LOCALIZATION OF THE ACOUSTIC AREA IN THE CEREBRAL CORTEX OF THE MONGOLIAN GERBIL (MERIONES UNGUICULATUS) AS DETERMINED BY CLICK STIMULATION.

by

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INTRODUCTION

The purpose of this work was to identify electrophysiologically the auditory area in the cerebral cortex of the Mongolian gerbil (Meriones unguiculatus).

I. Why Investigate the Gerbil

The Mongolian gerbil possesses a number of advantages characteristics for auditory neurophysiological research.

A. 'Good' Ears for Peripheral Work

These animals have large, inflated tympanic bullae that allow easy surgical access to the middle ear space, cochlea, and acoustic branch of the VIIIth nerve for electrophysiological recording with only minimal bleeding and without disturbing the sound conducting portions of the middle ear (Zwislocki and Sokolich, 1973; Vernon and Gillette, unpublished observations, 1974).

B. The Gerbil as a 'Robust' Experimental Animal

A second important characteristic is that the gerbil demonstrates a strong respiratory drive under barbiturate anesthesia (particularly Dial urethane), almost completely eliminating the problem of respiratory failure and resultant death during moderate anesthesia in acute experiments (Vernon and Gillette, unpublished observations, 1974). In addition, this particular rodent species is easily and cheaply obtained and adapts readily to the laboratory colony.

C. Literature on the Gerbil as an Auditory Research Subject

Other additional factors make this saltatory, desert-dwelling rodent an attractive auditory research subject. For example, basic information has already been published on the gerbil's auditory behavior

(Lay, 1972) and vocal repertoire (Finck and Goehl, 1968; DeGhett, 1974). The behavioral audiogram for the gerbil has also been recently determined with appetitive conditioning procedures (Alexander, Clark, Moody, and Stebbins, 1974). The auditory sensitivity of the Mongolian gerbil has recently been determined by Ryan (1975) using a shock avoidance technique. The two training procedures produced essentially the same audiogram. Galvani (1974) has also successfully trained gerbils with avoidance conditioning techniques to make auditory discriminations.

The peripheral auditory system of the gerbil has already been the focus of a series of investigations on cochlear histology (Webster and Stack, 1968; Lay, 1972) and AC cochlear potentials (Finck and Sofouglu, 1966; Finck and Goehl, 1968; Finck, Schneck, and Hartman, 1972; Lay, 1972; Vernon and Gillette, unpublished observations, 1974).

The central auditory system of the gerbil has also been the subject of a number of electrophysiological investigations in recent years. For example, single neuron (unit) electrophysiological recordings have been obtained with microelectrodes placed in the cochlear (VIIIth) nerve (Zwislocki and Sokolich, 1973; Sokolich and Zwislocki, 1974; Zwislocki and Sokolich, 1974) and cochlear nucleus (Smith, 1971; Smith and Zwislocki, 1971) of anesthetized subjects.

D. Lissencephalic Cortex of the Gerbil

The neocortex of lissencephalic mammals (including rodents) is particularly suited for correlative study of the functional and structural basis of motor and sensory functions. It is composed of the major classes of neurons arranged in the six-layered array (of Bevin Lewis) characteristic of neocortex of gyrencephalic mammals including man

(Lorente dè No, 1922; 1949). It also contains the same principle classes of intercellular connections, and in general, the cytoarchitectonic fields are fewer in number and distinctive in pattern with readily designated boundaries, undistorted by convolutions (Kreig 1946ab; Gerebtzoff, 1940; Hattori and Shoyama, 1970; Oliver, 1974; Caviness, 1975). This last point is of particular importance because electrophysiological investigation of sensory-cortical activity in "smooth-brained" species is not constrained by the difficult necessity of recording from cortical areas lying buried within fissures or sulci. The cortex of the Mongolian gerbil is lissencephalic (Loskota, Lomax, and Verity, 1975; Gillette and Keller, unpublished observations, 1975) and thus shares the above characteristics with other smooth-brained mammalian species.

As yet however, there is no information available on the anatomy or the electrophysiology of the auditory cortex of this species of rodent. As a consequence, information regarding the location of the auditory cortex of the Mongolian gerbil is needed before correlative studies can be undertaken.

II. The Evoked Potential Method

For some years now it has been customary for sensory neurophysiologists to use the evoked potential for the neuroanatomical mapping of cortical sensory receiving areas in the mammalian brain (Marshall, Woolsey, and Bard, 1941). Typically, when an electrode is placed on the cortical pial surface, it is possible to record a diphasic (initially positive) voltage change beginning shortly after natural or electrical stimulation of a sensory organ or receptor sheet, sensory nerve or thalamic relay nucleus (Eccles, 1951; Chang, 1959; Ruch, Patton, Woodbury,

and Towe, 1965; Thompson, 1967; Schlag, 1973). This earliest cortical response to sensory stimulation, the primary evoked potential, is found to be restricted generally to an area which corresponds to the thalamocortical terminal zone for axons from the specific thalamic relay nucleus of the modality of stimulation (Eccles, 1951, 1953; Brodal, 1969). Such responses have been used to map the projection of the body surface (Marshall, Woolsey, and Bard, 1937), retina (Talbot and Marshall, 1941), or cochlea (Bremer and Dow, 1939; Woolsey and Walzl, 1942; Tunturi, 1944; Walzl, 1947) on to the cortical sensory areas. This mapping is possible because the primary, cortical-evoked response results from the synchronous neuronal activity in the direct, fast-conducting sensory pathways leading from receptor sheet to cerebral cortex (Eccles, 1951, 1953; Ruch et al., 1965; Thompson, 1967; Brodal, 1969; Schlag, 1973).

III. Development of the Method

As early as 1939, Bremer and Dow utilized surface monopolar, evoked potential recordings to map the auditory cortex of the cat to click stimulation. Mounting the recording electrode in a movable holder, these workers systematically mapped the click-responsive cortex of one hemisphere to contralateral stimulation. Specifically, this was accomplished by placing one electrode well off the acoustic area (indifferent electrode) and moving the second (active) electrode in every direction, until the borders of the responsive area were located. Each point from which recording was attempted was carefully noted on a sketch of the exposed brain and the presence or absence of a response was indicated for each point sampled. Click-evoked potentials recorded from the acoustic area were characteristically of short latency and diphasic (initially positive) in waveform. This mapping procedure, and variants thereof, has been used

by auditory neurophysiologists since the work of Bremer and Dow up to the present for mapping the auditory cortex of various mammalian species.

IV. The Cortical Evoked Response in the Barbiturate-Anesthetized Preparation

Almost without exception, most auditory cortical mapping work has been done on barbiturate-anesthetized animals. It was Hawkins (1941) who first gave a detailed description of the characteristics of the primary, click-evoked response recorded from the auditory cortex of the anesthetized cat. Monopolar recordings were obtained from one hemisphere while click stimuli were presented to the contralateral ear.

Hawkins (1941) noted that the earliest component of the cortical response consists of several small deflections that appear to be subcortical in origin since they persist after thermocoagulation of the auditory area. They are recorded at the cortical surface presumably owing to electrical spread of the potentials from subcortical auditory centers (Hawkins, 1941; Ades and Brookhart, 1950). These wavelets are often followed by a small-amplitude negative wave occurring between 6 and 9 msec after the click stimulus. However, this wave is only observed with less intense click stimulation and in many cases there is no indication of the initial negative component for any stimulus intensity (Hawkins, 1941; Rosenzweig and Rosenblith, 1953). There is no direct evidence as to the origin of this initial, surface-negative deflection although it has been attributed to cortical cells by Hawkins (1941) and to thalamocortical radiation activity by Tunturi (1949).

The most characteristic and reliable component of the primary cortical evoked response in the barbiturate-anesthetized preparation is a large amplitude positive deflection called the "initial surface-positive

component" (Hawkins, 1941). The peak latency of this surface-positive wave varies depending upon the location of the recording electrode and the level of anesthesia (Hawkins, 1941; Ades and Brookhart, 1950; Mickle and Ades, 1953; Rosenzweig and Rosenblith, 1953; Goldstein, Kiang, and Brown, 1959; Pradhan and Galambos, 1963; Teas and Kiang, 1964). The amplitude of the surface positive wave may vary from a few microvolts to well over a thousand microvolts depending upon stimulus intensity, recording electrode location, and anesthetic level. With light levels of barbiturate anesthesia, the amplitude of the initial surface positivity is attenuated compared to its amplitude under moderate or deep anesthesia (Pradhan and Galambos, 1963; Teas and Kiang, 1964).

The surface-positive wave is often (but not always) followed by a negative waveform (late surface-negative component) depending again upon the anesthetic level. With moderate to deep levels of anesthesia this wave of negative polarity is greatly attenuated in amplitude and at times even absent (Hawkins, 1941; Ades and Brookhart, 1950; Rosenzweig and Rosenblith, 1953; Goldstein et al., 1959; Pradhan and Galambos, 1963; Teas and Kiang, 1964).

V. The Problem of Cortical Response Variability

Traditionally, auditory cortical mapping studies have been accomplished without the use of averaging techniques. However, as early as 1943, Ades noted that the evoked response amplitude recorded from cat auditory cortex showed a certain variability from stimulus to stimulus. The variable nature of the primary evoked response when recorded in 'moderately' or 'lightly' anesthetized preparations (and even more particularly in unanesthetized animals) often makes it difficult to obtain a 'typical'

or representative measurement of either amplitude or latency from a single response. An important consequence is that when attempting sensory cortical mapping with evoked potentials, the determination of the boundary or border of the cortical auditory field may be ambiguous. This ambiguity is due to the fact that responses recorded at the borders are usually of such small amplitude that it is difficult to decide whether a response has occurred at the sampled locus in the face of response variability from stimulus to stimulus.

Three methods for minimizing the effects of variability in the evoked cortical response have been discovered: (1) to use deep anesthesia (Marshall, Woolsey, and Bard, 1937; Woolsey and Walzl, 1942; Rosenzweig and Rosenblith, 1953; Goldstein et al., 1959; Pradhan and Galambos, 1963; Teas and Kiang, 1964), (2) application of strychnine patches to the cortical surface in order to enhance the amplitude of responses (Tunturi, 1950; Hind, 1953), or (3) to use response-averaging techniques (Goldstein et al., 1959). The first procedure has the disadvantage of compromising the physiological condition of the preparation. The second procedure is not practical when recording from small-brained animals. The third alternative, response averaging, is of considerable help in dealing with response variability. The important gain is that determination of response magnitude, latency, etc. is no longer made on a subjective basis (the old method in which the experimenter selects the "most representative" from among the traces recorded at a given point). Thus, the averaging procedure gives improved objectivity as well as reliability.

The principle of "averaging" has several advantages and disadvantages that are relevant to its application to the study of auditory

cortical responses in general. The technique uses a "signal averager", a device that adds together events presented sequentially and then gives the average value for these events. Auditory evoked responses generally occur at a certain time after the stimulus, depending on their origin; they are said to be "time-locked" to the stimulus. The averager can be used to record and summate brain potentials occurring within a set period after each of a series of stimuli, and as the auditory response always occurs in the same part of the record, subsequent responses add together arithmetically. The background noise of the electroencephalogram is assumed to be random, and theoretically the amplitude of the noise increases as the square root of the number of samples taken, as does the signal-to-noise ratio. The averaging rapidly increases the signal-to-noise ratio over a small number of samples, but further improvements need progressively larger samples, and the process then becomes time-consuming. The number of samples taken is therefore generally a compromise and depends on the requirements of the experiment. Another shortcoming of this procedure is that every response receives an equal weighting in the average. This may be undesirable if on some trials there were unusually large movements or other artifacts. So response averaging represents a compromise of all these factors. And greater reliability of measures is purchased at the price of some loss of speed in collecting the data. Even so, averaging is a useful means of recording small auditory responses, especially those responses observed at the borders of mapped auditory areas.

Averaging of cortical responses has been used by a number of investigators in recent years when recording from the auditory cortex of the hedgehog (Lende and Sadler, 1967), cat (Goldstein et al., 1959; Teas

and Kiang, 1964), rat (Borbély, 1970), guinea pig (Walloch, 1971; Ödkvist, Rubin, Schwarz, and Fredrickson, 1973), monkey (Arezzo, Pickoff, and Vaughn, 1975), and man (Celesia and Puletti, 1969; Celesia, 1975). Interestingly, in a mapping study of the auditory cortex of the hedgehog, Lende and Sadler (1967) defined the acoustic area with and without averaging in the same preparation. Both procedures yielded similar maps of click activation in the temporal cortex (c.f., Figure 2 of their study).

VI. The Use of Clicks As Mapping Stimuli

Synchronous neuronal activity is elicited best by stimuli which are of short duration or abrupt onset. In the auditory system, this type of activation can be achieved using clicks (Bremer and Dow, 1939; Rosenblith, 1950; Rosenzweig and Rosenblith, 1953; Rosenblith, 1954; Goldstein and Kiang, 1958). Clicks have been widely utilized in investigations of the mammalian auditory system probably because (1) they evoke very large, sharply-defined, and easily observable potentials and (2) they are easily generated. The question arises as to why such a transient acoustic pulse as the click is so effective in setting up synchronous activity in the auditory pathway leading from cochlea to cortex? Is it the short rise-time? Or is it the fact that a rapid rise-time leads to a wide frequency spread of sound energy (Licklider, 1951)? Goldstein and Kiang (1958) as well as Small and Gross (1960) have both addressed this question experimentally. They found that faster stimulus rise-times gave rise to larger amplitude evoked potentials and larger areas of cortical responsiveness. Conversely, as rise-times were lengthened, the cortical region found to be responsive to pure tone stimulation constricted in size. The rise-time of the stimulus is not the only determinant of response magnitude, however.

wide-band noise stimuli were found to be much less affected by slowing the rise-time than were tone-burst stimuli (Small and Gross, 1960). Thus a rich spectral content also contributes to optimal driving of the auditory afferents. Presumably, these observations explain the efficacy of click stimuli.

It has been known for some time that 'louder' (more intense) clicks produce larger amplitude cortical responses than do less intense click stimuli (Ades, 1941, 1943; Walzl and Woolsey, 1946; Rosenzweig and Rosenblith, 1953; Rosenblith, 1954; Horvath, 1969). The effect of changes in click intensity on the form (peak-to-peak amplitude and latency) of the cortical evoked potential has been rigorously investigated in only three cases. Both Rosenblith (1954) and Saunders (1970), studying auditory cortex of the cat, found that over an intensity range of 90 dB the peak-to-peak amplitude of the cortical response increased regularly up to intensities as great as 104 dB SPL. In addition, the latency to the peak of the first positive wave of the response was reduced from 19 to 13 msec (Rosenblith, 1954). Similar results were obtained in a study of the auditory cortex of the raccoon where click intensity was varied over a 70 dB range (Hertzler, Saunders, Gourevitch, and Herman, 1970).

In regard to stimulus rate, Pradhan and Galambos (1963) noted when recording from cat auditory cortex that increasing the frequency of click stimulation from 1 to 4 per second caused a decrease in the magnitude (peak-to-peak amplitude) of the initial surface positive component of the averaged evoked response. This phenomenon has also been reported by other investigators (Rosenzweig and Rosenblith, 1953; Goldstein et al., 1959; Wickelgren, 1968). The above researchers reported that no decrement in

evoked response amplitude was seen in cat auditory cortex when clicks were presented once every second. Borbély (1970) has studied the effect of click rate on evoked potentials recorded from the auditory cortex of the rat. He noted decrements in the peak-to-peak amplitude of evoked responses for click rates of 10 per second and higher but, found no change in response magnitude for click stimulation at a rate of 2 or 1 per second. Unpublished observations on the Mongolian gerbil (Gillette, 1975) confirms the above findings in yet another rodent species. Without exception, in all auditory cortical mapping studies published to date, a click rate of 1 per second has always been used.

Click stimulation presented to the ear contralateral of the cortical hemisphere recorded from gives rise to larger evoked responses than does ipsilateral click stimulation (Bremer, 1943; Tunturi, 1945, 1946; Rosenzweig, 1951; Gross, Small, and Thompson, 1967; Celesia and Puletti, 1969; Galli, Lifschitz, and Adrian, 1971). However, data regarding threshold or latency differences and side of stimulation were equivocal. When tone-burst stimuli are used, the area of cortical activation to contralateral stimulation is larger than that determined for ipsilateral stimulation (Gross et al., 1967; Galli et al., 1971).

VII. Specification of Click Stimulus Intensity: A Neglected Control

Surprisingly, in only one auditory cortical mapping study has the click stimulus used been characterized. In that study, the subject of which was the auditory cortex of the raccoon, Hertzler and colleagues (Hertzler et al., 1970) substituted a calibrated microphone for the animal preparation at the end of the hollow stereotaxic ear bar in order to measure various parameters of the stimulus (e.g., magnitude and wave-

form) and reference these values to an externally measureable physical dimension (dynes/cm^2 of sound pressure). The resulting lack of information in regard to stimulus specification for auditory cortical mapping studies is unfortunate because it makes comparison of results across species difficult at best. In addition, variability may be introduced into the data if the investigators do not have some way of specifying stimulus level. With these considerations in mind, this investigator has endeavored to specify in considerable detail the physical nature of the click stimulus used to map the acoustic area of the Mongolian gerbil (see comments by Vernon and Meikle, 1974, p. 33).

VIII. Cortical Auditory Response Fields: Single vs. Multiple Representations

The large majority of the auditory cortical mapping investigations have been done on the time-honored animal models: cat, dog, and monkey. Depending upon the type and level of anesthesia used, as many as eight click-responsive cortical fields have been delineated in the cat (Ades, 1943; Bremer, 1953; Mickle and Ades, 1953; Merlis and Lombroso, 1953; Perl and Casby, 1954; Desmedt, 1960; Thompson and Sindburg, 1960; Sindburg and Thompson, 1962; Thompson, Johnson, and Hoopes, 1963a; Thompson, Smith, and Bliss, 1963b; Gross et al., 1967; Goldring, Sheptak, and Karahashi, 1967). Some of the cortical auditory fields mapped in the cat were defined as "non-primary" or "secondary" fields on latency criteria alone (Ades, 1943; Bremer, 1953; Mickle and Ades, 1953) while others were defined on additional criteria; for example, as being "polysensory" (Desmedt, 1960; Thompson et al., 1963ab; Goldring et al., 1967). Of the regions defined, only the primary auditory area lying in the anterior and middle ectosylvian gyri of the cat appears to be the direct terminal zone for axons

comprising the geniculocortical radiations (Bremer and Dow, 1939; Ades, 1941; Rose and Woolsey, 1949, 1958). In addition, this region demonstrates a koniocortex cytoarchitecture (Bremer and Dow, 1939; Rose, 1949).

In another carnivore, the dog, Tunturi (1943) described a single click-responsive auditory focus in the ectosylvian cortex. Occasionally, responses were recorded from the middle sylvian gyrus and from the ventral margin of the suprasylvian gyrus. Within the click-responsive area, two different evoked response waveforms were observed depending on the location of the recording electrode. Evoked responses recorded from the anterior portion of the field were of small amplitude, short latency, and initially surface negative in polarity. In contrast, evoked potentials recorded from the center of the field were of much larger amplitude, of short latency (8-11 msec), and initially surface positive in polarity. As the recording electrode was moved caudally from the center of the area the recorded responses came to be predominantly monophasic positive and of somewhat longer latency. This click-responsive auditory field in the dog was located in a homologous area to that of the primary auditory field in the cat. Histologically, most of this click-responsive region in the dog has been shown to be koniocortex (Adrianov and Mering, 1959), particularly the ectosylvian area from which Tunturi (1943) could record initially surface positive evoked potentials.

A number of representative species of the Primate Order have been examined with regard to cortical responsiveness to click stimulation. For example, auditory cortical mapping has been accomplished in the tree shrew (Casseday, Oliver, and Eisenman, 1974), galago (Kanagasuntheram and Leong, 1966), cebus monkey (Hoffman, Walker, Kadoya, and Massopust, 1969),

and squirrel monkey (Massopust, Wolin, and Kadoya, 1968; Bignall and Singer, 1967; Bignall and Imbert, 1969; Hind, Benjamin, and Woolsey, 1958; Hardin and Castellucci, 1970). In general, a field of positive potentials of short latency encompassing the posterior two-thirds of the lower bank of the sylvian fissure has been found in these species characterized by an "arcuate" fissural pattern (Sanides, 1976). Histologically, this click-responsive auditory area has been shown to consist of koniocortex (Casseday et al., 1974; Kanagasuntheram and Leong, 1966; Sanides, 1976).

Similarly, a primary, click-responsive auditory area has also been described as occupying the lower bank and depths of the sylvian fissure in the macaque (Ades and Felder, 1942; Bailey, von Bonin, Garol, and McCulloch, 1943; Ades and Felder, 1945; Pribram, Rosner, and Rosenblith, 1954; Arezzo, Pickoff, and Vaughn, 1975), chimpanzee (Bailey et al., 1943; Hirsch, Anderson, Calvet, and Scherrer, 1960; Woolsey, 1971), and man (Celesia and Puletti, 1969; Celesia, 1975). Taking all the click mapping studies of the auditory cortex of higher primates as a whole, one finds remarkable agreement among the species examined in regard to the general anatomical location of the "primary" acoustic cortex with its short latency and large amplitude diphasic (positive-negative) evoked responses. Further, this auditory cortical field has a koniocortex cytoarchitecture (Pandya and Sanides, 1973; Bailey and von Bonin, 1950; Economo, 1929).

Besides the primary auditory field lying in the superior temporal gyrus, additional "non-primary" cortical areas responsive to click stimulation have been described in some of the above species depending upon the type and level of anesthesia used in the experiments. For example,

using latency criteria alone, as many as three additional auditory areas have been delineated besides the primary area (Kanagasuntheram and Leong, 1966; Massopust et al., 1968; Bignall and Singer, 1967; Pribram et al., 1954; Hirsch et al., 1960; Arezzo et al., 1975; Celesia and Puletti, 1969; Celesia, 1975). Further experiments have also demonstrated that these additional click-responsive cortical areas are 'true' auditory fields in that neural activity evoked from them is locally generated within the cortical grey matter (Bignal and Imbert, 1969; Hardin and Castellucci, 1970; Arezzo et al., 1975; Celesia and Puletti, 1969).

Other vertebrate species have been investigated in an effort to find cortical area(s) responding to click stimulation. A single click-responsive area has been mapped in the lissencephalic neocortex of the oppossum (Lende, 1963), armadillo (Royce, Martin, and Dom, 1975), hedgehog (Lende and Sadler, 1967), rabbit (Woolsey, 1971), and bat (Suga, 1965). However, two responsive foci have been identified in another lissencephalic species, the porcupine (Lende and Woolsey, 1956). In this study, the main auditory area was found in a region overlying the temporal cortex and was characterized by large amplitude and short latency evoked potentials of positive polarity. A second, smaller region of click responsiveness was found anterior to the first area. Evoked responses recorded from this area were also initially surface positive in polarity, but were somewhat longer in latency.

A single click-responsive auditory area has also been mapped in the gyrencephalic cortex of the echidna (Lende, 1964), pig (Woolsey and Fairman, 1946), sheep (Woolsey and Fairman, 1946), dolphin (Lende and Welker, 1972), seal (Alderson, Diamantopoulos, and Downman, 1960), and

raccoon (Hertzler et al., 1970). Conversely, in the sloth, both a single auditory focus (Meulders, Gybels, Bergmans, Gerebtzoff, and Goffart, 1967) and multiple auditory fields (Aaraiva and Magalhaes-Castro, 1975) have been delineated with click stimulation. Both studies were in agreement in regard to the location of the main (primary) auditory area but Saraiva and Magalhaes-Castro (1975) also found responses of smaller amplitude and longer latency in a second rostral area overlapping the second somatic-sensory area.

IX. Click Mapping Studies of Rodent Auditory Cortex

Some years ago LeMessurier (1948) used the evoked potential method to define the auditory cortex of the albino rat. Click stimulation produced an area of cortical activation centered over and encompassing Kreig's (1946ab) cytoarchitectonic field 41 (sensory koniocortex) lying in the temporal cortex. Click stimuli presented to the contralateral ear gave rise to evoked responses in the middle of the field which were large (peak-to-peak amplitude up to 1500 μV) and diphasic (initially positive), while responses of smaller amplitude were obtained from the remaining borders of the field. This main area measured approximately 4 mm wide (medio-laterally) and 5 mm long (antero-posteriorly). Another area which could be activated by sound was also described as being closely related to the face subdivision of somatosensory area II. Responses recorded from this second area varied widely in amplitude. Latency data was not reported for any of the responses.

More recently, Thomas Woolsey (1967) has mapped the acoustic cortex of the mouse with click stimulation. Monopolar recordings were obtained from the dural surface of the hemisphere with a 0.3 mm diameter steel wire. In the two animals investigated, a sharp auditory focus was found

consisting of a small number of click-responsive points clustered closely together in the temporal lobe. In one animal the auditory region measured 4.0 mm antero-posteriorly and 2.0 mm medio-laterally while, in the other preparation the click-responsive region measured 3.0 mm long and 2.5 mm wide. This area has been shown recently to have a koniocortex cytoarchitecture (Caviness, 1975). Within this region, click stimuli elicited diphasic potentials characterized by a large, initially positive waveform. The latency to onset of the evoked response was 8 msec on the average. The largest amplitude responses were found centrally within the field with smaller amplitude potentials making up the borders of the area. In one of the animals, the ventro-lateral boundary of the auditory area could not be determined; click-evoked responses were recorded up to the lateral bony edge of the cortical exposure. A second response focus or click field, such as that seen in the rat (LeMessurier, 1948) or the porcupine (Lende and Woolsey, 1956), was not apparent in the mouse.

The auditory cortex of the guinea pig has also been mapped in a number of investigations using click stimulation. Initially, Zeigler (1964) demonstrated with evoked potential recordings a single click-responsive focus in the temporal cortex of the guinea pig. Cortical responses were surveyed with a 0.5 mm diameter steel electrode moved in millimeter steps so as to sample cortical electrical activity from the entire hemispheric exposure. Click-evoked responses were recorded from a region measuring 8 mm long and 6 mm wide. The cortical responses recorded from within this area were diphasic (initially surface positive) in waveform with the peak of the positivity occurring some 14 to 21 msec after the presentation of the click to the contralateral ear. The greatest response

magnitudes (up to 1200 μV) were recorded from the middle of the field, with progressively decreasing response amplitudes seen at surrounding recording sites until the borders of the responsive area were reached. This single focus of click-evoked activity was restricted to a region of temporal cortex shown to have a koniocortex cytoarchitecture (Gerebtzoff, 1940).

Walloch (1971) has also recently mapped the acoustic cortex of the guinea pig with click stimulation. Clicks were presented to one ear of the animal preparation through a closed sound tube. Resultant evoked responses were recorded from an area in the contralateral hemisphere similar in location and size to that described by Zeigler (1964). In addition, Walloch (1971) noted that within the auditory area two groupings of evoked potentials could be discerned which differed in latency. Most of the responsive points within this auditory region were characterized by surface-positive waves of large amplitude (up to 1000 μV), with the peak of the positivity having a latency of 9 to 11 msec. In half the animals mapped, longer latency responses were consistently recorded from two locales within the acoustic field. Evoked responses with peak positive latencies of 18 to 22 msec were recorded from an antero-medial focus and a postero-lateral focus. Although the evoked potentials were only recorded from the temporal cortex, the exact boundaries of the acoustic area varied somewhat in location between animals. Tone-burst stimuli and electrical stimulation of the cochlear turns have also been shown to give rise to evoked potentials in this cortical area of the guinea pig (Kayser and Legouix, 1963; Kayser and Libouban, 1963; Walloch, 1971, 1975).

In a recent investigation of the guinea pig auditory cortex,

Ödkvist and colleagues (Ödkvist, Rubin, Schwarz, and Fredrickson, 1973) mapped the acoustic area by applying electrical stimulation directly to the VIIIth nerve. Electrical stimulation of the cochlear branch of the VIIIth (acoustic) nerve produced a field of responsiveness in the contralateral hemisphere that was essentially oval in shape. The auditory area so defined was approximately 7 mm long and 6 mm wide. The dimensions and general location correspond well with those already obtained for the guinea pig auditory cortex using click stimulation (Zeigler, 1964). The onset latency of the large, surface positive waves recorded from this area was 8 msec on the average. Again, the largest responses were recorded from the middle of the field while smaller amplitude potentials were obtained from points around this central core or 'hot spot'.

In an attempt to establish the source of the surface recorded evoked response, Ödkvist et al. (1973) obtained recordings at various cortical depths with a penetrating microelectrode at all the surface locations giving cortical responses. The resultant depth-distribution data on the various components of the evoked response assisted in determining whether the neural activity recorded at the surface was locally generated within the cortex or whether the surface response represented 'distant', volume-conducted sources. The border sampling points were found to be suspect, for the responses recorded from these loci did not show polarity reversals between surface and cortical white matter. Utilizing such data, the cortical acoustic area was defined as that area in which the initial surface-positive wave of the cortical evoked response reversed to negativity in the depths of the cortical grey matter. This 'true' auditory area was found to be smaller than the cortical area from

which surface responses could be obtained.

To summarize, in those rodent species investigated to date, one major auditory cortical field has been found consistently. There is also some evidence suggesting the possibility of additional fields in the rat and the guinea pig.

X. Aim of the Present Study

The aim of this study was to delineate the cerebral acoustic area in the Mongolian gerbil using click stimuli. Clicks were presented monaurally to the barbiturate-anesthetized gerbil while a surface electrode systematically sampled the evoked neuroelectric activity of the contralateral cortical hemisphere. It was hypothesized that the acoustic stimulation would give rise to a field of predominantly surface-positive potentials which would be confined to a small area in the contralateral temporal cortex of the gerbil as had previously been observed in other rodents (LeMessurier, 1948; Zeigler, 1964; Woolsey, 1967; Borbély, 1970; Walloch, 1971; Ödkvist et al., 1973). Because the brain, and therefore the cortical surface, is small in the Mongolian gerbil, the electrode chosen for recording from the cortical surface was also quite small (0.25 mm diameter ball tip) and sampling of evoked electrical activity was accomplished in steps which were as small as practical.

A second and separate question addressed in this study concerns the possibility that surface recordings obtained from the cerebral hemisphere may lead to an overestimation of the true extent of auditory cortex. The difficulty of assigning an anatomical boundary with the evoked potential method has been primarily due to the behavior of electric currents in a volume conductor. Since the brain is a volume conductor, the action

currents of nerve cells and fibers create electric fields which have extensive distribution in the brain medium (Lorente dé No, 1947ab; Hubbard, Llinás, and Quastel, 1969). With the usual methods of recording, whether monopolar of differential, the potentials of interest can be observed at considerable distances from the active elements which produce those potentials. For example, in studies related to electrical mapping of cortical sensory areas it is customary to place one recording electrode on the cortical surface and refer it to a distant one on bone or muscle. If a response appears to sensory stimulation and especially if it is of positive polarity the cortical area immediately beneath the recording electrode is tacitly considered to be a projection point of afferent thalamic fibers. Sensory areas localized by this method probably approximate the anatomical spatial distribution. However, on theoretical grounds, one may question the validity of any precise conclusions drawn from such studies. In a volume conductor, like the brain, it is only necessary that the recording electrodes be on disparate isopotential lines to record a potential difference. Thus a potential (positive or negative) may be recorded between cortical surface and 'distant' tissue such as bone, even when the surface electrode is at a considerable distance from the actual potential generator. This situation is made even more acute when averaging procedures are used, since the averaging is capable of revealing smaller potentials than are discernable from single responses, and thus potentials generated at a distance from the recording electrode may become visible (Kelly, Goldring, and O'Leary, 1965; Thompson, 1967).

How may the volume conduction problem be remedied in sensory-cortical mapping studies utilizing evoked potentials? A number of proced-

ures have been applied over the years including the use of (1) the strychine technique (Tunturi, 1950), (2) bipolar recordings (Bremer and Dow, 1939; Mickle and Ades, 1952, 1953), (3) Laplacian recordings (Perl and Casby, 1954), (4) transcortical recordings (Kelly et al., 1965), and cortical surface-to-depth recordings with a search for polarity reversal (Hawkins, 1941). The last mentioned procedure appears to be the most readily applicable to the study of the small, lissencephalic brain of the Mongolian gerbil. This procedure depends upon the observation that an evoked potential actually being generated below a point on the surface of the cortex will show a reversal in polarity if an electrode at that point is progressively lowered into the cortical grey matter. The depth of the polarity reversal is not necessarily the same for all components of the primary evoked response, but the fact of reversal itself is so general that the failure to obtain it should raise suspicion that the generator is not in the explored region (Thompson, 1967; Schlag, 1973). The reversal is thought to occur at the depth in which afferent thalamocortical axons terminate (Eccles, 1951; Brazier, 1968; Brodal, 1969; Schlag, 1973). This reversal procedure for determining the origin of the surface-recorded components of the evoked response has been used by a number of auditory physiologists to validate determinations of the auditory cortical areas of the cat (Hawkins, 1941; Ades and Brookhart, 1950; Cragg, 1954; von Euler and Ricci, 1958; Thompson et al., 1963ab; Kӧnig, Pujol, and Marty, 1972; Kӧnig and Marty, 1974), rat (Borbély, 1970), guinea pig (Ödkvist et al., 1973), monkey (Arezzo et al., 1975), and man (Celesia and Puletti, 1969).

For the reasons described above, the present observations obtained

from surface mapping in the gerbil were further refined and expanded by using a penetrating microelectrode to obtain both surface and depth recordings from various points shown to be responsive to click stimulation. With this procedure, the cortical location of the auditory field in the Mongolian gerbil was strictly defined as that area encompassed by click-responsive points at which the surface-positive potential reversed to negativity at some depth within the cortical grey matter.

In summary, the following specific objectives were addressed:

(1) Determination of the cortical projection area for click stimuli in the gerbil by mapping the temporal cortex with evoked potentials.

(2) Examination of the validity of the surface map by using a penetrating microelectrode to look for polarity reversals of the cortical response at representative 'border' points.

MATERIALS AND METHODS

I. Animal Preparation

A. Subjects

The experimental work was conducted on 16 healthy Mongolian gerbils (Meriones unguiculatus) with weights varying between 32 and 76 grams (Appendix I). It was estimated that the animal's ages ranged between 2 months and 7 months. The animals were housed independently or in pairs and maintained at the Kresge Hearing Research Laboratory following standard maintenance techniques. Elicitation of the Preyer reflex (pinna twitch visible as a response to a loud or brief auditory stimulus) with a loud hand-clap and visual inspection of the external auditory meati and drums were routinely used as screening procedures for the selection of prospective subjects. Animals showing signs of ongoing or previous ear infection or demonstrating a poor Preyer reflex response were not used in the study. Only two such animals were found. Animals passing these tests were anesthetized and prepared as follows.

B. Anesthesia

Anesthesia was induced with an intraperitoneal injection of a mixture of diallylbarbituric acid (80 mg/kg of body weight) and urethane (320 mg/kg). This particular barbiturate anesthetic combination when administered to the gerbil provides up to 10 hours of steady anesthesia following one intraperitoneal administration. Determination of an adequate and steady anesthetic level over the course of an experiment was accomplished by (1) periodically checking hindlimb pain reflexes elicited by pinching the hindpaws with a small hemostat, (2) checking the cornea reflex periodically by touching the cornea with a piece of hair, and (3) monitoring the baseline electrocortical activity with a

cortical surface electrode. A "moderate" level of anesthesia was sought in each experiment and defined as that level at which there was a slight limb withdrawal to pinching of the hindpaw but no corneal reflex (Pradhan and Galambos, 1963). With this procedure, supplementary injections of the anesthetic were seldom (only twice in sixteen experiments) required. The general effect of such a level of Dial-urethane anesthesia on auditory cortical evoked potentials is to consolidate individual components of the response until one observes only an initial, surface positive wave without secondary irregularities.

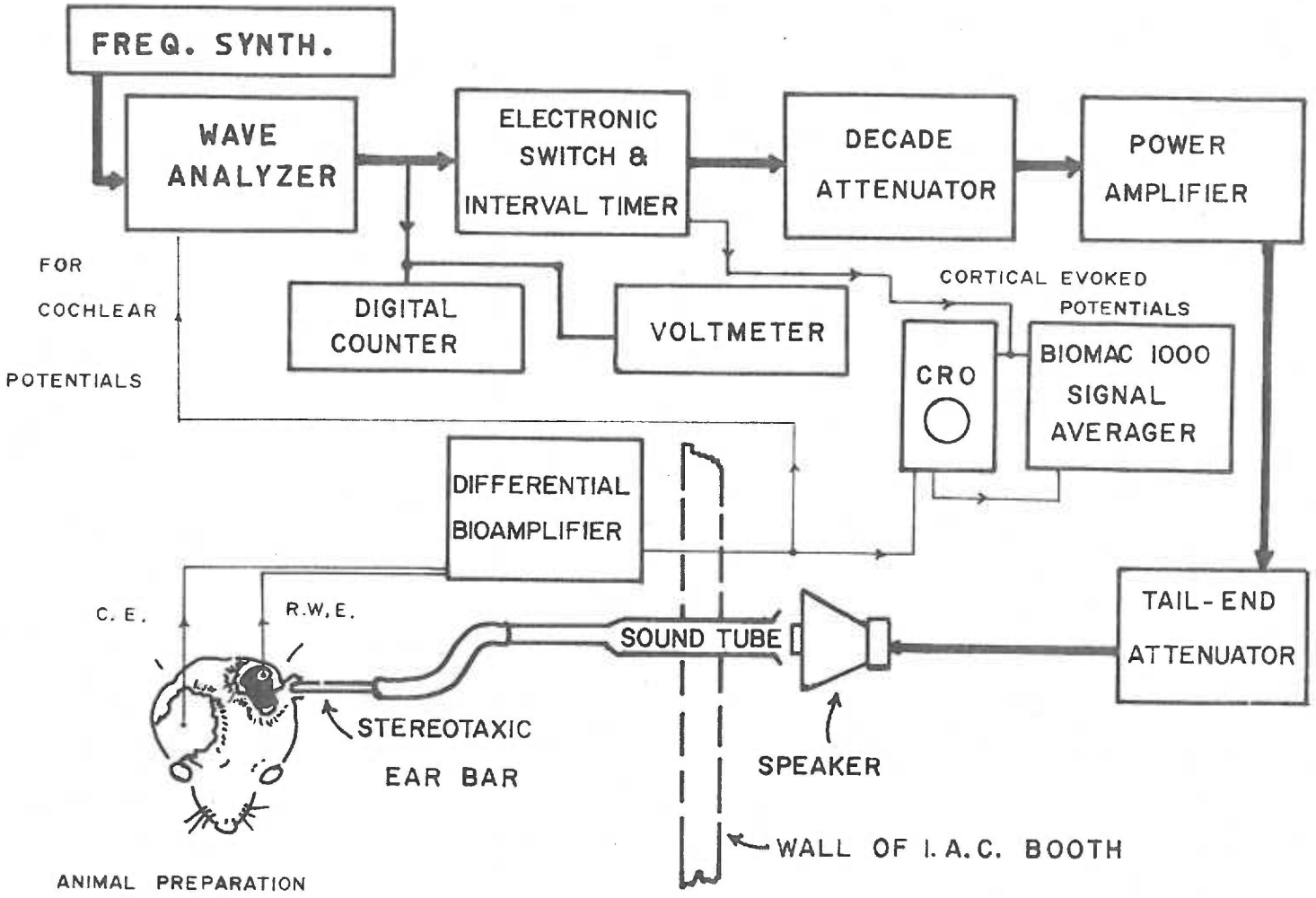
A small volume of lactated Ringer's solution was injected subcutaneously in two experimental preparations after 8 hours in the attempt to maintain proper water and electrolyte balance.

C. General Experimental Conditions

All surgical and electrophysiological recording procedures were carried out in a double-walled, sound insulated and electrically shielded Industrial Acoustics Company (IAC) chamber (Figure 1). Operating procedures were performed at 10 to 40 X magnification using a binocular dissecting microscope (Zeiss). Throughout the experiment, heart beat waveform (PQRST complex) and heart rate, cerebral vascular arterial-venous color difference, respiration rate, and rectal temperature were regularly monitored. The body temperature was maintained at 38.3 $\pm$ 1° centigrade. This is the normal range for the unanesthetized Mongolian gerbil (Gillette and Brummett, unpublished observations, 1975). Temperature maintenance within this normal range was accomplished with the aid of a heating pad (placed underneath the animal) in conjunction with a rectal thermister probe (Yellow Springs Instruments, model 46). Temperature maintenance is important because departures of 1.5 to 2.0°

FIGURE 1.

Schematic diagram of the sound-producing system (equipment connected by thick lines) and biological recording system (equipment connected by thin lines). C.E.: cortical electrode, R.W.E.: round window electrode. Note that the "indifferent" and "ground" electrodes and their connections between the animal preparation and the biological amplifier are not shown.


FREQ. SYNTH.
WAVE ANALYZER
ELECTRONIC SWITCH & INTERVAL TIMER
DECADE ATTENUATOR
POWER AMPLIFIER
FOR COCHLEAR POTENTIALS
DIGITAL COUNTER
VOLTMETER
CORTICAL EVOKED POTENTIALS
CRO
BIOMAC 1000 SIGNAL AVERAGER
DIFFERENTIAL BIOAMPLIFIER
C. E.
R.W.E.
SOUND TUBE
TAIL-END ATTENUATOR
STEREOTAXIC EAR BAR
SPEAKER
WALL OF I.A.C. BOOTH
ANIMAL PREPARATION

Celsius from the normal temperature range have been shown to affect the amplitude and waveform of auditory evoked potentials recorded from the cortex of the cat (Rosenzweig and Rosenblith, 1953) and guinea pig (Walloch, 1971). Evoked potentials recorded from the cortex of the Mongolian gerbil appeared to be similarly affected in preliminary observations made by the present author.

D. Respiration

It has proven to be very difficult to establish and maintain a proper level of mechanical ventilation in an animal as small as the Mongolian gerbil. Preliminary experiments had demonstrated that mechanical respiration was not well tolerated by the gerbil so all experiments were conducted without artificial respiration or tracheostomy. It is important to note that, unlike other small rodents that require mechanical ventilation when anesthetized with Dial-urethane, the Mongolian gerbil seems able to maintain adequate respiration without the need for mechanical assistance. With the level of anesthesia used in these experiments, the gerbil maintained steady and strong respiration without any mechanical assistance for periods as long as 10 to 12 hours, as long as the body temperature remained close to normal, So long as the body temperature was maintained within normal limits, respiration rates ranging between 80 and 120 breaths a minute were observed which is the range that we observed in the awake but resting gerbil.

It may be pertinent to mention the occurrence periodically of unusually deep breaths in the gerbils observed in the present experiments. After each such "sigh" the animal would return to the more typical steady rate of respiration. Such 'big breath' breathing is reportedly more physiologically 'normal' (because of the shift in

alveoli used) than is the steady ventilation imposed by mechanical respirators (Comroe, 1972). Further evidence that respiration was in general adequate comes from the observation that in all animals from which usable data were obtained (1) the cortical vasculature showed a characteristic artereo-venous color difference and, (2) consistently large evoked potentials could be recorded from the brain.

E. Preliminary Surgery

After the animal was anesthetized, both pinnas were removed and the external ear canals dissected free from surrounding tissue down to the bony meatus. This permitted clear access to the opening of the external auditory meatus for proper placement of the stereotaxic ear bars. The ear drums were then inspected visually under the dissecting microscope to be certain they were healthy and undamaged. Next, the left bulla was surgically exposed from a postauricular approach and its thin wall opened to allow the placement and securing of an electrode so round window membrane recordings could be obtained. This surgical procedure in the gerbil can be accomplished quickly without disturbing the sound conducting structures of the middle ear. The round window electrode was held in place by securely gluing it to the bulla bone with methacrylate tissue adhesive and cold-cure dental acrylic cement.

F. Stereotaxic Technique

The animal preparation was then placed in the headholder of a stereotaxic instrument (Kopf, model 1204) designed to handle small carnivores and rodents. A hollow stereotaxic ear bar with a tapering tip designed for small mammals was inserted into the left ear canal and was snugly fitted into the bony meatus. A solid ear bar was next placed

tightly into the right ear canal. Ear bar insertion was always accomplished while monitoring the responses of the left ear to click stimuli by 'listening in' on the AC cochlear potential with earphones. This procedure helped to insure an unimpeded acoustic coupling between the hollow ear bar and the animal's ear. Silicone grease was then placed around the coupling area between the hollow ear bar and the bony meatus to afford a tight acoustic seal. This procedure provided a sealed acoustic system, an important feature for proper calibration of the sound producing equipment.

G. Cortical Exposure

The scalp was incised along the midline with fine dissecting scissors and a large skin flap reflected back to expose the temporal musculature on the right side. The muscles were removed by blunt dissection down to the zygomatic arch to afford a clear approach to the extreme lateral aspect of the skull. The cranium was opened widely to expose the temporal cortex and surrounding regions of the right hemisphere. This was accomplished by carefully circumscribing the desired area using a small, high-speed, dental drill (Kerr, model ATM) without completely cutting through the cortical bone; that is, a 'thinning down' process was used. The entire flap of bone was then easily removed with a small elevator. This procedure was developed for the gerbil because of the minute dimensions of the skull. Even the smallest instrument available for breaking and trimming away skull bone was so large as to cause significant depression and trauma of the brain surface. Removal of the dura mater was then performed. This procedure proved to be a very delicate and tedious task and could only be successfully accomplished with the aid of a special tool (a discarded tungsten microelectrode with

a hook in the end) which was used in conjunction with an extremely fine-tipped pair of watchmakers forceps.

The brain exposure was unavoidably limited in a ventrolateral direction. It was found that most of the temporal cortex could be exposed by reflecting the eye ball away from the orbit and then removing the posterior third of the bony orbit. This allowed adequate cortical surface exposure in the anterior direction. However, if drilling was attempted as far lateral as the zygomatic crus, the delicate skull would often fracture down to the base of the braincase and cisternal bleeding would ensue, leading to poor condition of the preparation. As a result, in most of the mapping experiments, a more conservative lateral exposure was undertaken with the result that the far lateral borders of the auditory fields for these experiments were never really defined (see Results).

In order to protect the exposed pial cortical surface from fluid loss and drying, a small quantity of warm (38.0° C) mineral oil was frequently applied and allowed to flow across the exposed surface of the hemisphere.

II. Acoustic Stimulation: Sound System and Calibration Procedures

A. Stimulus Parameters

Acoustic stimuli used in these experiments were of two types: continuous pure tones and clicks. The acoustic transducer used to generate these stimuli was a Western Electric (model 555) speaker. This speaker was most efficient in the lower and middle frequencies with output falling off between 2 and 20 kHz. The acoustic transducer was located between the inner and outer walls of the IAC sound booth (Figure 1) and was connected to the ear of the animal preparation by way of a rigid

sound tube about 1 meter long, terminating in a flexible rubber tube attached to the hollow stereotaxic ear bar.

The electrical signals used to drive the speaker were produced by an oscillator which is part of a General Radio (model 1900) wave analyzer modified so as to be driven in its "tracking" mode by a General Radio Coherent Decade Frequency Synthesizer (model 1162A). The resulting sinusoidal signal(s) were led to a Grason Stadler Interval Timer (model 471-1) and Electronic Switch (model 829-E). For sustained tones, the switch was set to ignore the timer and to pass the input signal continuously. Operation during pulsed stimulation will be described below. The signals were then led to a General Radio Decade Attenuator (model 1450-TA) for control of signal level. This attenuator provides up to 110 dB of attenuation in 10 and 1 dB steps. The signals were then amplified by a McIntosh power amplifier (model MC-2105). A specially constructed power or 'tail-end' attenuator followed the amplifier in order to minimize amplifier noise in the acoustic system. This attenuator could provide 0, 20, 40, or 60 dB attenuation of the signal. It was found that 40 dB of tail-end attenuation was necessary to eliminate amplifier noise from the acoustic system. Finally, the electrical signal was led to the Western Electric speaker.

Pure tone stimuli at one of eighteen different frequencies (0.1, 0.2, 0.31, 0.5, 0.7, 1.0, 2.0, 3.0, 1.5, 4.0, 5.0, 7.0, 8.0, 10, 13, 15, 17, 20 kHz) were used for recording AC cochlear potentials from an electrode placed on the round window membrane of the left cochlea. Because the speaker was not flat in its output across frequencies for one level of input, careful calibration was required at the different

frequencies. Before the start of each experiment the attenuator setting in dB corresponding to a standard sound pressure level (1 μbar) was measured for each of the 18 frequencies. A 1/4 inch calibrated microphone (Bruel and Kjaer, model 4136) was used for this purpose. The microphone was coupled to the tapered end of the hollow stereotaxic ear bar (and hence the entire sound delivery system) with a short (1.5 cm. long) piece of rubber tubing (0.5 cm. inside diameter). This procedure is the so-called "substitution method" described by Vernon and colleagues (Vernon and Meikle, 1974; Vernon, Katz, and Meikle, 1976) and provides an estimate of the sound pressure level at the end of the ear bar. Because of the variation from animal to animal in regard to external and middle ear characteristics which will exert significant effects on the sound field, it was considered important to calibrate the sound equipment prior to each experiment (Vernon et al., 1976). A summary of the calibration data can be found in Appendix II. These data were used for calculating 1 μV isopotential curves of the AC cochlear potential.

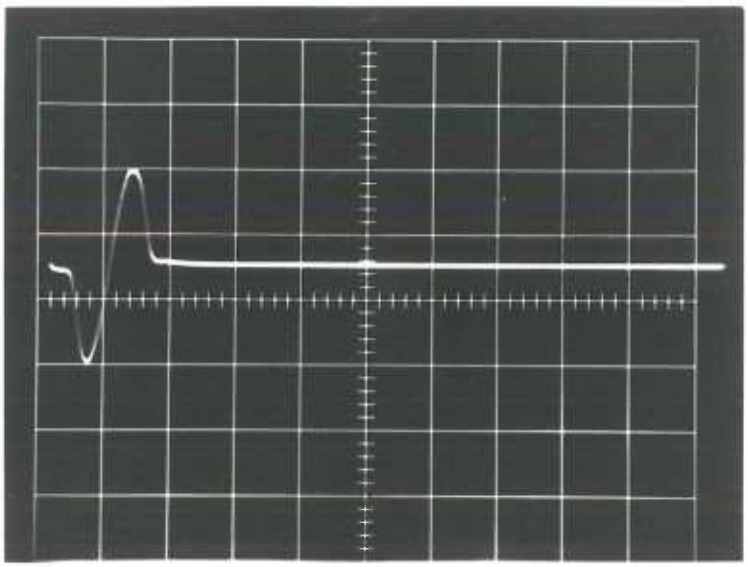
The acoustic system was also used to deliver an electrical transient of known dimensions to the speaker to produce a standard "click" stimulus. For this purpose, a sinusoidal (7 kHz) electrical signal was led to the Grason Stadler interval timer and electronic switch which were set so as to obtain a signal consistently of a single cycle (Figure 2a). The duration of the signal was 140 μsec. Its initial polarity was always negative going and its amplitude was 3 volts peak-to-peak. This signal was led through the various attenuation and amplification stages described above before reaching the Western Electric 555 speaker where it produced a sharp "click" sound.

FIGURE 2.

(a) Photographic record of the oscilloscope display of the electrical signal (1 cycle of a 7 kHz sinewave) used to drive the Western Electric 555 speaker to produce a "click" stimulus. Calibration: 1 V/cm, 100 μsec/cm. Positivity up.

(b) Photograph of the oscilloscope record of the standard click stimulus (at an intensity of 100 dB SPL) recorded with a calibrated microphone. Photograph is of a single sweep. Click produced by a Western Electric 555 speaker. Major frequency of the click is 833 Hz. Note that the click "rings" for 15 msec. Calibration: 1 mV/cm, 2 msec/cm. Positivity up.

a



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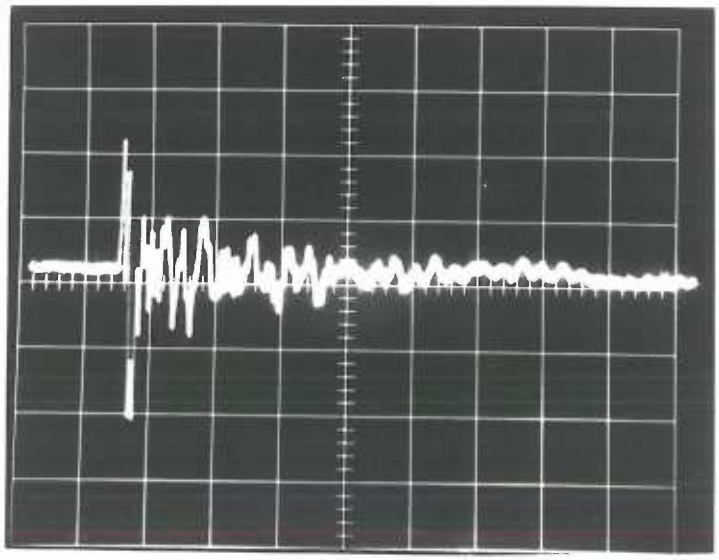


The standard "click" stimulus used in this investigation of the gerbil auditory cortex had a low major frequency of 833 Hz and a duration of 15 msec (Figure 2b). The click had a rapid onset and most of the energy of the stimulus was found to be concentrated within the initial 3 msec. Clicks were presented monaurally at a rate of 1/sec.

A click stimulus is easy to produce but difficult to quantify acoustically. Vernon and Meikle (1974) have pointed out that different speakers produce different clicks. Because of this unique characteristic of all speakers, it follows that it is never sufficient to describe a click stimulus by reporting only the voltage, duration, and shape of the electrical transient producing it. Instead, the actual sound output of the acoustic transducer must be recorded using a calibrated microphone and viewing its output on an oscilloscope. When this is done, the click can be seen to "ring" and the frequency of this ringing is an individual characteristic or signature of the speaker producing it. Thus, the major frequency, as well as the duration, of oscillation should therefore be reported (Vernon and Meikle, 1974). It has been also suggested that the magnitude of a click stimulus is fairly well approximated by measuring the peak-to-peak amplitude of the major deflection(s) (Vernon and Meikle, 1974; Vernon et al., 1976).

With the above points in mind, the following procedures were performed prior to each experiment. The click stimulus was recorded with the 1/4 inch calibrated microphone coupled to the end of the hollow stereotaxic ear bar, that is, 'substituted' for the animal preparation. The output of the calibrated microphone was led to an oscilloscope (Tektronix, model 504A) so that the waveform corresponding to the click could be displayed and photographed. The amplitude of the click stimulus

was defined as the peak-to-peak amplitude of the initial, major deflection of the click wave-form. A standard click amplitude was established by setting the attenuators so as to produce a signal amplitude of 4260 μV. This setting corresponded to a sound pressure level (SPL) of 26 dB re: 1 μbar (or 100 dB re: 0.0002 μbar). The output of the calibrated microphone is "flat" between 100 Hz and 20 kHz, therefore its use in measuring the amplitude of the transient (click) signal is permissible. This 'standard SPL' was used for all click stimuli presented throughout the entire experimental series. A standard click was considered important (and so used) as it makes comparisons between different animals valid.

This particular click intensity was chosen because it was found to produce evoked potentials of maximal amplitude in a variety of experimental animals anesthetized with barbiturates including the cat (Saunders, 1970), rat (Borbély, 1970), and raccoon (Hertzler et al., 1970). This conclusion was also born out in the present work with the gerbil. On theoretical grounds, it also seems reasonable to assume that a "loud" click would activate more neurons within the auditory pathway and auditory cortex than would a less intense click, and this supposition has been confirmed experimentally (Rosenzweig and Rosenblith, 1953; Rosenblith, 1954; Horvath, 1969). Thus a click of high intensity was used in the present experiments to maximize the probability of activating the entire population of acoustically-responsive neurons within the temporal cortex.

III. Recording System

A. Electrodes

AC cochlear potential and neural responses were recorded differ-

entially. An "active" silver ball (250 microns) electrode recorded responses from the round window membrane of the left cochlea (Figure 1). A stainless steel needle placed in muscle tissue near the left bulla acted as the "indifferent" electrode. The "ground" electrode was a stainless steel needle placed in the ipsilateral hind paw.

Cortical potentials evoked by clicks were also differentially recorded with either a silver ball (250 microns) electrode or a tungsten microelectrode (5 micron tip, 2-3 MΩ impedance at 1kHz). The indifferent and ground electrodes were stainless steel needles placed respectively in the temporal musculature and hind paw contralateral to the ear being stimulated (ipsilateral to the hemisphere recorded from). The "active" silver ball electrode was used to record from the cortical pial surface while the "active" microelectrode was used to record from various depths within the cortical grey matter.(Figure 1).

B. Recording Apparatus

All biological potentials were recorded and then amplified 1000 times with a differential biological amplifier (Princeton Applied Research, model TM 113). This amplifier has an input impedance of up to 100 MΩ in the AC recording mode. The output of this battery-driven amplifier was led outside the double-walled IAC booth and then in parallel to three recording devices: a General Radio (model 1900) wave analyzer for measurements of AC cochlear potentials, a Tektronix (model 564-B) oscilloscope for display of cochlear responses to the click stimulus and cortical evoked potentials, and a small, special-purpose computer (Data Laboratories, model Biomac 1000) for computation and display of averaged, cortical responses (Figure 1).

The filters of the biological amplifier were set during round

window recordings to pass the band from 30 Hz to 100 kHz. Cortical evoked potential recordings were obtained with the amplifier filters set to pass the band from 3 Hz to 3 kHz.

IV. Experimental Design and Protocol

A. Cortical Surface Mapping

In these experiments (Table I), the silver ball electrode, in light contact with the pia mater, was moved systematically in 0.5 mm steps over the exposed cortical surface to permit definition of the boundaries between acoustically 'responsive' and acoustically 'non-responsive' cortex. Sampling of cortical electrical activity was usuallly done along an anterior-posterior running line with 0.5 mm between recording points. Such exact steps were not always possible because occasionally blood vessels had to be avoided. After an anterior-posterior chord of recording points was sampled from, the electrode would be moved medially or laterally 0.5 mm and then another series of locations was recorded from until the bony edges of the exposure were reached. Parallel chords of recording points were consecutively recorded from until the entire temporal cortex had been sampled from with the ball electrode. The relative location of the first point to be recorded from in any one experiment was intentionally changed from experiment to experiment in order to minimize the possibility of sampling bias.

Each cortical point from which electrical activity was recorded was noted on a chart and its location referenced in three planes by way of stereotaxic coordinates. These recording locations could be returned to later in the experiment for further recordings as necessary, and for marking with a dot of india ink. Medial-lateral distances were

referenced to the midline (saggital suture) of the skull. Anterior-posterior (AP) distances were referenced to a "0" line represented by a line connecting the centers of the external auditory meati (inter-aural line). The inter-aural line was also utilized as the "0" coordinate for the vertical dimension. The skull was always maintained in the same horizontal plane from preparation to preparation by making sure that the incisor nose clamp was always set at the same vertical level ("0" mark) on the nose clamp support post of the stereotaxic frame. To further insure correct placement of the gerbil's skull in the stereotaxic instrument, a quick check of the alignment of the animal's skull in the instrument was done by using the recording electrode as a pointer and using the AP advancing mechanism of the stereotaxic to move it along the saggital suture (midline) of the skull. When the ear bars are properly placed, the saggital suture lies parallel to the AP axis of the stereotaxic unit. No deviation of the saggital suture from the AP axis was noted in any of the experiments as the pointer was moved along its length. Both 'click-responsive' and 'non-responsive' recording points were noted and referenced to the stereotaxic coordinate system.

Using averaging, a click-evoked response was defined as a consistently observable surface-positive potential beginning approximately 8 msec after the presentation of the click stimulus to the contralateral ear and with the peak of the positivity occuring 12 to 32 msec after the stimulus. If an averaged, click-evoked potential was not obtained at least two times out of three consecutive averaging episodes (16 responses per average), then the recording locus was defined as <u>not</u> showing a response.

As already mentioned, averaged responses were used because

of their high reliability from one average to the next, the improved signal-to-noise ratio, and the minimization of the subjective element in deciding (1) whether a response occurred (2) what the amplitude of the response is and (3) what the latency of the response is. This decision making problem is particularly acute in evoked potential mapping studies when recording responses from the border regions of the cortical sensory area for here response waveforms are quite variable in amplitude and latency and sometimes so small as to not be distinguishable from the background electrocorticogram. If a response is present, averaging will often bring it out of 'noise', and so make the decision easier on whether a response has occurred or not.

Photographs of the averaged response were taken at each 'responsive' cortical point. In addition, the following information was recorded: (1) peak-to-peak amplitude, (2) onset latency (in msec), and (3) latency to the peak of the major positive wave of the response.

B. Reversal Experiments

Four gerbil preparations were used in this portion of the study (Table I). First, the acoustic area of the right hemisphere was mapped with the surface ball electrode as outlined above. Next, a post-mapping cortical 'viability' recording was made by returning to the first 'click-responsive' point of the experiment (see Control Measures below). Then as many 'border' points as possible were returned to using the ball electrode and the stereotaxic coordinate system. At each such point, the ball electrode was withdrawn and a microelectrode took its place so cortical surface and depth recordings could be obtained. Care was always taken during the advancement of the microelectrode to penetrate the cortical tissue in a line as perpendicular to the cortical surface as possible

although sometimes this could not be achieved. The penetrating microelectrode, held in a table-mounted micromanipulator, was advanced through the cortex at these 'border' points to record sensory-evoked activity at various depths. The objective was to locate the point (depth) at which the waveform of the evoked potential showed a polarity reversal. The reason for using a microelectrode for cortical depth recording, as opposed to a larger electrode, was to minimize the possibility of producing tissue trauma or cortical speading depression, for the gerbil has an extremely small (Appendix I) and fragile brain.

The microelectrode was advanced through the cortex with the aid of a microdrive calibrated in 50 micron steps. Averaged, click-evoked responses were recorded with the microelectrode at (or just below) the pial surface and at various depths below the surface including: 250, 500, 750, 1000, 1250, 1500, 1750, and 2000 microns. Examination of the Mongolian gerbil brains used in the present experiments indicated that the temporal neocortex is approximately 1800 microns thick in formalin-fixed material (shrinkage unknown).

Averaged, click-evoked potential records were photographed at the various depths noted above. Information was also gathered at these various sampling depths concerning evoked response (1) waveform polarities, (2) latencies, and (3) amplitudes.

After the microelectrode recordings were obtained, the cortical viability check was again repeated (Table I) in order to see whether changes had occurred in the surface-recorded click response.

C. Control Measures

The major need for control measures (Table I) involves the possibility that the biological preparation may deteriorate during the

course of the experiment. The cortex is extremely labile and may become less responsive; the peripheral auditory apparatus is also susceptible to degradation; and the animal itself may show physiological deterioration as the experiment is prolonged.

The possibility of peripheral changes was checked by monitoring cochlear potentials, recorded from the round window. The monitoring procedure utilized both pure tones (at frequencies described above) and standard clicks.

AC cochlear potential "sensitivity" (or frequency) functions were obtained both before and after cortical mapping in 11 of the 16 experiments (Table I). The cochlear potential "frequency" function is a graphic description of the amount of sound required at each frequency of stimulation to elicit a constant (1 μvolt) cochlear output (see, for example, Wever and Lawerence, 1954). Discrepancies between the pre- and post-mapping sensitivity functions can reflect changes in stimulus conditions as well as changes in the physiological condition of the preparation over the course of the mapping experiment. A great advantage of the cochlear potential is its high degree of replicability which can be demonstrated over long periods of time. In the Mongolian gerbil (Vernon and Gillette, unpublished observations, 1975), as in other mammals similarly studied (Wever, 1966), a constant output of cochlear potential can be observed for periods of 8 to 10 hours if sufficient care is taken.

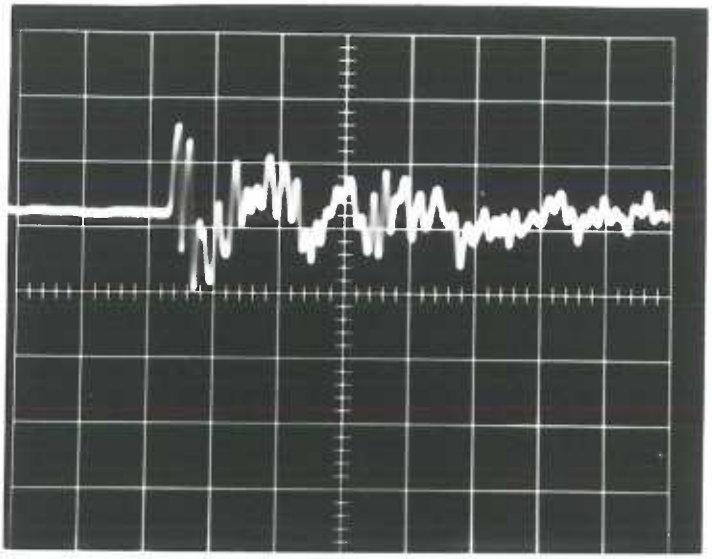
In some of the later experiments involving especially time-consuming procedures (e.g. combining surface mapping with microelectrode penetrations) it was considered more desirable to initiate cortical recording with minimum delay, therefore the cochlear potential recordings were

FIGURE 3.

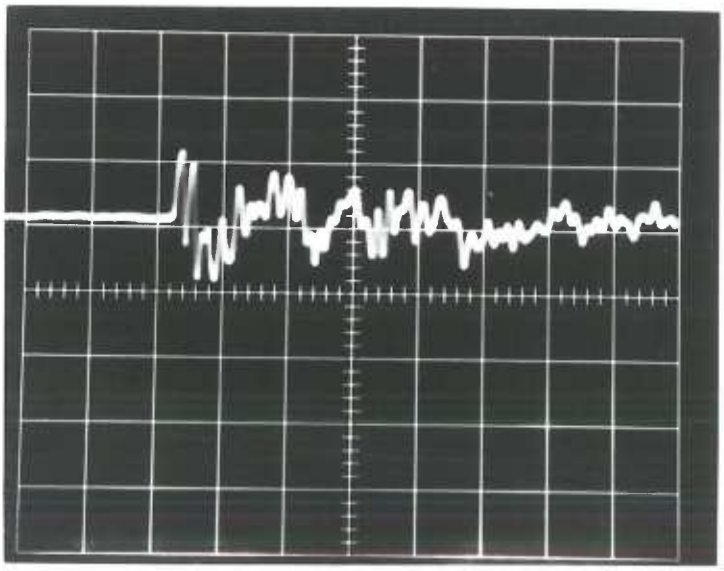
(a) Pre-mapping control record of a single response recorded from the round window membrane of the left cochlea of gerbil G11 5-5-75 to the standard click. Greatest peak-to-peak amplitude of the response is 2.6 mV. Recording obtained with the bulla open. Calibration: 1 mV/cm, 1 msec/cm. Positivity up.

(b) Post-mapping control record obtained from the round window membrane of the same animal three hours later. Note that the amplitude of the response has decreased to 2.0 mV. Same stimulus intensity and rate (1/sec). Calibration: 1 mV/cm, 1 msec/cm. Positivity up.

a



b



either abbreviated or eliminated from these last experiments (Table I).

The possible contribution of "radiation artifact" (Vernon and Meikle, 1974) to the recordings of AC cochlear potentials was checked for periodically during the course of each experiment.

AC cochlear potentials recorded from the round window to standard clicks were also routinely obtained (Table I) except in the microelectrode penetration experiments. An example of the round window response to the standard click both before and after cortical mapping is shown in Figure 3a and b. Such records served as a check for click stimulus constancy during the experiments. From photographs of such records it was possible to obtain information concerning the greatest peak-to-peak amplitude of the response and thus make comparisons between pre- and post-mapping records in an effort to see if changes in amplitude and waveform had occurred. This is possible because these responses are stable in amplitude, waveform, and latency from stimulus to stimulus if the biological preparation is in good condition and if the stimulus input is constant (Walzl and Woolsey, 1946; Rosenzweig and Rosenblith, 1953; Rosenblith, 1954; Peake and Kiang, 1962; Hertzler et al., 1970; Gillette, unpublished data, 1975).

The physiological condition of the cortex was checked by comparing cortical responses at the end of the experiment with those obtained at the beginning from the identical cortical location (Table I). This same procedure also served as a check on the general physiological condition of the animal.

The variability of cortical evoked responses makes it difficult to determine when significant changes in waveform and amplitude may

have occurred in the cortical records reflecting a change in the physiological condition of the cortex. An estimate of cortical response variability was therefore made from observations of consecutive, single click-evoked responses in 5 pilot experiments. On the basis of visual inspection of such records (Figure 4a and b), it was decided that changes in peak-to-peak amplitude of 20% or less between pre- and post-mapping records would be considered to be within the range of normal variability for cortical responses in these preparations. Conversely, it was taken as a 'rule of thumb' that decrements in cortical response amplitude of greater than 20% were arbitrarily considered to be indicative of deterioration in the physiological condition of the cortex, and mapping results obtained from these experiments considered suspect.

D. Marking Procedure

At the end of each experiment, every recording location which had given rise to a click-evoked response was then returned to with the aid of the stereotaxic coordinates and its position marked with a small dot of india ink (Lende and Woolsey, 1956). The animal was then given a lethal dose of Beuthanesia or Nembutal, and was then decapitated. The entire head was placed in a container of phosphate buffered formalin for eight days. After fixation, the entire brain was dissected free from the skull and the right hemisphere with its grid map of india ink dots photographed under 10 power magnification from two different perspectives; a dorso-lateral and a lateral view.

V. Data Presentation

A. Schematic Maps of Auditory Cortex

All cortical recording locations were plotted in three dimensions

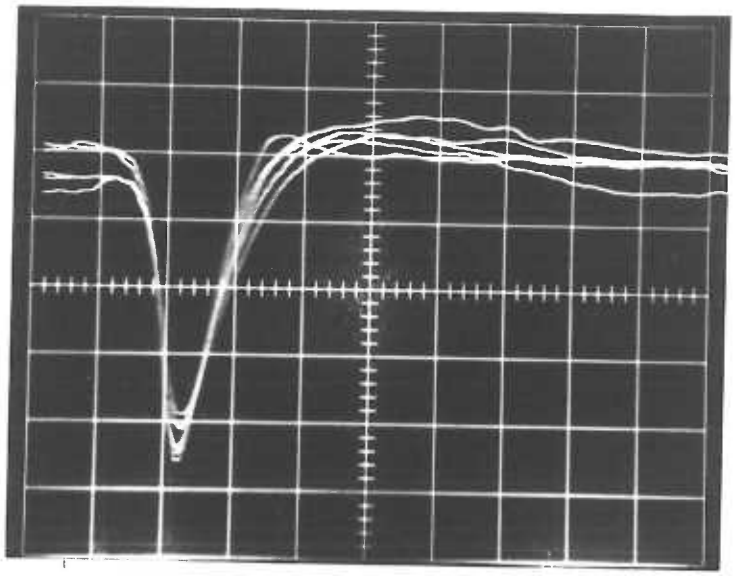
FIGURE 4.

Photographs of click-evoked responses obtained during cortical recording from two different gerbil experiments. These records are of superimposed traces intended to show the inter-response variability typical of gerbils anesthetized with Dial-urethane. All click stimuli were presented at the same intensity (100 dB SPL) at a rate of 1/sec.

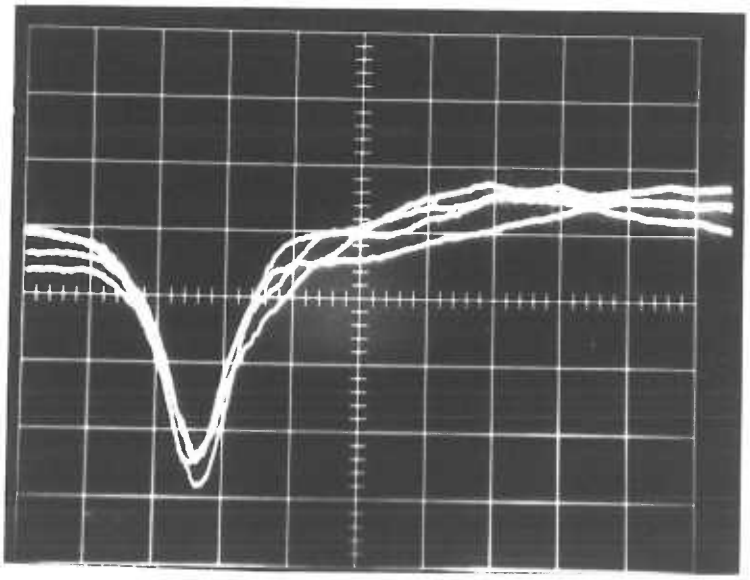
(a) Five consecutive click-evoked potentials recorded from the auditory cortex of pilot experiment Gp 11-7-74. Calibration: 500 μV/cm, 10 msec/cm. Positivity down.

(b) Four successive click-evoked potentials recorded from the auditory cortex of pilot experiment Gp 7-23-74. Calibration: 200 μV/cm, 10 msec/cm. Positivity down.

a



b



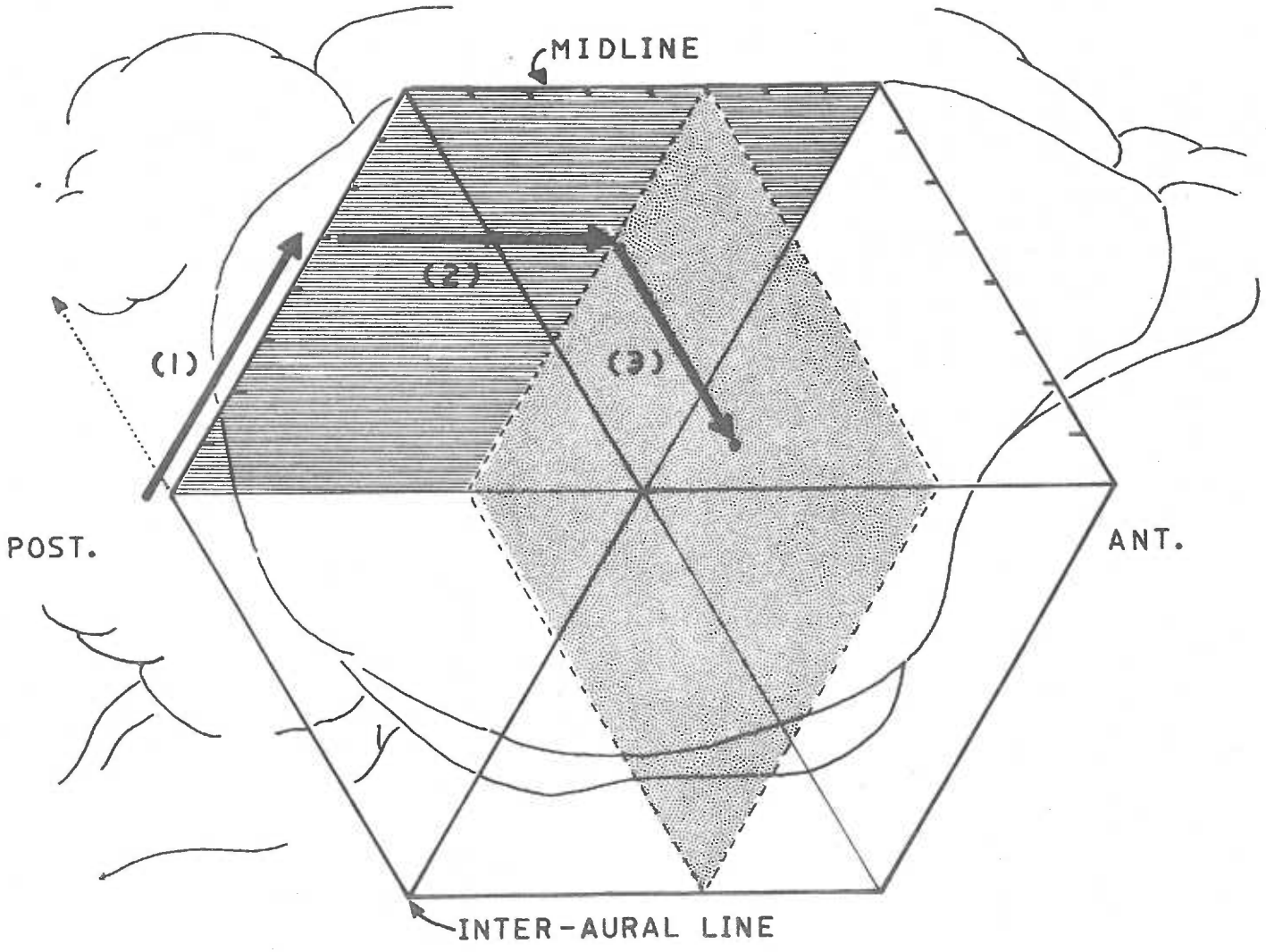
on a generalized outline of the right hemisphere of the gerbil brain. A recording locus was always represented by three numbers that referenced its location to the inter-aural line and the saggital suture of the skull. That is, a given point P (x, y, z) was plotted on triangular coordinate paper (Figure 5) by going (y) millimeters vertical from inter-aural "0", then (x) millimeters anterior of the same inter-aural line, and then (z) millimeters lateral of the midline (saggital suture) of the skull. A generalized outline of the right cerebral hemisphere of the Mongolian gerbil (viewed from a postero-lateral perspective) was superimposed upon the grid of graphed recording points to attempt a three-dimensional representation of the location of the neocortical area sampled (Figure 5 and 6; Appendix IV and V). Such maps were compiled for each cortical mapping experiment (Appendix IV and V). Points on the cortex where click-evoked responses could be recorded with a surface electrode are represented in these maps by a number denoting the peak-to-peak amplitude (in hundreds of microvolts) of the evoked potential recorded at that point. Loci where click-evoked potentials could not be recorded at the standard stimulus intensity are denoted in these schematic maps by large black dots.

B. India Ink Dot Maps

The auditory area defined with clicks can be seen in the photographs of the formalin-fixed right hemisphere of the gerbil brain (Appendix III) in four of the 'best' experiments. These photographs show clearly where the click-responsive cortex (denoted by the grid of india ink dots and pale overlay) lies relative to some of the more obvious cerebral landmarks; for example, the rhinal fissure and the middle cerebral artery.

FIGURE 5.

Schematic diagram showing how cortical recording points were plotted in three dimensions on a generalized outline of the right hemisphere of the gerbil brain. Anterior is to the right and posterior to the left in the diagram. The saggital plane (at the midline) is represented by the hatched surface while the coronal plane is represented by the dotted surface. A given recording point P (x, y, z) was plotted by going (y) millimeters vertical (arrow 1) from inter-aural "0", then (x) millimeters anterior of the same inter-aural line (arrow 2), and then (z) millimeters lateral of the midline (arrow 3). For the point plotted here, x=5, y=5, z=4; that is, P lies 5 mm above and 5 mm anterior to inter-aural "0" and 4 mm lateral of the midline.


MIDLINE
(1)
(2)
(3)
POST.
ANT.
INTER-AURAL LINE

RESULTS

I. Results of Cortical Surface Mapping Experiments

A. General Location, Size, and Shape of the Gerbil Auditory Area

When all the schematic maps for all the preparations (Appendix IV and V) are superimposed onto a single three coordinate plot the general size and location of the gerbil auditory field can be visualized for one hemisphere (Figure 6). The click-responsive auditory area overlies the temporal cortex and is bounded on its dorsal and anterior edge by the middle cerebral artery and on its ventral edge by a thin strip of cortex making up the upper bank of the rhinal sulcus (Appendix III). The auditory region varied slightly in location within the temporal area from preparation to preparation (Appendix III and VI), but not enough to qualify the general statements made above. In terms of size, the cortical auditory field for the gerbil is approximately 5 millimeters in length (anterior-posteriorly) and 4 millimeters in width (medio-laterally) (Appendix VI). The shape of the area is generally round or oval (Appendix III).

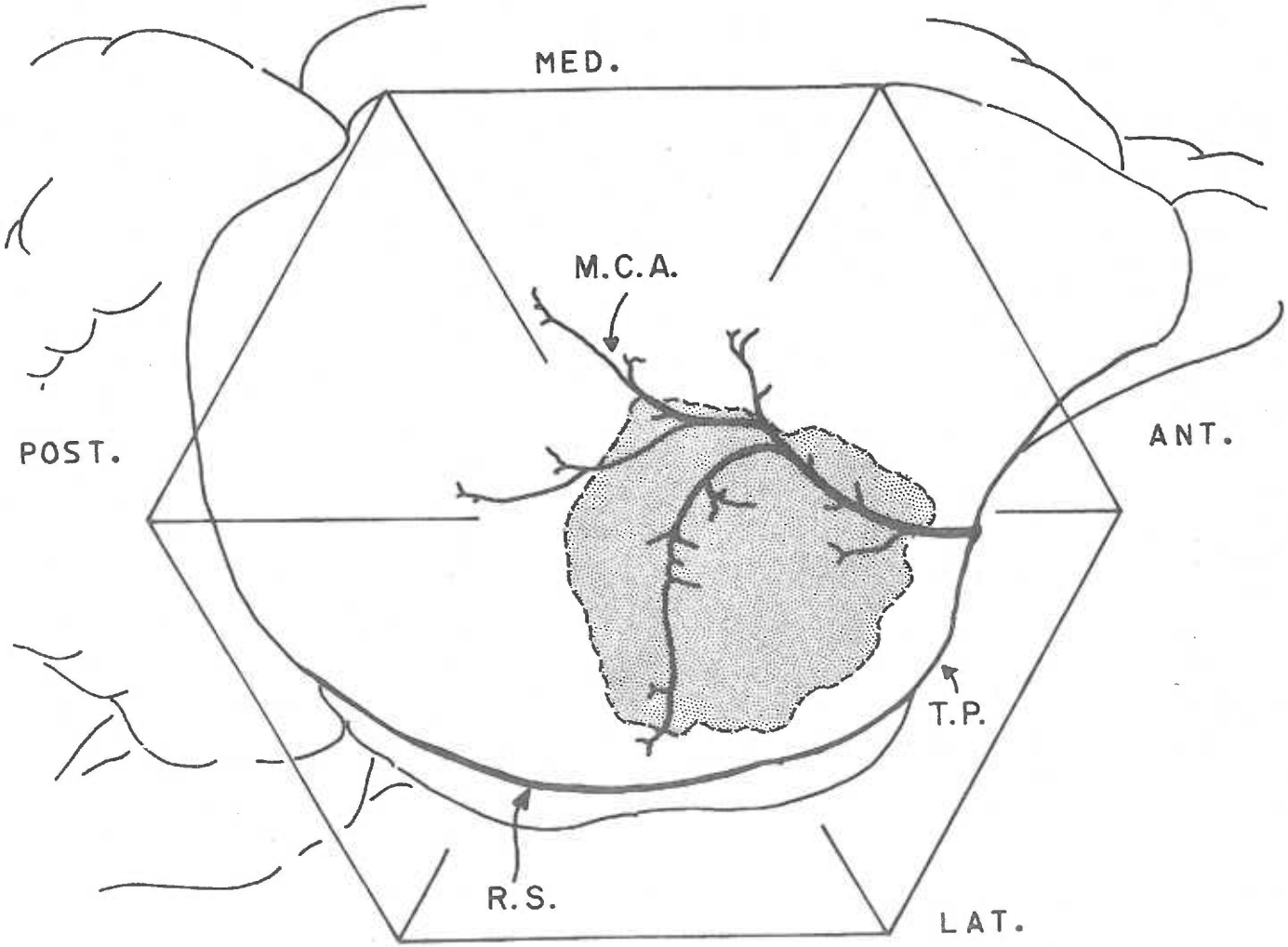
B. Results of Control Measures

Analysis of the control measures showed that the experimental population (16 Ss in total) could be divided into two groups depending upon whether the preparation was in "good" physiological condition (11 Ss) or "poor" physiological condition (5 Ss).

Peripherally, pre- and post-mapping amplitudes of round window responses to the standard click stimulus for all the preparations in which the monitor was used (Table I) are given in Table II. Most of the pre-mapping response amplitudes were around 2 mV. The discrepancy in pre-mapping amplitude between G2 2-25-75 and the rest of the animals

FIGURE 6.

Composite map of the gerbil auditory cortex derived by superimposing the click-responsive areas of all the animal experiments on to a three-dimensional depiction of right cerebral hemisphere. Maps used to derive this figure can be found in Appendix IV and Appendix V. Stippled area shows location of auditory field in the right hemisphere that results from the superimposing of all the maps. Abbreviations: M.C.A. for middle cerebral artery, R.S. for rhinal sulcus, and T.P. for temporal pole.


MED.
M.C.A.
POST.
ANT.
T.P.
R.S.
LAT.

(Table II) may be due to any or all of the following: (1) differences in acoustic coupling of sound tube to animal's ear, (2) differences in middle ear efficiency, or (3) differences in the physiological condition of the animals.

Within-subject variability for the round window responses to standard clicks is reflected in the pre- and post-mapping amplitudes for each animal found in Table II. It can be seen that a discrepancy exists between the pre- and post-mapping response amplitudes in at least four experiments (G2 2-25-75, G5 3-25-75, G7 4-1-75, G11 5-5-75). These records for gerbil G11 5-5-75 are shown in Figure 3a and 3b. The remaining animals demonstrated stable response amplitudes between the beginning and the end of the experiments.

The AC cochlear potential "sensitivity" functions generated before and after cortical mapping in eleven experiments (Table I) are presented in Appendix VII. Between-subject variability in sensitivity of the ear to 18 pure tone frequencies of stimulation is small and falls within the normal range of the AC cochlear potential output across frequencies for the Mongolian gerbil (Vernon and Gillette, unpublished data, 1975). The only exception was the pre-mapping function of gerbil G2 2-25-75 which showed much less (20 dB) sensitivity across frequencies when compared to the rest of the animals. As reported by others, the Mongolian gerbils used in this study demonstrated their greatest sensitivity to pure tone stimulation at lower frequencies (700 Hz through 3 kHz) with lesser sensitivity at the middle to higher frequencies.

Differences between the pre- and post-mapping sensitivity functions was only evident in two experiments: G5 3-25-75 and G7 4-1-75

(Appendix VII). All other experiments in which pre- and post-mapping sensitivity functions were obtained demonstrated over-lapping curves and hence no demonstrable changes over the course of the mapping experiments.

In summary, the peripheral control recordings showed that in at least four gerbil mapping experiments, the preparation started in (G2 2-25-75) or ended in (G5 3-25-75, G7 4-1-75, G11 5-5-75) questionable condition. This makes the surface mapping results in these experiments somewhat suspect.

Results from cortical control recordings support the above conclusion and add some additional important findings. Table III shows the peak-to-peak amplitudes of the averaged, click-evoked potentials recorded from the same cortical surface location both before and after cortical mapping in all the experiments (Table I). It can be seen that in five experiments (G2 2-25-75, G4 3-18-75, G5 3-25-75, G7 4-1-75, G11 5-5-75), there was a substantial drop (20% or greater in all cases) in response amplitude between pre- and post-mapping samples (Table IV). These five animals were thus considered "poor" preparations and the click maps obtained from them suspect. The remaining eleven animals and their auditory cortical maps were on the other hand considered "good" (Table IV).

C. Auditory Cortex Defined in the Good Preparations

Appendix IV contains the schematic maps of the click-responsive auditory field for all the "good" gerbil preparations. Ink dot maps of the acoustic area of the right hemisphere for four these animals (G8 4-12-75, G9 4-19-75, G10 5-3-75, G14 6-4-75) can be found in Appendix

III. The results of surface mapping in three representative animals of this group will be given in some detail below.

The auditory area of gerbil G8 4-12-75 was found to lie in the temporal cortex (Appendix III and IV). The largest amplitude evoked potentials were recorded in this experiment from a region located somewhat centrally and anteriorly within the field (Figure 7a). Smaller amplitude responses were recorded from sampling points around this central core or "hot spot". Click-evoked responses recorded from the field were biphasic (positive-negative) with an onset latency averaging 10 msec and a peak positive latency averaging 19.4 msec (Table V). Cortex not responsive to standard clicks was found to surround the auditory area on all sides except anteriorly. Here responses were recorded up to the edge of the cortical exposure. Interestingly, evoked responses with quite long onset and peak positive latencies were consistently recorded from the posterior-lateral border of the acoustic area (Figure 7b).

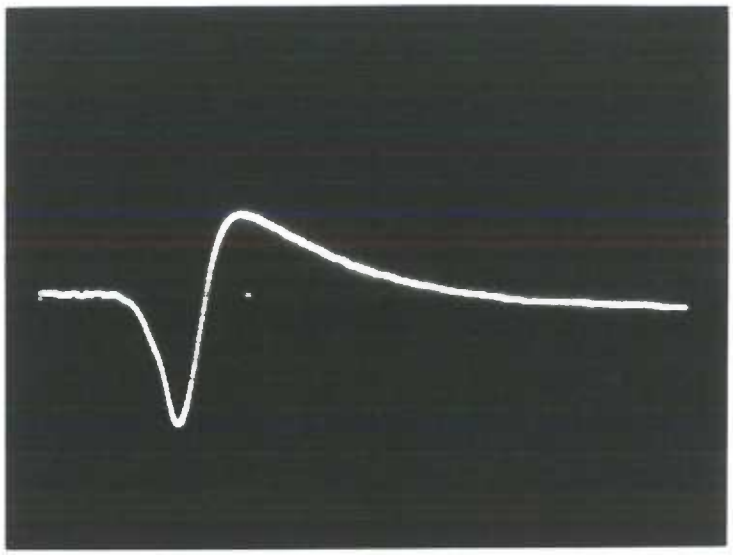
The auditory cortex mapped in gerbil G10 5-3-75 is, in terms of completeness of mapping, probably the best of the experimental series. The acoustic area for this animal was found to lie in the temporal area below the middle cerebral artery (Appendix III and IV). Responses recorded from this region were biphasic (initially positive going) with onset latencies averaging 10.2 msec and peak positive latencies averaging 22.2 msec. The largest amplitude potentials were localized centrally and somewhat anteriorly within the field with smaller amplitude responses recorded from surrounding areas. Cortex unresponsive to contralateral click stimulation was found to totally surround the aud-

FIGURE 7.

(a) Photographic record of averaged (16 sweeps), click-evoked potential recorded from locus 17 near the center of the auditory area of gerbil G8 4-12-75. The peak-to-peak amplitude of this response is 1700 μV. The latency to the peak of the positive wave is 16 msec. A downward deflection represents positivity at the electrode relative to the indifferent electrode. Calibration: 500 μV/cm, 8 msec/cm.

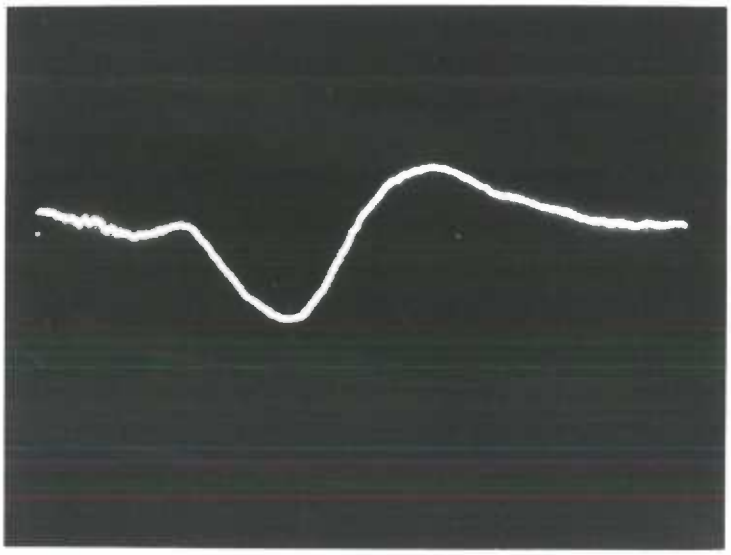
(b) Photographic record of averaged, click-evoked potential recorded from locus 1.3 at the postero-lateral border of the auditory area of gerbil G8 4-12-75. Peak-to-peak amplitude of the response is 130 μV. Latency to the peak of the surface-positive wave is 28 msec. This record represents a typical long-latency (27 msec $\leq$) response. Downward deflection represents positivity at the electrode relative to the indifferent electrode. Calibration: 50 μV/cm, 8 msec/cm.

a



L

b



itory area (black dots in schematic map of Appendix IV).

In both gerbil G15 7-17-75 and G16 7-28-75 an abbreviated surface mapping procedure was applied. The surface mapping was intentionally less complete in these two gerbil experiments in order to allow more time for investigating various click-responsive loci with a penetrating microelectrode. In these experiments, cortical, sensory-evoked electrical activity was sampled from points forming a line or chord running medio-laterally or anterior-posteriorly across the cortical exposure (Appendix IV).

The surface map of gerbil G16 7-28-75 (Appendix IV) was defined by two anterior-posterior chords of recording points crossed at right angles by a single, medio-laterally running chord of recording loci. Points that were unresponsive to contralateral click stimulation comprise the end loci of each chord of recording points (black dots in schematic map found in Appendix IV). Thus, the border of the auditory area for this animal was defined with surface recordings at six points; two anteriorly, two posteriorly, one dorso-medially, and one ventro-laterally. Thirteen recording locations produced click-evoked potentials that were typically biphasic (positive-negative) in waveform and polarity. The largest response amplitude was obtained from a location anteriorly within the field. Average onset and peak positive latencies for the responses recorded from this animal were 8 msec and 15.9 msec, respectively (Table V).

D. Latency Data

Frequency histograms of peak positive latencies for all experiments (Figure 8) as well as for the 11 best experimental preparations

FIGURE 8.

Latency histogram for the peak positive wave of the averaged, cortical evoked response for all click-responsive loci in all experimental subjects (N = 16 gerbils). Population: $\overline{X}$ = 20.4 msec, Mo = 20.0 msec, and Range = 13-32 msec. Latencies include the time required for the sound to reach the eardrum from the speaker $\cong$ 2.75 msec.

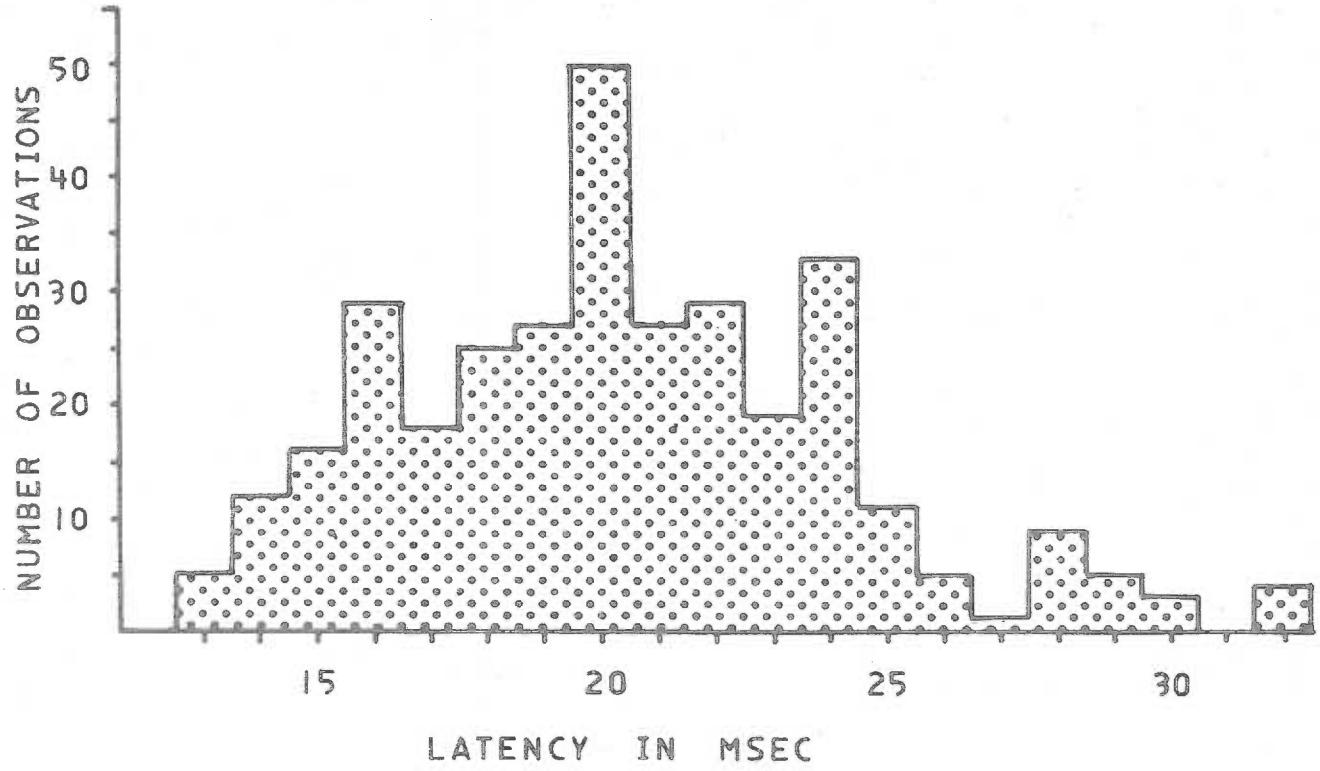
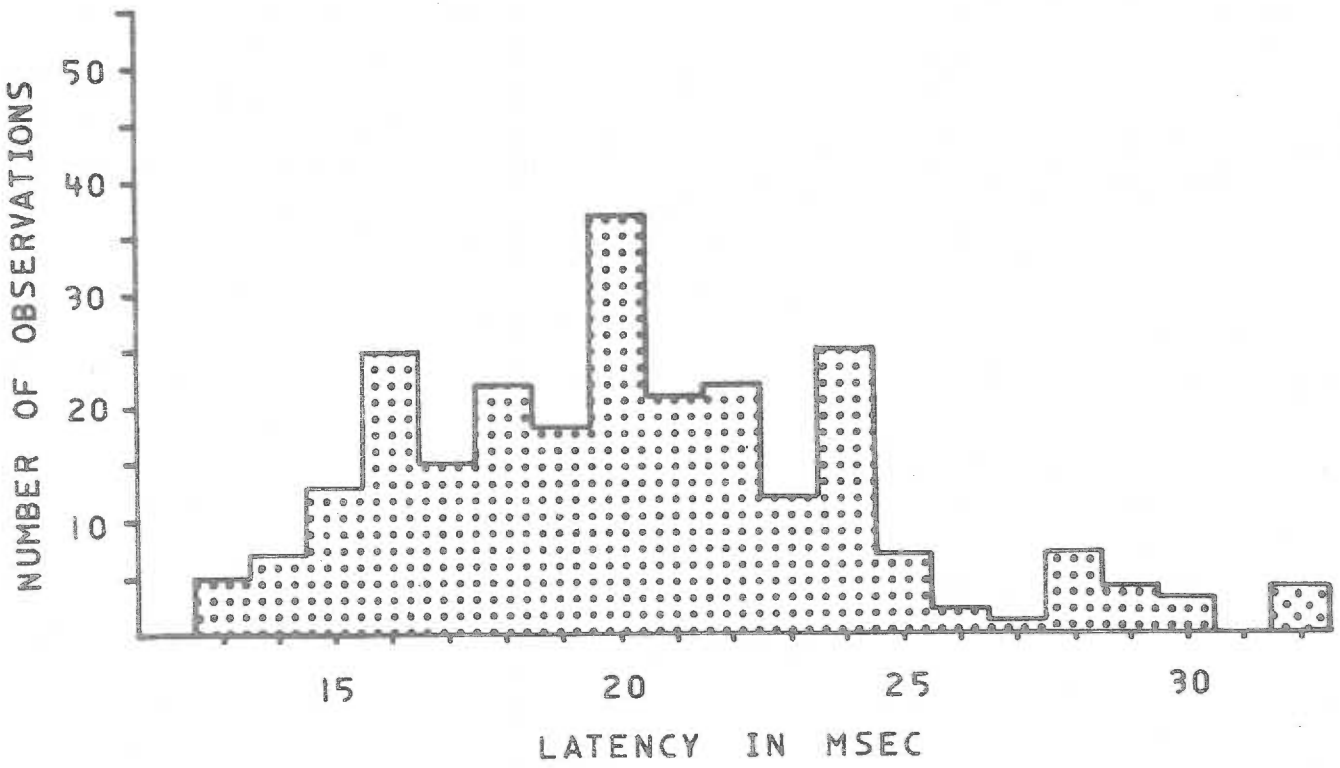

NUMBER OF OBSERVATIONS
50
40
30
20
10
15
20
25
30
LATENCY IN MSEC

FIGURE 9.

Latency histogram for the peak positive wave of the averaged, cortical evoked response for all click-responsive loci in the 'good' experimental preparations (N = 11 gerbils). Population: $\overline{X}$ = 19.9 msec, Mo = 20 msec, and Range = 13-32 msec. Latencies include the time required for the sound to reach the eardrum from the speaker $\tilde{=}$ 2.75 msec.


NUMBER OF OBSERVATIONS
50
40
30
20
10
15
20
25
30
LATENCY IN MSEC

(Figure 9) are essentially identical in showing that the characteristic is normally distributed. However, of some interest was the additional finding that click-evoked responses with rather long (27 msec ≤) first positive latencies (Figure 7b) were consistently recorded from points lying in the postero-lateral sector of the auditory area in a number of experiments (G2 2-25-75, G6 3-29-75, G8 4-12-75, G9 4-19-75, G10 5-3-75, G11 5-5-75, G14 6-4-75). These longer latency responses are denoted by the underlined numbers in the schematic maps for the above listed animal preparations (Appendix IV and V). Such long latency evoked potentials were usually recorded from only a few sampling points in the posterior region of the auditory cortex, although in one animal (G10 5-3-75) a cluster of five adjoining recording sites gave rise to long latency responses. A similarly located cluster of seven recording sites produced averaged responses with long first-positive latencies in the posterior region of the auditory area of gerbil G14 6-4-75. Such responses were much less frequently recorded from other regions within the acoustic cortex (see maps for gerbils G1 2-22-75 and G 14 6-4-75). The averaged response latencies obtained from the gerbil auditory cortex (Figures 8 and 9; Table V) include the air travel time required for the sound to travel down the sound tube to reach the ear of the gerbil. This travel time is approximately 2.75 msec.

II. Results from Microelectrode Recordings

A. Results of Control Measures

In four mapping experiments (Table I), surface-mapping was followed by microelectrode recordings from some of the click-responsive points located at the perimeter of the auditory field (Appendix IV). Tables II, III, and VI present data from peripheral (round window) and cortical control recordings that show that these four preparations remained in fairly stable condition over the course of the surface-mapping procedure.

However, within this group of four animals, the post-penetration control recordings (Table VI, Post-test$_2$) of three animals demonstrated some depression in peak-to-peak amplitude relative to earlier recordings (Table VI) and this was especially evident in gerbil G14 6-4-75. It was concluded from these data that the cortex was probably in fairly good condition during the microelectrode recordings in three of the animals (G13 6-2-75, G15 7-17-75, G16 7-28-75) and in a slightly depressed condition at the conclusion of the other penetration experiment (G14 6-4-75).

B. Results of the Search for Evoked Response Polarity Reversals

All except one click-responsive loci, when investigated with a penetrating microelectrode, showed evoked potential reversals in the depth of the cortex. So averaged responses recorded at the surface with a ball electrode probably reflect in these experiments acoustically-driven neuronal activity localized to the cortex immediately beneath the surface electrode. Thus the reversal results generally confirmed the validity of the surface maps.

Averaged, click-evoked responses recorded with a microelectrode at the cortical surface were always biphasic (positive-negative) in waveform (Figures 10a and 11a). The responses were also similar to evoked-responses obtained with the ball electrode in regard to onset and peak-positive latencies. However, peak-to-peak amplitudes of the evoked responses recorded with the microelectrode were almost always less than the response amplitudes obtained at the surface of the cortex with a silver ball electrode (Table VII). Evoked-potential recordings obtained at the surface and down to a cortical depth of 750 microns were positive-going and of short latency. Below 800 microns in depth the responses would reverse their polarity to become initially-negative going wave-

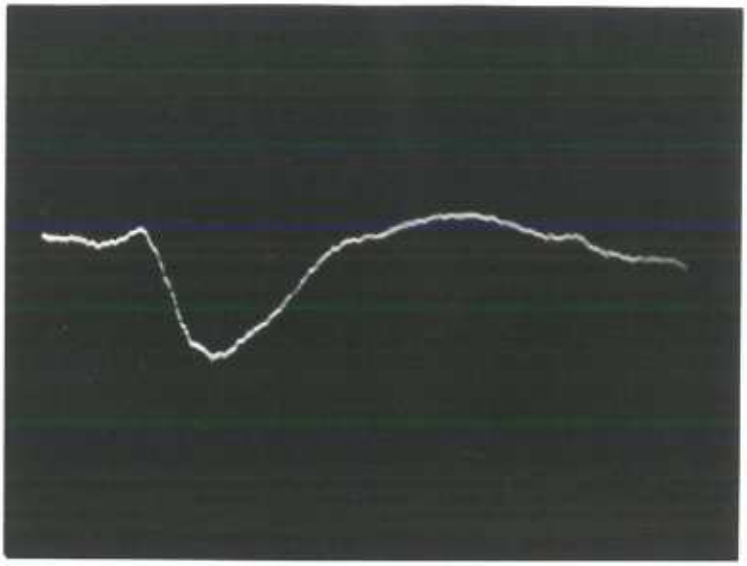
FIGURE 10.

Averaged, click-evoked responses recorded with a penetrating microelectrode from locus 3.2* at the dorso-medial fringe of the auditory area of the right hemisphere of gerbil G13 6-2-75. Clicks presented to the contralateral (left) ear at a rate of 1/sec.

(a) Averaged response recorded from just below the cortical surface. Note the surface-positive component with a latency of 18 msec. Calibration: 50 μV/cm, 8 msec/cm. Positivity down.

(b) Averaged response recorded at 900 microns below the cortical surface (read directly from the microdrive) showing an initially negative-going potential with a peak latency of 17 msec. Calibration: 50 μv/cm, 8 msec/cm. Positivity down.

a



b

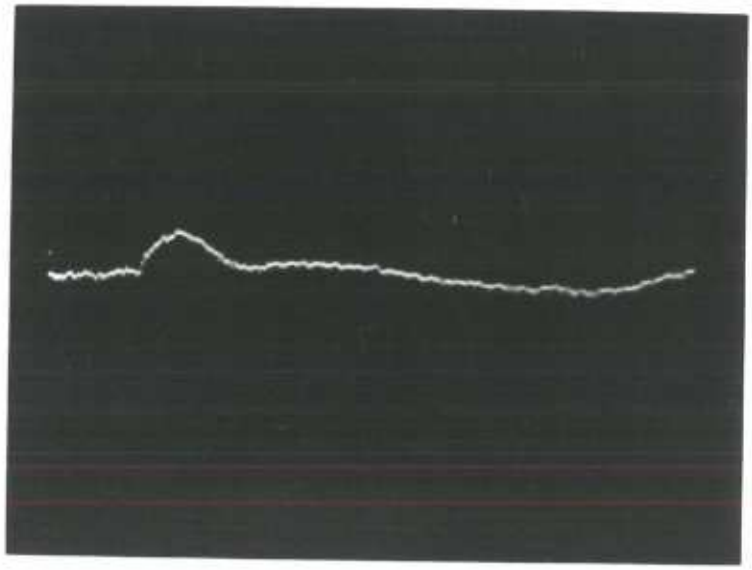


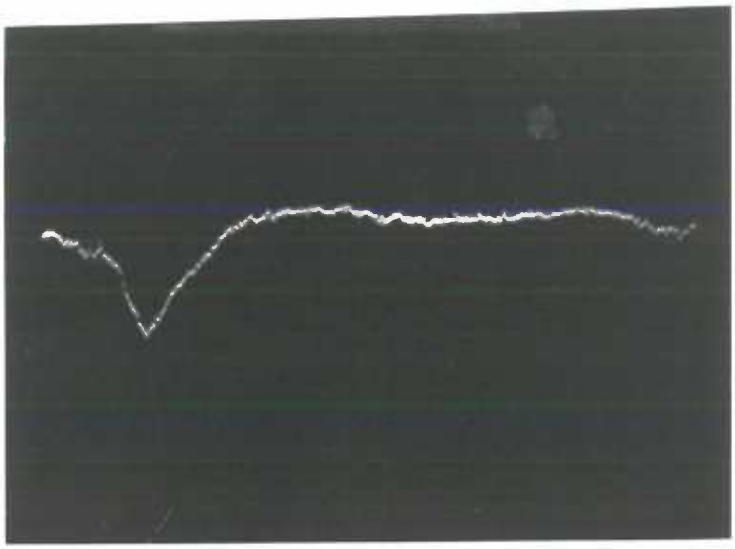
FIGURE 11.

Averaged, click-evoked responses recorded from point 1* at the posterior-lateral edge of the auditory field lying in the right hemisphere of gerbil G16 7-28-75. Recordings made with a penetrating microelectrode. Clicks presented to the contralateral (left) ear at a rate of 1/sec.

(a) Averaged response recorded from just below the cortical surface. Note that the potential is initially positive in polarity with a peak latency of 14 msec. Calibration: 25 μV/cm, 8 msec/cm. Positivity down.

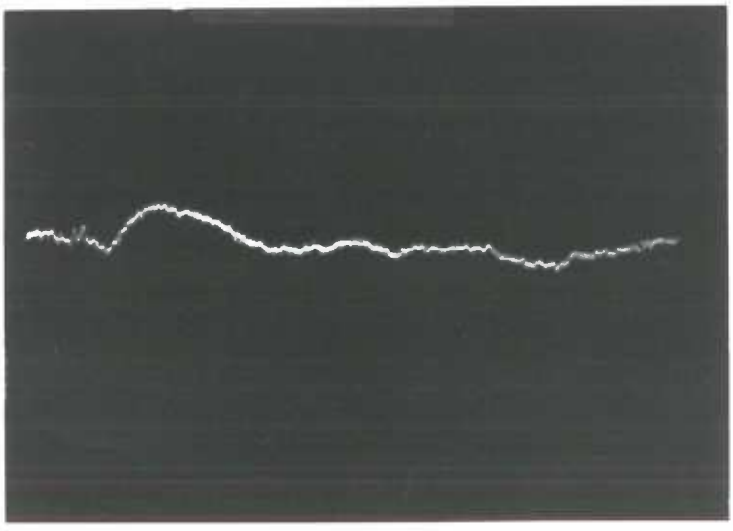
(b) Averaged response recorded at 800 microns below the cortical surface (read directly from the microdrive) demonstrating an initially negative-going waveform having its peak at 15 msec. Calibration: 25 μV/cm, 8 msec/cm. Positivity down.

a



L

b



forms at the same approximate latencies (Figures 10ab and 11ab). Data regarding the depth of reversals found in these experiments are presented in Table VII.

The results from each experiment will now be considered in turn. Waveform and polarity reversals were obtained at each point investigated with a penetrating microelectrode except one (point 2*) in gerbil G13 6-2-75 (Appendix IV). The reversals occurred at either 900 or 1000 microns (read directly from the microdrive) at six of the seven points examined (Table VII). In these cases the microelectrode entered the cortex at almost right angles to the surface. At the single point where reversal was not obtained, the electrode entered the cortex at an acute angle such that it traversed the cortical grey matter in an anterior-posterior direction as it penetrated. Strictly speaking, this microelectrode traverse did not truly sample cortical electrical activity directly beneath the surface recording location except in the upper cortical layers. Of the seven loci investigated with the microelectrode, four were locations defining the click-responsive border of the auditory area (Appendix IV) at its dorso-medial edge (points 2.1*, 2*, 3.2*, 1*). The three remaining points investigated were located within the confines of the acoustic area (points 5*, 3.5*, 2.6*).

In penetration experiment G14 6-4-75 (Appendix IV), three recording loci were investigated with a microelectrode and found to demonstrate reversals at around 1000 microns below the cortical surface (Table VII). Of these three recording locations, two (points 1.6* and 7.5*) defined the borders (posteriorly and anteriorly) of the acoustic field.

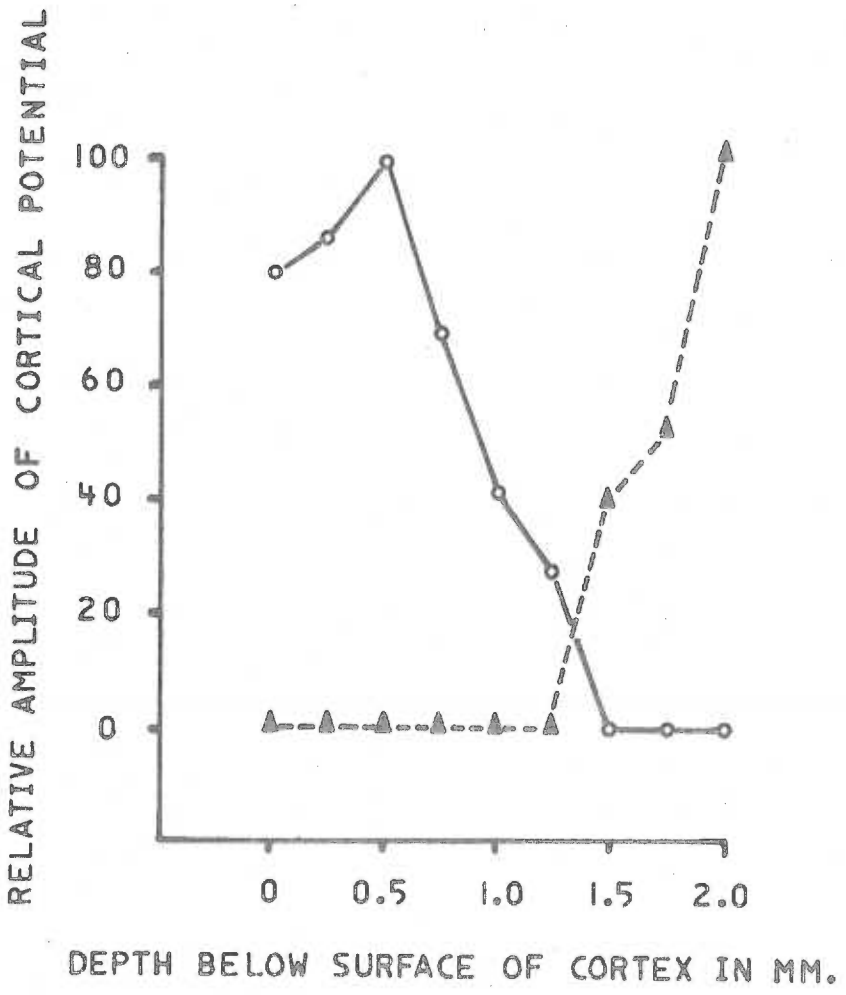
In the abbreviated, surface mapping experiment of gerbil G15

7-17-75 (Appendix IV), only two click-responsive points were investigated with a penetrating microelectrode and in both cases, polarity reversals were obtained (Table VII). The posterior border point (.5*) showed an evoked response polarity reversal at a depth of 1000 microns while the anterior border point (.5*) demonstrated an evoked response waveform reversal at 1500 microns. Figure 12 presents in graphic form the depth-distribution of the relative amplitude of the initial positive component and the initial negative component of averaged cortical responses recorded with the microelectrode at the anterior border point (.5*). The greater depth of reversal for this point is probably due to the fact that the microelectrode did not penetrate the cortex perpendicularly to the cortical surface as was the case at the other penetration point.

In the other incompletely mapped animal (G16 7-28-75), five border points were investigated with a penetrating microelectrode (Appendix IV). Averaged recordings obtained with a microelectrode at these loci (points .5*, .7*, 1*, .8*, .6*) demonstrated polarity inversions of the major components of the evoked responses between surface and depth (Table VII). The reversal obtained at point 1* is shown in the records of Figure 11.

FIGURE 12.

Graph plotting the relative amplitude of the initial positive component (line connecting open circles) and the initial negative component (line connecting solid triangles) of averaged cortical responses recorded with a microelectrode as a function of depth below the surface of the cortex at anterior point .5* in gerbil G15 7-17-75. Sample recordings obtained from 9 different depths below the cortical surface. Amplitude of positive component measured between baseline ('0' potential) and peak of initial positivity while amplitude of negative component was measured between baseline and peak of initial negativity.


RELATIVE AMPLITUDE OF CORTICAL POTENTIAL
100
80
60
40
20
0
0
0.5
1.0
1.5
2.0
DEPTH BELOW SURFACE OF CORTEX IN MM.

DISCUSSION

The primary auditory projection to the cerebral cortex of the Mongolian gerbil appears to be located generally in the same neocortical region as that reported for other rodent species. This area lies just lateral to the middle cerebral artery and just above the rhinal sulcus.

Histologically, the click-responsive cortex in the gerbil appears to be koniocortex (Gillette and Keller, unpublished observations, 1975). This agrees with other cytoarchitectonic studies of rodent neocortex (Kreig, 1946; Gerebtzoff, 1940; Hattori and Shoyama, 1970; Caviness, 1975).

I. Size and Shape of the Auditory Area

The size of the auditory area in the gerbil is generally similar to other rodents studied. More specifically, the acoustic area in the Mongolian gerbil is slightly smaller (5 mm long by 4 mm wide) than the auditory area defined by click stimulation in the guinea pig (8 mm long by 6 mm wide) by Zeigler (1964) and Walloch (1971). Yet, the gerbil's auditory field, as defined in this study, measures slightly larger than the same area defined in the mouse (4 mm long by 2.5 mm wide) by Woolsey (1967). The gerbil's click map matches most closely the click map of the rat (also 5 mm long by 4mm wide) defined some years ago by Le Messurier (1948).

From one experiment to the next the maps showed slight variation in size (Appendix VI) and location (Appendix III, IV, V). Such variability in cortical auditory field location and size has been noted in other click mapping studies of mammals including investigations of the rat (Le Messurier, 1948), mouse (Woolsey, 1967), and guinea pig (Walloch,

1971). Differences between individual maps in the same species may well reflect 'true' anatomical differences or they may be the result of errors derived from improper placement of the animal in the stereotaxic instrument. Because of the extreme care taken in mapping experiments to control for or minimize the latter possibility, it seems more likely that the differences are due to true anatomical variability (Ades, 1941; Rose and Woolsey, 1949; Walloch, 1971).

Because the surface mapping of the gerbil auditory cortex was accomplished in the present experiments by the use of averaging procedures, the question arises as to whether the same results (i.e., the same click map) would have been obtained using single responses. The work of Lende and Sadler (1967) on the auditory cortex of the hedgehog has shown that click maps derived from 'averaged' and 'non-averaged' responses were essentially equivalent in every way. Since similar experiments have yet to be attempted on the Mongolian gerbil, the question remains open whether or not a similar equivalence can be assumed for the gerbil.

II. Evoked Response Characteristics

Averaged, click-evoked potentials recorded from the gerbil auditory cortex were almost always diphasic (positive-negative), but occasionally they were found to be monophasic positive. The initial, surface positive wave was the most characteristic and reliable component of the averaged response in terms of waveform, amplitude, and latency while the following negativity was much more variable. This is consistent with findings made by other investigators on both single response and averaged responses recorded from auditory cortex (Rosenzweig and Rosenblith,

1953; Goldstein et al., 1959; Teas and Kiang, 1964; Borbély, 1970; Walloch, 1971, Walloch, 1975; Ödkvist et al., 1973; Lende and Sadler, 1967; Arezzo et al., 1975; Celesia and Puletti, 1969).

In regard to evoked response latencies, data on peak positive latencies from the present study on the gerbil auditory cortex indicate a somewhat greater range than has been reported for other rodent species. Walloch (1971) and Zeigler (1964), for example, found a latency range of 9 to 22 msec for the peak positivity at the guinea pig auditory cortex while the present investigation on the gerbil shows a 13 to 32 msec range for the same component of the response (Figures 8 and 9). These differences between the gerbil and the guinea pig may well be due to differences in the level of anesthesia used. The present investigation on the gerbil was made under a 'moderate' (Pradhan and Galambos, 1963) level of barbiturate anesthesia (see Methods, section I., B.) while a 'deeper' level of anesthesia was utilized in both the guinea pig studies. Indeed, a lighter level of anesthesia is known to produce greater variability in peak positive latencies of click-evoked responses than is a 'deep' level of barbiturate anesthesia (Mickle and Ades, 1953; Pradhan and Galambos, 1963; Teas and Kiang, 1964; Horvath, 1969). This may be why the gerbil data show a greater variability in peak positive latencies.

The peak-to-peak amplitude of the averaged, click-evoked response recorded from the gerbil auditory cortex shows considerable variation depending upon the location of the recording electrode within the field. Although surface positive potentials were elicited by clicks over a cortical area of several square millimeters, in each cortex there was always

at least one point at which response amplitude was found to be maximal. These 'hot spots' were usually (but not always) surrounded by a 'fringe' area in which the evoked potentials were of decreasing amplitude, until finally at the borders of the auditory field, no evoked responses could be recorded. (It should be recalled that only one stimulus intensity, that of the standard click at 100 dB SPL, was employed.) This type of amplitude response pattern has been reported in click mapping studies of cats (Walzl and Woolsey, 1946; Mickle and Ades, 1953; Perl and Casby, 1954) and rodents (Le Messurier, 1948; Zeigler, 1964; Woolsey, 1967; Walloch, 1971). The largest amplitude evoked responses were generally recorded from a region located centrally and somewhat anteriorly within the acoustically-responsive field of the gerbil (Appendix IV and V).

This graded pattern of evoked response amplitudes has also been found in sensory cortical mapping studies using other modalities of stimulation (Marshall et al., 1937; Talbot and Marshall, 1941). This phenomenon appears to be a ubiquitous characteristic of sensory cortical mapping studies utilizing the evoked potenial technique.

The question arises as to why a graded pattern of response amplitudes is obtained? A number of hypotheses may be entertained in order to explain such results. First, the averaging procedure itself might give rise to this pattern if for example the evoked responses recorded from the fringe of the gerbil auditory area were more variable in latency and waveform than those potentials recorded from more central portions of the field. Resultant averages of variable responses would be of lesser amplitude than averages of responses having little to no variability. However, this is probably not the case because similar

gradients in response amplitude are seen in auditory cortical maps regardless of whether averaging is used or not (Lende and Sadler, 1967; Walloch, 1975; Gillette, unpublished observations, 1975).

A second possible factor which might be responsible for the graded amplitudes seen in click mapping studies is changes in the level of anesthesia. Even though this is a plausible explanation based upon what we know about the effects of anesthesia on the form and variability of evoked responses (Pradhan and Galambos, 1963), other evidence argues against such an influence. Specifically, in click mapping studies of cat (Ades, 1941) and seal (Alderson et al., 1960) auditory cortex, it was found that maps derived under two different levels of barbiturate anesthesia in the same preparation were essentially identical. Maps obtained under the two different anesthetic levels were similar in areal size, anatomical location, and had identical response amplitude gradations with large amplitudes centrally located and smaller amplitude responses surrounding the central 'hot spot'.

Another possible explanation for the described phenomenon could be volume conduction. That is, the smaller amplitude 'border' and 'fringe' responses recorded from the auditory field would be the result of electrotonic spread from the active zone or hot spot of that field. This does not appear to be likely however, since studies employing recording procedures that control for the possibility of volume conduction (e.g., bipolar, Laplacian, or transcortical recordings) in click mapping of auditory cortex have reported response amplitude gradients like those obtained with monopolar recordings (Bremer and Dow, 1939; Mickle and Ades, 1953; Perl and Casby, 1954; Arezzo et al., 1975).

A fourth possible explanation for the response gradients observed in mapping of the auditory cortex relates to the spectral (frequency) content of the click stimulus. In the following arguement, two facts are crucial. First, while clicks are spectrally rich stimuli they tend to concentrate most of their energy in a limited frequency band which is determined by the physical characteristics of the transducer producing them (Vernon and Meikle, 1974; Vernon et al., 1976). The click used in the present study, for instance, was found to have a low major frequency of 833 Hz. The second crucial fact is that auditory cortex is known to be tonotopically organized (Woolsey, 1971). That is, for a number of species, rostral portions of the auditory cortex appear to be more sensitive (and hence show larger evoked responses) to low frequencies of acoustic stimulation (Tunturi, 1944; Walloch, 1971), or to electrical stimulation of the apex of the cochlea (Woolsey and Walzl, 1942; Kayser and Libouban, 1963), while caudal parts of the auditory area appear to be more responsive to high acoustic frequencies or to electrical stimulation of the basal turn. The middle cochlear turns (corresponding to intermediate acoustic frequencies) activate cortical tissue in between the apical and basal representations (Woolsey and Walzl, 1942; Tunturi, 1944, 1949; Kayser and Libouban, 1963; Walloch, 1971). Putting together the above facts, one could argue that the click stimulus used in the present study was most effective in activating (and hence producing larger evoked responses) that region of the gerbil auditory cortex which was most sensitive to the middle and lower frequencies. By analogy with other tonotopic studies, that region would be the central and rostral portions of the acoustic field. Other frequen-

cies which were present at lower acoustic energy levels would be less effective in activating the corresponding portions of the cortex, so that small amplitude potentials would result. In short, the locational specificity of the 'hot spot' and the graded response pattern of the click map might be produced by the fact that the click stimulus is not "flat" across frequencies (Walzl and Woolsey, 1946).

The amplitude gradient pattern may well be due to structural features of the auditory cortex and/or its thalamic afferent input. For example, auditory koniocortex shows gradual changes in histological structure as it grades into surrounding isocortex in carnivores (Rose, 1949; Rose and Woolsey, 1949; Adrianov and Mering, 1959), primates (Casseday et al., 1974; Kanagasuntheram and Leong, 1966; Pandya and Sanides, 1973; Bailey and von Bonin, 1950; Economo, 1929), and rodents (Gerebtzoff, 1940; Krieg, 1946ab; Caviness, 1975; Gillette and Keller, unpublished observations, 1975). The pattern may also be a reflection of, at least in part, a gradation in the density of afferent thalamocortical input (or their axonal collaterals) to the auditory cortex (Rose and Woolsey, 1949; Kleist, 1962). Unfortunately, definitive anatomical data are not presently available to help to decide this question.

Whether the amplitude gradient results from anatomical factors or stimulus factors, or a combination of both, is impossible to determine given our present knowledge (or lack of knowledge) of the gerbil auditory cortex, or the auditory cortex of any other species for that matter. Hopefully, future experimentation will help clarify the issue.

III. Some Limitations Inherent in the Present Surface Maps

An important limitation of the results in this study of the gerbil auditory cortex relates to the incompleteness of mapping. In all the surface mapping experiments except one (G10 5-3-75), the anteriolateral border of the click-responsive area was poorly defined or not defined at all because skull bone prevented further sampling with the recording electrode (see comments in METHODS). This difficulty was not unique to the present experiments for it has been noted in other click-mapping studies of rodent auditory cortex (Woolsey, 1967; Walloch, 1971).

Click stimuli were presented monaurally in the present investigation, and only contralateral responses were observed. It may well be that the area of cortical activation to contralateral stimulation is larger than that area delineated with ipsilateral stimulation (Galli, Lifschitz, and Adrian, 1971). Further, binaural stimulation has been used in a number of studies (Bremer, 1943; Tunturi, 1946; Rosenzweig, 1951; Gross, Small, and Thompson, 1967; Galli et al., 1971; Celesia, 1969), and such stimuli might have produced slightly different results in the present case. It is known, for example, that response amplitudes are different for binaural stimuli than for monaural. And it might also be the case that the responsive area is larger when stimuli are presented binaurally.

The present experiments utilized broad-spectrum stimuli (that is, clicks), to map the gerbil auditory cortex. Tone burst stimuli (Tunturi, 1944; Small and Gross, 1961; Galli et al., 1971; Walloch, 1971), noise burst stimuli (Small and Gross, 1961), or electrical stimulation of the cochlea (Woolsey and Walzl, 1942; Downman, Woolsey, and Lende,

1960; Kayser and Libouban, 1963) may have given rise to different mapping results in the gerbil.

It should also be appreciated that a different anesthetic (e.g., alpha chloralose) may have given rise to different results in the gerbil. For example, 'non-primary' click-responsive areas (as well as polysensory areas) have been reported in cat (Thompson and Sindburg, 1960; Sindburg and Thompson, 1962; Thompson et al., 1963ab; Goldring et al., 1967) and rat (Bliss and Petrinovich, 1964) cortex under chloralose anesthesia. Such areas, if they exist, remain to be identified in the gerbil.

IV. Single versus Multiple Auditory Response Fields

There is no clear dichotomy (for example, between lissencephalic and gyrencephalic species) in regard to those species shown to have a single auditory field in each hemisphere and those that appear to have multiple response fields. Interestingly, in two click-mapping studies of the sloth auditory cortex done under similar conditions (e.g., type and level of anesthesia), different results were obtained. In one study (Meulders et al., 1967) only a single responsive field was found while in the other study (Aaraiva and Magalhaes-Castro, 1975), two seperate responsive areas were found. Similar contradictory results have been reported for the guinea pig (Zeigler, 1964; Walloch, 1971; Odkvist et al., 1973). The type of anesthesia appears to be of considerable importance. Usually one, or at most two click fields are found when barbiturates are used; for example, studies in the rat (Le Messurier, 1948) and the mouse (Woolsey, 1967). Conversely, other less depressant anesthetics like alpha chloralose apparently allow additional fields to be seen.

For example, the work of Bliss and Petrinovich (1964) on the rat and the study of the cat by Thompson and associates (Thompson et al., 1963ab).

Under the anesthetic conditions of the present study on the Mongolian gerbil, only a single click-response field was found. This agrees with the results published on the mouse (Woolsey, 1967) and guinea pig (Zeigler, 1964; Walloch, 1971; Ödkvist et al., 1973) auditory cortex. In contrast, Le Messurier (1948) described two fields responsive to clicks in the rat with the primary area localized to the temporal cortex and the second area closely associated with the second somatic-sensory area (SII) more rostrally.

Although the evoked response latencies obtained from auditory cortical recordings in the gerbil were found to be distributed in a unimodal form (Figures 8 and 9), it is interesting that the evoked potentials with the longest latencies were consistently recorded from the posterior-lateral portion of the auditory field (Appendix IV and V). This is very similar to findings in the guinea pig auditory cortex reported by Walloch (1971). This type of finding is suggestive that there may be two fields, one short latency and one with somewhat longer latencies, but much anatomical and electrophysiological work is needed in order to consider this question adequately.

V. Validity of the Surface Map: Microelectrode Results

Microelectrode recordings of averaged, click-evoked responses in the gerbil demonstrated a polarity reversal of the initial positive component between cortical surface and underlying white matter at every point investigated except one. From these data it was concluded that the surface map in the gerbil is a true reflection of immediately under-

lying cortical events produced by acoustic stimulation. So the actual size and shape of the click-responsive cortex in the gerbil is probably well approximated by the surface map.

Interestingly, the polarity reversal results of the present study are in sharp contrast to the findings in the guinea pig using a similar technique. Ödkvist and colleagues (Ödkvist et al., 1973) found that only the central core area of their surface map would give evoked response polarity inversions. The surrounding 'finge' points in their surface map did not show reversals. It was argued by these investigators that only the central core of the surface map represented 'true' auditory cortex. In the present study of the gerbil auditory cortex, all surface points (except one) investigated with a penetrating microelectrode (including 'border' points) demonstrated polarity reversals. The discrepancy between these two studies is difficult to account for since both investigations used similar techniques and anesthesia. One thing that did differ between the two studies was the type of auditory stimulation used (clicks versus electrical stimulation of the second cochlear turn), but how this might account for the different results is unknown.

The surface positive component of the cortical response recorded in the gerbil was found to reverse in polarity, to an initially negative going wave with approximately the same latency, at around 1000 microns below the cortical surface (Table VII). The finding that reversal of the initial major component of the primary evoked response occurs at this depth agrees well with results from other rodents similarly investigated; for example, the rat (Borbély, 1970) and the guinea pig (Ödkvist et al., 1973). The reversals appear to occur in these rodent species

at about the midpoint of the cortical thickness, which would approximate the level of Layer IV of auditory koniocortex in these species (Gillette and Keller, unpublished observations, 1975; Kreig, 1946; Gerebtzoff, 1940; Caviness, 1975). However, in none of these rodent studies have microelectrode marking experiments been performed to confirm the above relationship between the anatomy and the electrophysiology. Relatedly, it has recently been confirmed that Layers III and IV of rat auditory koniocortex are the termination sites for axons arising from the medial geniculate body (Ryugo and Killackey, 1974). Thus the present electrophysiological findings of waveform reversal are consistent with the anatomical evidence available on the structure of rodent auditory cortex, and the afferent inputs thereto.

Despite the limitations enumerated above, the data presented here clearly demonstrate a click-responsive auditory area for the gerbil encompassing much of the temporal cortex between the middle cerebral artery and the rhinal fissure.

SUMMARY AND CONCLUSION

An investigation of the auditory projection area in the contralateral cerebral cortex of the Mongolian gerbil was made, using click stimuli at a standard intensity to map the temporal cortex by the evoked potential method. The major results of the study can be summarized as follows:

(1) As is typical for other mammals, click-evoked responses characterizing the gerbil auditory area were initially surface-positive potentials with short peak latencies. Amplitude of the responses ranged from about 100 μV to about 1.7 mV. Latencies for the initial positive wave ranged from 13 to 32 msec.

(2) Only one click-responsive field was found in the temporal area. However the data suggest that this area may actually represent two seperate projections to the cortex, in that a small sub-area, characterized by longer response latencies, was located posteriorly within the click field in a number of animals.

(3) The size (5 mm long by 4 mm wide) and location of the gerbil auditory cortex are consistent with mapping results obtained in other rodents.

(4) The validity of the surface maps was confirmed in four cases by demonstrating that the evoked responses reversed polarity between the cortical surface and underlying white matter. The reversal was demonstrated by recording with a penetrating microelectrode at representative 'border' points.

Even though the Mongolian gerbil is a rather small rodent, it has proven to be a most 'robust' experimental preparation for auditory neurophysiological research.

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TABLE I. Summary of experimental and control procedures applied to each animal in the experimental series. Asterisk denotes that surface mapping and/or depth recordings were undertaken.

	EXPERIMENT NO.															
	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10	G11	G12	G13	G14	G15	G16
PRE - TEST	a b c	a b c	a b c	a b c	a b c	c	a b c	a b c	a b c	a b c	a b c	a b c	b c	c	c	c
MAP SURFACE	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
POST - $TEST_1$	a b c	c	a b c	a b c	a b c	c	a b c	a b c	a b c	a b c	a b c	a b c	b c	c	c	c
DEPTH RECORD.													*	*	*	*
POST - $TEST_2$													b c	c	c	c

a: Round-window-recorded responses to pure tones at 18 frequencies

b: " " " " to clicks

c: Cortical responses evoked by clicks, measured at identical spot PRE and POST

TABLE II. Peak-to-peak amplitudes (in millivolts) of responses recorded from the round window membrane to click stimuli in the 'best' experimental preparations (above the line) and the 'poor' experimental preparations (below the line).

EXPERIMENT NO.	PRE-MAPPING AMPLITUDE	POST-MAPPING AMPLITUDE
G1 2-22-75	2.1	2.0
G3 3-6-75	2.0	1.8
G8 4-12-75	2.0	1.8
G9 4-19-75	2.6	2.5
G10 5-3-75	2.0	2.0
G12 5-6-75	2.0	1.8
G13 6-2-75	1.9	1.8
G2 2-25-75	0.9	*
G4 3-18-75	1.9	1.8
G5 3-25-75	2.0	1.0
G7 4-1-75	1.6	0.4
G11 5-5-75	2.6	2.0

TABLE III. Peak-to-peak amplitudes (in microvolts) of averaged, click-evoked responses recorded from the same neocortical location before (Pre-map) and after (Post-map) cortical mapping in the 'best' experimental preparations (those listed above the line) and the 'poor' experimental preparations (those listed below the line).

EXPERIMENT NO.	PRE-MAPPING AMPLITUDE	POST-MAPPING AMPLITUDE
G1 2-22-75	850	750
G3 3-6-75	1200	1000
G6 3-29-75	500	600
G8 4-12-75	600	1100
G9 4-19-75	1000	1000
G10 5-3-75	290	270
G12 5-6-75	300	340
G13 6-2-75	260	250
G14 6-4-75	750	700
G15 7-17-75	400	360
G16 7-28-75	300	290
G2 2-25-75	400	50
G4 3-18-75	800	430
G5 3-25-75	700	300
G7 4-1-75	700	0
G11 5-5-75	375	275

TABLE IV. Percent change in peak-to-peak amplitudes of round window and cortical responses to clicks between PRE and POST mapping samples. The 'best' preparations are listed above the line, the 'poor' preparations are listed below the line.

EXPERIMENT NO.	PER CENT CHANGE ROUND WINDOW CLICK RESPONSE	PER CENT CHANGE CORTICAL EVOKED RESPONSE	CONDITION OF EXPERIMENTAL PREPARATION
G1 2-22-75	5% Decrease	12% Decrease	Good
G3 3-6-75	10% Decrease	17% Decrease	Good
G6 3-29-75	___[1]	20% Increase	Good
G8 4-12-75	10% Decrease	83% Increase	Good
G9 4-19-75	4% Decrease	0% Change	Good
G10 5-3-75	0% Change	7% Decrease	Good
G12 5-6-75	10% Decrease	13% Increase	Good
G13 6-2-75	5% Decrease	4% Decrease	Good
G14 6-4-75	___[2]	7% Decrease	Good
G15 7-17-75	___[2]	10% Decrease	Good
G16 7-28-75	___[2]	3% Decrease	Good
G2 2-25-75	___[3]	87% Decrease	Poor
G4 3-18-75	5% Decrease	46% Decrease	Poor
G5 3-25-75	50% Decrease	57% Decrease	Poor
G7 4-1-75	75% Decrease	100% Decrease	Poor
G11 5-5-75	23% Decrease	27% Decrease	Poor

1: Round window electrode wire broke before records could be obtained
2: Recordings were not attempted
3: Animal died before post-mapping record could be obtained

TABLE V. Click-evoked potential latencies (in msec) derived from averaged cortical recordings in the 11 'best' gerbil preparations. Data uncorrected for travel time of stimulus between speaker and ear drum (2.75 msec).

EXPERIMENT NO.	INITIAL				FIRST POSITIVE PEAK			
	N	RANGE	$\bar{X}$	Mo	N	RANGE	$\bar{X}$	Mo
G1 2-22-75	24	8-16	10.3	8	24	20-28	21.6	21
G3 3-6-75	12	8-10	8.7	8	12	15-24	20.3	20
G6 3-29-75	19	8-15	8.7	8	19	14-29	20.6	20
G8 4-12-75	19	8-14	10.0	9	19	17-32	19.4	19
G9 4-19-75	25	8-16	9.5	9	25	16-32	21.7	20
G10 5-3-75	26	8-18	10.2	8	26	14-29	22.2	16
G12 5-6-75	36	8-10	8.5	8	36	14-25	20.5	24
G13 6-2-75	27	8-13	8.9	8	27	16-25	18.7	18
G14 6-4-75	32	8-18	9.2	8	32	14-32	22.9	22
G15 7-17-75	16	8-9	8.1	8	16	13-19	15.4	15
G16 7-28-75	15	8	8.0	8	15	13-20	15.9	16

Population $\bar{X}$ = 9.1

Pop. Range = 8-10.3

Population $\bar{X}$ = 19.9

Pop. Range = 13-32

TABLE VI. Peak-to-peak amplitudes (in microvolts) of averaged, click-evoked potentials recorded from the same cortical location before surface mapping (PRE-TEST), after surface mapping (POST-$TEST_1$), and after microelectrode recordings (POST-$TEST_2$) in four gerbil experiments.

EXPERIMENT NO.	PRE-TEST AMPLITUDE (uV)	POST-TEST$_1$ AMPLITUDE (uV)	POST-TEST$_2$ AMPLITUDE (uV)
G13 6-2-75	260	250	280
G14 6-4-75	750	700	150
G15 7-17-75	400	360	200
G16 7-28-75	300	290	200

TABLE VII. Averaged, evoked response data derived from micro-electrode recordings at various cortical depths.

EXPERIMENT NO.	MAP POINT NO.	EVOKED RESPONSE AMPLITUDES (Peak-to-peak)		POLARITY REVERSAL	DEPTH OF REVERSAL (Microns below surf)
		BALL ELECTRODE	MICROELECTRODE		
G13 6-2-75	2.1*	210 μV	100 μV	Yes	1000
	2*	200 μV	40 μV	No	
	3.2*	320 μV	120 μV	Yes	900
	1*	100 μV	75 μV	Yes	1000
	5*	500 μV	100 μV	Yes	900
	3.5*	350 μV	190 μV	Yes	1000
	2.6*	260 μV	60 μV	Yes	1000
G14 6-4-75	7.5*p	750 μV	140 μV	Yes	1300
	1.6*	160 μV	25 μV	Yes	1000
	7.5*a	750 μV	45 μV	Yes	1000
G15 7-17-75	.5*p	50 μV	48 μV	Yes	1000
	.5*a	50 μV	29 μV	Yes	1500
G16 7-28-75	.5*	50 μV	30 μV	Yes	1000
	.8*	80 μV	75 μV	Yes	1000
	.7*	70 μV	40 μV	Yes	1000
	1*	100 μV	45 μV	Yes	800
	.6*	60 μV	25 μV	Yes	1000

a: anterior

p: posterior

APPENDIX I

Listings of experimental subjects, weights, sex, and brain dimensions.

EXPERIMENTAL SUBJECTS	WEIGHT IN GRAMS	SEX	LENGTH OF CEREBRUM IN MILLIMETERS*	WIDTH OF CEREBRUM IN MILLIMETERS*
G1 2-22-75	67	Male	14.0	7.8
G2 2-25-75	76	Male	15.0	8.0
G3 3-6-75	48	Female	13.7	7.0
G4 3-18-75	40	Female	13.8	7.4
G5 3-25-75	41	Male	14.5	8.0
G6 3-29-75	45	Male	14.0	7.6
G7 4-1-75	33	Male	14.0	8.0
G8 4-12-75	41	Female	14.0	7.6
G9 4-19-75	45	Male	14.0	7.9
G10 5-3-75	38	Male	14.0	7.8
G11 5-5-75	39	Female	14.5	8.0
G12 5-6-75	32	Male	14.0	7.3
G13 6-2-75	54	Male	14.4	7.5
G14 6-4-75	56	Male	14.2	7.7
G15 7-17-75	46	Male	14.0	7.8
G16 7-28-75	47	Male	14.3	7.6

*Greatest length and width of right hemisphere when looking directly down on the dorsal surface.

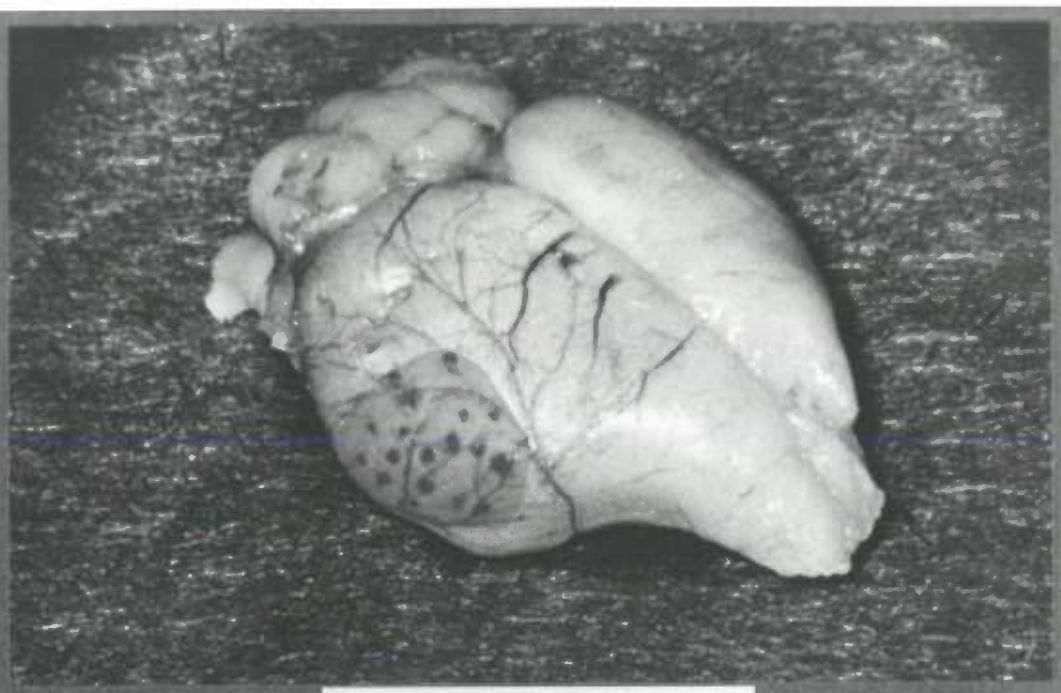
APPENDIX II

Calibration data for 18 pure-tone frequencies used for generating AC cochlear potentials. Values represent dB of attenuation necessary to produce 1 ubar of sound pressure as measured with a calibrated microphone in a closed (pressure) system. Calibration by "substitution method". Underlined values represent dB extremes for that frequency across experiments.

SOUND	EXPERIMENT NO.												
FREQUENCY	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10	G11	G12	RANGE
100 Hz	97	97	84	84	84	85	85	77	82	85	85	85	20
200 Hz	112	112	99	99	99	100	99	93	96	102	102	102	19
310 Hz	107	107	93	93	93	95	93	86	91	98	98	98	21
500 Hz	116	116	102	103	103	104	103	96	100	99	99	99	20
700 Hz	119	119	107	106	107	107	107	100	105	108	108	108	19
1 kHz	103	103	90	91	91	91	90	83	88	92	92	92	20
1.5 kHz	104	102	91	88	90	92	92	85	88	98	98	98	19
2 kHz	101	101	89	88	88	90	89	80	86	90	90	90	21
3 kHz	76	98	69	70	70	68	68	63	68	50	50	50	48
4 kHz		95		82	82	83	82	75	80	82	82	82	20
5 kHz	91	93	80	81	81	80	77	68	74	73	73	73	25
7 kHz	93	97	82	83	84	82	78	73	79	82	82	82	24
8 kHz		78		62	64	60	60	58	60	57	57	57	21
10 kHz	68	71	55	59	56	66	52	48	53	57	57	57	23
13 kHz				65	66	63	63	53	62	62	62	62	13
15 kHz	72	76	62	60	63	56	55	50	55	59	59	59	26
17 kHz				76	59	54	53	55	51	45	45	45	31
20 kHz	49	58	40	43	43	32	26	33	39	43	43	43	32

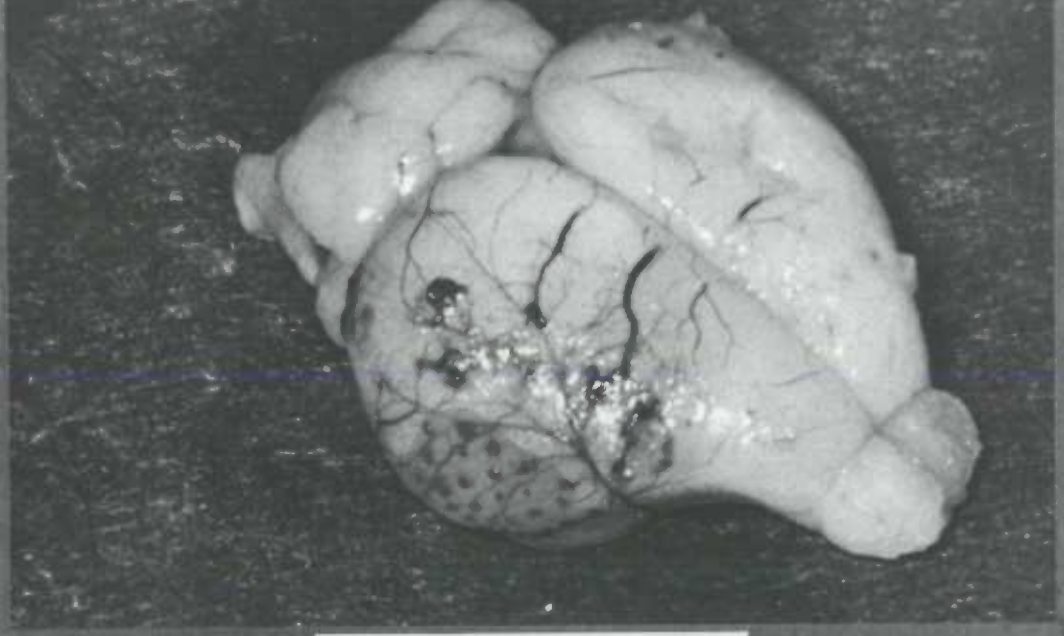
APPENDIX III

Photographs of the formalin-fixed right hemispheres of four representative "good" gerbil preparations that were completely mapped with a surface ball electrode. Both a dorso-lateral and a lateral perspective of the hemisphere are presented for each animal. The shaded area denotes the auditory area for the animal and overlies the grid of recording loci (each point denoted by an india ink dot) responsive to contralateral click stimulation. Note the very slight differences in shape and location of the click-responsive region between the animals. Photographs were obtained under 10 power magnification.

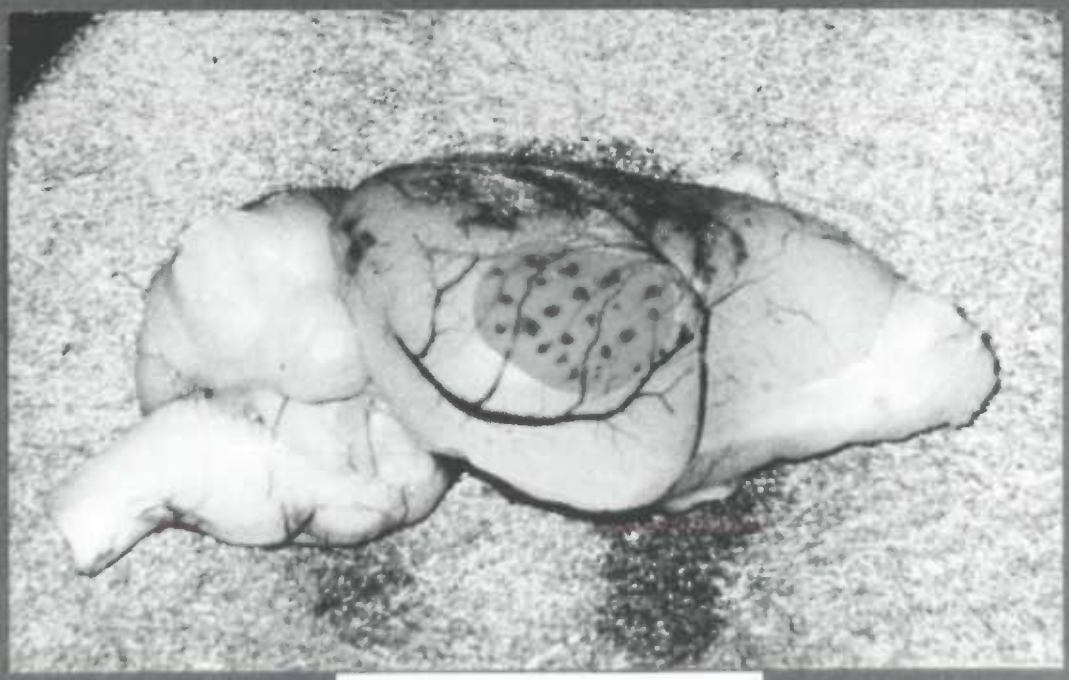


G8 4-12-75

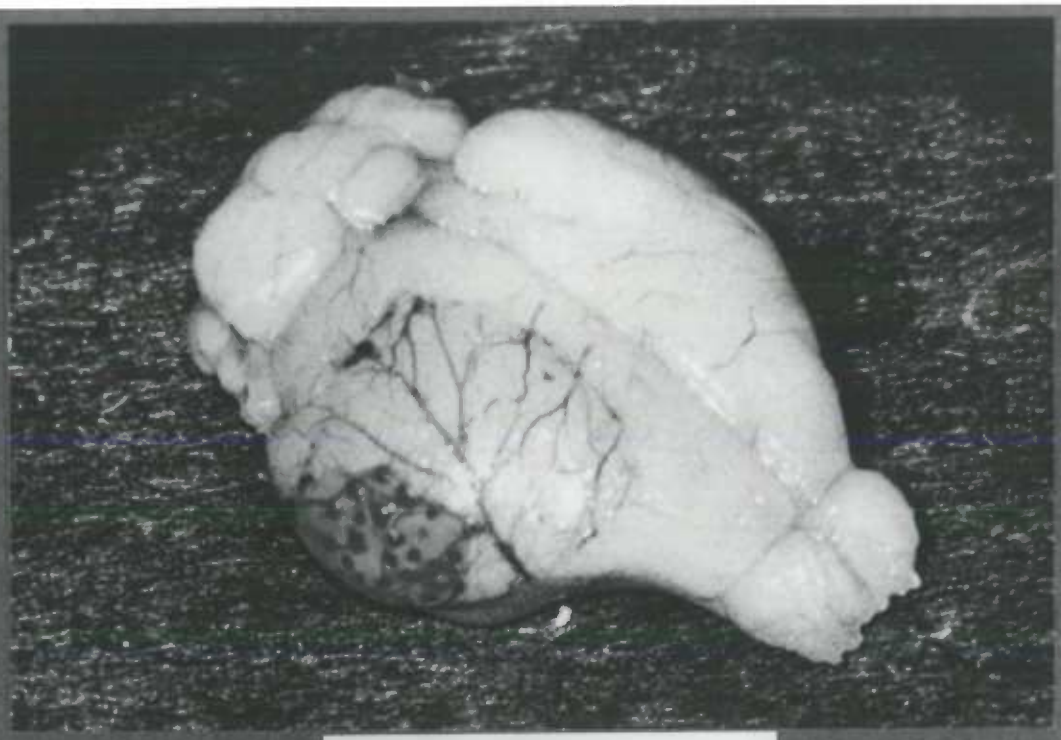
G8 4-12-75



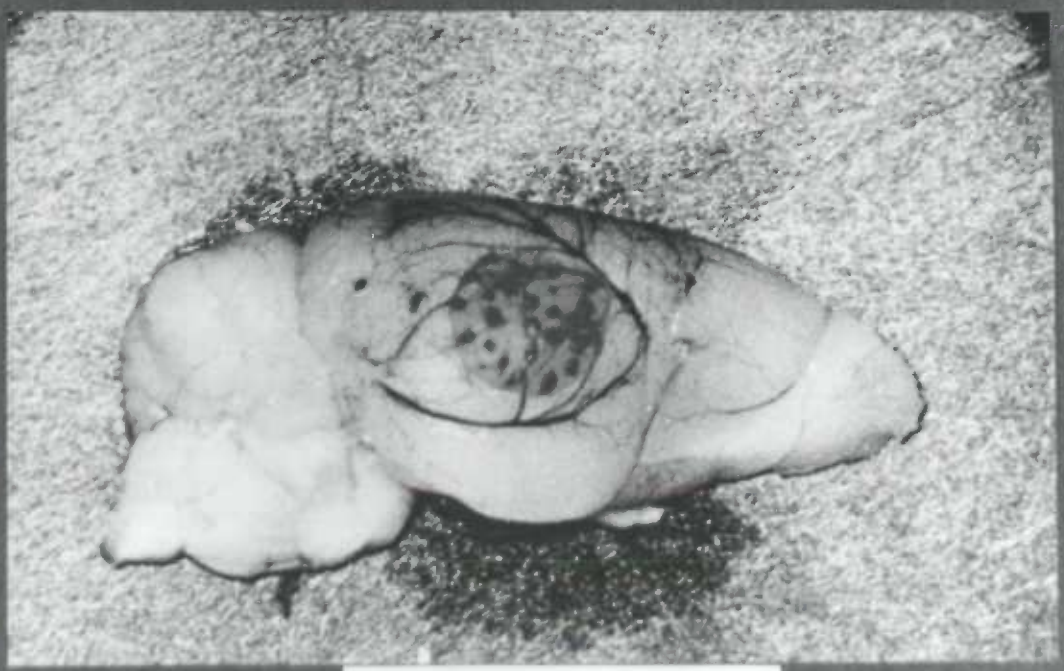
G9 4-19-75



G9 4-19-75

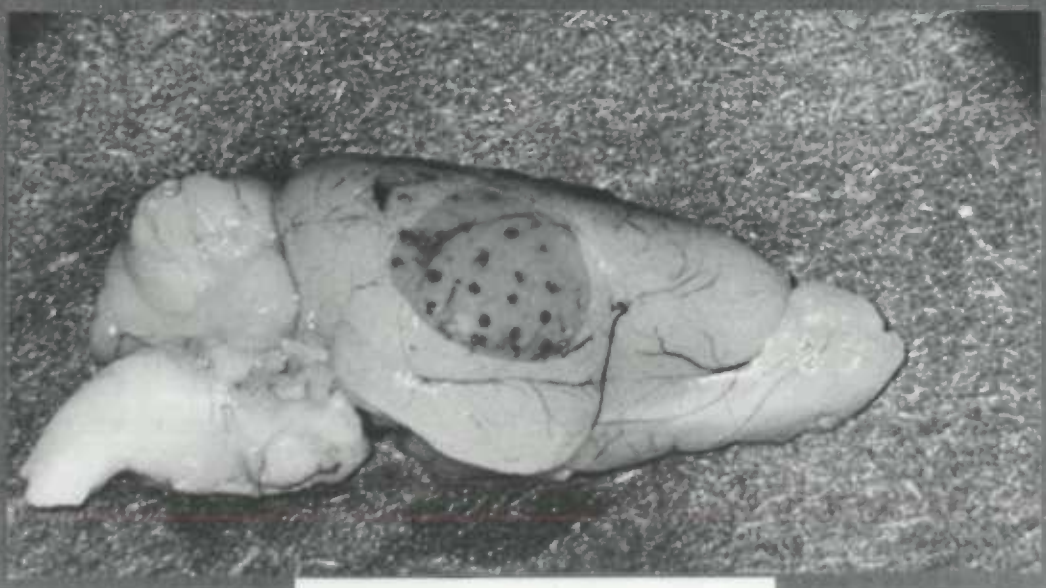


G10 5-3-75



G10 5-3-75

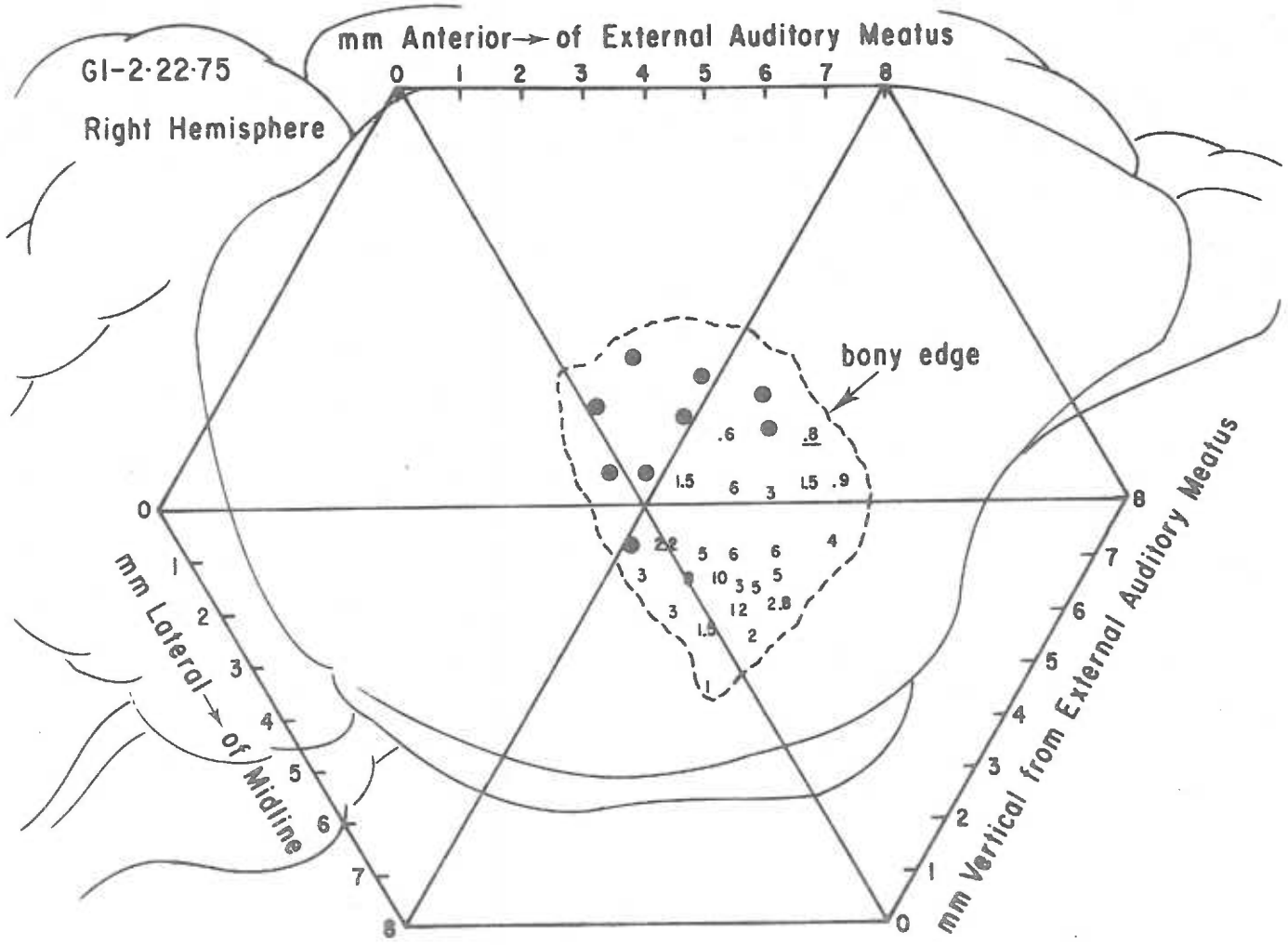
G 14 6-4-75

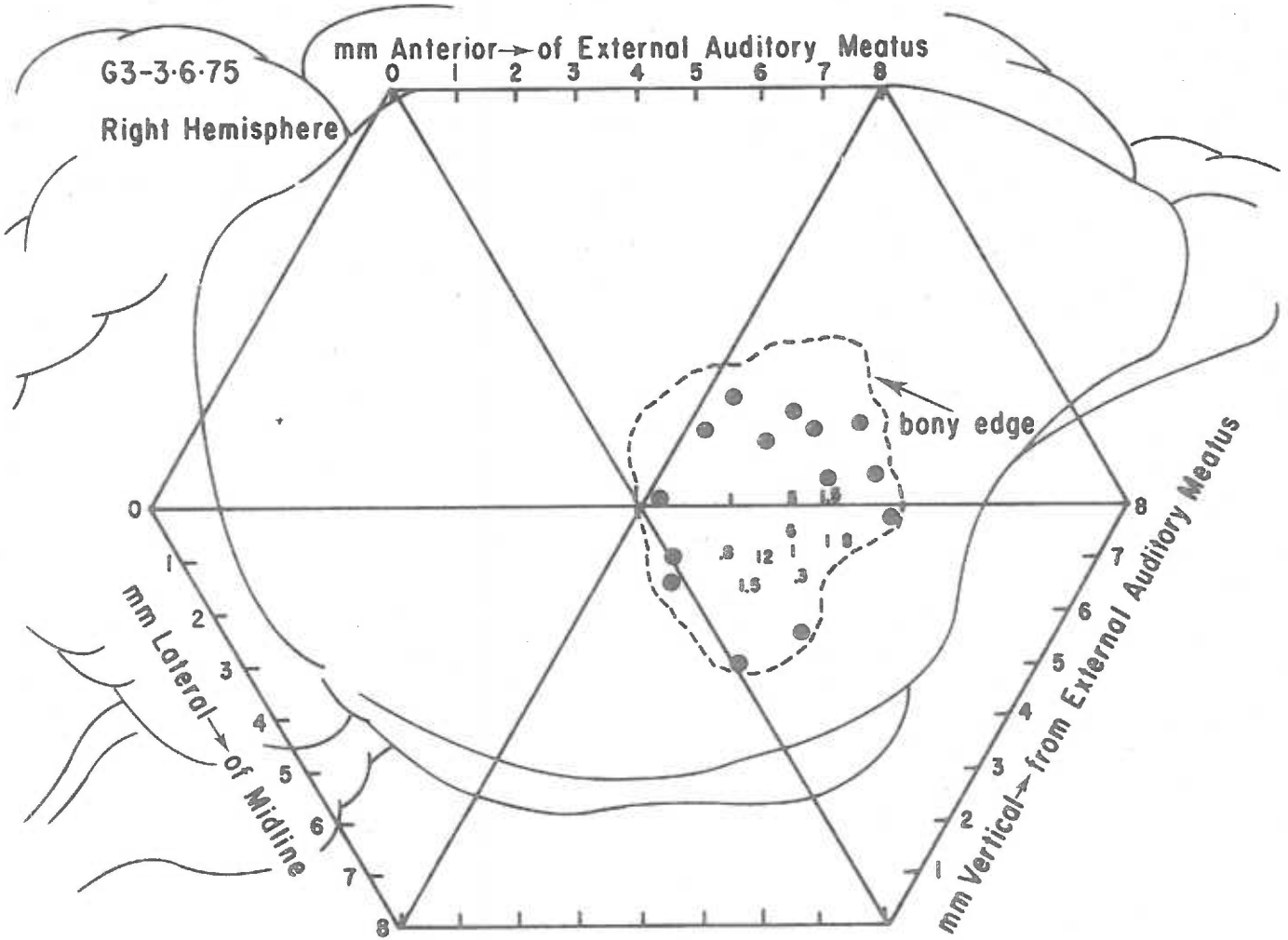


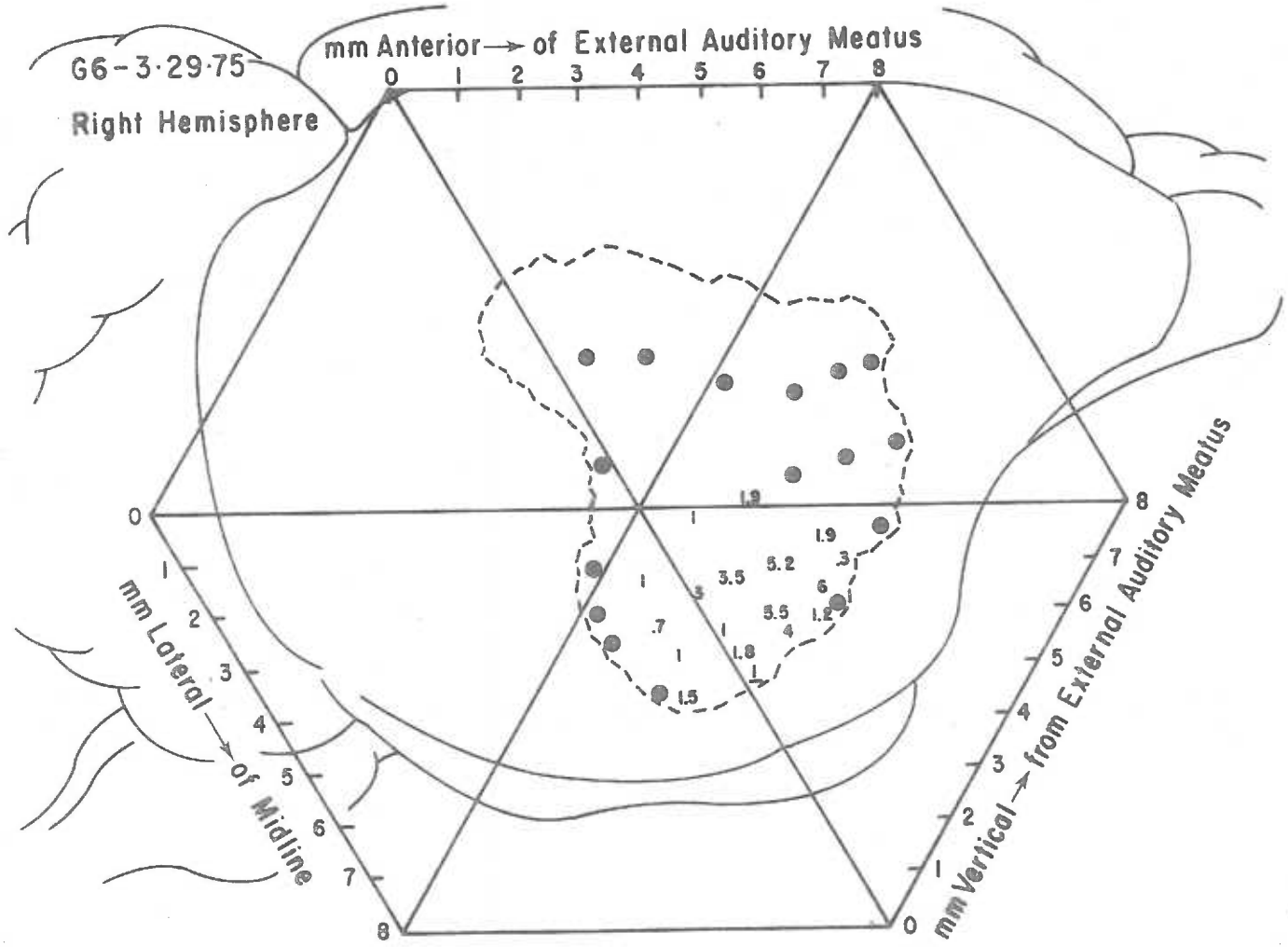
G 14 6-4-75

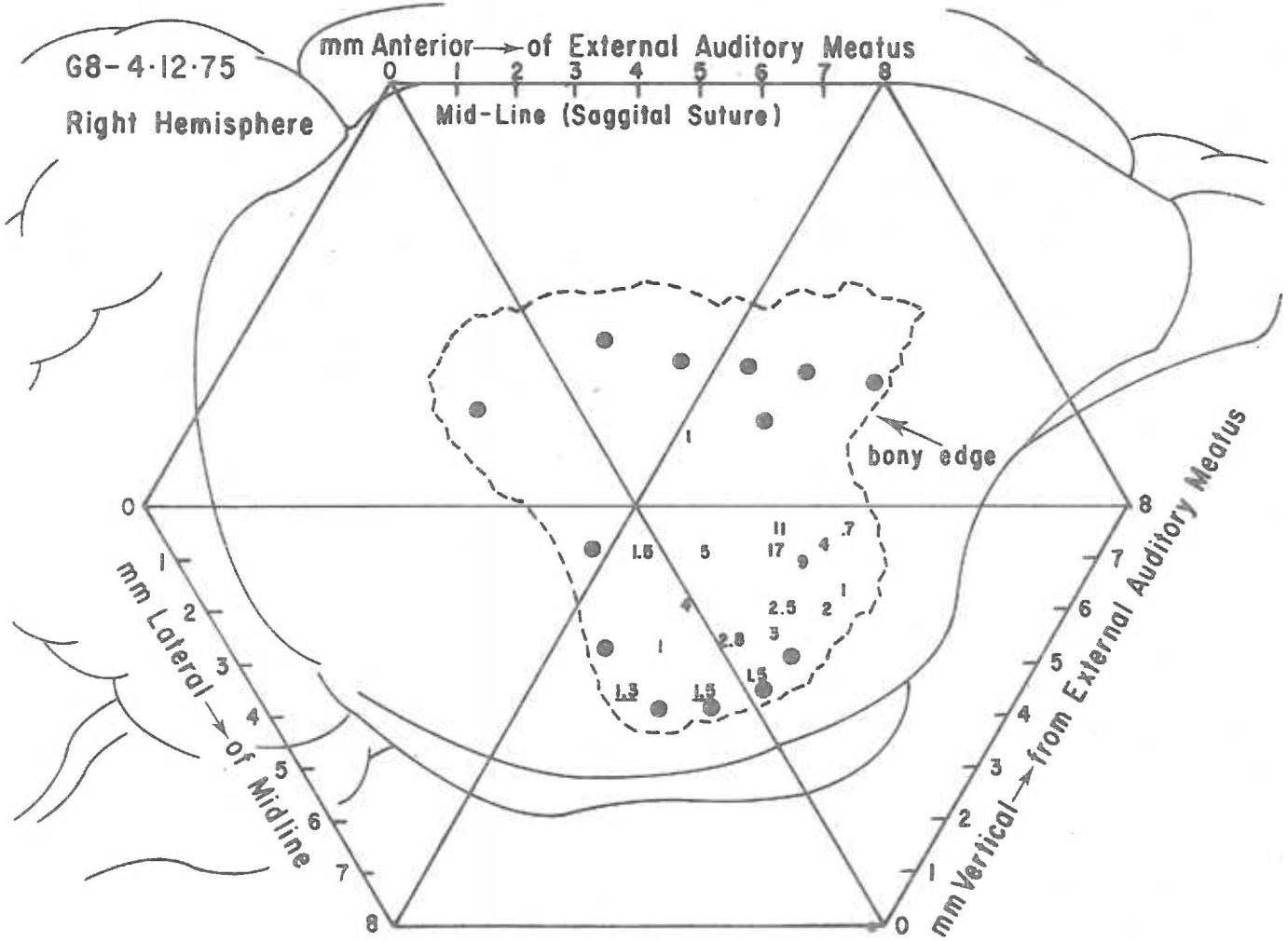
APPENDIX IV

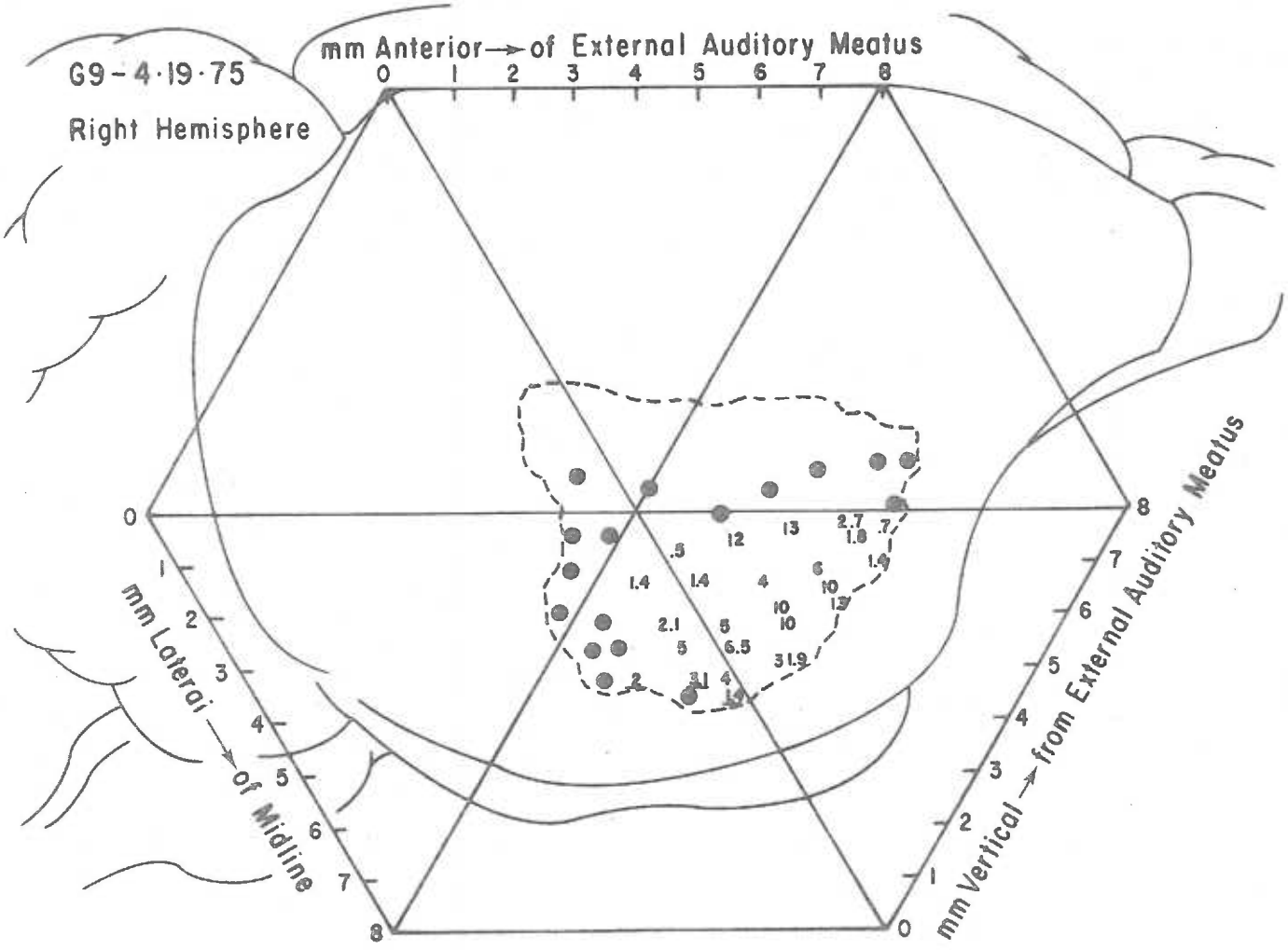
Schematic maps of the auditory cortex defined in all the 'good' experimental preparations. In each map, recording loci are plotted in reference to three coordinates (see Figure 5 for description of this procedure) on a three-dimensional depiction of the right cerebral hemisphere of the Mongolian gerbil. Click-responsive recording sites are denoted by a number which represents the peak-to-peak amplitude (in 100's of μV) of the evoked response recorded from that spot with a ball electrode. Underlined numbers represent click-responsive sites where the recorded evoked response had a peak positive latency of 27 msec or greater. Numbers with asterisks denote locations where a penetrating microelectrode was used to record averaged, evoked responses. Recording sites giving no response to the standard click stimulus are denoted by large black dots. Anterior is to the right and posterior is to the left in the diagrams. The dashed line represents the bony edge of the cortical exposure.

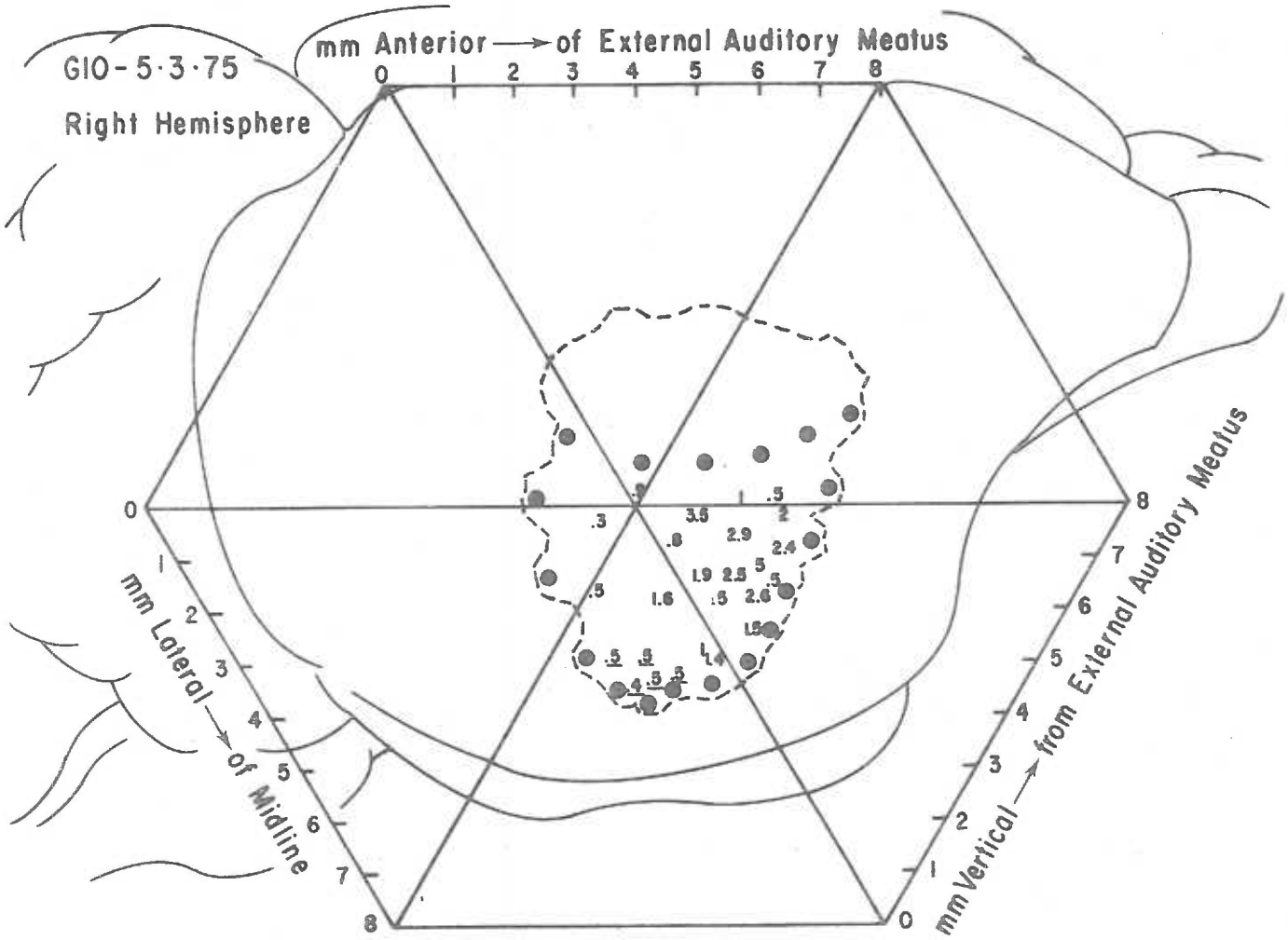

GI-2-22-75
Right Hemisphere
mm Anterior→ of External Auditory Meatus
0 1 2 3 4 5 6 7 8
bony edge
.6 .8
1.5 6 3 1.5 .9
2.2 5 6 6 4
3 10 3 5 5
12 2.8
3 1.5 2
1
mm Lateral→ of Midline
mm Vertical from External Auditory Meatus

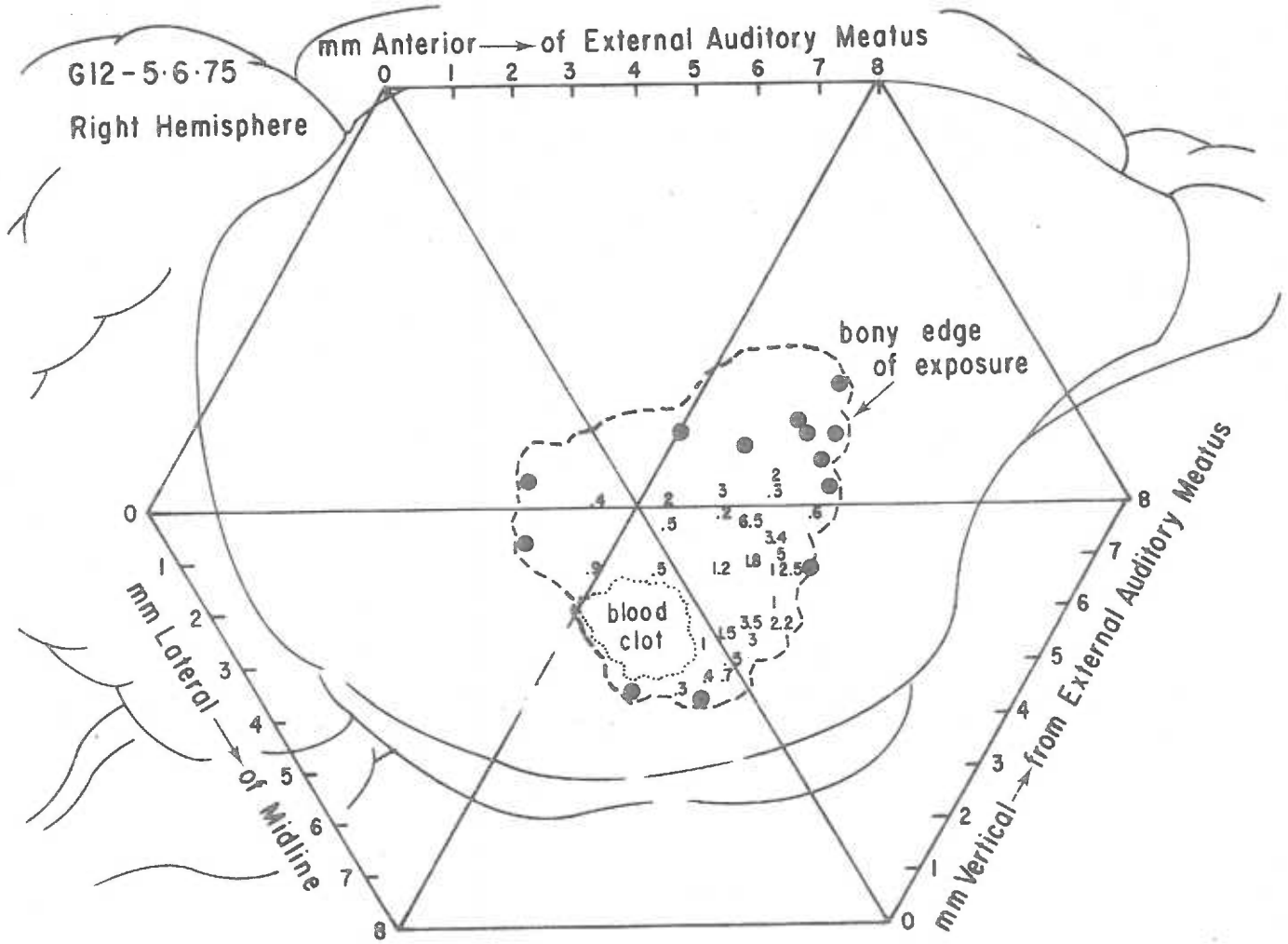

G3-3·6·75
Right Hemisphere
mm Anterior→of External Auditory Meatus
0 1 2 3 4 5 6 7 8
bony edge
mm Lateral→of Midline
mm Vertical→from External Auditory Meatus

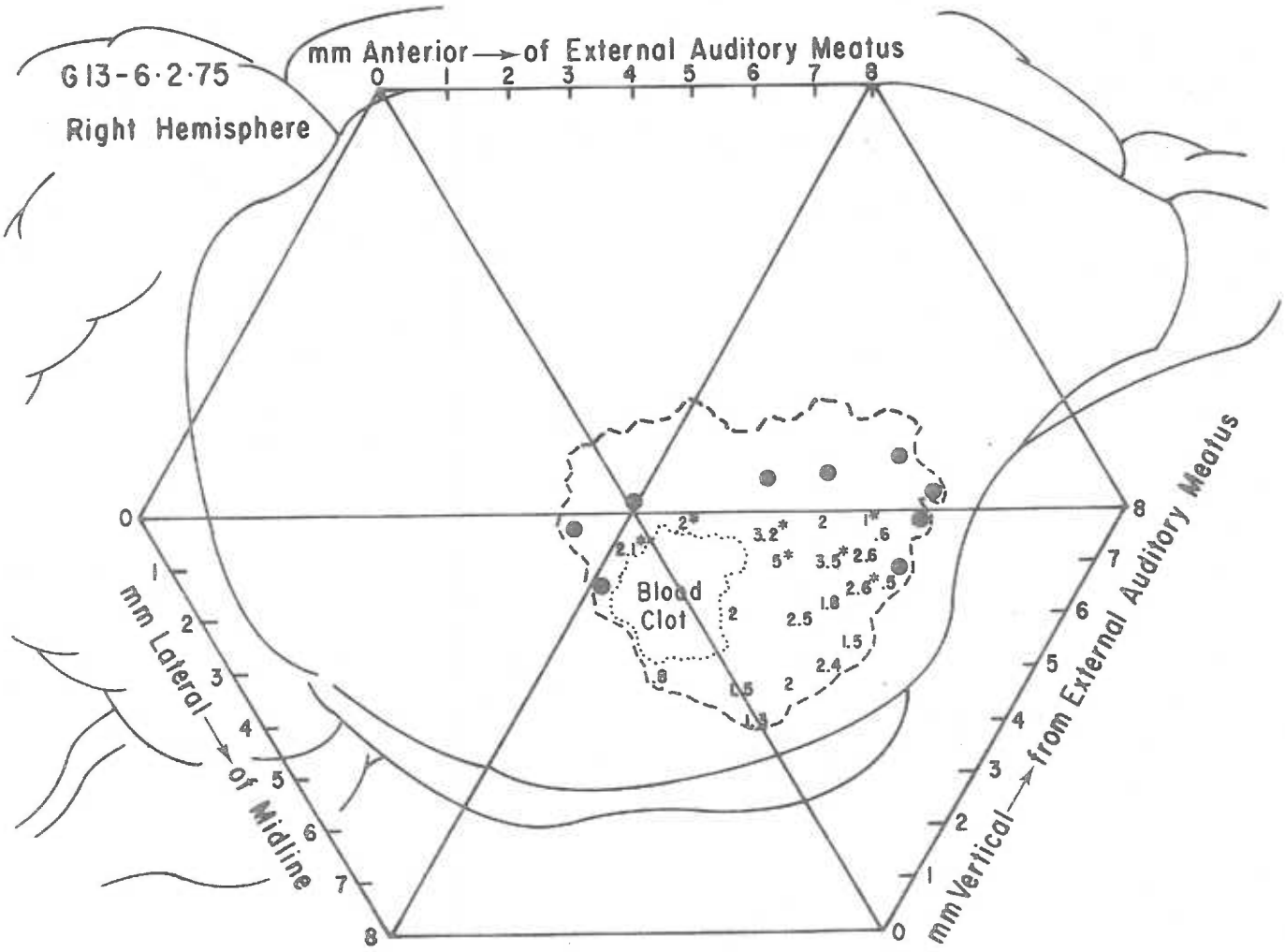

G6-3-29-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
1.9
1
1.9
.3
5.2
3.5
6
5.5
1.2
4
.7
1
1.8
1.5

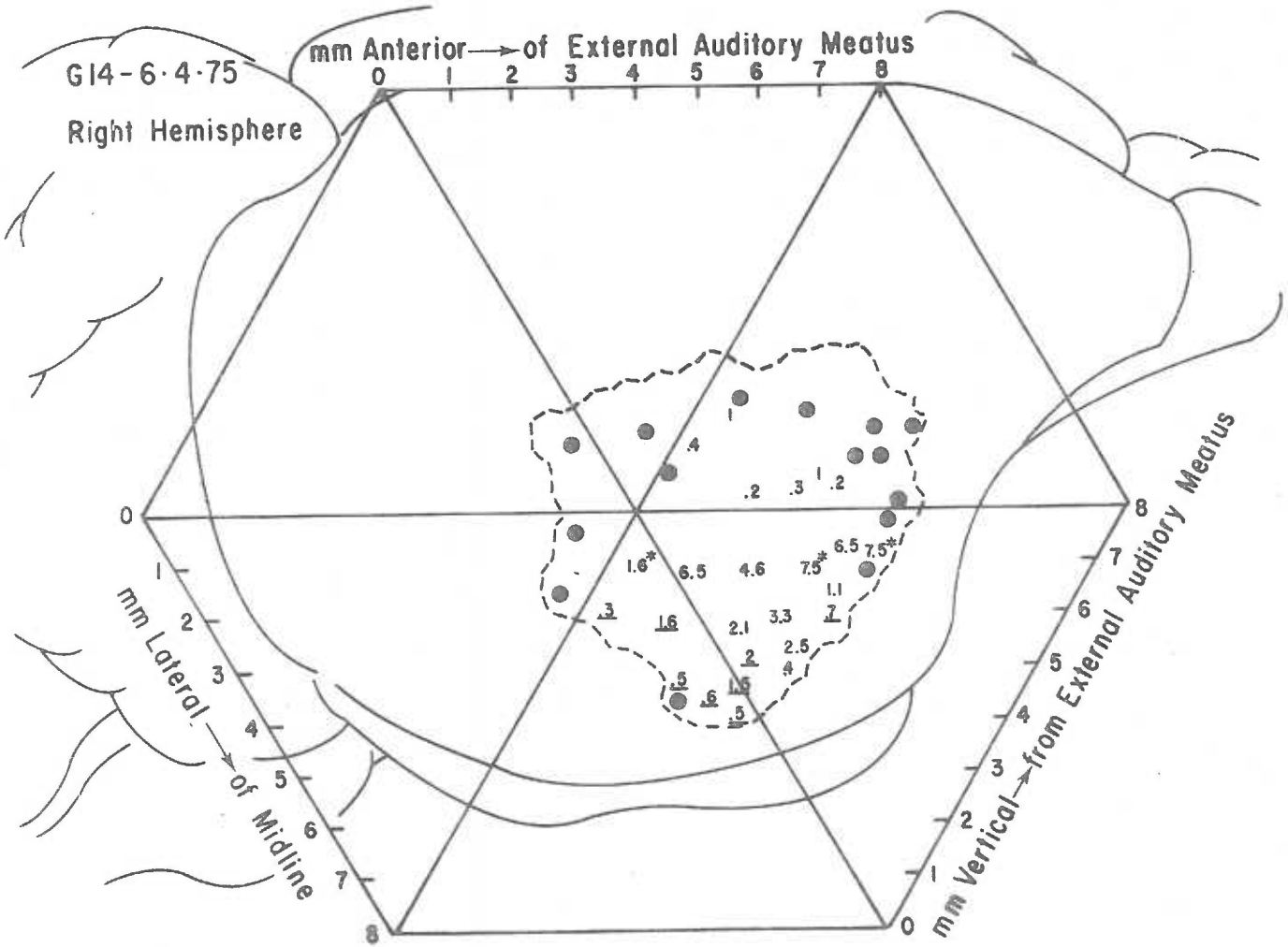

G8-4-12-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
Mid-Line (Saggital Suture)
bony edge
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
1
1.5
5
11
17
9
4
.7
2.5
2
2.8
3
1.5
1.3
1.5

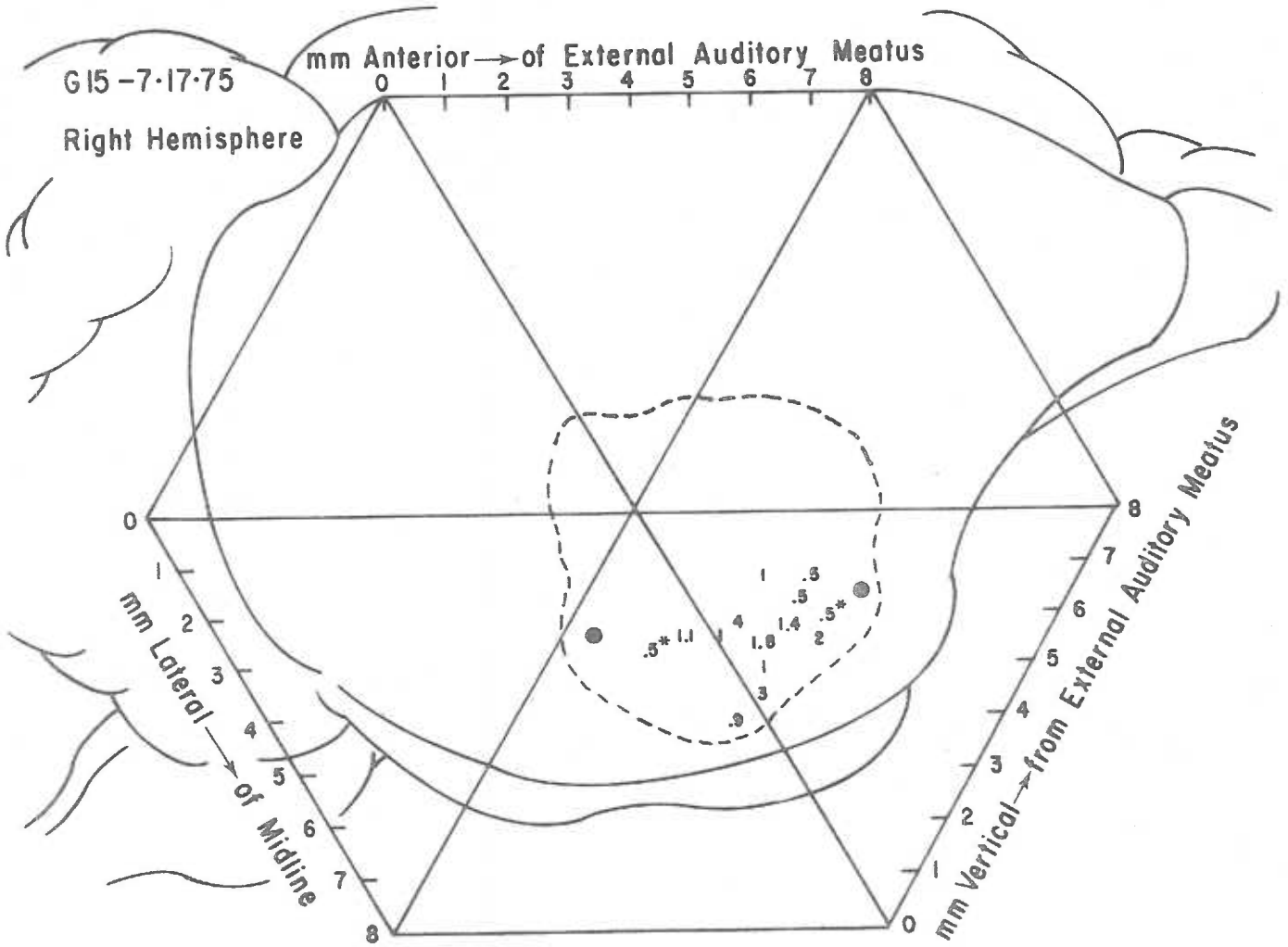

G9-4-19-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.5
1.2
1.3
2.7
1.8
.7
1.4
1.4
1.4
4
6
10
1.9
10
10
2.1
5
5
6.5
3
1.9
2
3.1
4
1.9

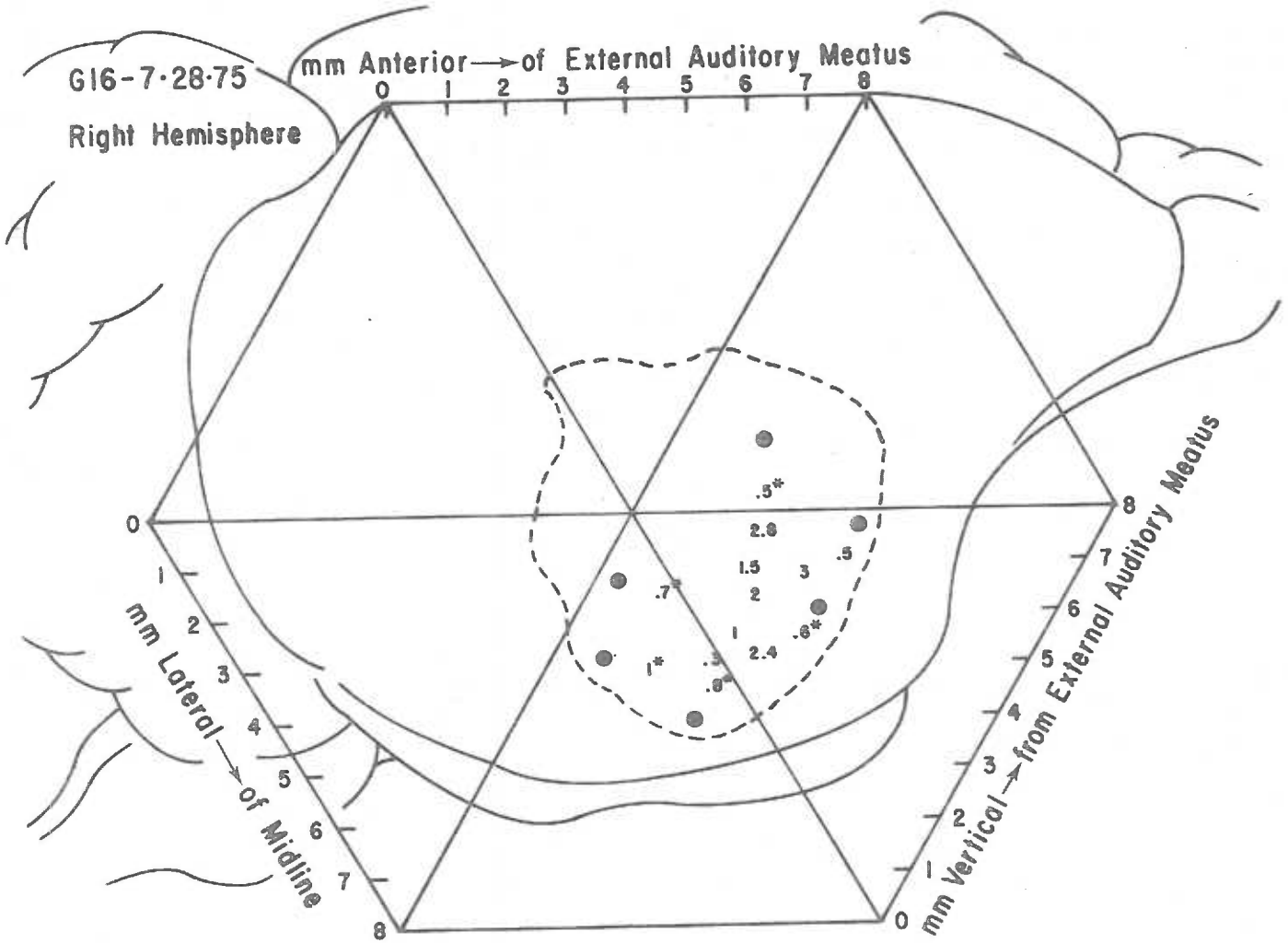

G10-5-3-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.3
.5
3.5
2
.8
2.9
2.4
1.9
2.5
5
.5
.5
1.6
.5
2.6
1.5
.5
.5
1.4
.4
.5
.5


G12-5·6·75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
bony edge
of exposure
blood
clot
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus


G13-6-2-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
Blood Clot
2.1*
2*
3.2*
2
1*
.6
5*
3.5*
2.6
2.6*
.5
1.8
2.5
1.5
2.4
1.8
1.5
2
1.5

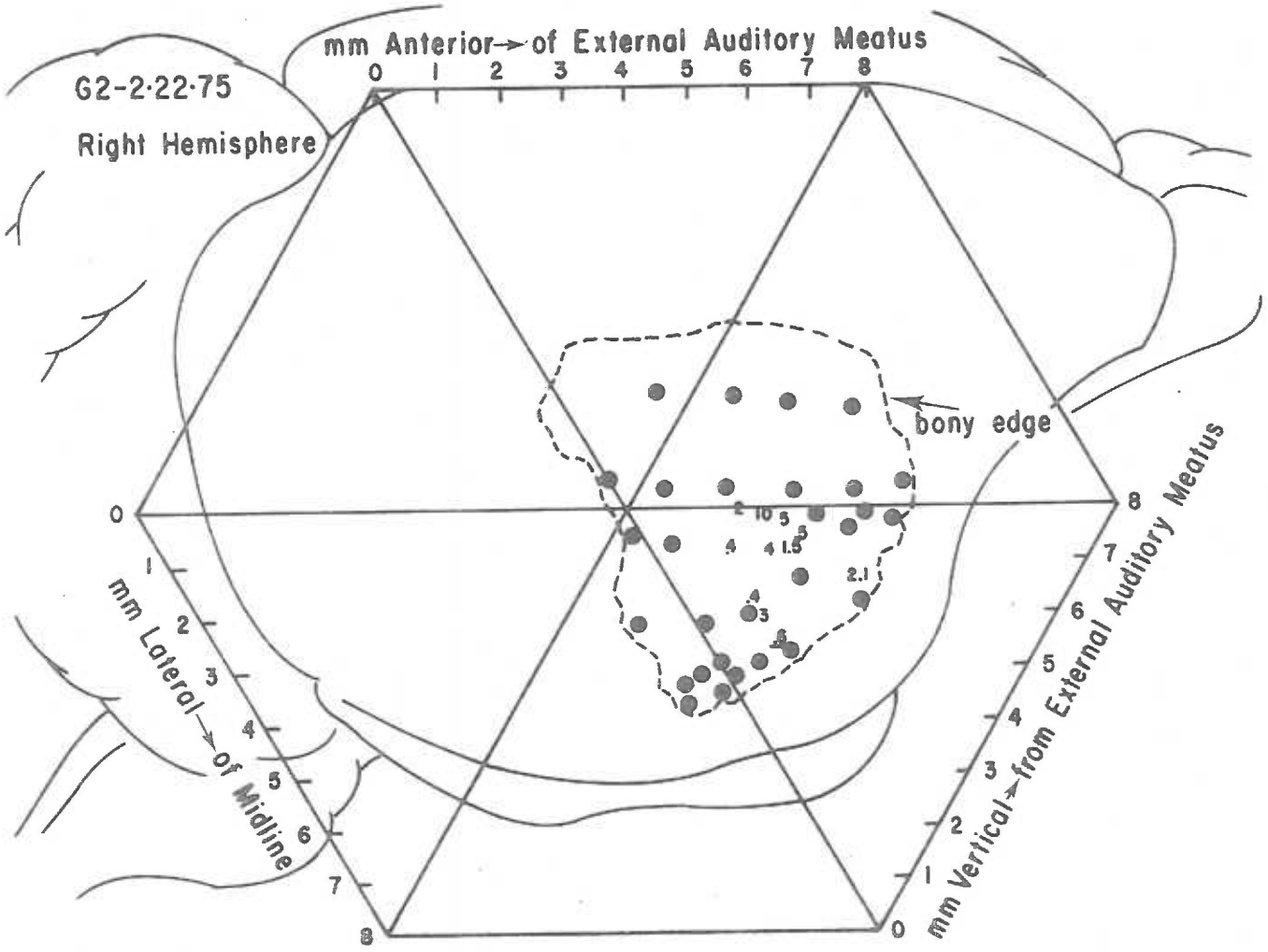

G14-6·4·75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.4
1
.2 .3 1 .2
1.6*
6.5
4.6
7.5*
6.5
7.5*
1.1
.3
1.6
2.1
3.3
7
2
2.5
4
.5
.6
1.5
.5

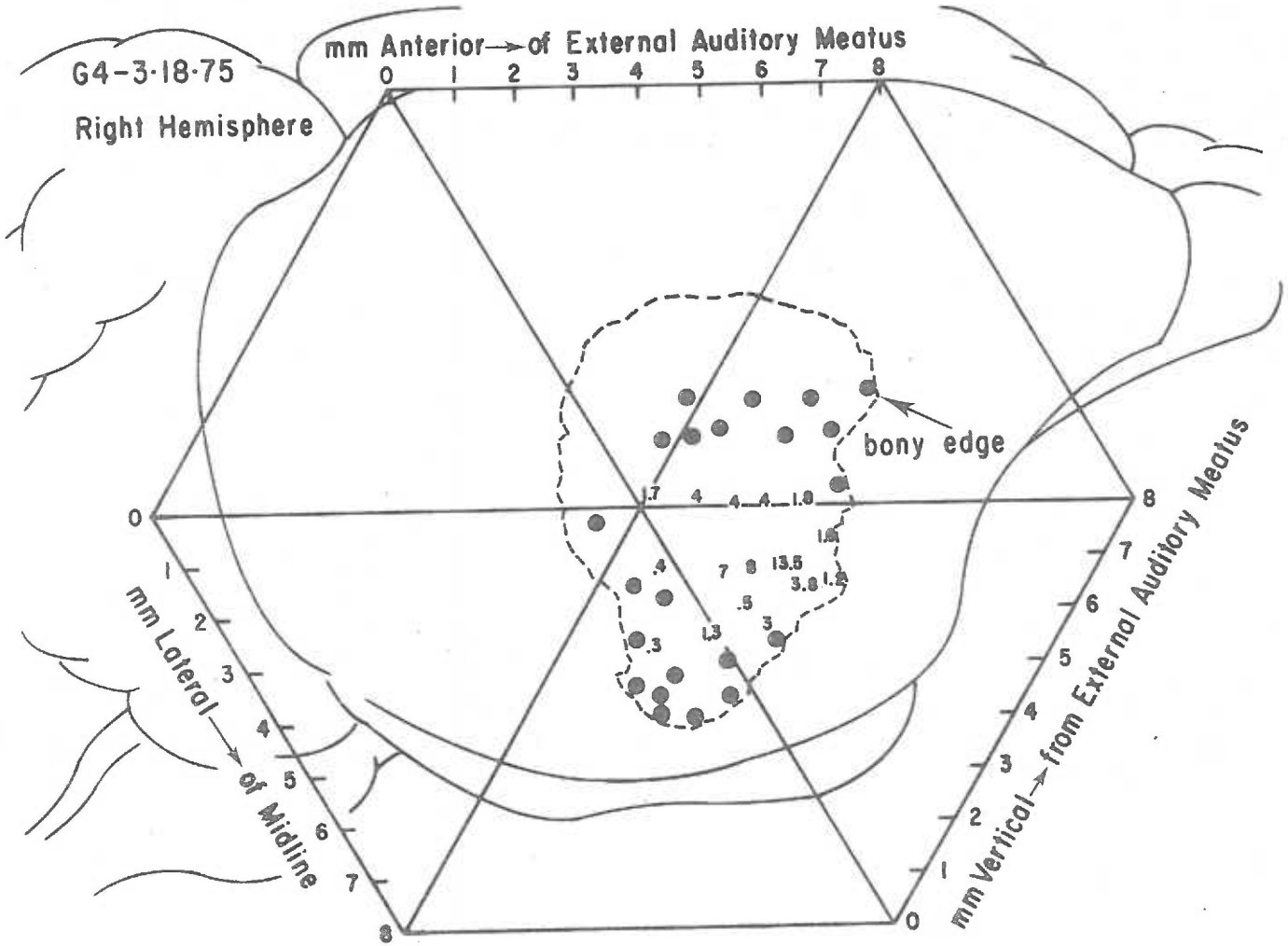

G15-7-17-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.5* 1.1
1 .5
.5
.5*
4 1.4
1.8 2
3
.9

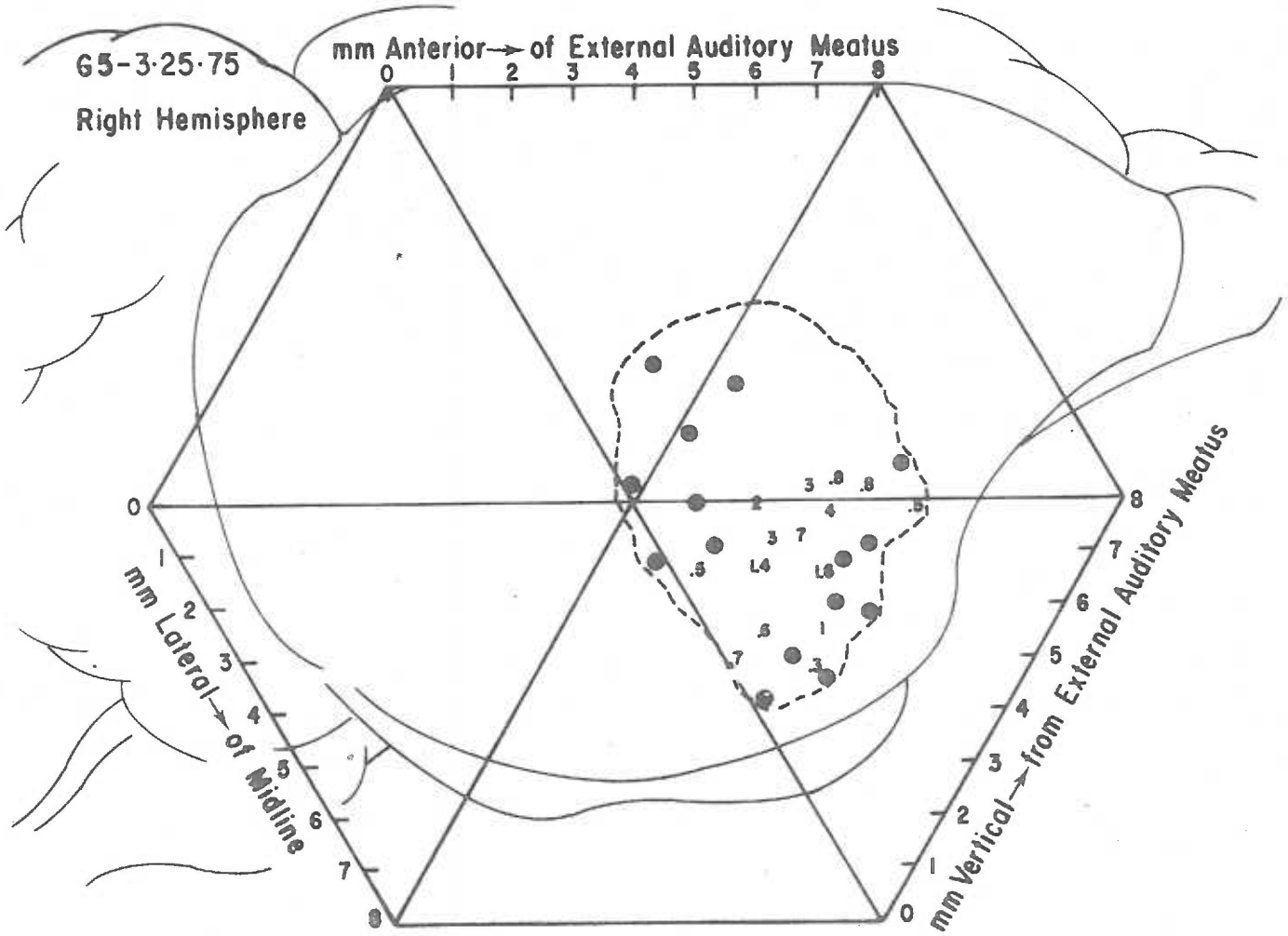

G16-7-28-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.5*
2.8
.5
1.5
3
.7*
2
.6*
1
2.4
1*
.8*

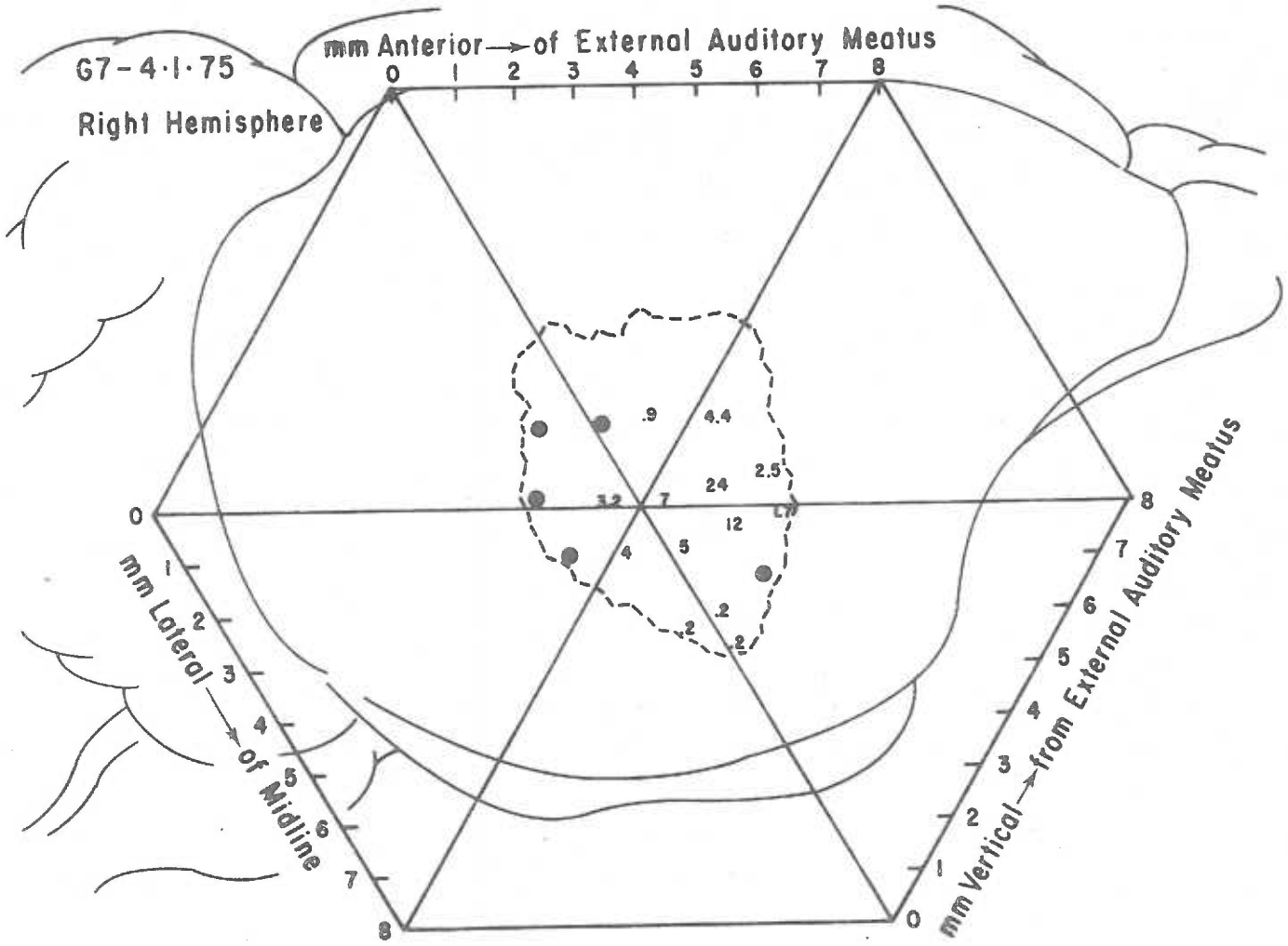
APPENDIX V

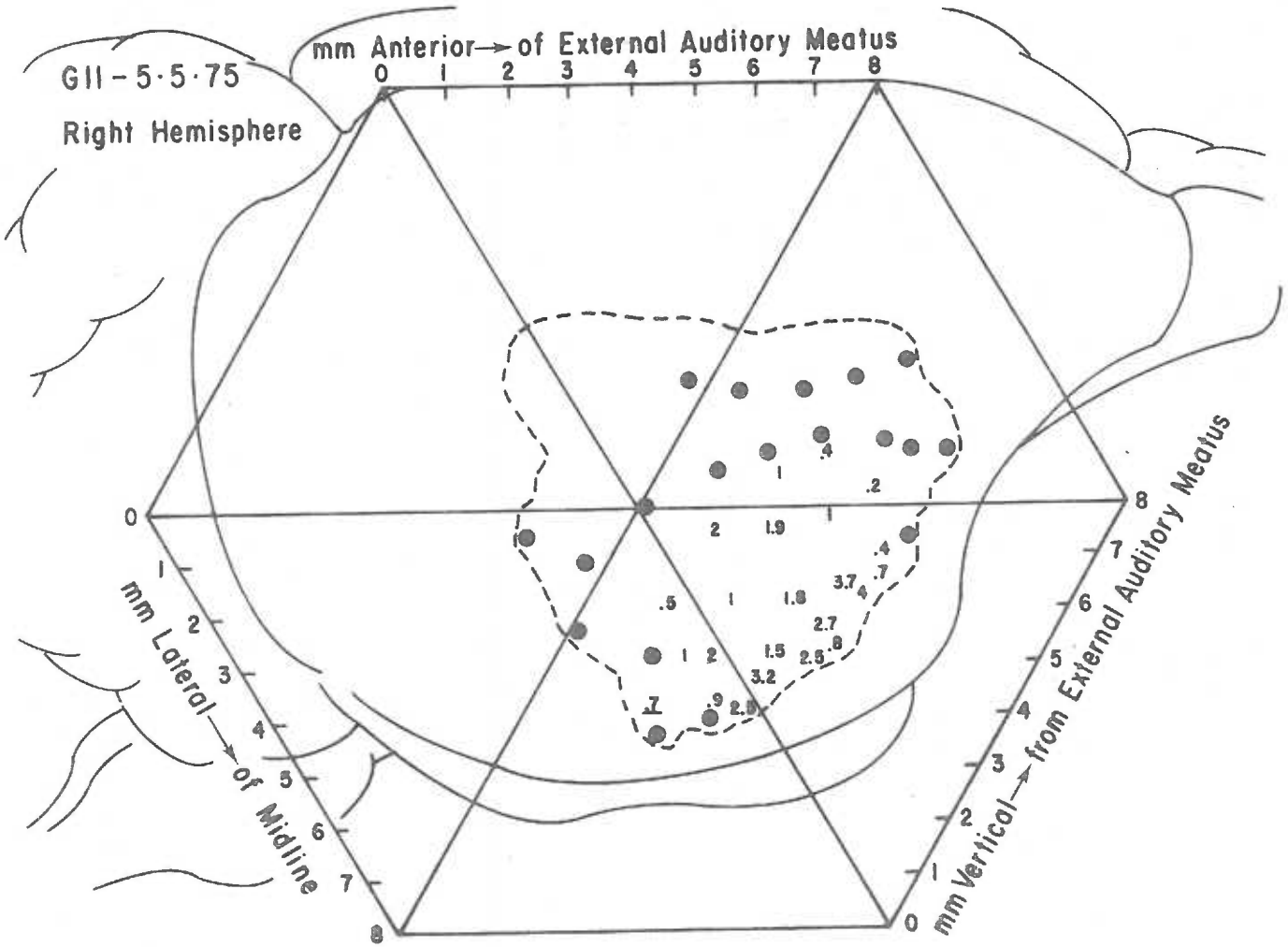
Schematic maps of the auditory cortex defined in the 'poor' experimental preparations. In each map, recording loci are plotted in reference to three coordinates (see Figure 5 for description of this procedure) on a three-dimensional depiction of the right cerebral hemisphere of the Mongolian gerbil. Click-responsive recording sites are denoted by a number which represents the peak-to-peak amplitude (in 100's of μV) of the evoked response recorded from that spot with a ball electrode. Underlined numbers represent click-responsive sites where the recorded evoked response had a peak positive latency of 27 msec or greater. Numbers with asterisks denote locations where a penetrating microelectrode was used to record averaged, evoked responses. Recording sites giving no response to the standard click stimulus are denoted by large black dots. Anterior is to the right and posterior is to the left in the diagrams. The dashed line represents the bony edge of the cortical exposure.


G2-2-22-75
Right Hemisphere
mm Anterior→of External Auditory Meatus
0 1 2 3 4 5 6 7 8
bony edge
mm Lateral→of Midline
mm Vertical→from External Auditory Meatus


G4-3-18-75
Right Hemisphere
mm Anterior→of External Auditory Meatus
0 1 2 3 4 5 6 7 8
bony edge
.7 4 4 4 1.8
1.8
.4
7 8 13.5
3.8 1.8
.5
3
.3
1.3
mm Lateral→of Midline
mm Vertical→from External Auditory Meatus


65-3-25-75
Right Hemisphere
mm Anterior→ of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral→ of Midline
mm Vertical→ from External Auditory Meatus


G7-4-1-75
Right Hemisphere
mm Anterior → of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral → of Midline
mm Vertical → from External Auditory Meatus
.9
4.4
2.5
24
12
5
.2
.2


G11-5·5·75
Right Hemisphere
mm Anterior→ of External Auditory Meatus
0 1 2 3 4 5 6 7 8
mm Lateral→ of Midline
mm Vertical→ from External Auditory Meatus
.4
1
.2
2
1.9
1
.4
.7
3.7
4
.5
1
1.8
2.7
.8
1
2
1.5
2.5
3.2
.7
.9
2.5

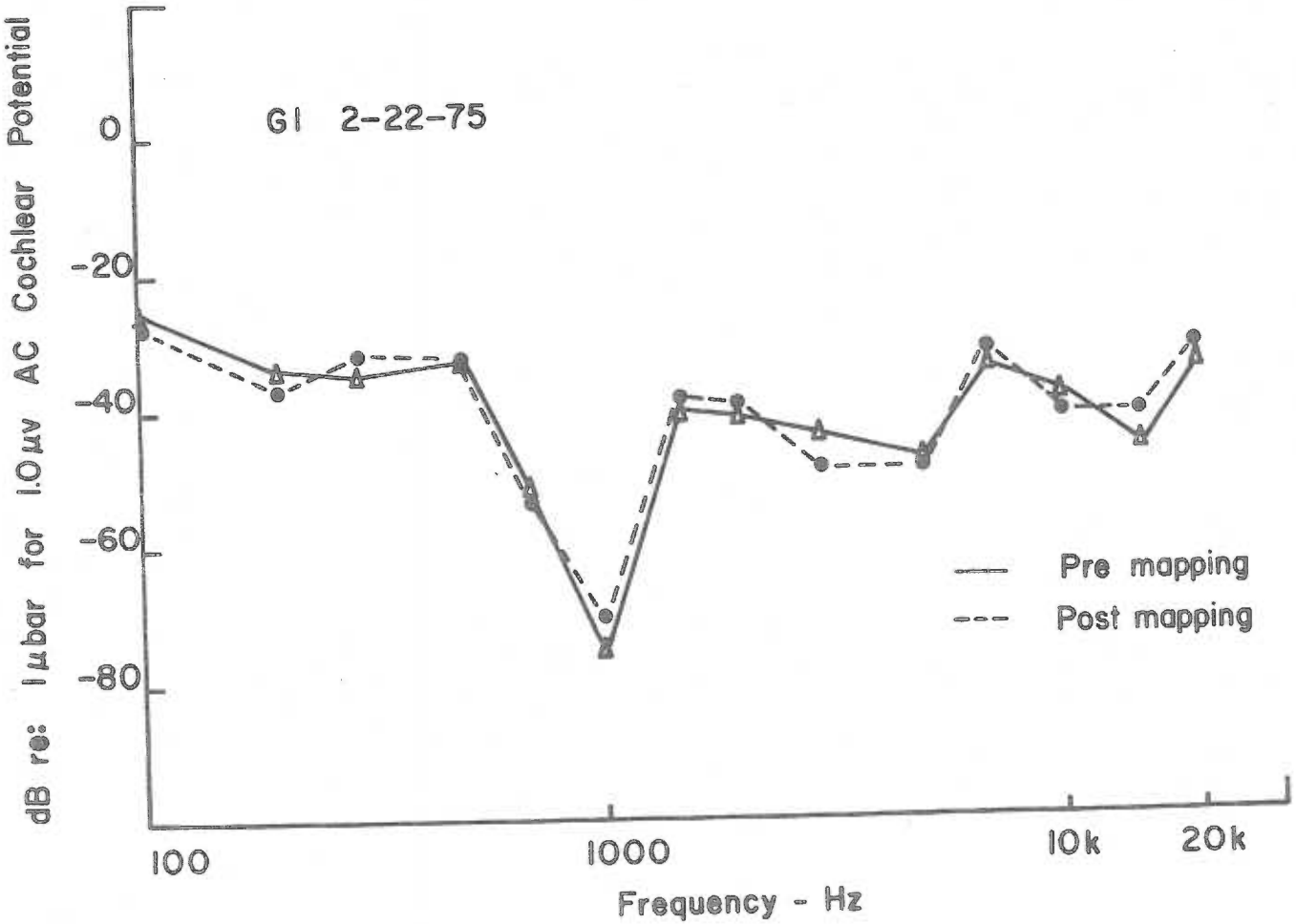
APPENDIX VI

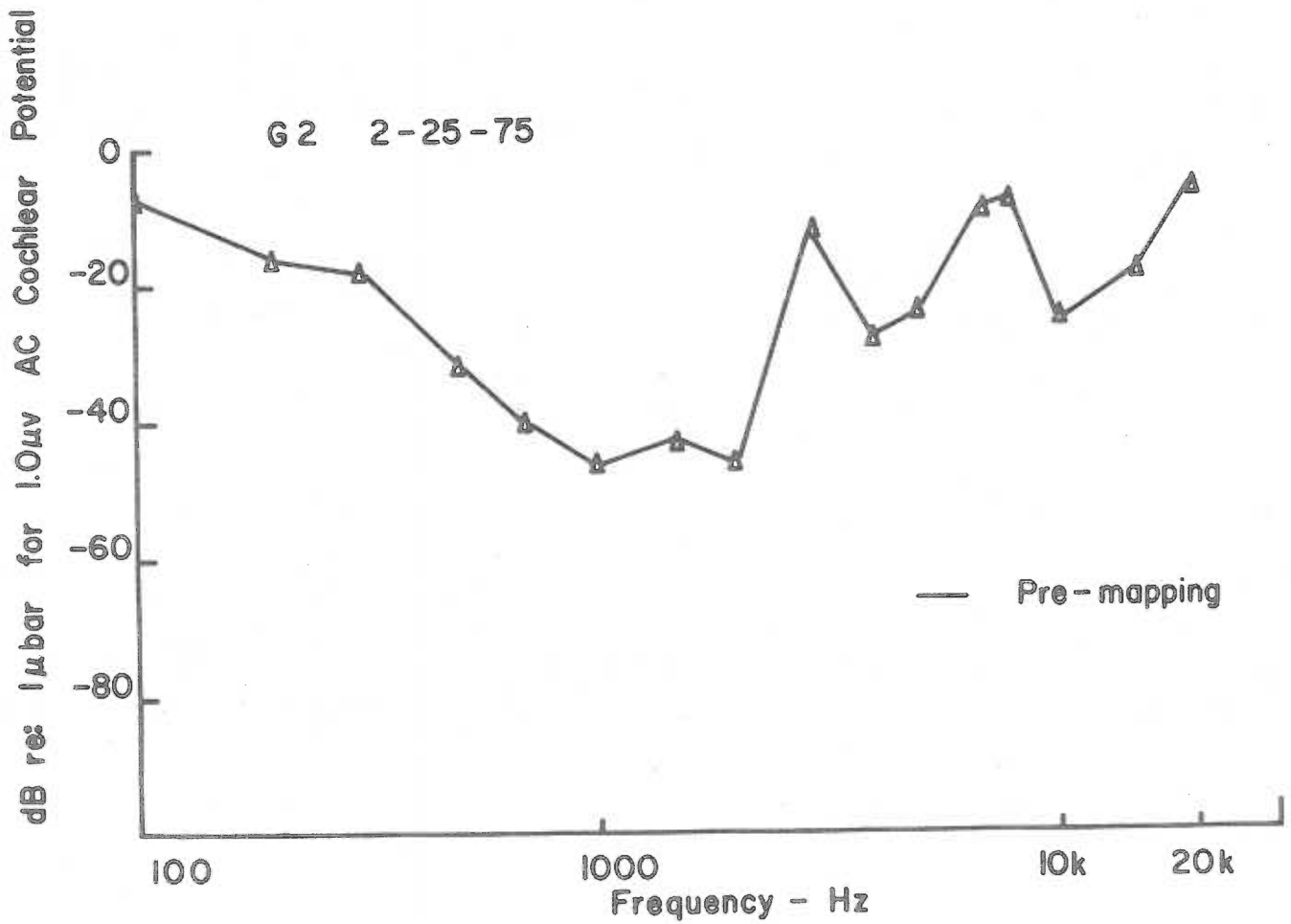
Data representing stereotaxic extremes for the (click-responsive) borders of the auditory area defined in each experiment of the study. Underlined values denote the population extremes for each coordinate.

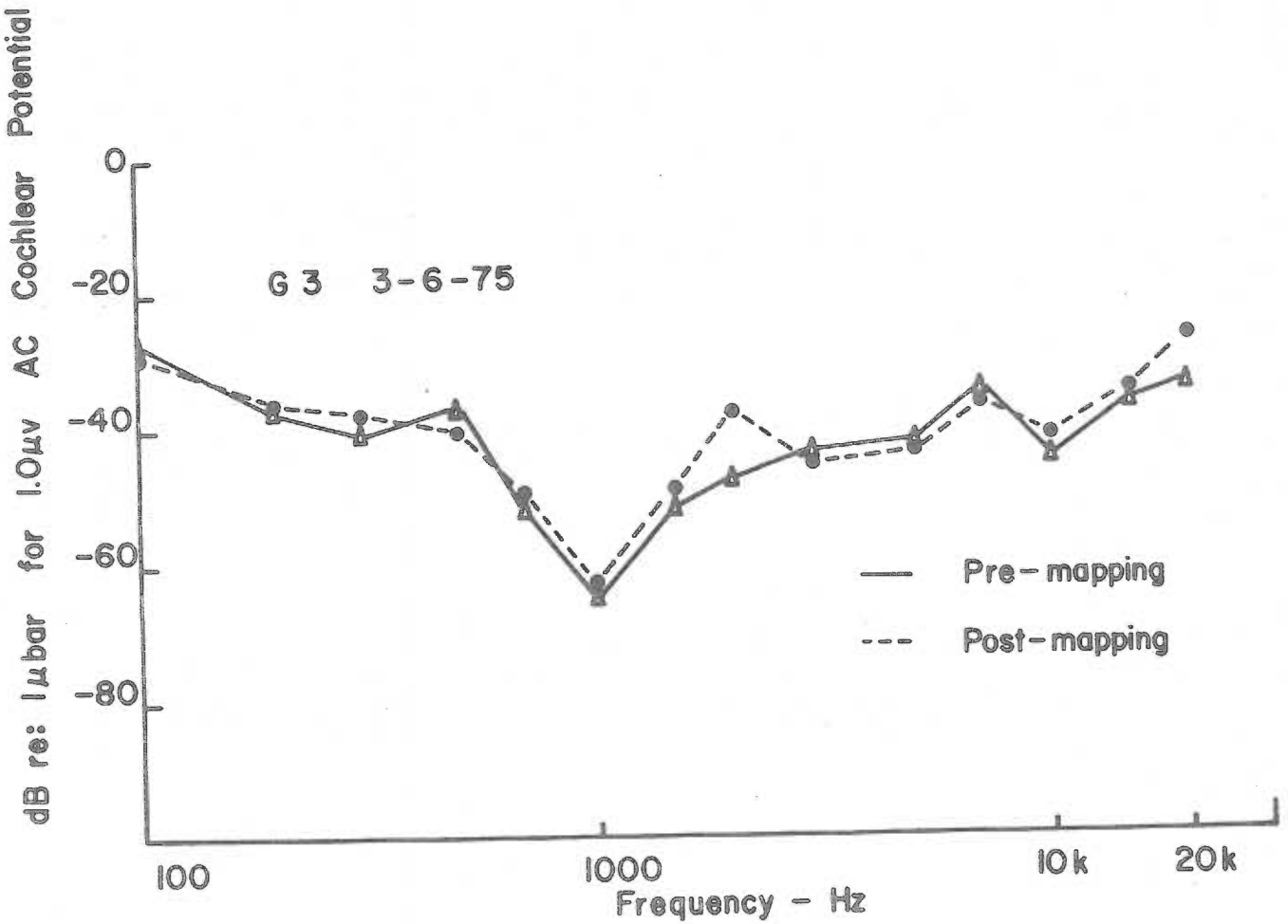
EXPERIMENT NUMBER	MM. ANTERIOR OF INTER-AURAL LINE	MM. LATERAL OF MIDLINE	MM. DORSAL OF INTER-AURAL LINE
G1 2-22-75	1.3 - 5.0	4.4 - 7.2	3.7 - 7.2
G2 2-25-75	3.6 - 5.6	6.2 - 7.1	4.4 - 6.4
G3 3-6-75	2.2 - 5.7	5.4 - 6.3	3.7 - 7.2
G4 3-18-75	2.3 - 5.9	5.6 - 6.9	4.5 - 5.8
G5 3-25-75	2.6 - 6.6	6.0 - 7.6	4.6 - 6.5
G6 3-29-75	2.1 - 6.0	5.8 - 7.1	3.3 - 7.2
G7 4-1-75	2.0 - 5.5	4.3 - 6.4	3.2 - 6.1
G8 4-12-75	1.5 - 6.3	3.7 - 7.3	3.1 - 6.8
G9 4-19-75	2.1 - 6.6	5.6 - 7.0	3.4 - 6.2
G10 5-3-75	1.8 - 4.8	5.3 - 6.9	3.0 - 6.3
G11 5-5-75	2.0 - 6.5	6.1 - 7.6	3.6 - 7.3
G12 5-6-75	2.0 - 5.0	5.9 - 7.5	3.7 - 6.5
G13 6-2-75	1.2 - 6.0	6.6 - 7.9	3.8 - 6.1
G14 6-4-75	1.7 - 6.0	5.3 - 7.4	3.4 - 7.1
G15 7-17-75	2.2 - 5.3	6.9 - 7.5	3.7 - 5.7
G16 7-28-75	2.5 - 5.7	6.2 - 7.3	3.9 - 6.7

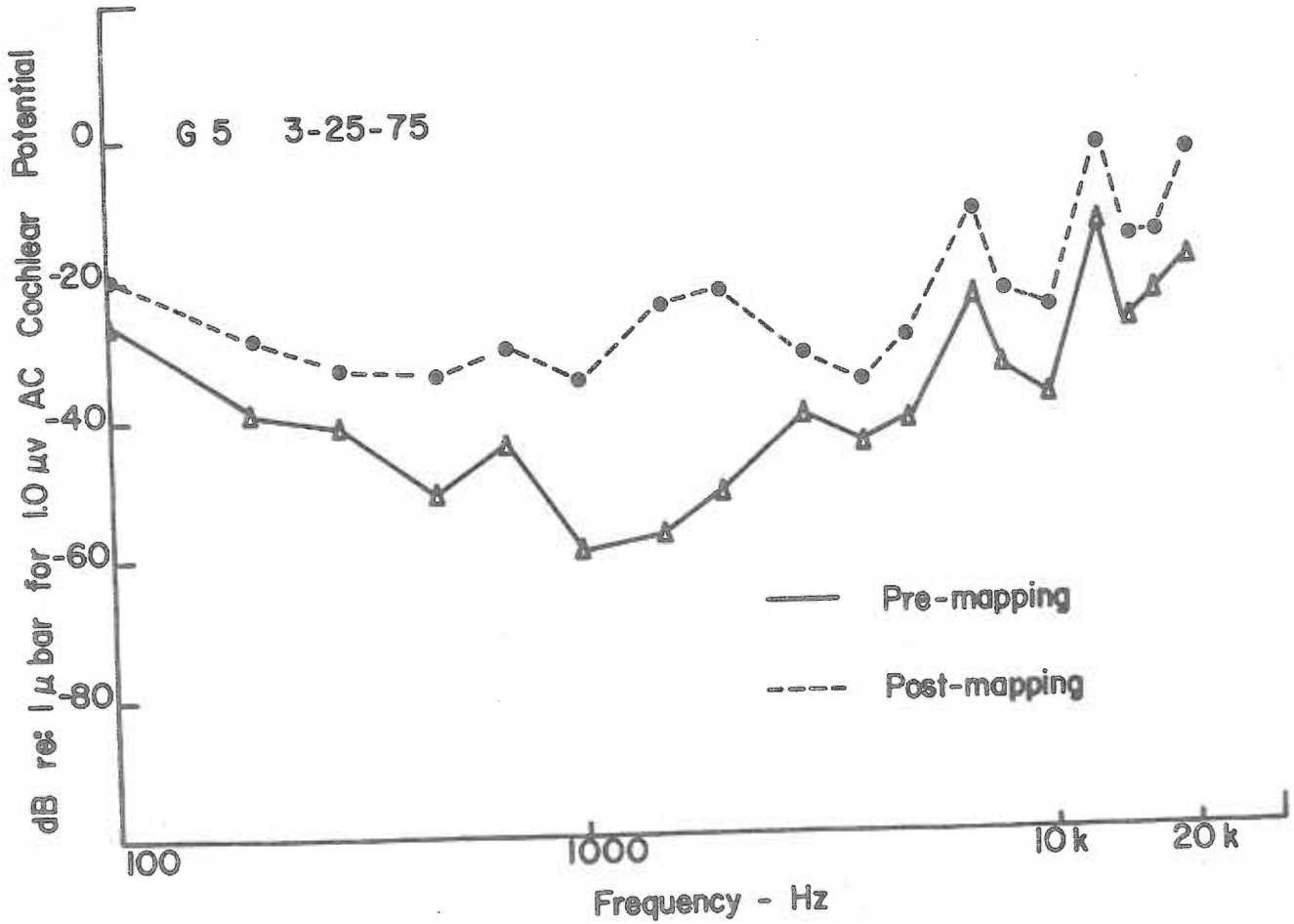
APPENDIX VII

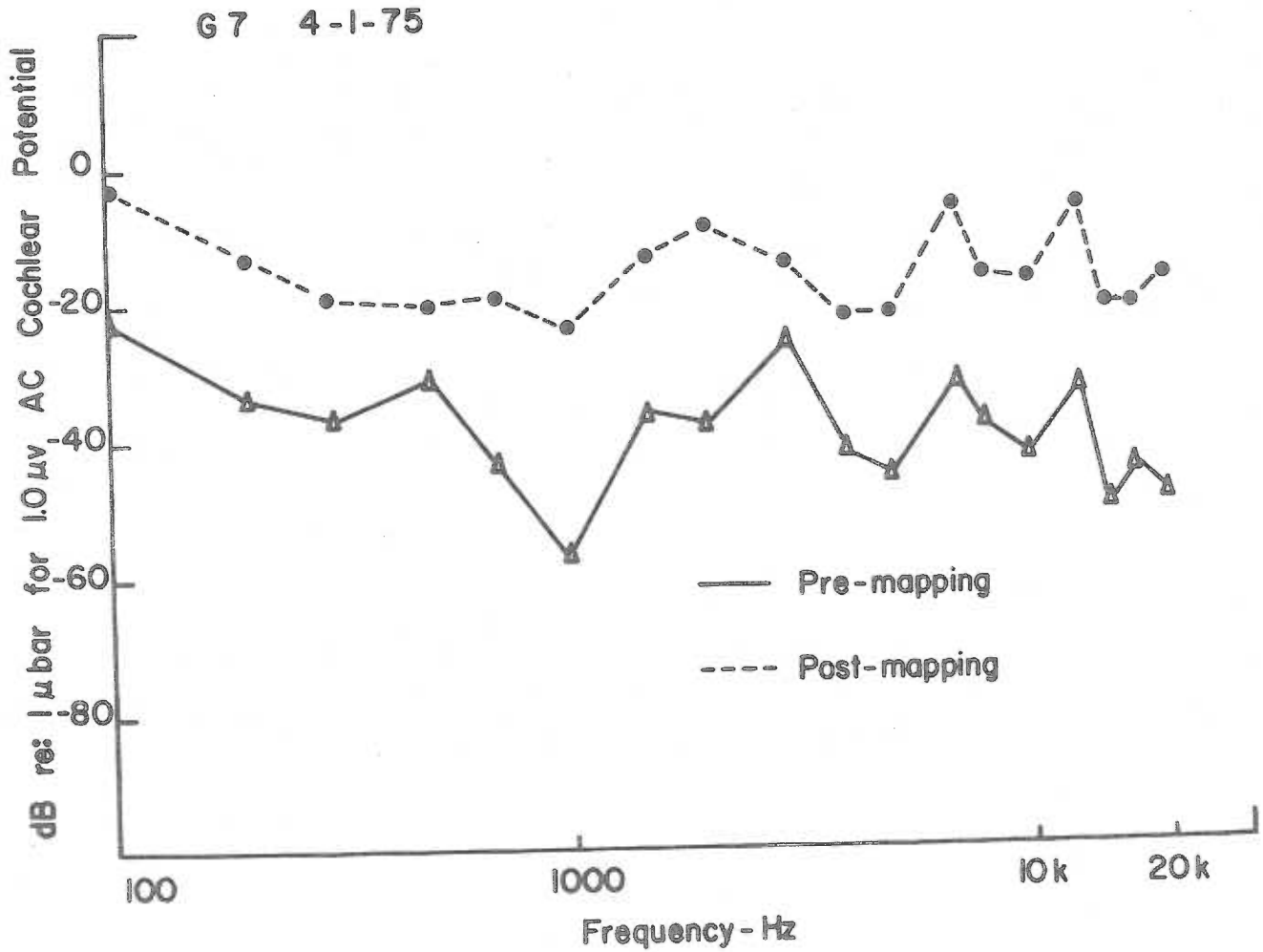
AC cochlear potential frequency (or 'sensitivity') functions generated before (solid line function) and after (dashed line function) cortical mapping in 11 experiments. Recordings made with a silver ball electrode resting on the round window membrane of the left cochlea. All recordings obtained with the bulla open. Eighteen pure tone frequencies presented to the left ear. The 1 μV isopotential curve is a graphic description of the amount of sound required at each of the 18 stimulating frequencies to elicit a constant (1 μV) cochlear output. The AC cochlear potenial was read directly, as rms voltage, from the wave analyzer voltmeter. A 3 Hz bandwidth was used during recording.

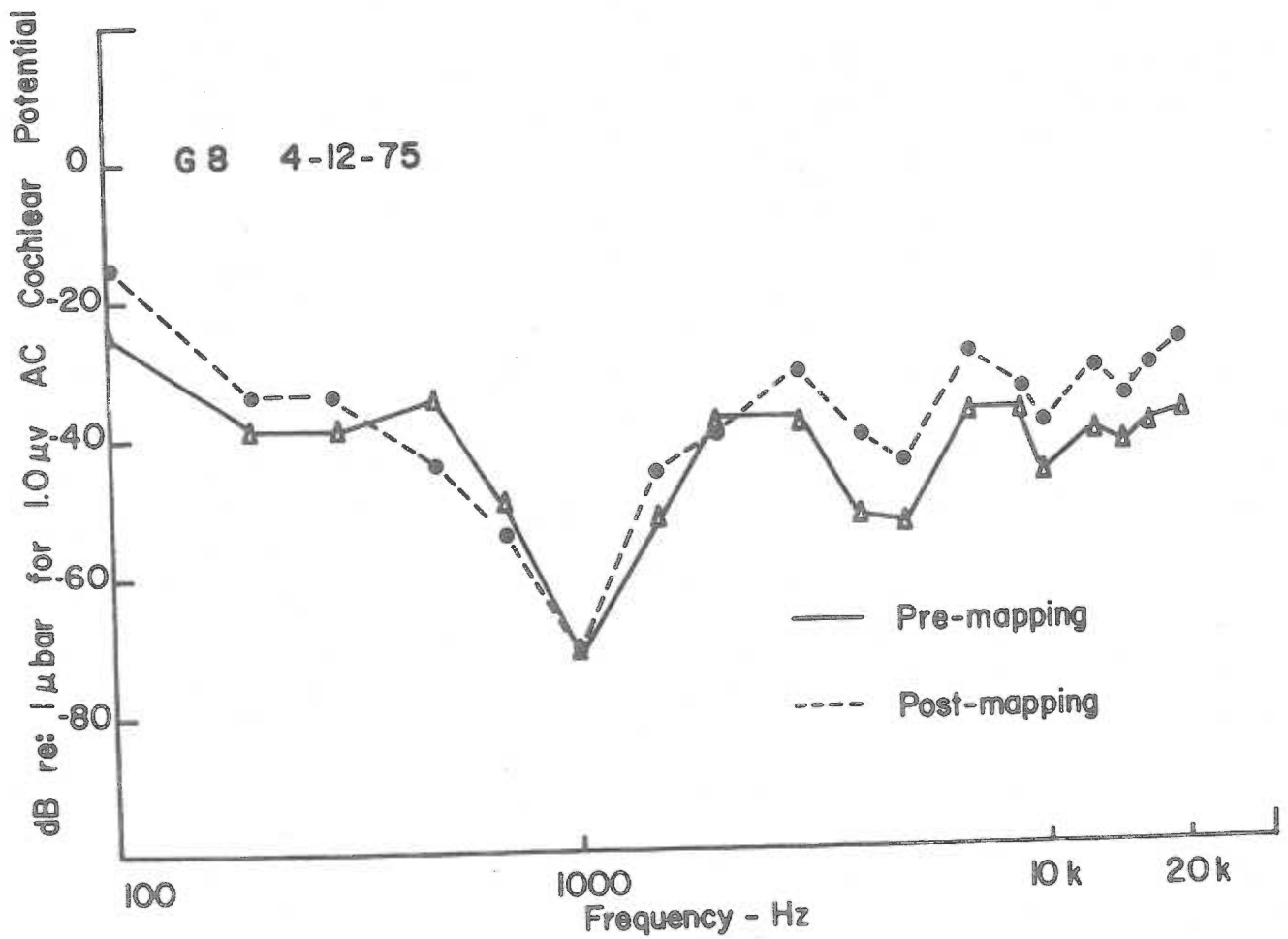

G1 2-22-75
dB re: 1 μbar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
100
1000
10k
20k
Frequency - Hz
Pre mapping
Post mapping

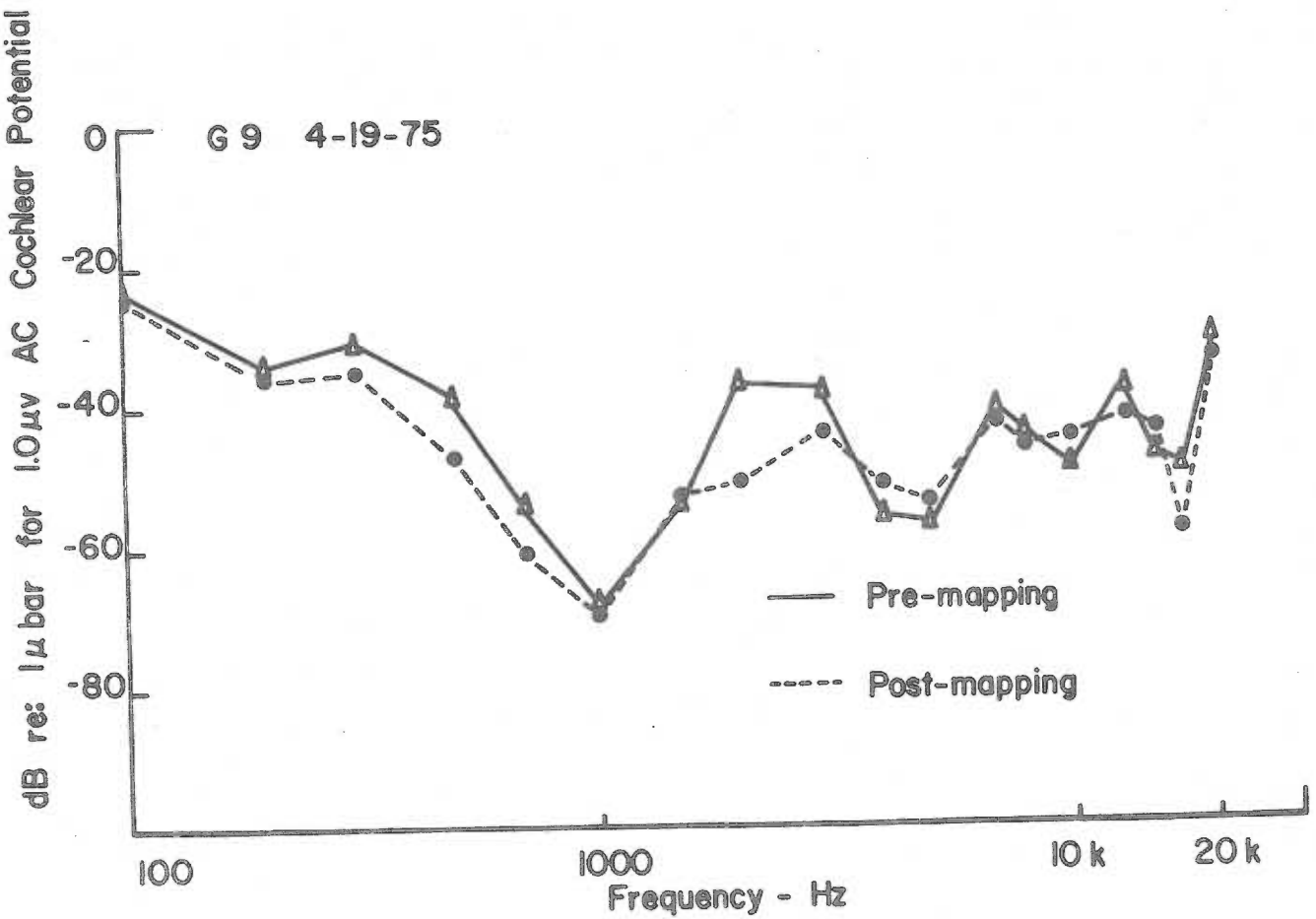

G2 2-25-75
dB re: 1 μbar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
Pre-mapping
100
1000
10k
20k
Frequency - Hz

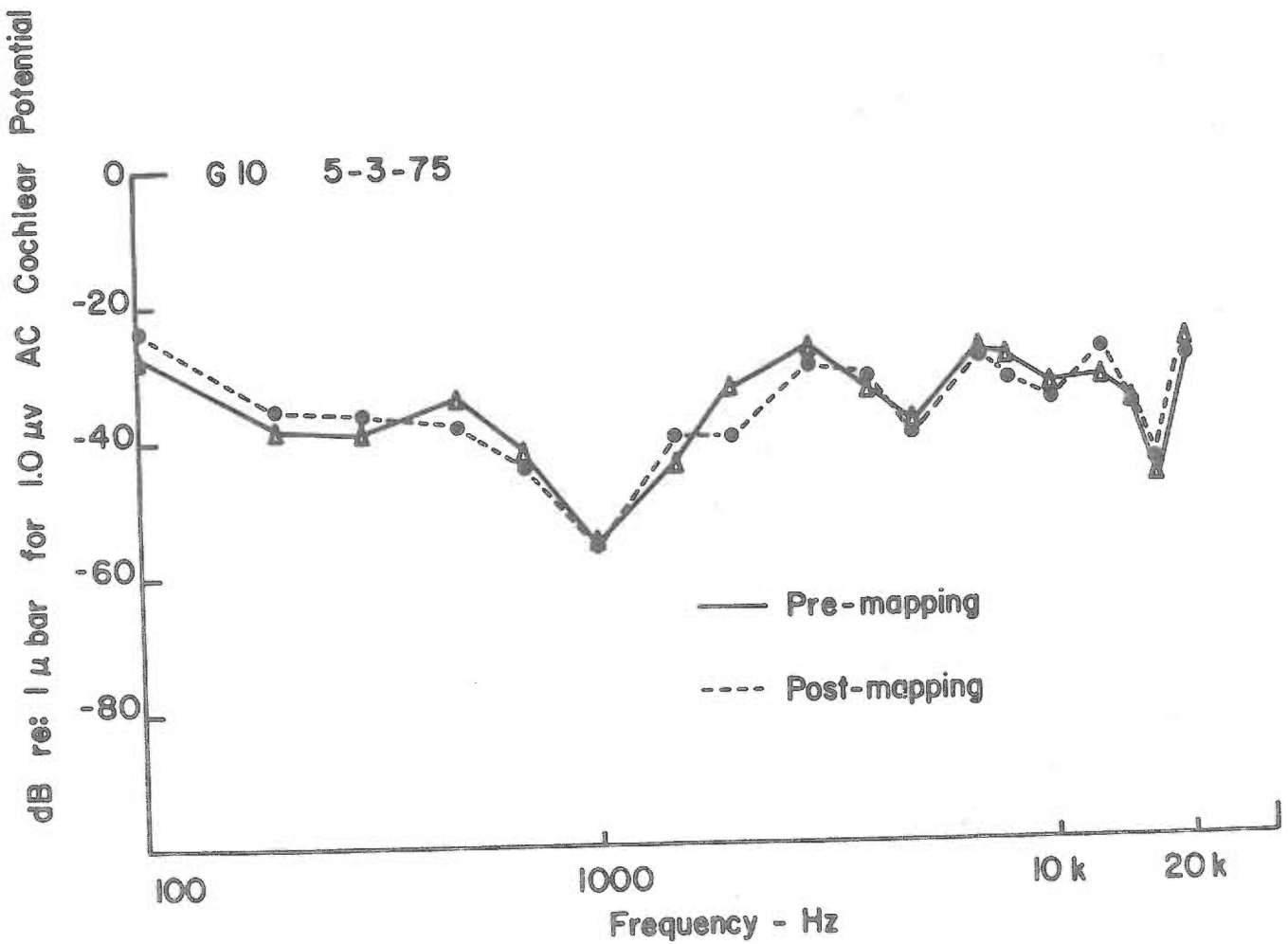

dB re: 1 μbar for 1.0μv AC Cochlear Potential
0
-20
-40
-60
-80
G 3 3-6-75
Pre-mapping
Post-mapping
100
1000
10k
20k
Frequency - Hz

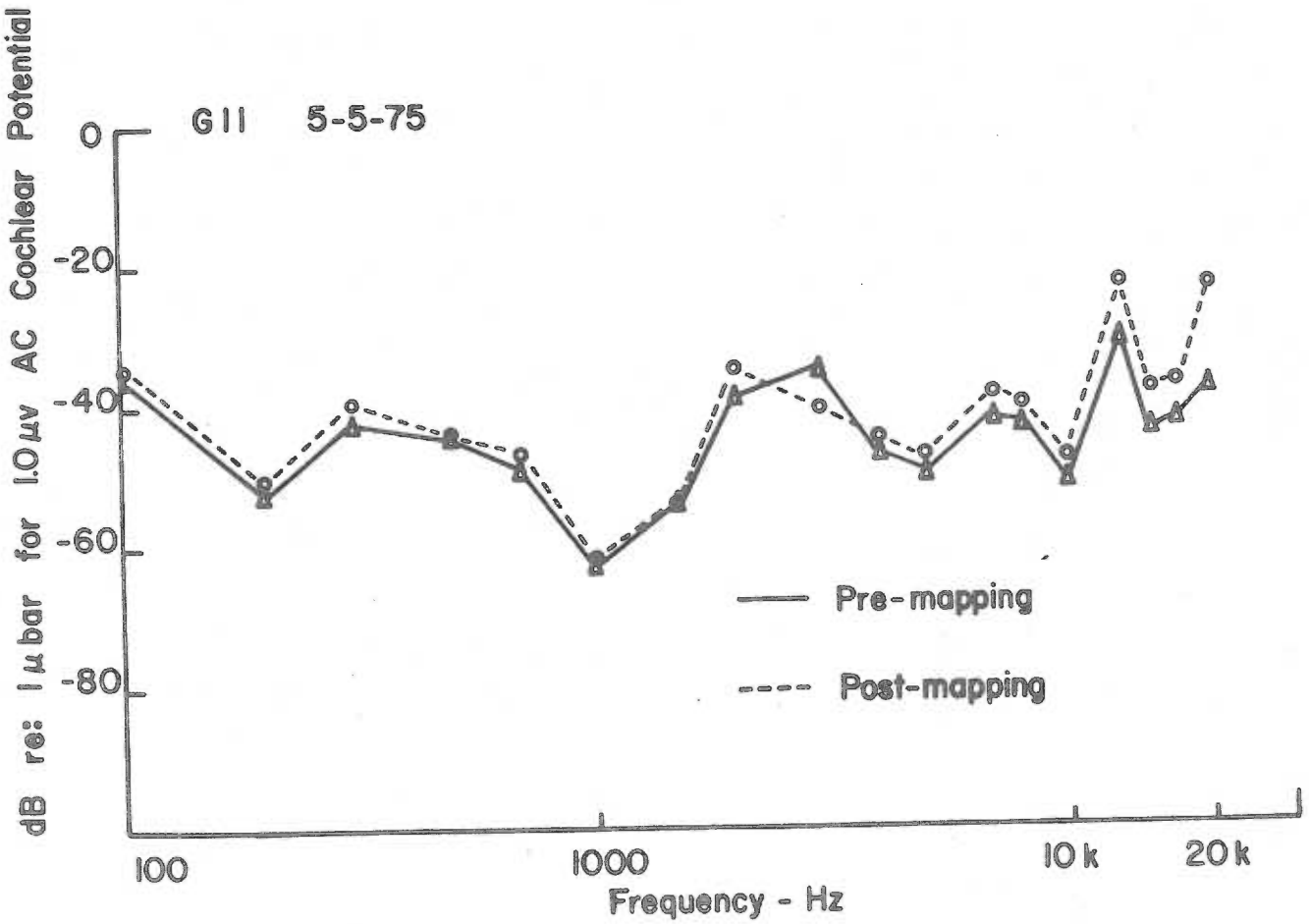

G 5 3-25-75
dB re: 1 μ bar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
100
1000
10 k
20 k
Frequency - Hz
Pre-mapping
Post-mapping

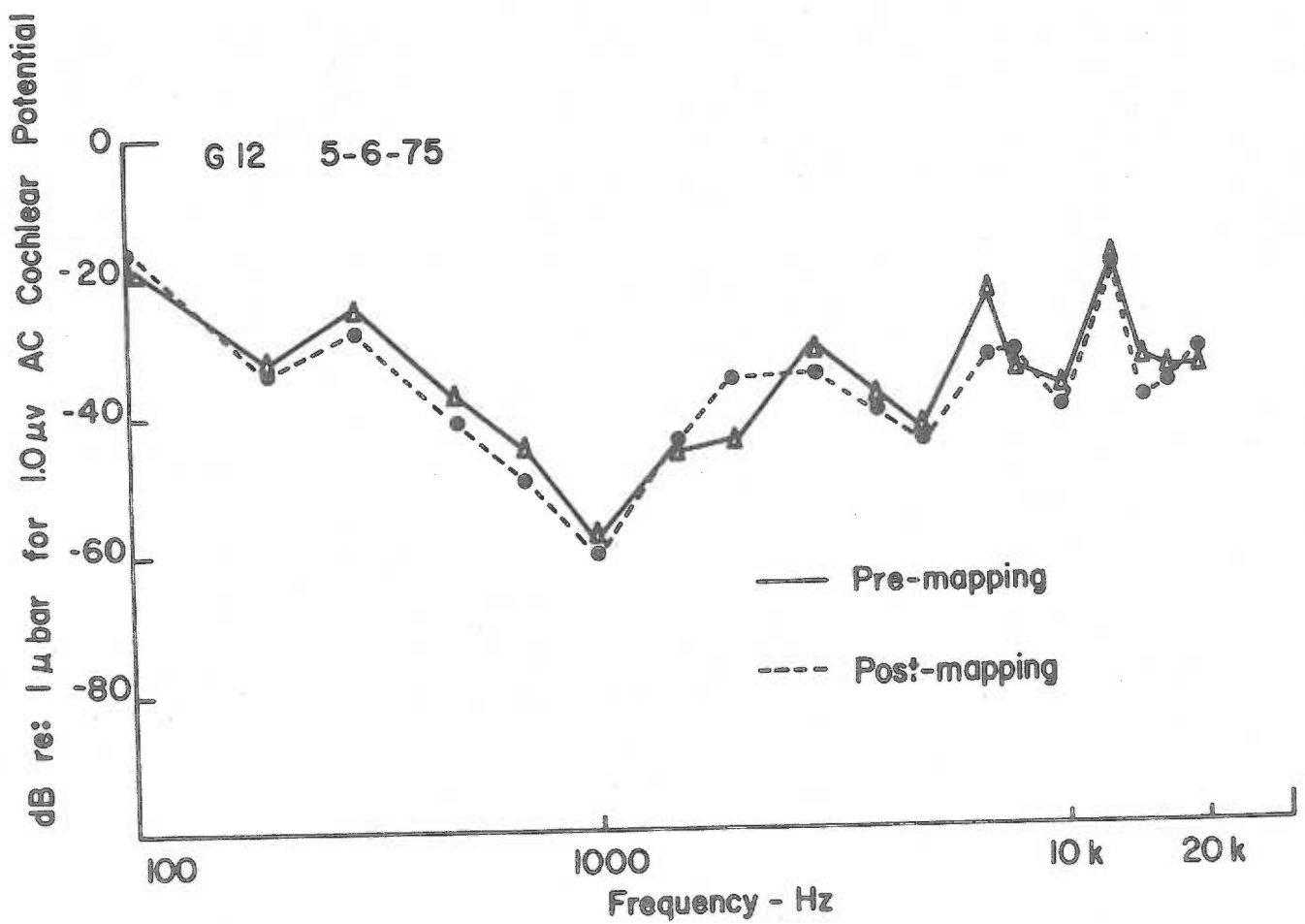

G7 4-1-75
dB re: 1 μbar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
100
1000
10k
20k
Frequency - Hz
Pre-mapping
Post-mapping


dB re: 1 μbar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
G 8 4-12-75
Pre-mapping
Post-mapping
100
1000
10 k
20 k
Frequency - Hz


G 9 4-19-75
dB re: 1μ bar for 1.0μv AC Cochlear Potential
0
-20
-40
-60
-80
100
1000
10 k
20 k
Frequency - Hz
Pre-mapping
Post-mapping


dB re: 1 μ bar for 1.0 μv AC Cochlear Potential
0
-20
-40
-60
-80
G 10 5-3-75
Pre-mapping
Post-mapping
100
1000
10 k
20 k
Frequency - Hz


G11 5-5-75
0
-20
-40
-60
-80
dB re: 1 μbar for 1.0 μv AC Cochlear Potential
Pre-mapping
Post-mapping
100
1000
10 k
20 k
Frequency - Hz


G 12 5-6-75
0
-20
-40
-60
-80
dB re: 1 μbar for 1.0 μv AC Cochlear Potential
Pre-mapping
Post-mapping
100
1000
10 k
20 k
Frequency - Hz