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GRADUATE COLLEGE

THE IMMEDIATE EFFECT OF SECTIONING HOMOLATERAL AUDITORY CENTRIFUGAL FIBERS ON THE COCHLEAR MICROPHONIC AND ACTION POTENTIAL IN GUINEA PIG

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

DOCTOR OF PHILOSOPHY

BY

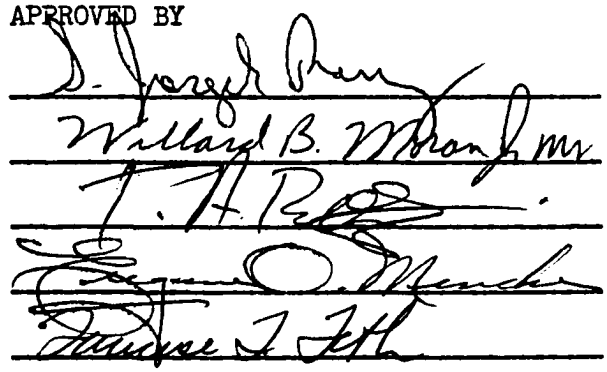
RICHARD E. TALBOTT

Oklahoma City, Oklahoma

1973

THE IMMEDIATE EFFECT OF SECTIONING HOMOLATERAL AUDITORY CENTRIFUGAL FIBERS ON THE COCHLEAR MICROPHONIC AND ACTION POTENTIAL IN GUINEA PIG

APPROVED BY



DISSERTATION COMMITTEE

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THE IMMEDIATE EFFECT OF SECTIONING HOMOLATERAL AUDITORY CENTRIFUGAL FIBERS ON THE COCHLEAR MICROPHONIC AND ACTION POTENTIAL IN GUINEA PIG

CHAPTER I

INTRODUCTION

Since the early attempts of Cramer and Bournilli to define the relationship between the magnitude of a physical stimulus and the magnitude of the psychological response, investigators have tried to understand the coding of sensory systems. Progress toward this goal has been limited by the lack of sufficient information concerning the anatomy and physiology of the systems under study. This is especially true in the case of audition. For many years the auditory system was considered to function solely through innervation of special somatic afferent fibers carrying impulses toward the central nervous system. In 1942, however, Rasmussen discovered the existence of a system of special visceral efferent fibers which innervated the end organ of the auditory mechanism. He designated this system the olivo-cochlear bundle (OCB). Rasmussen's discovery stimulated a flurry of neuroanatomic and neurophysiologic investigations and

copious speculation as to the role of the efferent fibers during auditory stimulation.

Originally, Rasmussen (99) located only the general course of the auditory efferent fibers. His observations revealed a complex bundle of 500 special visceral efferent fibers of three to five microns in diameter coursing from a point medial to the accessory nucleus of the superior olive through the brain stem, beneath the facial genu, and across the floor of the fourth ventricle. Some of the fibers terminated in the medial angle of the medial vestibular nucleus, but the majority proceeded laterally to the dorsal border of the descending route of the trigeminal nerve where they joined the afferent brances of the VIII cranial nerve and from there were distributed to the several turns of the cochlea. Rasmussen designated these efferent fibers the crossed olivo-cochlear bundle (COCB). At that time, he failed to observe the final termination of the fibers.

In the same study, Rasmussen also observed homolateral efferent fibers arising from the accessory nucleus. These fibers coursed with the cochlear and vestibular afferent fibers into the cochlea. Galambos (59) and others have also observed centrifugal fibers coursing from the inferior colliculus to the cochlear nuclei. The final termination of these efferent fibers remained obscure for many years following their initial discovery.

Fernandez (49) was the first to suggest that collateral fibers of the efferent system were directed to the inner hair cells of the cochlea. Churchill and his co-workers (18) used a histochemical approach in an attempt to specify the location of the distal endings of the efferent fibers. Acetylocholine had long been accepted by physiologists as one of

the primary efferent synaptic transmitters in other efferent systems of the body (19). Relying on the assumption that the presence of acetylcholinesterace (AcHE), an enzyme associated with acetylcholine activity, was an indicator of acetylocholine concentration, Churchill and his colleagues isolated AcHE in the regions of both the inner and outer hair cells of cats and guinea pigs. They concluded that efferent innervation existed in this area. Rossi (112) observed the presence of AcHE in the efferent fibers forming the intraganglionic spiral bundle. Visual observation of hair cell innervation by efferent fibers, however, had not as yet been accomplished.

Smith and Sjöstrand (132) succeeded in visualizing the cochlear efferent innervation through the use of the high magnification made possible by the electron microscope. They demonstrated two different major types, and one sub-type, of nerve endings innervating the outer hair cells. At a later date Kimura and her associates (77) confirmed the original observations of Smith and Sjöstrand. She observed the nerve endings of the efferent fibers to be vesiculated and similar in their morphological characteristics (numerous vessicles) to motor end plates and other presynaptic neural junctions which also generally are considered to be efferent fibers.

Numerous investigators have directed their efforts toward the observation of the effect of stiumulation of the olivo-cochlear bundle on the cochlear microphonic, endocochlear potential, summating potential and action potential. Galambos (56) was one of the first investigators to use electric shock to stimulate the OCB and to achieve the effect of this stimulation on the eighth nerve action potential (AP). Galambos observed a

complete elimination of the AP following OCB stimulation. Fex (51), using similar stimulation, observed an increase in the cochlear microphonic (CM) voltage following OCB stimulation. Fex also noticed an increase in the positive resting, or endocochlear, potential (EP) following OCB stimulation. Konishi and Slepian (77) observed that the summating potential became more negative with electrical stimulation of the COCB. In all instances the four potentials (AP, CM, SP, EP) returned to their original value following the withdrawal of the electrical stimulation of the OCB. Desmedt (32), Konishi and Slepian (80) and Rossi (111), all confirmed the initial observations of Galambos and Fex.

Several hypotheses have been offered to explain the activity of the auditory efferent system. Hernandez-Peon (70) suggested that the system may function as a gating mechanism for the separation of meaningful from non-meaningful material and characterized the auditory centrifugal fibers as being part of a feedback loop functioning in a self-regulating manner. Bekesy (5) discussed the possible role of inhibitory efferent nerve fibers in auditory localization phenomenon. The results of different investigations and the conclusions drawn from them are inconclusive and the role of the efferent auditory system in audition remains obscure.

It had been noted that small changes in stimulus parameters (electrical or acoustic) used in stimulation of the efferent system have been observed to produce large variations in the experimental results. Consequently, Pfaltz (96) has suggested that the changes observed in the cochlear potentials when using electrical stimulation may not be the result of efferent fiber activity but rather may represent an artifact induced by the electrical stimulation itself.

While all investigators using electrical stimulation of the efferent system have observed similar changes in cochlear potentials, none has been able to observe a similar response using contralateral acoustic stimulation. This led Pfaltz (96) and Spong (126) to suggest that the efferent system may be functioning as a homolateral feedback network rather than as an inhibiting system on the contralateral cochlea. They propose that both the COCB and the HOCB may have an ipsilateral function as well as a contralateral function as had been previously suggested. They point out that while it is true that the majority of the efferent fibers from the superior olivary complex cross to the contralateral side, the afferent input to each complex comes from both the homolateral and the contralateral cochlear nuclei. The anatomical possibility for a homolateral feedback mechanism is thus available.

While a great amount of data has been accumulated pertaining to the auditory efferent system, no unifying hypothesis has evolved with regard to its exact function. In part, the problem lies with the complexity of the system itself, reflecting the need to gather more information as to the activity of the individual sub-units thereof. The general purpose of this particular investigation is to examine the effect of eliminating all homolateral efferent input to one cochlea. The specific intent of this study is to determine the influence, if any, of homolateral efferent fibers on the auditory afferent input. To this end, the cochlear microphonic and action potential were measured before and after sectioning the homolateral olivo-cochlear fibers and the homolateral lateral lemniscus in eight guinea pigs. The rational for sectioning both the efferent fibers in the lateral lemniscus and the homolateral olivary complex fibers was to

examine in this study the gross effect of eliminating all efferent input to one cochlea. The following chapter is devoted to a review of the literature pertinent to the anatomy and physiology of centrifugal fibers to the cochlea.

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

The human auditory system is a complex network of neurons which exhibits all of the capabilities of the nervous system in general. It is composed of both afferent and efferent neurons which facilitate the coding of peripheral sensory input into neural messages which enable the perception of acoustic events. The efferent fibers of the auditory system course from several nuclei in the brain stem to terminate peripherally on the hair cells of the cochlea or on some central afferent neurons. This chapter is devoted to a discussion of the anatomy and physiology of these auditory efferent fibers.

There appears to be a unique relationship between the auditory afferent and efferent systems which allows for the modification of afferent neural activity by the efferent system. The afferent input seems to trigger efferent fiber activity at several levels of the brain stem which in turn may facilitate or inhibit the homolateral or contralateral afferent input. Only the advent of new measurement techniques and the use of the electron microscope has allowed a detailed mapping of the location of the neural fibers in the auditory system. The discovery of the exact

pathways of the auditory centrifugal fibers has naturally led to speculation and experimentation with regard to their function. While a great deal of both anatomic and physiologic information has been accumulated, many unanswered questions remain. The following section is a review of the literature with regard to the anatomic, physiologic and psychophysical studies of the auditory centrifugal system.

Anatomic Evidence of the Existence of Auditory Centrifugal Nerve Fibers

Rasmussen (99) was first to report the existence of efferent fibers coursing from the superior olive toward both the contralateral and ipsilateral cochleas. Using a degeneration technique, Rasmussen was able to trace what he termed the crossed olivo-cochlear bundle (COCB) from its point of origin in the superior olive to the basal turn of the cochlea. Destruction of the multipolar cells situated medial to the accessory olive and dorsal to the trapezoid body revealed degenerating fibers rising ventrally through the brain stem and moving to the floor of the fourth ventricle. The fibers formed a compact bundle and crossed the floor of the fourth ventricle rostral to the facial genu. Rasmussen further observed that some of the fibers entered the medial angle of the medial vestibular nucleus and terminated while the majority ran laterally to the dorsal side of the descending trigeminal nerve where they joined the afferent vestibular nerve. The bundle then left the medulla running parallel to the vestibular and facial nerves. The fibers then proceeded to the area of Scarpa's ganglion. In the area of Scarpa's ganglion, the fibers left the vestibular nerve to form Oort's anastomosis with the cochlear division of the eighth cranial nerve.

Rasmussen (100) was later able to trace the efferent fibers beyond Oort's anastomosis. He identified three of four well defined fasciculi (small bundles or clusters of nerves). The largest of these passed through the groove between the basal and second turns of the cochlea before entering Rosenthal's canal. These fibers then proceeded toward the second and apical turns of the cochlea. The second fascicle coursed almost parallel to the afferent cochlear nerve supply of the basal turn. The third fascicle was inconsistent and could be found in the spiral ganglia of the middle of the basal turn. All of these fibers were shown to collect to form what is now known as the intraganglionic spiral bundle.

In a later study, Rasmussen (102) identified a homolateral component of the efferent bundle where fibers pass dorsolaterally with respect to the ascending limb of the crossed component arising from the same general location in the superior olive. Rasmussen observed that the COCB was comprised of approximately 500 three-to-five micron fibers while the HOCB contained approximately one-fifth as many fibers of the same diameter. Collateral fibers from both the HOCB and the COCB far exceeded the parent fibers in number. COCB fibers were observed to connect directly to the ventral cochlear nucleus through collateral branches. The innervation in the ventral cochlear nucleus was diffuse, however, and the precise termination of these fibers was not demonstrated. Rasmussen was also able to show that the origins of both HOCB and COCB in the superior olive were innervated by afferent fibers from both cochlear nuclei.

Fernandez (49) was able to trace the course of the spiral fibers discovered by Rasmussen through the cochlea. Fernandez's research revealed that portions of the interganglionic spiral bundle run apically inside the

spiral ganglion as much as one-fourth of a turn or more. These fibers gave off many collateral fibers which could be traced to the region of the inner hair cells. Fernandez concluded that the inner hair cells had both afferent and efferent innervation. Fernandez further observed that the interganglionic spiral bundle had more neurons in the basal turn with a decreasing population of fibers toward the apical turns. Portmann and Portmann (98) replicated Fernandez's work with similar results. The initial investigations discussed above all used degeneration and staining techniques to observe the course of the efferent fibers. About this time (1959), however, other investigators turned to histochemical investigations to further confirm the course of these newly discovered efferent fibers.

The first of the histochemical investigations was carried out by Churchill and his co-workers (18). Their study was designed to take advantage of previous information regarding the presence of acetylcholine as a neural-transmitter in certain efferent systems. Acetylcholine is recognized as the chemical mediator of impulses at all autonomic ganglia, all parasympathetic postganglionic terminations, sympathetic postganglionic endings at sweat glands, and motor nerve endings at skeletal muscles. Acetylcholinesterase is an enzyme which reduces acetylcholine to acetic acid and choline following activation of a succeeding neuron at the synaptic junction. While acetylcholine cannot be measured directly, the assumption is generally accepted by physiologists that the acetylcholine concentration parallels that of acetylcholinesterase (AcHE). Churchill, etal (19) was able to demonstrate the presence of AcHE activity in the region of both the inner and outer hair cells of cats and guinea pigs. He did not try, however, to definitely link this AcHE activity to olivocochlear bundle activity.

Schuknecht (123) and Schuknecht, Churchill, and Doran (124) demonstrated that the presence of AcHE in the cochlea was dependent on the integrity of the olivo-cochlear bundle. Following transection and degeneration of the COCB and the HOCB, AcHE activity was no longer observable in the region of the outer hair cells. It was concluded that the outer hair cells were the final terminations for the efferent fibers.

Other investigators attempted to confirm the presence of these efferent terminations visually through the use of electron microscopy. Engstrom and his co-workers (48), Spoendlin (135), Iurato (74), Smith (127), and Smith and Sjöstrand (132) among others demonstrated the existence of several structurally different types of nerve endings at the base of the cochlear hair cells with the use of the electron microscope. Nerve terminals of the first row of outer hair cells were large and granulated (numerous vessicles), however, the inner row contained a number of smaller less granulated fibers. Engstrom (48) also noted a double-walled postsynaptic membrane that could be identified inside the hair cell at the point of contact with the large granulated endings. Smith hypothesized that the granulated fibers were part of the efferent system.

Smith and Sjöstrand (132) demonstrated the existence of two different types of nerve endings at the base of the outer cells as well as one subtype. Type I endings were small and sparsely vesciculated with diameters from 0.1 to 1.0 possessing a well defined plasma membrane and containing few mitochondria (small granules) and vescicles. A "synaptic bar" consisting of a rod-shaped osmiophilis (readily subject to osmosis) structure surrounded by a single layer of vescicles was observed to divide the space between the synaptolemma and the hair cell plasma membrane. They

(Smith and Sjöstrand) also described some large densely vesciculated nerve endings measuring up to five inches in length and one-to-three microns in diameter. These fibers contained numerous closely packed vescicles. They also contained numerous mitochondria grouped in the portion of the nerve cell distal to the hair cell. No synaptic bar was observed in this group of fibers. The nerve endings designated as type 2a have an identical structure to those of type II but their endings were not in contact with the hair cells and connected mainly with other nerve endings of fibers.

Smith and Sjöstrand (132) classified the individual hair cells depending upon the type of nerve endings which innervated them. The hair cells were termed type A if they were in contact with both type I and type II nerve endings and were termed type B if they were in contact with the type I endings. Both Smith and Sjöstrand and Spoendlin observed that the hair cells progress in number from predominantly type A to predominantly type B from base to apex respectively. Kimura and her co-workers (77) demonstrated that in man there are also two types of nerve endings where synaptic connections exist between the efferent axon and the afferent dendrite, both in the region of the outer spiral bundle and at the base of the hair cells. Smith and Sjöstrand considered both type 2 and type 2a nerve endings to be efferent fibers.

Other centrifugal connections have also been demonstrated within the auditory system. Van Gehuchten (141) demonstrated fibers supplying both the cochlear and vestibular apparatus of the ipsilateral side coming from cells in the reticular formation of the pons and medulla. Rasmussen (106) recently confirmed the existence of the reticulo-cochlear fibers. Galambos (61) and others have observed the presence of centrifugal fibers

descending from the inferior colliculus in the lateral lemniscus to the ipsilateral cochlear nuclei. Figure I presents a simplified diagram of the brain stem at the level of the cochlear nuclei.

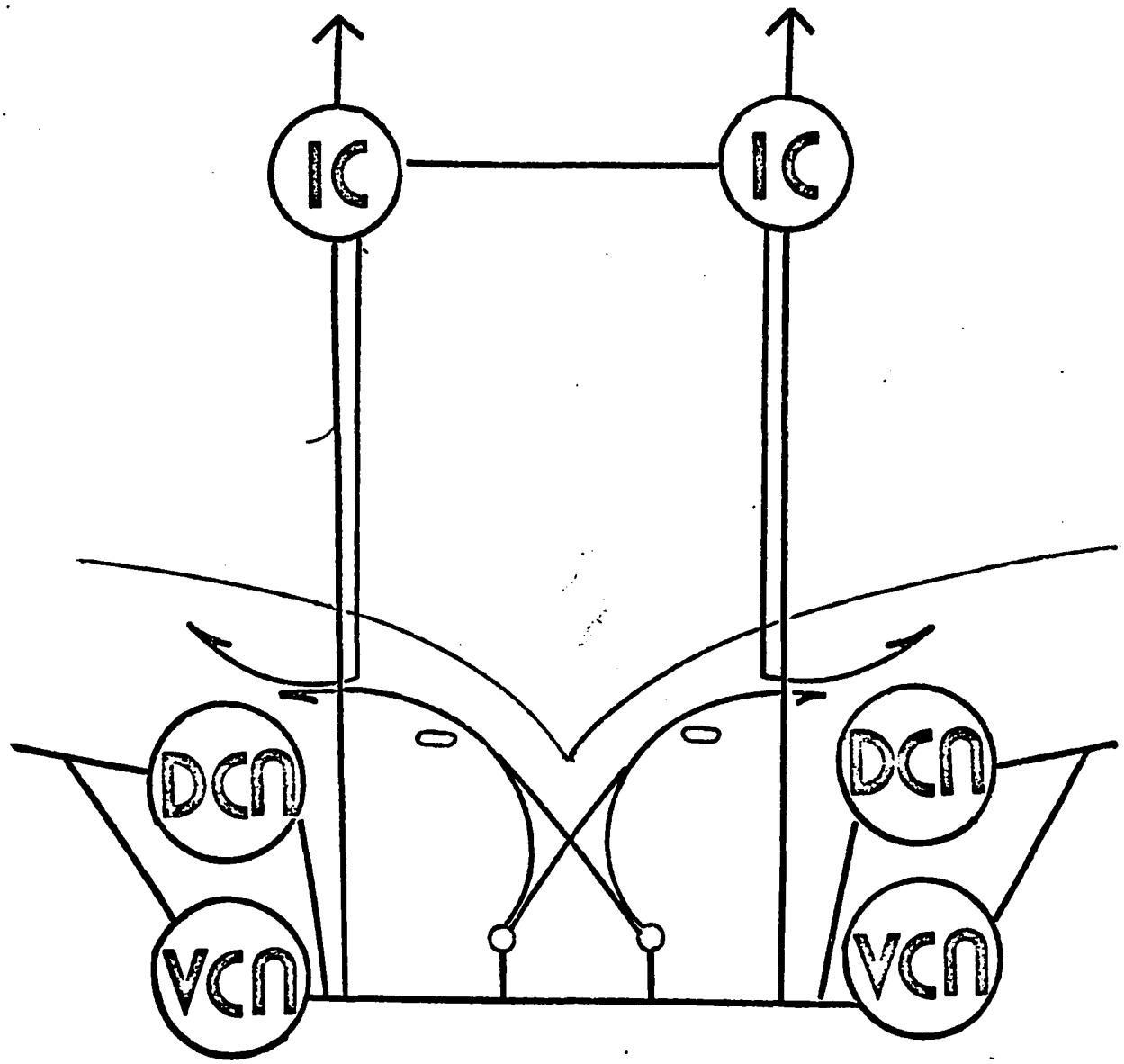
The anatomical evidence for the location of the auditory centrifugal fibers is fairly conclusive. Based on the investigations cited above and others, the existence of both a crossed and a homolateral efferent innervation of the outer hair cells from the superior olivary complex has been established. The physiological significance of this system, however, has not been so clearly demonstrated. The investigations pertaining to the physiology of the auditory efferent system are discussed in the following section.

Physiology of the Auditory Efferent System

The study of the physiology of the auditory efferent system was initiated by Galambos (56). Galambos investigated the effect of stimulation of the COCB on the action potential (N_1) in the eighth nerve of cats. He stimulated COCB fibers in the floor of the fourth ventricle with electrical square waves. The N_1 response was abolished by this stimulation. There was an indication of an inconsistent but direct relationship between the frequency of the electrical shock and the amount of N_1 reduction. Optimal reduction was observed at 100 shocks per second. Full recovery of the N_1 response was observed two seconds after electrical stimulation of the COCB was terminated. Placement of the stimulating electrode was found to be crucial for observation of the reduction of N_1. A location of $\pm$2mm rostral to the obex of the medulla was necessary for the reduction. While Galambos did not discuss the effect of stimulation on the cochlear

FIGURE I

Graphic Representation of the Brain Stem Illustrating The Cochlear Nuclei (DCN-VCN), The Inferior Colliculus (IC), The Superior Olivary Complex (SOC), and The Facial Genu (F.G.)



microphonic (CM), inspection of his data reveals that the CM was potentiated by the stimulation.

In 1962, Fex (50) studied the effect of electrical stimulation of the COCB on both the cochlear microphonic and the endocochlear potentials. The procedure used in this study is typical of the majority of investigations using electrical stimulation to elicit efferent fiber firing. Fex used decerebrated cats anesthetized with ether, throgenal and flanedil. He observed an increase of approximately three dB in the CM during stimulation of the COCB. Single fibers were studied to observe the effect of stimulating the efferent fibers electrically. Fex was able to locate 505 efferent fibers in his experimental animals. Of these, thirty-five showed resting activity which was different from typical afferent resting activity. The efferent fibers showed a regular firing of varying frequency in contrast to the typical bursts of firing observed in the afferent fibers. While afferent fibers were shown to generate firing rates up to 1000 impulses per second, efferent fibers responded to tone pips of 60dB SPL at a rate of only thirty to fifty per second with most fibers having a dynamic range of only 30dB (A dynamic range similar to afferent eighth nerve fibers). Fibers were observed to exhibit an absolute refractory state after twelve milliseconds of stimulation.

The electrical stimulation of the COCB was of 17 to 75 msec. duration. The most effective inhibition of the N_1 component of the AP response with this stimulus was observed using approximately 250 shocks per second. As the N_1 response decreased while the shock was presented, the cochlear mocrophonic was observed to increase by a maximum of three decibels. The endocochlear resting potential was also observed to increase

as a function of increasing the electrical stimulation of the COCB. The maximum increases observed were .5mV (average potentials of approximately 80mV are typical). Further increases in the stimulus strength above this did not increase the resting potential voltage.

In his summary, Fex suggests that the following statements can be made with regard to the activity of the OCB: (1) Acoustic stimulation will stimulate the auditory efferennt fibers; (2) Electrical stimulation of the COCB in the floor of the fourth ventricle will cause a decrease in the N_1 response of the eighth nerve; (3) Electrical stimulation of the COCB in the floor of the fourth ventricle will cause an augmentation of both the cochlear microphonic potential and the DC endocochlear resting potential in the cochlea. Implicit with his discussion is the suggestion that the OCB is functioning primarily as a contralateral inhibitor of afferent activity. Fex did not, however, attempt to demonstrate whether or not contralateral acoustic stimulation would have the same effect as midline electrical stimulation on the action potential, cochlear microphonic, or endocochlear potential. In another experiment Fex injected strychnine (a known efferent inhibitor) intraveneously into his experimental animals. He observed that all effects on the cochlear microphonic and action potential attributable to the efferent activity disappeared.

In 1966, Wiederhold and Chance (144) investigated the effect of changing the stimulus parameters employed on the efferent inhibition of afferent firing. They used barbituate anesthesia in cats whose middle ear muscle tendons had been sectioned, and delivered a train of shocks to the floor of the fourth ventricle, followed by presentation of an acoustic stimulus. The CM responses were averaged on a digital computer. The

results indicated that the N_1 response was significantly reduced in amplitude for the lowest click levels presented to the ear but not for the highest click levels. Even very strong OCB stimulation did not reduce N_1 amplitude at high sound pressure levels. The authors suggest that this may be the result of the differences in the waveforms of the stimuli that activate the nerve endings of the auditory nerve fibers as well as their location along the cochlea. Other investigators have also observed the dependence of afferent activity on the stimulus parameters.

Dallos (22) has suggested that when measurement of the action potential in the basal turn of the cochlea was achieved by using a differential electrode technique, the observation could only be made when using a high frequency acoustic stimulation (8Khz) since the CM amplitude masked out the AP response. The differential technique allows for a local measurement of the cochlear microphonic and a distant measure of the action potential. On the other hand Konishi and Slepian (80) observed that electrical stimulation of the efferent system resulted in CM changes only when the frequency of the acoustic stimulation was approximately 1KHz. Fex (51), Rossi, etal (117), Galabmos (57) and others have all reported that the effects of efferent stimulation are maximal when the frequency of the electrical stimulation is approximately 250 shocks per second. Konishi (80) observed an inhibitory effect on the summating potential in guinea pig using electrical stimulation of the COCB; however, he cautions that a great variation of effect was observed depending on the parameters of the acoustic signals, the parameters of the electrical stimulation of the COCB, and even the interval between COCB stimulation and the presentation of the acoustic stimulus.

The influence of one cochlea on the contralateral cochlea is well documented. It appears that the mechanisms by which this cochleo-cochlear interrelationship is effected may be found in the auditory efferent system.

Galambos, and his co-workers (62) were the first to study the cochleo-cochlear inter-relationships. The recorded the N_1 response following stimulation of one ear by a click. When the contralateral ear was exposed to a similar click, preceding the other one by 1.25 mSec., a decrease in the ipsilateral N_1 response was observed. These results were, however, discounted when it was later observed that similar results could be observed after sectioning the ipsilateral acoustic nerve.

The existence of functional cochleo-cochlear connections has been demonstrated (62). These are not connections limited to peripheral organs alone but are integrated and complemented by other connections at higher neural centers. Changes in hearing acuity of one ear associated with pathologic processes in, or following surgery of the contralateral ear have been suggested. The exact manner in which afferent-efferent interaction influences the auditory mechanism is still obscure; however, the activity of the auditory centrifugal fibers provides at least one possible explanation of the behavioral observations mentioned above. Following are some of the more important of these observations.

Investigators have hypothesized that collateral auditory efferent fibers function as a sharpening or funneling mechanism (5). Both frequency and intensity discrimination have been considered in the hypothesis. While the results of the behavioral studies in some instances tend to support this hypothesis, behavioral investigations concerning the olivo-cochlear system have not yielded conclusive evidence in this regard.

Galambos (61) using classical conditioning techniques investigated absolute thresholds for tones of 300, 500, and 1500 Hz in the presence of an unspecified masking noise before and after transection of the COCB in cats. The results revealed no change in the absolute threshold. Using implanted electrodes, the N_1 potentials were measured bilaterally in sleep and wakefulness, during anesthesia, while the animal was excited and while the animal was observing a mouse (a condition which produced changes in the neural activity in other parts of the CNS). No consistent and reliable changes were found in the ear with the middle ear muscles cut. Although conditioned responses were evident, no effect on the OCB could be observed.

Brugg, Anderson and Aitkin (14) in their study of the dorsal nuclei of the lateral lemniscus suggested that inhibitory effects in the lateral lemniscus suggested that inhibitory effects in the lateral lemniscus due to contralateral acoustic stimulation are due to impulses arriving over pathways directly from the cochlear complex of the contralateral side. They suggest that possibly the effects of stimulation of the ipsilateral ear arise from neurons in the superior olivary complex and which project to neurons in the dorsal nucleus on the same side.

In 1969, Pfalz (94) studied the effect of contralateral acoustic stimulation of the cochlear potentials in guinea pigs. A differential electrode technique was used by Tasaki, Davis and Legouiz in 1952 for recording the N_1, N_2 and CM. No changes in the action potentials or cochlear microphonic were observed by Pfaltz as a result of contralateral acoustic stimulation with pure tones or clicks. In his discussion, Pfalz suggests that the lack of evidence for a function of the olivo-cochlear

bundle is only in conflict with the findings of other investigators if it is assumed that there must necessarily be a crossed function of the bundle under non-experimental conditions. Pfalz points out that in studying crossed efferent activity,

> generally each of the two ears must be stimulated separately, for only at the level of the cochlea and the cochlear nucleus can efferent crossed action best be studied. The chief difficulty in such an experiment is in rebutting the opinion that a reduction of a potential such as the N_1/N_2 is not due to neural inhibition but rather to peripheral physical crossed masking (90).

Electrical overstimulation may yield non-physiologic inhibition due to the electrical activity itself.

> It is generally the integrative action of the synapse which limits excitation in a neural pathway whereas the nerve usually can be electrically driven to far higher spike-rates of excitation if its synaptic junction is bypassed (90).

This is the case with electrical stimulation of the COCB in the floor of the fourth ventricle since the synapse is located in the superior olivary complex.

Pfalz (94) further discussed the lack of 'natural' presentation during previous studies of the efferent system. For an example of this he refers to the stimulation of one ear using a 1KHz tone of 90dB and the other ear with a 1KHz tone of 30dB as Fex had done. Differences of this magnitude between the two ears do not occur under normal conditions in life. Rasmussen (102) as early as 1953 emphasized the function of the OCB as being, most likely, homolateral. Primary afferent fibers from the left cochlea proceed through the left cochlear nucleus to the ipsilateral and contralateral superior olivary complex. The homolateral efferent fibers to the left cochlea arise from the left superior olive while the

contralateral efferent fibers to the left cochlea arise from the right superior olive. Pfalz (94) suggests that this functionally unilateral circuit may be inhibited or potentiated by higher auditory centers such as the inferior colliculus or the medial geniculate body by way of centrifugal pathways which may contact the left olivocochlear system in the left cochlear nucleus or in the superior olivary complexes of both sides. The possibility of the right cochlea contributing to the activity of the left efferent system is thus not excluded and may be effected via other centrifugal systems.

In summary, while the centrifugal auditory system has been studied quite extensively, the physiological and behavioral data are sometimes equivocal. There are several possible sources for lack of agreement in the studies of the auditory efferent system. The use of different experimental animals may in itself be on source. In the cat, for example, no reticulo-efferent fibers have been demonstrated. The use of different levels, or type of, anaesthesia may contribute to the variations observed. Variation due to changes in stimulus (acoustic or electrical) parameters have been shown to produce equivocal results. There is even evidence to suggest the possibility that use of electrical stimulation as a means of investigating the efferent system may produce artifactual results. It is clear that additional investigation is necessary before the specific function or functions of the auditory centrifugal system will fully be understood. Persuant to this need, the present investigation examines the effect of eliminating all efferent feedback to one cochlea in guinea pig. The following chapter will present in detail the methods used in this investigation of the auditory centrifugal system.

CHAPTER III

DETAILS OF THE EXPERIMENT

Introduction

Several different techniques have been used to examine the activity of the auditory centrifugal system as has been indicated in earlier chapters. The majority of the previous studies of the physiologic activity of the efferent system have used electrical stimulation to trigger the neurons in the olivo-cochlear bundle. In the present investigation a procedure was used for sectioning the auditory efferent fibers on one side of the brain stem. Table I indicates the temporal measurement sequence. A detailed description of the experimental animals, apparatus and procedures used in this study follows.

Experimental Animals

Eight healthy white guinea pigs weighing between 400 and 500 grams served as experimental subjects for this investigation. As control for normal hearing, a normal Preyer reflex (pinna reflex to whistle) was required before the animal was accepted. The external auditory meatus and tympanic membrane were examined to eliminate guinea pigs with otitis externa or otitis media.

Surgical Preparation

The surgical preparation used in this experiment was a typical ventrolateral approach as originally described by Davis, Gernandt and Riesco-MacClure (31). The animals were anesthetized by intraperitoneal injections of sodium pentobarbital (Nembutal) using .45cc/Kg body weight as dosage. Immobilization of the animal was accomplished by intravenous injection of curare following cannulation of the left jugular vein.

Following the anesthesia a midline saggital incision of approximately 2cm was made using surgical scissors. The trachea was then cut in half anteriorally and a glass "t" cannula, with a rubber tube and a clamp regulator attached, was tied into the trachea. The animal was then fastened to a head holder which consisted of two hollow steel rods in a "C" clamp. The rods were then inserted into the ear canals and a nose clamp attached to the snout.

The auditory bulla was then exposed by deflecting the overlying tissue. The tissue on the left side of the trachea was deflected to expose the left jugular vein. This vein was then cannulated and connected to a 2-way syringe for injection of more anesthesia or curare as needed. Following this, an artificial respirator (Harbard) was connected to the glass regulator and set for 75cc per stroke with 60 strokes per minute. Surgical thread (00 size) was guided along the medial surface of the left mandible and under the tissue of the neck to exit lateral to the right carotid artery. The neck tissue was then tied loosely and pulled toward the left to allow better observation of the right auditory bulla. The right sternocleidomastoid muscle was then broken free from its insertion and deflected superiorly to expose the bulla. The right mandible was

then broken distally to broaden the field of cision around the bulla. The mandible and muscles of masticulation were tied lateralward to keep them from covering the bulla area. The right bulla was then opened to expose the cochlea within.

A dental drill (Emesco) was used to drill a kidney shaped hole (with convex side medialward) in the bulla from a point inferior to the tympanic membrane medialward in order to allow observation of the entire cochlea. Care was taken not to damage the tympanic membrane during this procedure. Following this, with the aid of an operating microscope, two holes were drilled in the basal turn of the cochlea, one in scala vestibuli and the other in scala tympani. These holes were drilled by using a needle which had been sharpened to a three sided point and attached to a hand holder. By observing the changes in the color of the bone chips when first dampened by cochlear fluid it was possible to stop penetration of the needle with a minimal loss of the perilymph. Care was taken to keep the cochlea dry with suction during drilling in order to facilitate observation of the bone penetration. At this time the pickup electrodes were introduced into scala media and scala tympani.

Measurement of the Cochlear Microphonic and Action Potential

Measurement of the cochlear microphonic (CM) and action potential (AP) was accomplished by using two stainless steel electrodes and a modified differential electrode technique as suggested by Dallos. The steel electrodes were coated with a paint (Targon) except for approximately 500 microns of the tip. The bulla was isolated from the surrounding tissue by

means of an ear speculum which had been cut back to expose an area of approximately two cm by one-and-one-half cm and attached to the head holder by a steel connecting rod. The electrodes were inserted into scala media and scala tympani and fixed to the sides of the speculum. The electrodes were held in place by fastening them to the sides of the speculum with dental cement (Emesco).

The electrodes were then attached to two preamplifiers, one an inverting and the other a non-inverting amplifier. The outputs of the two amplifiers were directed to a switching box for selection of either the CM or AP mode for display (Figures 2 and 3). In both the CM and AP modes the reference electrode was grounded to indifferent tissue via the head holder inserted into the external auditory meatus. The signal was directed to the differential input amplifier (Tektronix 2A61) of a dual beam oscilliscope. An oscilliscope camera was used to photograph the CM and AP. Photographs of both the CM and AP were made prior to cerebellar excision, following cerebellar excision and following centrifugal sectioning. A pulsed acoustic stimulation with a 250 msec duty cycle of the cochlea was maintained from the time that the electrodes were attached to the preparation until the second photograph of the cochlear microphonic and action potential was obtained.

Surgical Sectioning of Centrifugal Fibers

The course of the crossed olivo-cochlear bundle across the midline in the floor of the fourth ventricle and superior to the facial genu is well documented (60, 99, 100, 101). The homolateral efferent fibers of the superior olive have been demonstrated to loop around the ipsilateral

FIGURE II

Block Diagram of the Amplifier Configurations for the Cochlear Microphonic and Action Potential Measurements

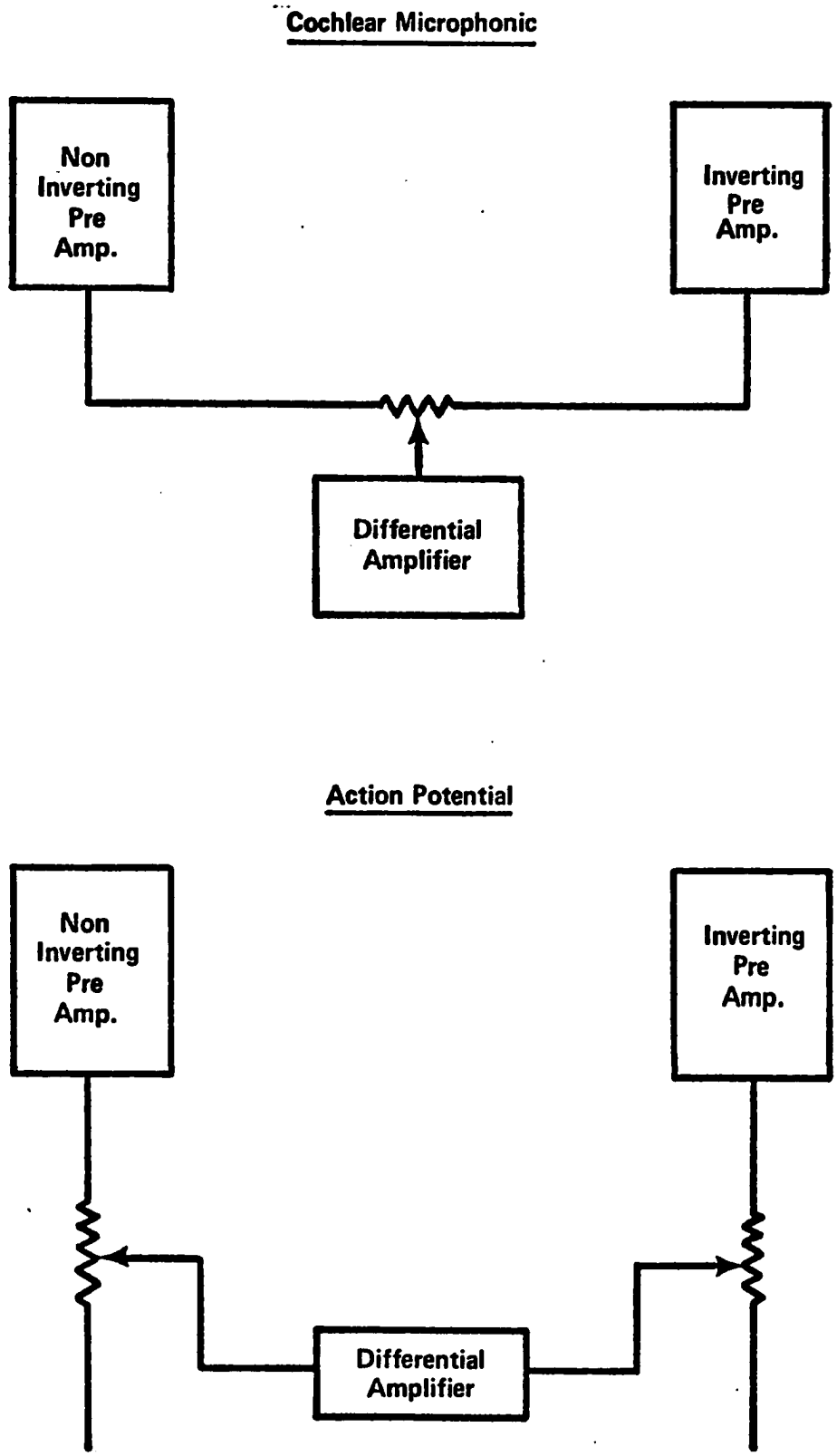
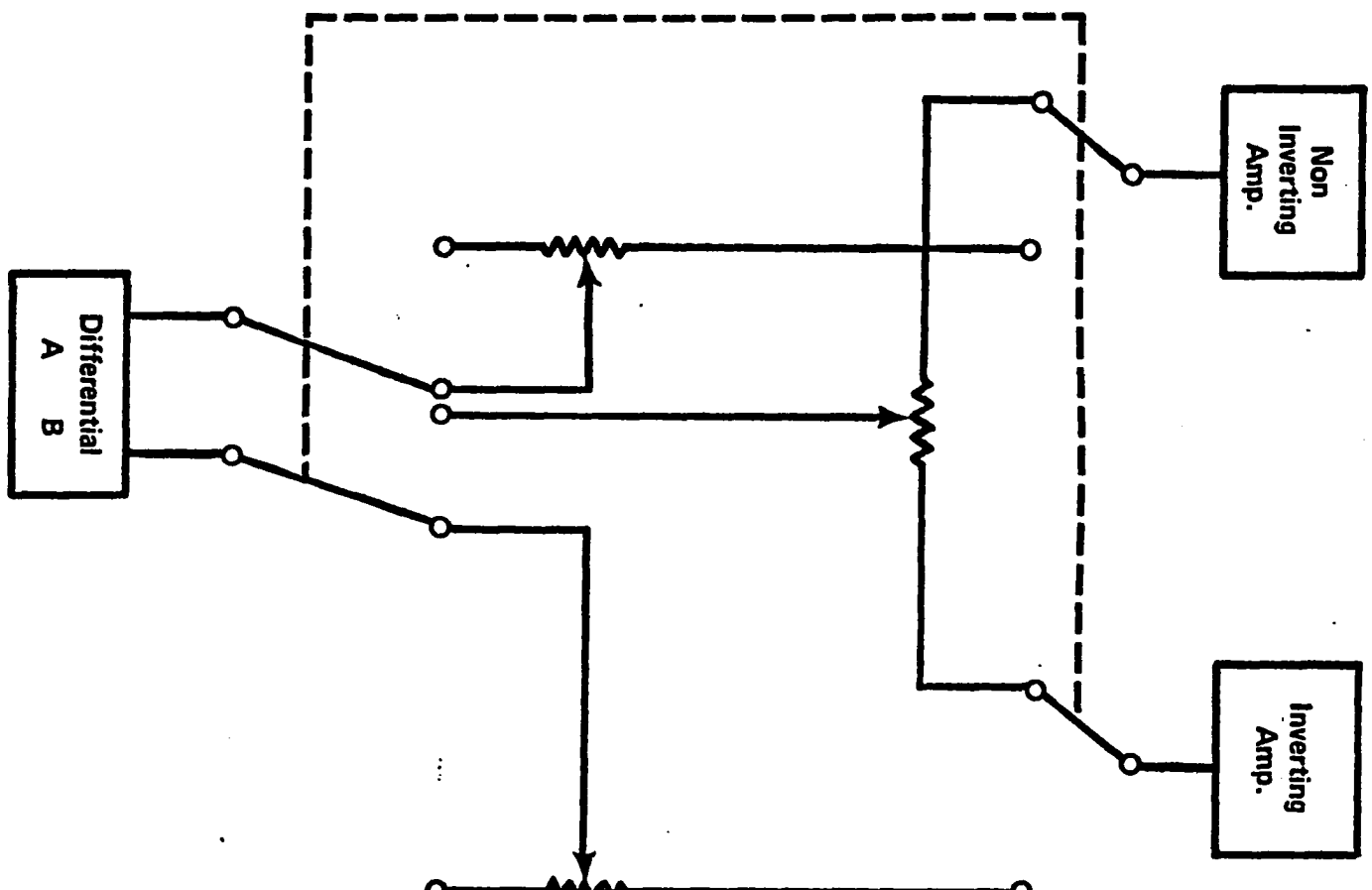


FIGURE III

Schematic Diagram of the Circuitry Used to Enable Instantaneous Switching Between the Amplifier Configurations Illustrated in Figure II



facial genu (100). Centrifugal fibers from the inferior colliculus have been shown to proceed inferiorly along the lateral lemniscus to synapse in the cochlear nuclei (38). In order to eliminate any efferent activity to the homolateral cochlea, two surgical sections were made in the brain stem of the guinea pig. Using a number ten scalpel (Board Parker), a saggital section was made approximately one mm to the right of the midline and approximately .5 mm deep running just superior to the facial genu. The second incision was a transverse section at a point .5 cm superior to the first incision on the right side of the brain stem and deep enough to section the lateral lemniscus on that side. The location of both these incisions was confirmed following one of the experimental runs by fixing the brain stem with Heidenhein-Susa solution, imbedding in collodion and staining with blue stain for microscopic examination. Figure 4 presents a schematic of the surgical lesions.

Acoustic Stimulation

A sine wave generator (Hewlett Packard 200 ABR) was used to generate a 1000Hz signal which was used to stimulate the right ear of the guinea pig. The pure tone signal was electronically switched (Grason Stadler 829C) to generate a 250mSec. pulsed tone with a 25mSec. rise and decay time for the cochlear microphonic measurement action potential measurement. The timing of the electronic switch was controlled by the use of a wave form generator (Tektronix) and two pulse generators (Tektronix). Figure 5 presents a block diagram of the apparatus used to generate the acoustic signals. Sound pressure level calibration at the earphone tip was accomplished by use of a probe microphone and microphone complement (Bruel and Kjaer).

FIGURE III

Graphic Representation of the Brain Stem Illustrating
The Cochlear Nuclei (DCN-VCN), The Inferior
Colliculus (IC), The Superior Olivary
Complex (SOC), The Facial Genu (F.G.),
And The Two Surgical Sections (1 2)
Made in this Experiment

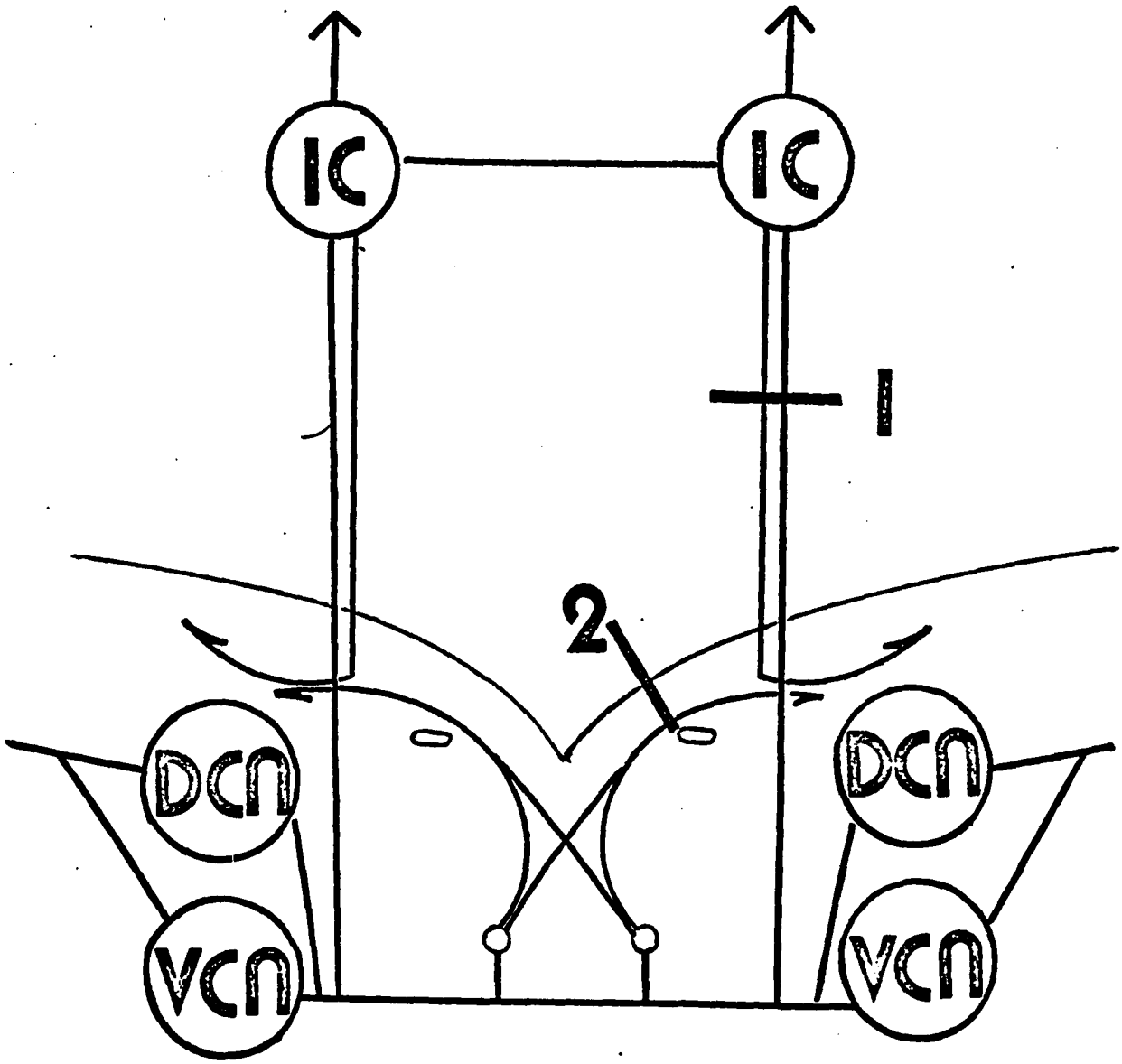
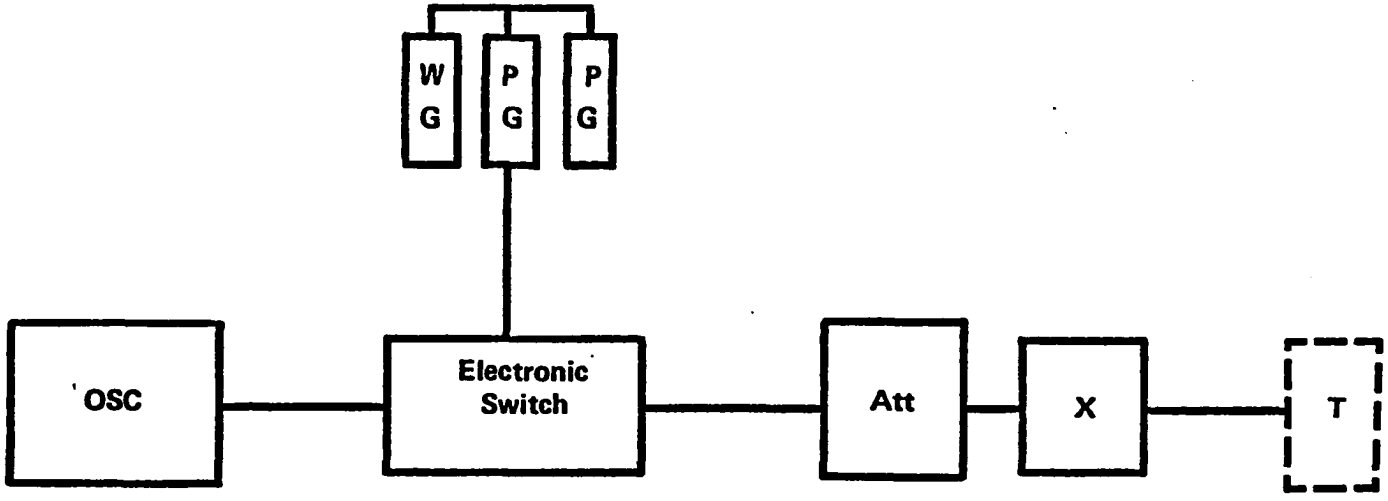


FIGURE V

Simplified Block Diagram of the Apparatus Used to Generate the Acoustic Stimulus. Shown are the Pure Tone Oscillator (OSC), the Wave Form and Pulse Generators (W.G. and P.G.), the Attenuator (Att), the Transformer (X) and Hearing Aid Transducer.



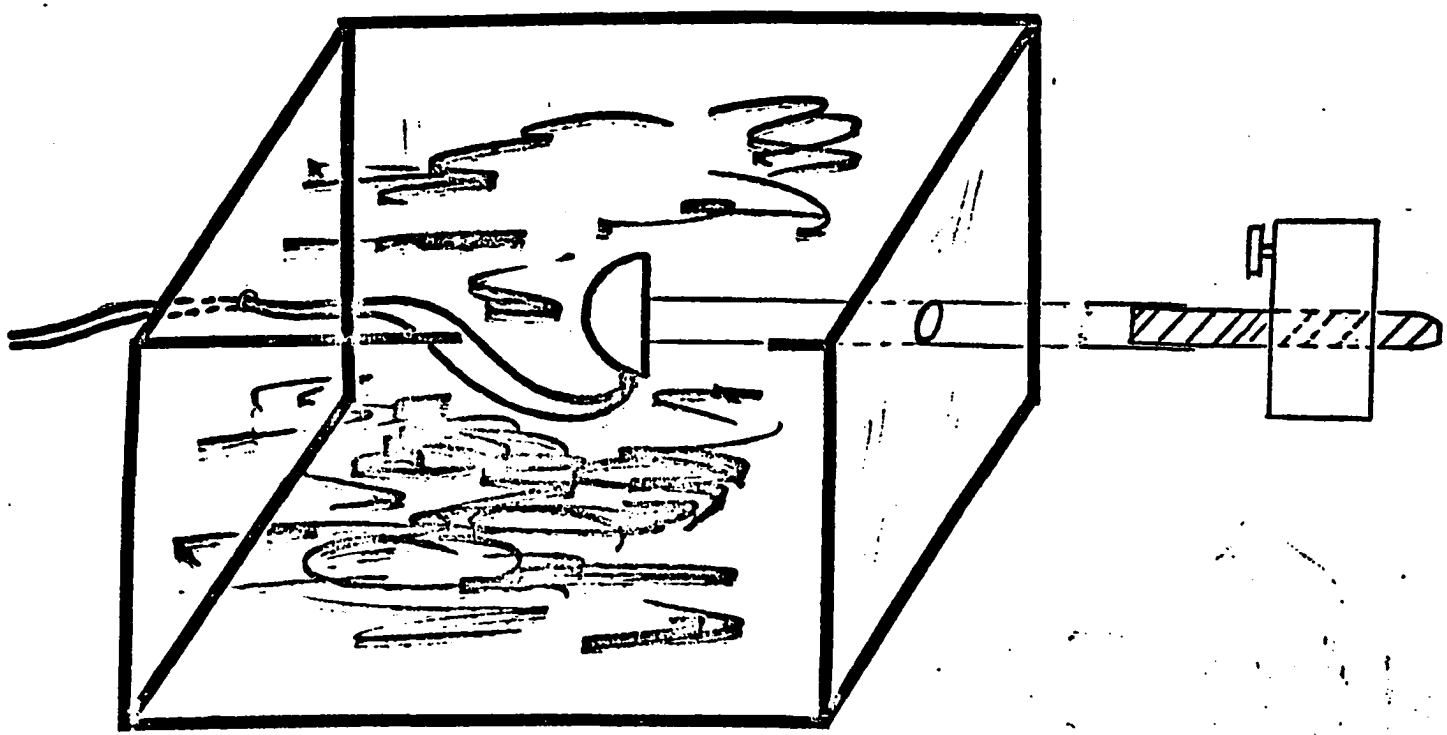
In order to isolate auditory stimulation to one ear the sound was transduced by a hearing aid receiver (50 ohms) which was acoustically isolated within a small (3"x4"x2") electrically shielded metal box packed with cotton. The sound was directed to the right ear canal by means of a polyethylene tube which was connected to a hollow metal ear holder fixed in the bony external auditory meatus. Figure 6 illustrates the transducer housing and linkage to the head holder. During all measurements the animal was isolated in a single wall acoustically treated booth (IAC).

Summary of Experimental Design

The purpose of the present study was to examine the immediate effect of sectioning the homolateral olivo-cochlear bundle and the desing centrifugal fibers in the lateral lemniscus on the cochlear microphonic and the action potential of the homolateral cochlea. The olivo-cochlear bundle was sectioned just superior to the facial genu in the floor of the fourth ventricle. The lateral lemniscus was sectioned approximately 5 cm superior to the initial incision and inferior to the inferior colliculus. To this end the effect of sectioning the efferent innervation of one cochlea on the cochlear microphonic (CM) and action potential (AP) of that same cochlea was studied. This purpose was achieved by observing the cochlear microphonic and action potential of guinea pig's cochlea under two conditions. First, the CM and AP were observed and photographed during acoustic stimulation of the right ear with a 1000 Hz pure tone at 90dB sound pressure level (SPL). Secondly, the CM and AP were observed and photographed during stimulation with the same acoustic stimulus but following surgical sectioning of the homolateral auditory

FIGURE VI

Detailed Drawing of the Electrostatically Shielded Box Housing the Transducer and the Method of Coupling the Acoustic Signal to the Ear of the Experimental Animal.



centrifugal efferent fibers of the superior olivary complex and the inferior colliculus. Observation of the cochlear microphonic after surgical excision of the cerebellum was used as an experimental control to rule out the possibility that the observed result was attributable to the trauma associated with cerebellar excision.

The following chapter presents a discussion of the results of the experiment and the conclusions drawn from them.

CHAPTER IV

RESULTS, DISCUSSION, AND SPECULATION

Introduction

The specific function of the auditory efferent fibers in the neural coding of acoustic input is yet to be explained. While several investigators have examined the activity of these fibers, no unifying hypothesis has been developed to explain their complete role. A pressing need in this area is the accumulation of sufficient information about the groups of auditory efferent bundles to allow speculation with regard to their contribution to auditory input control. The intent of this particular investigation was to contribute further information regarding the activity of this system. The experimenter examined the immediate effect of sectioning both the homolateral olivo-cochlear efferent fibers (OCB) and the homolateral centrifugal fibers from the inferior colliculus using the methods previously described.

Results

The results obtained in this investigation were analyzed with three basic questions in mind. First is the question of whether or not a generalized trauma to the posterior cranial fossa itself would cause

any significant changes in the cochlear microphonic and/or action potential; second, the effect on the cochlear microphonic sectioning of the OCB and homolateral lateral lemniscus; third, the effect of sectioning the OCB and lateral lemniscus on the action potential. Each of these questions are considered separately below.

Effect of Cerebellar Excision

In general no significant changes in either the cochlear microphonic or the action potential were observed following cerebellar excision in any of the eight animals. In all cases the absolute voltage changes observed were less than that seen in the ongoing variation prior to or following cerebellar excision. In all animals, the maximum and minimum voltages in the pre-cerebellar excision time period were within ± 4mV of the maximum and minimum voltages observed in the post-cerebellar excision time period for the cochlear microphonic.

Effect of Sectioning Homolateral OCB and Lateral Lemniscus on Cochlear Microphonic

The immediate effect of sectioning the homolateral OCB fibers and the lateral lemniscus was to produce an increase in the cochlear microphonic in every experimental animal. The measurement of the differences observed was accomplished by visual observation and noting in a ledger the maximum and minimum voltages during the various time periods previously specified. It was realized that a better technique would have been a continuous recording of the CM throughout the entire time period but due to the lack of the necessary equipment for such measurement the less desirable sampling method was chosen. The pre-section and post-section

maximum and minimum voltages were recorded and the voltage ratios of these differences were then calculated. Based on these voltage ratios the decibel equivalent was then calculated. Table II presents the voltage differences observed and the accompanying voltage ratios and decibel differences for each animal. The photographic reproductions in Illustration I typify the observations made during the measurement of the cochlear microphonic.

Since only two data points, maximum and minimum voltages, were gathered for the pre- and post-section conditions, no assumptions were made with regard to the homogeneity of variances or the normalcy of the distributions of the measure. In order to test for significant differences between the pre- and post-section conditions a powerful non-parametric test of differences was sought. Since the Walsh test of differences is considered to be a very powerful test and when compared to the parametric t test has a power efficiency of 95% for most values of N and , it appeared as the statistical test of choice (122). The only assumption underlying this test is that the populations are symmetrical, so that the mean is an accurate estimator of central tendency and equal to the median. Measurement of voltage met the requirement of measurement at an interval scale. It was felt that by using mid-range points between the manimum and minimum voltages it would not be in violation of these assumptions to apply the Walsh test to these data. The results of this test are presented in Table III and indicate that the post-section voltages were significantly larger than the pre-section voltages (.008 level of confidence).

TABLE II

SUMMARY OF COCHLEAR MICROPHONIC CHANGES OBSERVED

Voltage ratios expressed represent the variation observed in the pre section and the post section cochlear microphonic voltages.

Pre Section

Animal	Min. Voltage	Max. Voltage	Voltage Ratio	Decibel Equiv.
1.	51mV	58mV	1.137	0.595
2.	54mV	70mV	1.296	1.159
3.	70mV	84mV	1.200	0.792
4.	58mV	64mV	1.103	0.425
5.	70mV	79mV	1.128	0.461
6.	56mV	60mV	1.071	0.297
7.	65mV	71mV	1.092	0.342
8.	62mV	69mV	1.112	0.461

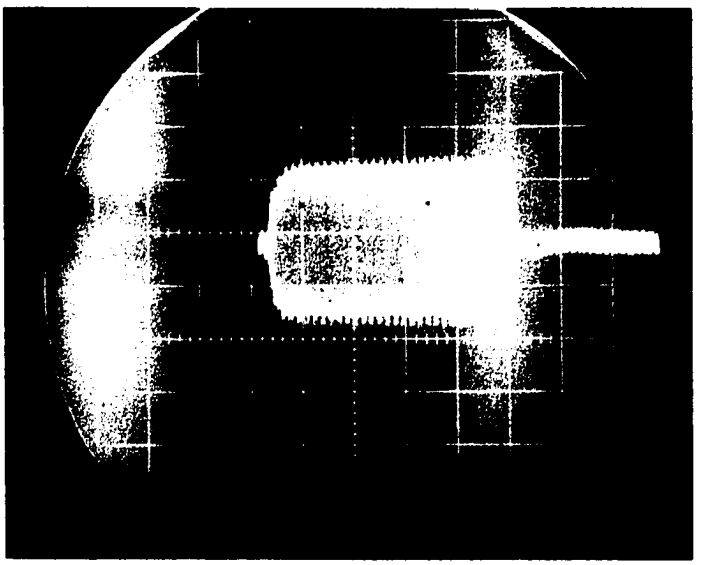
Post Section

1.	95mV	104mV	1.094	0.390
2.	115mV	126mV	1.095	0.394
3.	119mV	120mV	1.008	0.034
4.	102mV	111mV	1.088	0.366
5.	105mV	112mV	1.066	0.277
6.	104mV	110mV	1.057	0.212
7.	130mV	141mV	1.084	0.350
8.	126mV	130mV	1.031	0.128

ILLUSTRATION I

Photographs of Cochlear Microphonic Before and After Section of Centrifugal Fibers

BEFORE SECTION



AFTER SECTION

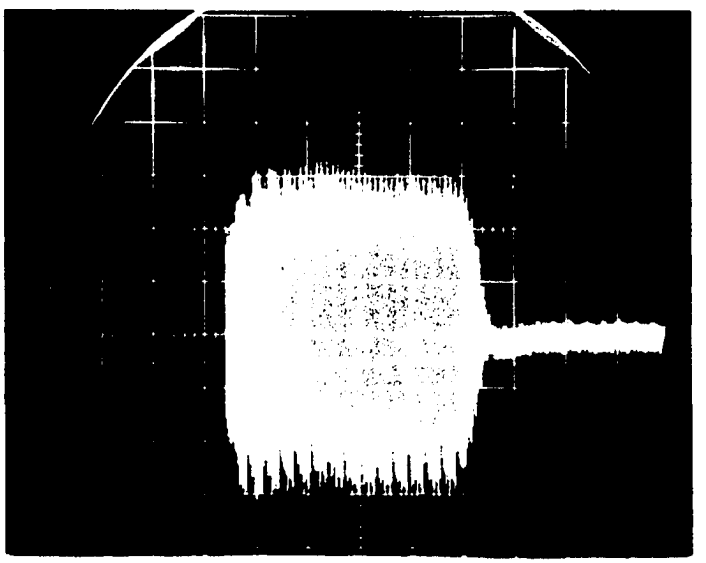


TABLE III

Summary of the Statistical Analysis
of the Cochlear Microphonic.

Animal	Pre Section Mid Range	Post Section Mid Range	Difference Scores	Decibel Difference	Rank Order Differences
1.	55.0mV	100.0mV	45.0	2.595	d_4 45.0
2.	62.5mV	120.0mV	57.5	2.833	d_6 57.5
3.	77.5mV	119.5mV	42.0	1.701	d_2 42.0
4.	62.5mV	106.0mV	44.5	2.294	d_3 44.5
5.	75.0mV	107.5mV	32.5	1.562	d_1 32.5
6.	57.5mV	107.0mV	49.5	2.616	d_5 49.5
7.	67.5mV	135.0mV	67.5	3.013	d_8 67.5
8.	65.0mV	128.0mV	63.0	2.942	d_7 63.5

Statistical Summary of Walsh Test

If d_8 0 or d_1 0 with N=8
Scores are significantly different at .008 level

Effect of Sectioning the Homolateral OCB and Lateral Lemniscus on the Action Potential

The immediate effect of sectioning the homolateral OCB fibers and the lateral lemniscus was to produce a reduction of the action potential. As with the cochlear microphonic the measurements were obtained by visual observation of the oscilliscope for the time period specified. The maximum and minimum voltages for the pre-section and the post-section conditions were then recorded. Table IV presents the maximum and minimum voltages, the voltage ratios and the decibel equivalents for these ratios observed in both the pre- and post-section conditions for all animals. In four of the animals the reduction of the action potential was greater than the minimum discernable AP voltage on the oscilliscope (10mV). In each of these cases, the voltage was taken to be less than 10mV and this figure was used to calculate the difference scores. The photographic reproductions in Illustration II typify the observations made of the pre- and post-section action potentials.

As in the case of the cochlear microphonic it was felt that a non-parametric test of differences would be most applicable in this case. Again, the Walsh test of differences was chosen and the results of this test indicate that the pre- and post-section action potential voltages were significantly different at the .008 level of confidence. Table V summarizes the statistical analysis used.

In summary, it appears that sectioning the centrifugal input to one cochlea has a specific effect on the cochlear microphonic and action potential of that cochlea which is not the result of a generalized neural trauma to the posterior cranial fossa. The following section discusses the results obtained in this investigation.

TABLE IV

SUMMARY OF ACTION POTENTIAL CHANGES OBSERVED

Voltage ratios expressed represent the variation observed in the pre section and the post section cochlear microphonic voltages.

Pre Section

Animal	Min. Voltage	Max. Voltage	Voltage Ratio	Decibel Equiv.
1.	70mV	80mV	1.142	0.569
2.	58mV	70mV	1.206	0.792
3.	60mV	76mV	1.266	1.004
4.	76mV	84mV	1.105	0.607
5.	50mV	68mV	1.360	1.335
6.	64mV	70mV	1.093	0.374
7.	50mV	66mV	1.320	1.206
8.	68mV	70mV	1.029	0.086

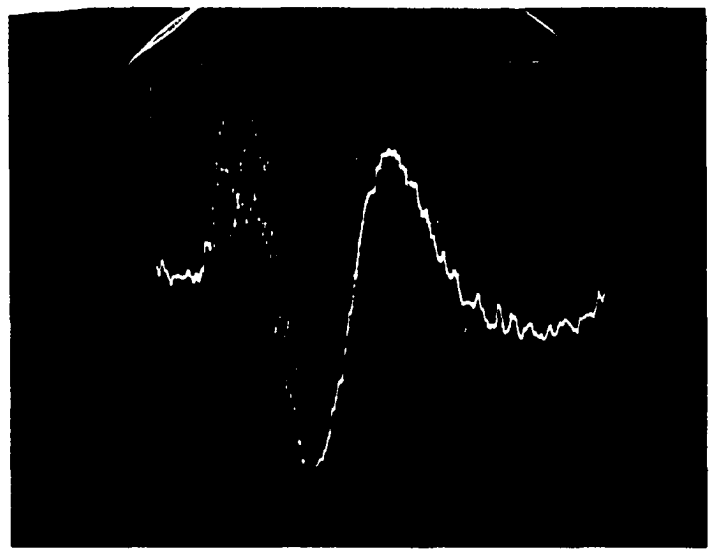
Post Section

1.	10mV	10mV	1.000	0.000
2.	10mV	10mV	1.000	0.000
3.	10mV	10mV	1.000	0.000
4.	26mV	30mV	1.153	0.607
5.	14mV	20mV	1.426	1.523
6.	30mV	42mV	1.400	0.128
7.	10mV	10mV	1.000	0.000
8.	10mV	10mV	1.000	0.000

ILLUSTRATION II

Photographs of Action Potential Before and After Surgical Section of Centrifugal Fibers

BEFORE SECTION



AFTER SECTION

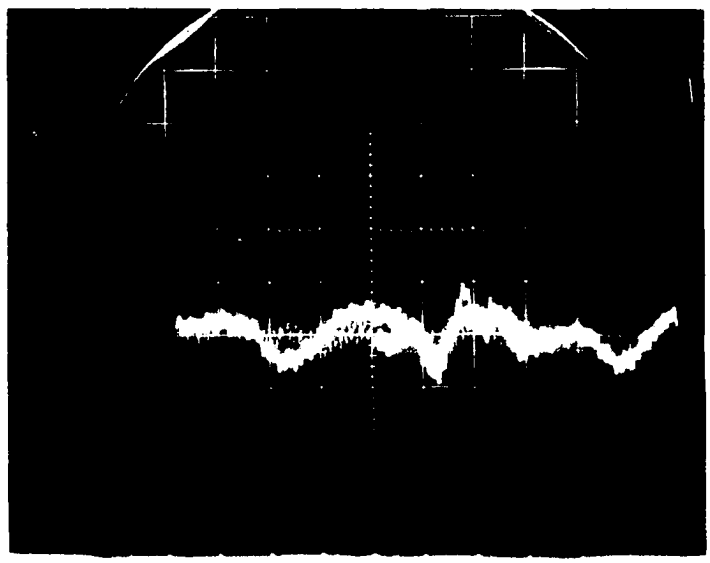


TABLE V

Summary of the Statistical Analysis
of the Action Potential

Animal	Pre Section Mid-Range	Post Section Mid-Range	Difference Scores	Decibel Difference	Rank Order Differences
1.	75.0mV	10.0mV	65.0	8.750	d_8 65.0
2.	64.0mV	10.0mV	54.0	8.061	d_5 54.0
3.	68.0mV	10.0mV	58.0	8.325	d_6 58.0
4.	80.0mV	28.0mV	52.0	4.559	d_4 52.0
5.	59.0mV	17.0mV	42.0	5.403	d_2 42.0
6.	67.0mV	36.0mV	31.0	2.697	d_1 31.0
7.	58.0mV	10.0mV	48.0	7.634	d_3 48.0
8.	69.0mV	10.0mV	59.0	9.390	d_7 59.0

Statistical Summary of Walsh Test

If d_8 0 or d_1 0 with N=8,
Scores are significantly different at .0008 level.

Discussion

The primary concern of this investigation was to establish the immediate effect of sectioning the homolateral centrifugal fibers to one cochlea on the cochlear microphonic and action potential recorded from that same cochlea. The conclusion based on the results obtained is that there is indeed an immediate effect observed by sectioning the homolateral centrifugal fibers, the effect being an increase in the cochlear microphonic voltage and a decrease in the action potential voltage. This effect is similar to that observed in investigations using electrical stimulation in the floor of the fourth ventricle to trigger olivo-cochlear fiber activity.

The results observed in this study suggest several possible conclusions as to the cause of these changes. Of consideration, first is the question of whether or not the effects observed are the result of generalized neural trauma secondary to the surgical procedures involved, rather than to the section of the OCB and lateral lemniscus per se. Second, is the consideration of whether or not the results in whole or part, derive from damage to other structures or neural pathways. Finally, if the results are, indeed, attributable solely to the sectioning of the OCB and lateral lemniscal fibers, then is this effect a short-term effect of acute trauma or is it a permanent effect truly representative of the interruption of the pathways. Each of these questions will be considered separately in the following discussion.

Generalized Neural Trauma

It is doubtful that the changes in the cochlear potentials were due to general trauma since one would expect to see these changes following cerebellar excision inasmuch the trauma to the posterior cranial fossa would far exceed that which is created by the sectioning of the auditory centrifugal fibers. Since in this as well as several other investigations, cerebellar excision itself did not produce changes in the control potentials (CM and AP), it seems reasonable to rule out a general traumatic effect as the cause of the changes in the cochlear potentials due to the nueral trauma. Also, in one animal in this study a ten hour observation of the CM following cerebellar excision produced no significant changes. Previous investigation has indicated that sectioning of only the auditory afferent fibers does not produce significant changes in the cochlear microphonic (59). If no changes in the CM were observed following afferent sectioning, it is doubtful that the sections used in this study would cause such changes due to the trauma alone. If the effect observed was then due to interruption of the OCB and lateral lemniscus pathways, it is doubtful that the effects observed would diminish following recovery from the trauma of the sectioning since the central nervous system does not have the capability for regeneration of nerve fibers in their original pathway.

Direct trauma to the first order afferent neurons of the VIII nerve was avoided in this investigation by the location of the site for surgical sectioning of the centrifugal fibers. The section of the olivocochlear fibers was achieved by cutting these fibers dorsal to the facial genu. The descending fibers of the inferior colliculus were cut in the lateral leminscus which would only involve second order afferent neurons.

Also the general trauma to the posterior cranial fossa induced by cerebellar excision would far exceed that produced by OCB sectioning alone, thus suggesting that the effects observed are the direct result of the interruption of the efferent fibers.

Damage to Other Structures or Pathways

With regard to the second consideration, that being the question as to whether the results observed were the effect of some neural activity other than the auditory centrifugal system, it is again doubtful that this would explain the cause of the observed effects. In the first place, the location of the olivo-cochlear bundle has been confirmed in several investigations and the superficial location of these fibers provides easy access to sectioning superior to the facial genu. The location of the lateral lemniscus is also well documented and surgical section used in this investigation was deep enough so as to insure that these fibers were included in the section. The question of whether or not sectioning of neural fibers not associated with either the crossed olivo-cochlear bundle or the descending centrifugal fibers of the lateral lemniscus may influence the Ap and CM potentials is also pertinent. While no histological confirmation of all fibers sectioned was obtained, the depth of the section at the level of the facial genu should preclude direct damage to any but the crossing olivo-cochlear fibers. While no histological confirmation to assure that only a partial section of these fibers was not effected, reference to a sterotaxic atlas was used in an attempt to prevent this possibility. Further, at the level of section of the lateral lemniscus, the fibers involved would include only some of the brachium

conjunctivium, the central tegmental tract, and the medial lemniscus, none of which would seem likely to influence either the VIII nerve action potential as recorded from the cochlea or the cochlear microphonic.

Included in the question of whether or not the effect observed was the result of OCB and lateral lemniscal efferent activity alone is the implication that the auditory efferent system is functioning as both an inhibitory and a facilatory network. If this is the case then the results seem more logical.

The results obtained in this investigation were the product of cutting both the homolateral olivo-cochlear bundle and the descending centrifugal fibers in the lateral lemniscus which complicates comparison with the studies using electrical stimulation. The sub-cortical control centers such as the olivo-cochlear bundle are probably subservient to higher cortical control centers which are phylogenetically the younger systems. The activity of the descending centrifugal fibers may influence the auditory input by way of their action on the sub-cortical control centers. Apparently, the net results of the activity of the higher centrifugal and subcortical control centers is an interplay of excitation and inhibition resulting in neural coding for perception of subtle acoustic differences.

The magnitudes and temporal order of events occurring at the two ears must be reflected in some usable neural code. Sensitivity of an auditory neuron to the interaural phase difference of low frequency tones, for example, is the result of convergence of periodic excitatory and inhibitory events evoked by stimulation of each ear (103). The importance of the olivary complex in this coding is demonstrated by the phase

sensitivity of neurons in the superior olivary complex which is highly correlated with the relative timing of the periodic excitatory and inhibitory events evoked by stimulation of each ear (67).

It is recognized that the limits of this particular investigation restrict the latitude of speculation possible, however, with the direction of future investigation in mind, the possible dual function (inhibitory and facilitory) of the auditory efferent system is suggested.

Short Term Trauma Effect Versus True Pathway Interruption Effect

That stimulation and destruction of the same neural fibers would produce similar results, as previously mentioned, is disconcerting. Perhaps the effect observed in the studies using electrical stimulation was the result of a potentiation of the nerve fibers creating a condition similar to that observed when the nerve is in absolute refractory period. It has been further suggested that the effect of electrical stimulation in the floor of the fourth ventricle does not represent normal physiologic activity since electrical stimulation bypasses all the synapses of the compound olivo-cochlear system.

> It is generally the integrative action of the synapse which limits excitation in a neural pathway, whereas the nerve usually can be driven to far higher spike-ratios of excitation if its synaptic junction is bypassed (96).

If, then, the results of the previous investigations are due to 'over-driving' the nerve rather than to the normal physiologic response, perhaps the similarity between those results and the results obtained in the present study is a product of the electrical shock having a similar effect as the surgical sectioning.

The current information with regard to the specific function of the auditory efferent system is limited and the results of previous investigations seem to be ambiguous. This, however, is often the case in attempts to explain neural phenomena by investigators using different approaches. The following section will attempt to present one possible explanation of the results obtained in this and previous investigations which will generate a working hypothesis for further investigation, if nothing else.

Speculation Based on Current Findings And an Overview of the Literature

Several studies pertaining to the activity of the auditory centrifugal system indicate possible explanations of the manner in which it functions.

Investigations of the ventral cochlear nucleus indicate the possibility that this may be one focal point for both homolateral and contralateral centrifugal activity. Observations of decreases and even complete elimination of the action potential in the ventral cochlear nucleus as a result of contralateral acoustic stimulation have been attributed to the auditory efferent system (92). The observations are especially significant in attempting to explain localization phenomenon. A commissurectomy in the trapezoid body of cats reduces their localization capabilities by a factor of two. The surgical effect is to prevent efferent fibers from crossing to the ventral cochlear nucleus and thus the inhibitory activity of this system is retarded.

The effect of the centrifugal fibers on second-order afferent neurons has also been suggested. Dunker and his co-workers (33) have

observed inhibition of the second-order afferent neurons as a result of contralateral acoustic stimulation. As in all previous studies the latency and magnitude of the effect was influenced by the frequency and intensity of the acoustic stimulation.

The study of the activity of the olivo-cochlear system is further complicated by the presence of corticofugal fibers which connect the temporo-insular cortex with the inferior colliculus (35). From this location, further centrifugal fibers descend to the cochlear nuclei (104). Fibers have been shown to connect the ventral cochlear nucleus of the contralateral side (33). The ventral cochlear nucleus also receives ipsilateral fibers from cells within the superior olivary nucleus (107). The existence of these several centrifugal systems complicates overall speculation in any specific instance; however, the observation of the behavior of the system as a unit suggests certain possible roles for the auditory centrifugal fibers.

Increases in the differential threshold upon contralateral stimulation with a signal of the same frequency have been observed by Chocholle (16). A decrease in the differential threshold, however, has been observed when the contralateral stimulus was of a different frequency. The dependence of the specific efferent effect on the stimulus parameters in physiologic studies may explain this differential effect. Galambos and his collegues (62), suggest that it is the inhibitory activity of the reticular centrifugal fibers. The reduction of the recruitment sensation in one ear by exposing the contralateral ear to the same sound is explained as a product of "recruitment-compensating" crossed neural inhibitory efferents while degeneration of efferent inhibitory tracts may result in central

recruitment (33). The recruitment phenomenon itself has been attributed to the elimination of an inhibitory effect that certain sections of hair cells exert upon their surrounding cells which may be effected through the efferent fibers there. This phenomenon in the sense of vision is well documented in studies of Mach band activity of collateral afferent fibers. Perstimulatory adaptation which employs a monaural stimulation technique can be inhibited using dichotic stimulation which suggests the effect of an intercochleo-bulbo-cochlear efferent activity.

The interference of other sensory systems on the auditory system has also been attributed to the activity of the auditory centrifugal fibers (126). Hahn and Demechelis have assessed auditory adaptation using the tone decay test. In one of the experimental conditions a light signal was also applied. In all of the subjects, the introduction of the light stimulus shortened the time of perception of the signal at threshold. The authors suggested the efferent cochlear fibers as the physiologic bases for their results.

The role of the reticular formation of the brain stem has also been studied with respect to its effect on the control of auditory input. Connections from the auditory afferent fibers to the reticular formation have been demonstrated both from the mesencephalon and the metencephalon (104). Acoustically evoked potentials have been recorded from the reticular substance (107). In turn collateral fibers from the reticular formation have been described coursing to all sensori-nuclei of the brain stem. In general, the reticular formation have been described coursing to all sensori-nuclei of the brain stem. In general, the reticular formation serves as a cortical arousal system and changes in the auditory evoked potentials

have been observed as a result of changes in the reticular system activity (117). Thus, the general activity of other auditory centrifugal fibers may well be modified by the excitatory state of the cortex or lower brain stem neurons, or on the other hand, impulses reaching the auditory areas may modify the excitatory state of the reticular substance (116).

If, then, one can accept the apparent duality of function in the auditory centrifugal system, a plausable hypothesis with regard to its overall activity evolves. Neural system activity in general is recognized as being the product of a combination of both inhibitory and excitatory processes as observed in the generation of exictatory and inhibitory post synaptic potentials. Evidence previously mentioned, suggests this same phenomenon exists within the auditory centrifugal system. Eventually all changes in the auditory centrifugal system could influence activity at the ventral cochlear nucleus. Even centrifugal fibers from the temporal insular cortex which proceed to the inferior colliculus are indirectly connected through lateral lemniscal fibers to the ventral cochlear nucleus. Complex interaction through collateral fibers have been demonstrated between the ventral cochlear nucleus and the superior olivary complex. It is suggested, therefore, that this is the most likely point for afferent-efferent interaction and whether the primary control is from the superior olive to the ventral cochlear nucleus or the reverse is still open to speculation. If, then, the effect of all centrifugal fibers is a combination of inhibition and excitation depending on the specific auditory input, a mechanism for central coding of auditory information is available. In the specific instance of this investigation an unusual acoustic stimulation (stimulation at a level low enough so as not to produce any visable

CM in the contralateral ear) was used to trigger auditory afferent activity. In cases of natural acoustic stimulation (bilateral stimulation in the environment) the perception of variation in signal location is most likely effected through contralateral inhibition and ipsilateral facilitation of afferent input. If one elminiates the ipsilateral facilitation of the afferent input, a reduction in the ipsilateral action potential would be expected which is the very observation made in this particular study. This hypothesis suggests only one of the probably many functions of the auditory centrifugal system, that of localization facilitation; however, the data obtained in this study may be reflecting the activity of this system as it functions in an intrasensory gating capacity.

The total effect of the combination of auditory centrifugal systems is a complex system for control of auditory input as well as cross modality coding. A self regulating network which has the capacity for control at various levels within the brainstem is thus observed. The morphologic and physiologic evidence previously presented indicated the existence of a system which from any level can modify the activity of any other level in the transmission of the auditory action potential to the cerebral cortex. This network allows for feedback which can alter the auditory input from something as simple as changing the position of the head to complex biochemical changes affecting the coding of neural information at the hair cells or attenuation of the input stimulus via the middle ear muscle reflex.

In order to further specify the exact nature of the centrifugal activity in several different situations, simultaneous measurement of changes in the major brain stem and cortical centers as a function of

very specific stimulation and/or sectioning of individual units of the centrifugal fibers would be of much benefit in further describing their function. The activity of the centrifugal system during stimulation of other sensory systems would also contribute to understanding the general area of cross modality inhibition as well as the specific activity of the auditory system's efferent activity. The following chapter summarizes the present investigation.

CHAPTER V

SUMMARY AND SUGGESTIONS FOR FURTHER RESEARCH

Introduction

The mechanisms by which the auditory system decodes the acoustic stimulus striking the tympanic membrane into useable neural symbols are highly complex. One of the most difficult to understand is the function of the auditory centrifugal system. Investigators have studied the activity of this system primarily by examining the effect on cochlear potentials of either sectioning or stimulating the fibers. The results of these investigations have not as yet led to the development of a unifying hypothesis with regard to the exact manner in which the centrifugal fibers function in the control of afferent neural input.

Experimental Design

The purpose of the present investigation was to examine the function of the efferent centrifugal fibers in the brain stem of the guinea pig. The major concern of this study was the activity of the homolateral olivo-cochlear bundle and the centrifugal fibers of the lateral lemniscus on two specific indicants of cochlear activity: the cochlear microphonic

and action potential. This goal was accomplished by sectioning the OCB at a point superior to the facial genu in the fourth ventricle and sectioning the lateral lemniscus at a point between the inferior colliculus and cochlear nuclei. Recordings of the cochlear microphonic and action potential of the VIII nerve were made from the basal turn of the cochlea using electrodes placed in scala tympani and scala vestibuli.

Results and Conclusions

The results of this investigation indicate that sectioning of the homolateral efferent feedback to the cochlea causes an immediate reduction in the action potential and an increase in the cochlear microphonic of that cochlea. It is suggested that the auditory efferent system functions both to inhibit and facilitate auditory afferent input to the central nervous system. It is hypothesized that the control of the auditory centrifugal system is effected by the activity of the superior olivary complex in conjunction with and via collateral connections to the ventral cochlear nucleus. While the specific activity of the several centrifugal divisions within the auditory system may be further clarified as more information is obtained, the above mentioned hypothesis serves as one possible explanation of the results observed in this and previous investigations of that system.

Suggestions for Future Research

Much of the confusion with regard to the function of the auditory centrifugal system may lie in the use of unnatural stimulus conditions during the experiment to elicit responses from the auditory fibers and the cochlea. Two important considerations in studying this system are

suggested. First, the acoustic stimulation of the cochlea should be attempted using binaural stimulation and varying the levels to the two ears while observing central nervous system changes. Second, simultaneous measurements of centrifugal activity in several locations seems necessary to furnish information with regard to the total effect of this system on the afferent input. Electrical stimulation in locations providing a synaptic junction between the location of the electrical stimulation and the measurement of neural or cochlear activity would reduce the possibility of the electrical stimulus itself influencing the results obtained. The complex interaction of all of the centrifugal fibers prohibits valid speculation with regard to the system as a whole in experiments examining only individual units thereof.

BIBLIOGRAPHY

OF SOURCES CONSULTED

1. Agin, D., and Lowy, K. Effect of electrical stimulation on peripheral auditory responses. Laryngoscope, 1962, 72: 361-366.

2. Aitkin, M., Anderson, S., and Brugge, T. Tonotopic organization and discharge characteristics of single neurons in the nucleus of the lateral lemniscus of the cat. J. Neurophysiol., 1970, 33: 421-440.

3. Appleby, S. V., McDermick, P., and Scott, J. W. The sound evoked cerebral response as a test of hearing. EEG Clin. Neurophysiol., 1963, 15: 1050-1055.

4. Barnes, W. T., Magoun, H. W., and Ranson, S. W. The ascending auditory pathway in the brainstem of the monkey. J. Com. Neurol., 1943, 79: 129-152.

5. Bekesy, G. von. Funneling in the nervous system and its role in loudness and sensation intensity on the skin. J. Acoust. Soc. Amer., 1958, 30: 399-412.

6. Bekesy, G. von. Experiments in Hearing. New York: McGraw-Hill, 1960, 314-321.

7. Bickford, R. G. Nature of computer averaged evoked potentials in man. Fed. Proc., 1963, 22: 678.

8. Black, S., and Walter, W. G. Effects on anterior brain responses of variation in the probability of association between stimuli. J. Psychosom. Res., 1965, 9: 33-34.

9. Bocca, E. Notes on the innervation of the cochlea. I.. Arch. Otolaryng., 1952, 55: 188-205.

10. _____. Notes on the innervation of the cochlea. II. Arch. Otolaryng., 1953, 58: 690-703.

11. Borsanyi, S. J., and Blanchard, C. L. Auditory evoked brain responses in man. Arch. Otolaryng., 1964, 80: 149-154.

12. Bradley, P. B., and Mollica, A. The effect of adrenaline and acetylcholine on single unit activity in the reticular formation of the decerebrate cat. Arch. Ital. Biol., 1958, 96: 168-186.

13. Brazier, M. A. B. Some uses of computers in experimental neurology. Exp. Neurol., 1960, 2: 123-143.

14. Brugge, T., Anderson, S., Aikin, M. Responses of neurons in the dorsal nucleus of the lateral lemniscus of cat to binaural tonal stimulation. J. Neurophysiol., 1970, 33: 441-458.

15. Chang, H. T. The repetitive discharge of corticothalamic reverberating circuit. J. Neurophysiol., 1950, 13: 235-258.

16. Chocholle, R. Le seuil differentiel d'intensite en presence d'un son controlateral de frequence differente. Acustica, 1959, 9: 309-315.

17. Candiollo, L., Filogamo, G., Rossi, G. The morphology and function of auditory input control. Translations of the Beltone Institute for Hearing Research. 1967, p. 20.

18. Churchill, J. A., Schukneckt, H. F., and Doran, R. Acetylcholinesterase activity in the cochlea. Laryngoscope, 1956, 66: 1-15.

19. _____. The relationship of acetylocholinesterase in the cochlea to the olivocochlear bundle. Henry Ford Hosp. Bull., 1959, 7: 202-210.

20. Cioce, C., and Pestalozza, G. a: Considerazioni sull'adattamento binaurale e monoaurale. Societe Internationale d'Audiologie. 4eme Congres, 1958, pp. 386-394.

21. Dallos, P. J. Dynamics of the acoustic reflex: phenomenological aspects. J. Acoust. Soc. Amer., 1964, 36: 2175-2183.

22. Dallos, P. J. Northwestern University, Evanstown, Ill. Personal Communication, 1971.

23. Davis, H. Slow cortical responses evoked by acoustic stimuli. Proc. of a conference held in Toronto, Canada. Acta. Otolaryng., 1964, Supp. 206, 128-134.

24. _____. Some principles of sensory receptor action. Physiol. Rev., 1961, 41: 391-416.

25. _____. Advances in the neurophysiology and neuroanatomy of the cochlea. J. Acoust. Soc. Amer., 1962, 34: 1377-1385.

26. Davis, H., Davis, P. A., Loomis, A. L., Harvey, E. N., and Hobart, G. Electrical reactions of the human brain to auditory stimulation during sleep. J. Neuro-Physiol., 1939, 2: 500-514.

27. Davis, H. and Yoshie, N. Human evoked cortical responses to auditory stimuli. Physiologist, 1963, 6: 164.

28. Davis, P. A. Effects of acoustic stimuli on the waking brain. J. Neurophysiol., 1939, 2: 494-499.

29. Davis, H., and Derbyshire, A. J. The action potential of the auditory nerve. Amer. J. Physiol., 1935, 113: 476-504.

30. Davis, H., Gernandt, B.E., and Riesco Mac-Clure, J. S. Threshold of action potentials in ear of guinea pig. a. J. Neurophysiol., 1950, 13: 73-87.

31. Davis, H., Gernandt, B. E., and Riesco-MacClure, J.S. Threshold of action potential in ear of guinea pig. b. J. Neurophysiol., 1950, 13: 98-101.

32. Davis, H., Tasaki, I., and Goldstein, R. Peripheral origin of activity with referenee to the ear. Cold. Spr. Harb. Symp. Quant. Biol., 1952, 17: 143-154.

33. Desmedt, J. E. Neurophysiological mechanisms controlling the auditory acoustic input. Neural Mechanisms of the Auditory and Vestibular Systems; G. L. Rasmussen and W. F. Windle, Eds., 1960, pp. 152-164.

34. Desmedt, J. E. and Monaco, P. Suppression par la strychnine de l'effet inhibiteur centrifuge exerce par le faisceau olivo-cochleaire. Arch. Int. Pharmacodyn, 1960, 129: 244-248.

35. Desmedt, J. E. Descending activity in the auditory system. Science, 1964, 146: 433-443.

36. Desmedt, J. E. and Delwaide, P. J. Particularites fonctionelles de l'inhibition efferente cochleaire chez le pigeon. Arch. Int. Bioch., 1964, 72: 341-346.

37. Desmedt, J. E. and La Grutta, G. The effect of selective inhibition of pseudocholinesterase on the spontaneous and evoked activity of the cat's cerebral cortex. J. Physiol., 1957, 136: 20-40.

38. _____. Function of the uncrossed efferent olivo-cochlear fibres in the cat. Nature, 1963, 200: 472-474.

39. Desmedt, J. E., and Mechelse, K. Suppression of acoustic input by thalmic stimulation. Proc. Soc. Exp. Bio., 1958, 99: 772-775.

40. _____. Corticofugal projections from temporal lobe in cat and their possible role in acoustic discrimination. J. Physiol., 1959, 147: 17P-18P.

41. Desmedt, J. E. and Monaco, P. Suppression par la strychnine de l'effet inhibiteur centrifuge exerce par le faisceau olivo-cochleaire. Arch. Int. Pharmacodyn., 1960, 129: 244-248.

42. _____. a: Mode of action of the efferent olivo-cochlear bundle on the inner ear. Nature, 1961, 193: 1263-1265.

43. _____. b: Stimulation sterotaxique des vois afferentes dans le systeme nerveux auditif de chat. (Demonstration). Arch. Int. Pharmacodyn., 1961, 132: 492-494.

44. _____. The pharmacology of a centrifugal inhibitory pathway in the cat's acoustic system. Proc. First Intern. Pharmacol. Meet., 1962, Vol. 8: 183-188.

45. Desmedt, J. E., LaGrutta, G., and LaGrutta, V. Auditory response characteristics by efferent olivo-cochlear bundle (OCB) inhibition. Fed. Proc., 1963, 22: 677-687.

46. Engstrom, H. Electron micrographic studies of the receptors of the organ of Corti. Neural Mechanisms of the Auditory and Vestibular Systems, G. L. Rasmussen and W. F. Windle, Eds., 1960, pp. 48-64.

47. _____. Discussion of the paper of C. A. Smith, "Innervation of cochlea". Trans. Amer. Otol. Soc., 1961, 44: 58-60.

48. Engstrom, H., Sjoestrand, F. S., and Wersell, J. The fine structure of the tone receptors of the guinea pig cochlea as revealed by the electron microscope. Proceedings of the Fifth International Congress of Otorhinolaryngology, Amsterdam, 1953, pp. 563-568.

49. Fernandez, C. The innervation of the cochlea (guinea-pig). Laryngoscope, 1951, 61: 1152-1172.

50. Fex, J. Augmentation of the cochlear microphonics by stimulation of efferent fibres to cochlea. Acta Otolaryng. (Stockh.), 1959, 50: 540-541.

51. Fex, J. Auditory activity in centrifugal and centripetal cochlear fibres in cat. A study of a feedback system. Acta Physiol. Scand., 1962, 55: suppl. 189.

52. _____. Centrifugal activity in the olivo-cochlear bundle: a single unit analysis from a feedback system. Intern. Audiol., 1963, 2: 45-47.

53. _____. Auditory activity in uncrossed centrigugal cochlear fibres in cat. A study of a feedback system, II. Acta Physiol. Scand., 1965, 64: 43-57.

54. Fish, U. P., and Ruben, R. J. Electrical acoustical response to click stimulation after section of the eighth nerve. Acta Oto-Laryng. (Stockh.), 1962, 54: 532-542.

55. Fischer, G. L., and Harrison, J. M. Some functions of the superior olivary complex in auditory intensity discrimination. J. Comp. Neurol., 1963, 119: 269-279.

56. Galambos, R. Suppression of auditory nerve activity by stimulation of efferent fibres to the cochlea. Fed. Proc., 1955, 14: 53-63.

57. _____. a: Suppression of auditory nerve activity by stimulation of efferent fibers to cochlea. J. Neurophysiol., 1956, 19: 424-437.

58. _____. b: Some recent experiments on the neurophysiology of hearing. Ann. Otol. (St. Louis), 1956, 65: 1053-1059.

59. _____. a: Neural mechanisms in audition. Laryngoscope, 1958, 68: 388-401.

60. _____. b: Physiological study on the olivocochlear bundle of Rasmussen. Societe Internationale d'Audiologie. 4eme Congres, Padova, 1958, 304-306.

61. _____. Studies of the auditory system with inplanted electrodes. Neural Mechanisms of the Auditory and Vestibular Systems, G. L. Rasmussen and W. F. Windle, Eds., 1960, 137-151.

62. Galambos, R., Rosenblith, W. R., and Rosenweig, M. R. Physiological evidence for a cochlea-cochlear pathway in the cat. Experientia (Basel), 1950, 6: 438-440.

63. Galambos, R., Schwartzkopff, J., and Rupert, A. Microelectrode study of superior olive nuclei. Amer. J. Physiol., 1959, 197: 527-536.

64. Garner, W. R. The effect of frequency spectrum on temporal integration of energy in the ear. J. Acoust. Soc. Amer., 1933, 5: 82-108.

65. Gisselsson, L. The effects of acetylcholine inhibiting substances on the muscles of the middle ear and on the latency of the cochlear potentials. Acta Oto-Laryng. (Stockh.), 1952, 42: 208-218.

66. _____. Effect on microphonics or acetylcholine injected into the endolymphatic space. Preliminary report. Acta Oto-Laryng. (Stockh.), 1960, 51: 636-638.

67. Goldberg, J. M., Diamond, I. T., and Neff, W. D. Frequency discrimination after ablation of cortical projection areas of the auditory system. Fed. Proc., 1958, 17: 55.

68. Haider, M., Spong, P., and Lindsley, D. B. Attention, vigilance, and cortical evoked potentials in humans. Science, 1964, 145: 180-182.

69. Harrison, J. M., and Warr, W. B. A study of the cochlear nuclei and ascending auditory pathways of the medulla. J. Comp. Neurol., 1962, 119: 341-380.

70. Hernandez-Peon, R. Central mechanisms controlling conduction along the central sensory pathways. Acta Neurol. Lat-Amer., 1955, 1: 256-264.

71. _____. Reticular mechanisms of sensory control. Sensory Communication, W. A. Rosenblith, Ed. New York: The M.I.T. Press and John Wiley and Sons, Inc., 1961, pp. 497-520.

72. Hilding, D., and Wersaell, J. Cholinesterase and its relation to the nerve endings in the inner ear. Acta Oto-Laryng. (Stockh.), 1962, 55: 205-217.

73. Hillyard, W. A., and Galambos, R. Effects of stimulus and response contingencies on a surface negative slow potential shift in man. EEG clin. Neurophysiol., 1967, 22: 297-304.

74. Iurato, S. Efferent fibers to the sensory cells of Corti's organ. Exp. Cell. Res., 1962, 27: 162-164.

75. John, E. R., Herrington, R. N., and Sutton, S. Effects of visual form and the evoked response. Science, 1967, 155: 1439-1442.

76. Kiang, N. Y. S., Crist. The use of computers in studies of auditory neurophysiology. Trans. Amer. Acad. Ophthal. Otolaryng., 1961, 65: 735-747.

77. Kimura, R., and Wersaell, J. Termination of the olivo-cochlear bundle in relation to the outer hair cells of the organ of Corti in the guinea-pig. Acta Oto-Laryng. (Stockh.), 1962, 55: 11-32.

78. Kimura, R., Schuknecht, H. F., and Sando, I. Fine morphology of the sensory cells in the organ of Corti of man. Acta Oto-Laryng. (Stockh.), 1964, 58: 390-408.

79. Koelle, G. B., and Friedenwald, J. S. A histochemical method for localizing cholinesterase activity. Proc. Soc. Exp. Biol. (N.Y.), 1949, 70: 617-622.

80. Konishi, T. and Slepian, S. Effects of the electrical stimulation of the COCB on cochlear potentials recorded with intracochlear electrodes in guinea pigs. JASA, 1971.

81. LaGrutta, V., and Desmedt, J. E. Contrastes entre les actions centrales de la conline et de la strychnine. Arch. Int. Pharmacodyn, 1964, 151: 289-296.

82. Lamb, L. E., and Graham, J. T. Influence of signal variables on evoked response to sound. J. Speech Hearing Res., 1967, 10: 257-267.

83. Leibrandt, C. C. The significance of the olivo-cochlear bundle for the adaptation mechanism of the inner ear. Acta Oto-Laryng. (Stockh.), 1965, 59: 124-131.

84. Lombroso, C. T., and Duffy, E. H. Auditory evoked potentials during alterations in attention. EEG Clin. Neuro-Physiol., 1967, 23: 93.

85. Lorente de No, R. Anatomy of the eighth nerve III. General plan of structure of the primary cochlear nuclei. Laryngoscope (St. Louis), 1933, 43: 327-350.

86. Lowell, E. L., Toffer, C. I., Ballinger, R. M., and Alvig, D. P. Measurement of auditory threshold with a special purpose analog computer. J. Speech Hearing Res., 1961, 4: 105-112.

87. Miller, G. A. The perception of short bursts of noise. J. Acoust. Soc. Amer., 1948, 20: 160-170.

88. Moller, A. The acoustic reflex in man. J. Acoust. Soc. Amer., 1962, 34: 1524-1534.

89. Neff, W. D. Neural mechanisms of auditory discrimination. Sensory Communication, W. A. Rosenblith, Ed., New York: The M.I.T. Press and John Wiley and Sons, Inc., 259-278.

90. Nomura, Y., and Schukneckt, H. F. The efferent fibers in the cochlea. Ann. Otol. (St. Louis), 1965, 74: 289-302.

91. Palmer, C. W., Derbyshire, A. J., and Lee, A. W. A method of analyzing individual cortical responses to auditory stimuli. EEG Clin. Neurophysiol., 1966, 20: 204-206.

92. Papez, J. W. The superior olivary nucleau: its fiber connection. Arch. Neur. Psychiat. (Chic.), 1930, 24: 1-20.

93. Pestalozza, G. in: Pirodda, E., and Pestalozza, G. "I fenomeni di adattamento nell'apparato uditivo." Boll. Soc. Ital. Fon., 1960, 10:213-375.

94. Pfalz, R. K. J. a: Centrifugal inhibition of afferent secondary neurons in the cochlear nucleus by sound. J. Acoust. Soc. Amer., 1962, 34: 1472-1477.

95. _____. c: Nachweis der akustischen Efferenz und ihre Wirkung auf die schallaufnehmende Peripherie (Nucleus cochlearis; Cochlea). XXXIII Jahresversammlung der Deutschen Gesellschaft der Hals-Nasen-Ohrenarzte, Mannheim 3-7 Juni. (Zbl. Hals.-,Nas.-u. Ohrenheilk), 1962, 74: 9.

96. _____. Absence of a function for the crossed olivo-cochlear bundle under physiological conditions. Arch. Klin. exp. Ohr.-, Nas.-u. Kehlk. Heilk., 1969, 193: 89-100.

97. Portmann, G., Portmann, M., and Portmann, Cl. La double innervation de l'organe de Corti. Acta Oto-Laryng. (Stockh.), 1953, 43: 226-238.

98. Portmann, M., and Portmann, Cl. Efferent nerve fibres of cochlea. Arch. Oto-Laryng., 1954, 59: 543-555.

99. Rasmussen, G. L. An efferent cochlear bundle. Anat. Rec., 1942, 82: 441-442.

100. _____. The olivary penducle and other fiber projections of the superior olivary complex. J. Comp. Neurol., 1946, 84: 141-219.

101. _____. Further observations on the termination of the so-called olivary peduncle. Anat. Rec., 1950, 106: 235-236.

102. _____. a: Further observations on the efferent cochlear bundle. J. Comp. Neurol., 1953, 99: 61-74.

103. Rasmussen, G. L. b: Recurrent or "feed-back" connections of the auditory system of the cat. Anat. Rec., 1953, 115: 361-362.

104. _____. Descending or "feedback" connections of the auditory system of the cat. Amer. J. Physiol., 1955, 183: 653P.

105. _____. Anatomical discussion of the paper given by Dr. Galambos. Laryngoscope (St. Louis), 1958, 68: 404-406.

106. _____. Efferent fibers of the cochlear nerve and cochlear nucleus. Neural Mechanisms of the Auditory and Vestibular Systems, G. L. Rasmussen and W. F. Windle, Eds., Springfield, Ill.: Charles C. Thomas, 105-115.

107. _____. Anatomic relationships of the ascending and descending auditory system. Neurological Aspects of Auditory and Vestibular Disorder, W. S. Field and B. R. Alford, Eds., Springfield, Ill.: Charles C. Thomas, 1-19.

108. Rose, J. E., Galambos, R., and Hughes, J. H. Microelectrode studies of the cochlear nuclei of the cat. Bull. Johns Hopk. Hosp., 1959, 104: 211-251.

109. Rose, J. E., and Woolsey, C. N. Cortical connections and functional organization of the thalamic auditory system of the cat. Biological and Biochemical Bases of Behavior, H. F. Harlow and C. N. Woolsey, Eds., Madison: University of Wisconsin Press, 127-150.

110. Rosenblut, B., Bilger, R. C., and Goldstein, R. Electrophysiologic responses to sound as a function of intensity, EEG pattern and sex. J. Speech Hearing Res., 1959, 2: 28-39.

111. Rossi, G. F., and Brodal, A. Corticofugal fibres to the brain stem reticular formation. An experimental study in the cat. J. Anat. (Lond.), 1956, 90: 42-62.

112. Rossi, G. Acetylcholinesterase in the ganlionic cells of the eighth nerve. Ital. Gen. Rev. Oto-Rhino-Laryng., 1960, 2: 587-596.

113. _____. L'acetylcholinesterase au cours du developpement de l'oreille interne du cobaye. Acta Oto-Laryng. (Stockh.), 1962, supple. 170.

114. Rossi, G., and Cortesine, G. Acetylcholinesterase activity in the efferent cochlear fibres after destruction of the organ of Corti and afferent fibres. Acta Oto-Laryng. (Stockh.), 1965.

115. _____. The action of strychnine sulphate on AChE activity in the organ of Corti of the guinea-pig. (unpublished data), 1965.

116. _____. The efferent innervation of the inner ear. A historical-bibliographical survey. Laryngoscope (St. Louis), 1965, 75: 212-235.

117. Rossi, G., Voena, G., Cortesine, G., and Buongiovanni, S. Changes in the cochlear microphonic potential due to resection of the efferent cochlear fibres. J. Acoust. Soc. Amer., 1964, 36: 1845-1849.

118. Roth, M., Shaw, J., and Green, J. The form, voltage distribution and physiological significance of the K-complex. EEG Clin. Neurophysiol., 1956, 8: 385-402.

119. Ruben, R. J., and Sekula, J. Inhibition of central auditory response. Science, 1960, 131: 163-164.

120. _____. Central inhibition of auditory input following stiumlation of the olivo-cochlear bundle in cat. J. Acoust. Soc. Amer., 1962, 34: 732-733.

121. Satterfield, J. H. Evoked cortical response enhancement and attention in man. A study of responses to auditory and shock stimuli. EEG Clin. Neurophysiol., 1965, 19: 470-475.

122. Siegel, Sidney. Nonparametric Statistics. McGraw-Hill Book Company, Inc., New York, New York, 1956, pp. 83-85.

123. Schukneckt, H. F. Acetylcholinesterase and the olivo-cochlear tract of Rasmussen (Abstract). Laryngoscope, 1958, 68: 627-628.

124. Schuknecht, H. F., Churchill, J. A., and Doran, R. The localization of acetycholinesterase in the cochlea. Arch. Oto-Laryng., 1959, 69: 549-559.

125. Spong, P., Haider, M., and Lindsley, D. B. Selective attention and cortical evoked potentials. EEG Clin. Neurophysiol., 1965, 18: 523.

126. Spong, P., Haider, M., and Lindsley, D. B. Selective attentiveness and cortical evoked responses to visual and auditory stimuli. Science, 1965, 148: 395-397.

127. Smith, C. A. Electron microscopic studies of the organ of Corti. Anat. Rec., 1955, 121: 451-452.

128. _____. Innervation pattern of the cochlea. The internal hair cell. Ann. Otol. (St. Louis), 1961, 70: 504-527.

129. Smith, C., and Rasmussen, G. Ultrastructural changes in the efferent cochlear nerve endings following transection of the olivo-cochlear bundle in the chinchilla. Anat. Rec., 1963, 145: 287-288.

130. _____. Recent observations on the olivo-cochlear bundle. Ann. Otol. (St. Louis), 1963, 72: 489-506.

131. _____. Recent observations on the olivo-cochlear bundle. Trans. Amer. Otol. Soc., 1963, 51: 85-104.

132. Smith, C. A., and Sjoestrand, F. A synaptic structure in the hair cells of the guinea pig cochlea. J. Ultra-struct. Res., 1961a, 5: 184-192.

133. _____. Structure of the nerve endings on the external hair cells of the guinea pig cochlea as studied by serial section. J. Ultra-struct. Res., 1961b, 5: 523-556.

134. Sohmer, H. The effect of contralateral olivo-cochlear bundle stimulation on the cochlear potentials evoked by acoustic stimuli of various frequencies and intensities. Acta Oto-Laryng. (Stockh.), 1965, 60: 59-70.

135. Spoendlin, H. H. Ultrastructural features of the organ of Corti in normal and acoustically stimulated animals. Ann. Otol. (St. Louis), 1962, 71: 657-677.

136. _____. Ultrastructural features of the organ of Corti. Trans. Amer. Otol. Soc., 1962, 50: 61-82.

137. Spoendlin, H. H., and Gacek, R. R. Electromicroscopic study of the efferent and afferent innervations of the organ of Corti in the cat. Ann. Otol. (St. Louis), 1963, 72: 660-686.

138. Starr, A. Influence of motor activity on click-evoked responses in the auditory pathway of waking cats. Exp. Neurol., 1964, 10: 191-204.

139. Starr, A., and Salomon, G. Electromyografic study of middle ear muscle activity during shock evoked motor activity in cats. Int. Audiol., 1965, 4: 28-30.

140. Stevens, S. S. The psychophysics of sensory function. In W. A. Rosenblith, Ed., Sensory Communication, New York: Wiley, 1961, 1-33.

141. Van Gehuchten, P. Recherches experimentales sur les terminaisons du nerf vestibulaire et sur les voies vestibulaires centrales. Rev. Oto-neuro-opthal., 1927, 5: 777-791.

142. Walter, W. G. The convergence and interaction of visual auditory and tactile responses in human nonspecific cortex. Ann. N. Y. Acad. Sci., 1964, 112: 320-326.

143. Walter, W. G. Slow potential waves in the human brain associated with expectancy, attention, and decision. Arch. Psychiat. Nervenkr., 1964, 206: 309-322.

144. Wiederhold, M. L., and Chance, E. K. Effects of olivo-cochlear bundle stimulation on acoustically evoked potentials. Quarterly Progress Report No. 72. Research Laboratory of Electronics, M.I.T., 1963, 311-313.

145. Organization of cortical auditory system. Sensory Communication, W. A. Rosenblith, Ed. New York, London: The M.I.T. Press and John Wiley and Sons, Inc., 1961, 235-257.