvolts
14
24
39
49
61
Hours

DISCUSSION

The experimental evidence indicates that evoked responses to either peripheral auditory, tactile, or visual stimuli can be recorded from the suprasylvian gyrus of the unanesthetized and unrestrained cat. These responses are similar in their characteristics and waveform to those previously described in the chloralose preparation. When unanesthetized cats with chronic electrodes were subsequently anesthetized with chloralose, evoked responses similar to those seen in the waking state were noted, with the exception that the amplitudes of the evoked responses were greater in magnitude and exhibited less variability.

The latency differences described for evoked responses to the three modalities of stimulation using chloralose maintain the same order in the waking animal, with auditory having the shortest latency of response, visual responses having the longest, and tactile responses being intermediate in length. While most characteristics of the responses were equivalent under both conditions it appears the evoked responses recorded using chloralose were more limited in their superficial extent along the gyrus. These findings would seem to confirm Buser and Imbert (8) who suggested the effect of chloralose was to decrease the superficial extent of the association areas while enhancing the voltage of the evoked response.

One of the problems encountered in this investigation was the apparent extreme sensitivity of the association cortex. Implantation of bipoler electrodes in a number of instances appeared to damage the

cortex to a degree incompatible with the recording of meaningful evoked responses. Usually when responses were obtainable from one electrode they could be elicited from most leads along the gyrus, similarly, when no responses were elicitable from one electrode they were usually absent from the others as well. Thus, almost identical electrode positions along the suprasylvian gyrus in two cats could result, in one case, in an absence of evoked activity, while in the other it might be possible to record evoked responses to all three modalities of stimulation. Almost invariably when evoked responses from one modality were recorded, similar responses to the other two modalities of stimulation could be elicited.

The effect of novel stimuli upon the amplitude of the evoked responses to repetitively occurring auditory, tactile, or visual stimulation is consistent with a number of reports in the literature describing evoked responses in the primary sensory pathways. Since the first report by Hernandez-Peon and Scherrer (19), evoked responses in all primary sensory pathways have been reported to be reduced with the presentation of a novel stimulus (18). Since "attention" implies selective awareness, it was thought "focusing of attention" presupposed suppression of sensory input other than that which was being attended. Hernandez-Peon (18) speculated that the reticular formation is able to control the sensory input between the first and second order neurons in all three principal sensory pathways by modulation of a tonic descending inhibitory pathway. It was thought selective inhibition might operate simultaneously for various sensory modalities leaving one or more unaffected. Thus, when a cat perceives a visual

stimulus (a white rat enclosed in a bell jar) the auditory input is suppressed to focus "attention" upon the rat. If orientation to a novel stimulus is preadaptive in the sense that it is an attempt to define its qualities by the integration of sensory information it seems unlikely that information obtained from one sensory modality would be totally excluded. Pavlov, as reported by Magoun (29), describes the ability of the novel stimulus to give rise to the "investigatory reflex with pricking up of the ears, fastening of gaze, turning of the head to stimulus and sniffing the air", all of which seems designed to maximize sensory input.

Sokolov (40, 41) explains the induction of the orienting reflex by novel stimuli by proposing a cortical cell assembly which preserves information about the modality, intensity, duration, and order of presentation of earlier stimuli with which analogous aspects of the novel stimulus may be compared. When the parameters of the novel stimulus do not coincide with the neuronal model, the orienting reflex takes place and when, upon repetition of the stimulus, accordance of the stimulus and the model takes place, habituation of the orienting reflex occurs.

Horn (22) suggested that depression of an evoked response does not mean the particular sensory pathway is being blocked, but rather it is possible for the activity to be manifested in a different way. He concludes "depression of an evoked response occurs in the modality actually being used for examining the sensory field. Thus when a cat is called or receives some other non-visual stimulus, the visual evoked responses are attenuated as a correlate of the search for visual

information not because the visual information is irrelevant." (22) Thus, reduction of evoked responses upon presentation of a novel stimulus implies altered activity, not blocked activity.

If we can assume that the association areas represent the cortical terminus of the non-specific pathways (ARAS), it would not be surprising that evoked activity in these areas is quite sensitive to changes in the peripheral environment. Our experiments indicate that evoked responses in these areas to either repetitive auditory, tactile, or visual stimuli are reduced in amplitude when a novel stimulus which may be either auditory, tactile, or visual in quality is presented. These findings would seem to be consistent with the hypothesis suggested by Horn (22). Reduction of auditory, tactile and visual evoked responses recorded from the same cortical locus upon presentation of the same novel stimuli at different intervals would be more easily acceptable as manifestations of altered central activity rather than the blocking of input to the sensory pathways. This can only be determined by further research.

It is our suggestion that an evoked association response to any discrete modality of stimulation occurs most synchronously when the animal is in a state of "non-attention". Reduction of evoked response amplitude with presentation of novel stimuli suggests that "attention mechanisms" or the increased sensory input associated with novel stimuli alters the activity of the association system in such a way that the evoked responses to a repetitive stimulus are greatly reduced or are absent. All of our results appear understandable in the light of this hypothesis.

The orientation experiment is unique for several reasons: First, there is no repetitive presentation of a discrete stimulus. Second, the novel stimulus is a discrete stimulus which is capable of eliciting an evoked response from the association cortex. Last, attention directed toward the novel stimulus (the click) may be graded by rating the degree of head orientation using the method of Thompson and Welker (49). Presentation of an auditory click from either one or the other speakers to a naive cat resulted in head orientation. The evidence indicates that orientation to a novel click is associated with reduced amplitudes and that as the click is repeated and habituation of the orienting reflex takes place there is a concomitant increase in the amplitude of the evoked responses. This suggests that "attention" as defined by head orientation interferes with the ability of the discrete novel click to give rise to an evoked response. And it is only when the level of attention is decreased, as determined by little or no head orientation that the evoked responses become maximally manifested. In a sense the reduced amplitude of the click evoked responses associated with head orientation may be said to habituate just as the orienting reflex habituates. The possibility exists that the generalized EEG arousal reaction as a component of the orientation reflex (40, 41) interferes with the evoked responses to a discrete stimulus by desynchronization of the "association system". It may be that as the arousal reaction habituates, the evoked responses become greater in amplitude (3, 7).

The changes in the amplitude of the evoked responses for each day over trials shows a progressive increase through the ten trials. This

suggests that in future studies a greater number of trials should be presented each day to determine when the amplitude of the click evoked response begins to level off.

Several control procedures were utilized to exclude head position and head rotation as possible factors in the reduction of evoked responses. The placement of a microspeaker within the external auditory canal of a cat was associated with reduction of mean evoked responses to click upon presentation of a novel stimulus. Mean evoked responses recorded in the chloralosed preparation in various positions relative to a free field speaker failed to indicate any significant difference in amplitude. Observations by the experimenter failed to implicate the importance of head position or head rotation in determining the amplitude of evoked responses in the unanesthetized cat. A click stimulus was introduced to the cat in the orientation experiment only when his head was perpendicular to a line joining the two speakers.

The reduction of the mean amplitude of the evoked responses occurring to either auditory, tactile, or visual repetitive stimuli with heightened bodily activity relative to lesser degrees of activity was consistent with our hypothesis. The increased "awareness" and sensory input associated with increased bodily activity may disrupt synchronization of the input to an extent incompatible with the elicitation of well defined evoked responses.

The failure of habituation, per se, of the evoked responses to click stimulation every two seconds over a variable time course (61-74 hours) is consistent with our hypothesis. In a situation in which a discrete auditory stimulus is continuously presented in a monotonous

fashion within a non-changing environment, we would expect little activation of "attention mechanisms". Under these conditions, the discrete stimulus should be able to produce synchronized evoked responses in the association system over the designated time course. Although habituation did not occur, waxing and waning of the amplitude was evident. This may reflect changes in bodily activity or in the intrinsic state of alertness.

While the general hypotheses have been confirmed, further investigations seem to be warrented:

1. Studies to determine if habituation of the reduced amplitudes of evoked responses occurs upon continued presentation of the novel stimulus.

2. Repetition of the orientation experiment using a greater number of trials per day.

3. Repetition of the orientation experiment using other modalities of stimulation.

4. Analysis of possible central mechanisms responsible for alterations in evoked association response amplitudes.

SUMMARY

Evoked responses recorded from the suprasylvian gyrus of the unanesthetized and unrestrained cat to auditory, tactile, and visual stimuli were found to have a waveform and latency of response similar to those recorded in the chloralose preparation. These responses appeared more widespread in the waking state and were of smaller amplitude than those recorded under chloralose.

It was found that the amplitude of association evoked responses was quite variable in the waking animal but related to behavioral state (measured by a rating scale). With increased activity the mean amplitude of the evoked responses was reduced. Evoked responses occurring to either auditory, tactile, or visual stimulation were found to be reduced in amplitude when a novel auditory, tactile or visual stimulus was briefly presented. Upon removal of the novel stimulus, the response amplitudes returned to their control level within two minutes.

An experiment to determine the relationship of the amplitude of click evoked association responses to the degree of head orientation to the click stimulus indicated the relationship was an inverse one. As habituation of the orientation reflex occurred to the click stimulus, there was a concomitant increase in the amplitude of the click evoked response. It was suggested that habituation of head orientation was associated with habituation of the reduced amplitudes of the evoked responses.

Habituation to a click stimulus every two seconds for time intervals varying from 61 to 74 hours was tested with a total of eight

electrode placements in three cats. Although no consistent changes in amplitude were noted over the time intervals, waxing and waning of the responses were seen in several leads.

All these findings are consistent with the behavioral hypothesis that activation of "attention" or increases in sensory input alters the activity of the association system. As a consequence, the evoked responses recorded from the suprasylvian gyrus to a discrete auditory, tactile, or visual stimulus are reduced in amplitude or are absent.

REFERENCES

1. Albe-Fessard, D. and Rougeul, A. Activities bilaterales tardines evoquees sur le cortex du chat sous chloralose par stimulation d'une voie somasthesique. J. Physiol. Path. Gen., 1955, 47:69-72.

2. Albe-Fessard, D. and Rougeul, A. Activities d'origine, somesthesique evoquees sur le cortex non-specifique du chat anesthesie au chloralose; role du centre median du thalamus. EEG Clin. Neurophysiol., 1958, 10:131-151.

3. Albe-Fessard, D., Mallart, A., and Aleonard, P. Responses cerebrales evoquees enregistrees chez le chat eveille libre et comportment attentif. J. Physiol., Paris, 1960, 52:7.

4. Amassian, V. E. Studies on organization of a somesthetic association area, including a single unit analysis. J. Neurophysiol., 1954, 17:39-58.

5. Bremer, F. Some problems in neurophysiology, Vol. 9. London: Univ. of London, 1953, p. 79.

6. Buser, P., Borenstein, P., and Bruner, J. Etude des systemes "associatifs" visuels et auditifs chez le chat anesthesie au chloralose. EEG Clin. Neurophysiol., 1959, 11:305-324.

7. Buser, P. and Borenstein, P. Responses somesthesiques, visuelles et auditives, recueillies au niveau du cortex "associatif" suprasylvien chez le chat curarise non anesthesie. EEG Clin. Neurophysiol., 1959, 11:285-304.

8. Buser, P. and Imbert, M. Sensory projections to the motor cortex in cats: a microelectrode study. In: Sensory communication, edited by W. A. Rosenblith. Cambridge, Mass.: Technology Press, 1961, pp. 607-626.

9. Clare, M. H. and Bishop, G. H. Responses from an association area secondarily activated from optic cortex. J. Neurophysiol., 1954, 17:271-277.

10. Dawson, G. D. Cerebral responses to electrical stimulation of peripheral nerve in man. J. Neurol., Neurosurg., and Psych., 1947, 10:134-140.

11. Diamond, I. T. and Chow, K. L. Biological Psychology. In: Psychology a study of science, Vo. 4, edited by Sigmund Koch. New York: McGraw-Hill Book Company, Inc., 1962, pp. 195, 206-208.

12. Dixon, W. and Massey, F. Introduction to statistical analysis. New York: McGraw Hill Book Company, Inc., 1957, pp. 272-275.

13. Evarts, E. V. Effect of ablation of prostriate cortex on auditory, visual association in monkeys. J. Neurophysiol., 1952, 15:191-200.

14. Fernandez-Guardiola, A., Roldan, E., Fanjul, L., and Castells, C. Role of the pupillary mechanism in the process of habituation of the visual pathways. EEG Clin. Neurophysiol., 1961, 13:564-576.

15. Flechsig, P. E. Brain Physiology and theories of volition (Gehirnphysiologie and Willenstheorien). In: Some papers on the cerebral cortex, edited by Gerhardt von Bonin. Springfield, Ill.: Charles C. Thomas, 1960, pp. 181-200.

16. Galambos, R., Sheatz, G., and Vernier, V. Electrophysiological correlates of a conditioned response in cats. Science, 1956, 123:376.

17. Hernandez-Peon, Raul. Neurophysiological correlates of habituation and other manifestations of plastic inhibition. In: The moscow colloquium on electroencephalography of higher nervous activity, edited by H. H. Jasper and G. D. Smirnov. EEG Clin. Neurophysiol., Suppl. 13, 1960.

18. Hernandez-Peon, R. Reticular mechanisms of sensory control. In: Sensory comminication, edited by W. A. Rosenblith. Cambridge, Mass.: Technology Press, 1961, pp. 607-626.

19. Hernandez-Peon, R. and Scherrer, H. Habituation to acoustic stimuli in cochlear nucleus. Fed. Proc., 1955, 14:71.

20. Hernandez-Peon, R., Scherrer, H., and Jouvet, M. Modification of electrical activity in cochlear nucleus during "attention" in unanesthetized cats. Science, 1956, 123:331.

21. Hernandez-Peon, R, Guzman-Flores, C., Alcarez, M and Fernandez-Guradiola, A. Photic potentials in the visual pathways during attention and photic habituation. Fed. Proc., 1956, 15:91-92.

22. Horn, G. Electrical activity of the cerebral cortex of the unanesthetized cat during attentive behavior. Brain, 1960, 83:57-76.

23. Huttenlocher, P. R. Effects of arousal on click responses in the mesencephalic reticular formation. EEG Clin. Neurophysiol., 1960, 12:819-827.

24. James, W. The principles of psychology, Vol. 1. New York: Holt, 1890, pp. 48-50.

25. John, E. R. and Killam, Keith. Electrophysiological correlates of avoidance conditioning in the cat. J. Pharm. Therapeutics, 1959, 125:252-273.

26. Lashley, K. S. The mechanism of vision. XVII Autonomy of the visual cortex. J. Genet. Psy., 1942, 60:197-221.

27. Lindsley, D. B. Attention, consciousness, sleep and wakefulness. In: Handbook of physiology, Vol. 3, Sect. I, edited by J. Field, H. W. Magoun, and V. E. Hall. Washington, D. C.: American Physiological Society, 1960, pp. 1553-1593.

28. Lindsley, D. B., Bowden, J., and Magoun, H. W. Effects upon the EEG of acute injury to the brain stem activating system. EEG Clin. Neurophysiol., 1949, 1:475.

29. Magoun, H. W. The waking brain, 2nd Ed. Springfield, Ill.: Charles C. Thomas, 1963, p. 109.

30. Marsh, J. T., Worden, F. G., and Hicks, L. Some effects of room acoustics on evoked auditory potentials. Science, 1962, 137:280-282.

31. Marsh, J. T., McCarthy, D. A., Sheatz, G., and Galambos, R. Amplitude changes in evoked auditory potentials during habituation and conditioning. EEG Clin. Neurophysiol., 1961, 13:224-234.

32. Marshall, W. H., Talbot, S. A., and Ades, H. W. Cortical response of the anesthetized cat to gross photic and electrical afferent stimulation. J. Neurophysiol., 1943, 6:1-15.

33. McNemar, Q. Psychological statistics. New York: John Wiley and Sons, Inc., 1962, pp. 198-201.

34. Meulders, M., Massin, J., Colle, J., and Albe-Fessard, D. Effect d'ablations telecephaliques sur l'amplitude des potentiels evoques dans le centre median par stimulation somatique. EEG Clin. Neurophysiol., 1963, 15:26-38.

35. Moruzzi, G. and Magoun, H. W. Brain stem reticular formation and activation of the EEG. EEG Clin. Neurophysiol., 1949, 1:455.

36. Palestini, M. Discussion. In: The central nervous system and behavior, edited by M. Brazier. New York: Josiah Mach, Jr. Foundation, 1959, p. 239.

37. Prescott, W. G. Distribution of auditory, visual and somatic sensory "association" responses in the thalamus of cat. Unpublished Master's dissertation, University of Oregon Medical School, 1963.

38. Santibanez, G., Trouche, E., and Albe-Fessard, D. Etude de l'evolution au cours du temps de l'amplitude des activites corticales et thalamiques evoquees par des stimuli somatiques repetes. J. de Physiologie, 1963, 55:335-336.

39. Sharpless, S. and Jasper, H. H. Habituation of the arousal reaction. Brain, 1956, 79:655.

40. Sokolov, E. N. Neuronal models and the orienting reflex. In: CNS and Behavior, Vol. 3, edited by M. A. B. Brazier. New York: Josiah Macy, Jr. Foundation, 1960, pp. 187-276.

41. Sokolov, E. N. Higher nervous functions: the orienting reflex. In: Annual review of physiology, edited by V. E. Hall. Palo Alto, Calif.: Annual Review, Inc., 1963, pp. 545-580.

42. Sperry, R. W. Cerebral regulation of motor coordination in monkeys following multiple transections of sensorimotor cortex. J. Neurophysiol., 1947, 10:275-294.

43. Starzl, T. E. and Whitlock, D. G. Diffuse thalamic projection system in monkey. J. Neurophysiol., 1952, 15:449-467.

44. Starzl, T. E. and Magoun, H. W. Organization of the diffuse thalamic projection system. J. Neurophysiol., 1951, 14:133-146.

45. Thompson, R. F. Thalamocortical organization of association responses to auditory, tactile and visual stimuli in cat. Intern. Congr. Physiol. Sci., 21st, Leiden, 1962, Series No. 48, 1057.

46. Thompson, R. F. and Sindberg, R. M. Auditory response fields in association and motor cortex of cat. J. Neurophysiol., 1960, 23:87-105.

47. Thompson, R. F., Smith, H. E., and Bliss, D. Auditory, somatic sensory, and visual response interactions and interrelations in association and primary cortical fields of the cat. J. Neurophysiol., 1963, 26:365-378.

48. Thompson, R. F., Johnson, R. H., and Hoopes, J. Organization of auditory, somatic sensory, and visual projection to association fields of cerebral cortex in the cat. J. Neurophysiol., 1963, 26:343-364.

49. Thompson, R. F. and Welker, W. I. Role of auditory cortex in reflex head orientation by cats to auditory stimuli. J. Com. Physiological Psy., 1963, 56:996-1002.

50. Von Bonin, G. and Bailey, P. The neocortex of macaca mulatta. Chicago: University of Illinois Press, 1947, pp. 21.

51. Woolsey, C. N. Organization of somatic sensory and motor areas of the cerebral cortex. In: Biological and biochemical basis of behavior, edited by H. E. Harlow and C. N. Woolsey. Madison: University of Wisconsin Press, 1958, pp. 63-81.

52. Worden, F. G., and Marsh, J. T. Amplitude changes of auditory potentials evoked at cochlear nucleus during acoustic habituation. EEG Clin. Neurophysiol., 1963, 15:866-881.