Section 3 Auditory Physiology

Chapter 1 Signal Transmission in the Auditory System

Chapter 1. Signal Transmission in the Auditory System

Academic and Research Staff

Professor Lawrence S. Frishkopf, Professor Nelson Y.S. Kiang, Professor William T. Peake, Professor William M. Siebert, Professor Thomas F. Weiss, Dr. Robin L. Davis, Dr. Bertrand Delgutte, Dr. Donald K. Eddington, Dr. Dennis M. Freeman, Dr. Barbara Fullerton, Dr. Miriam Furst, Dr. Jill C. Gardner, Dr. John J. Guinan, Jr., Dr. James B. Kobler, Dr. Robert A. Levine, Dr. Xiao Dong Pang, Dr. William M. Rabinowitz, Dr. John J. Rosowski, Dr. Sylvette R. Vacher, Patricia A. Cuneo

Visiting Scientists and Research Affiliates

Dr. Jay T. Rubenstein, Debra S. Louison, Frank J. Stefanov-Wagner, David A. Steffens

Graduate Students

Kathleen M. Donahue, Farzad Ehsani, Donna K. Hendrix, Michael P. McCue, Jennifer R. Melcher, Michael E. Ravicz, Jenny S. Yu

Technical and Support Staff

Susan M. Ross

1.1 Introduction

Sponsors

National Institutes of Health
Grants 5 T32 NS07047, 5 P01 NS13126, 8 R01 DC00194, 5 R01 NS25995, 8 R01 DC00238, 5 R01 NS20322, 5 R01 DC00235, 5 R01 NS20269, 1 P01 NS23734
Johnson and Johnson Foundation
Unisys Corporation Doctoral Fellowship

Research on the auditory system is carried out in cooperation with two laboratories at the Massachusetts Eye and Ear Infirmary (MEEI). Investigations of signal transmission in the auditory system involve the Eaton-Peabody Laboratory for Auditory Physiology. Our long-term objective is to determine the anatomical structures and physiological mechanisms that underlie vertebrate hearing and to apply that knowledge to clinical problems. Studies of cochlear implants in humans are carried out at the MEEI Cochlear Implant Laboratory. The ultimate goal of these devices is to provide speech communication for the deaf through electric stimulation of intracochlear electrodes to elicit patterns of auditory nerve fiber activity that the brain can learn to interpret.

1.2 Signal Transmission in the External- and Middle-Ear

1.2.1 Structure-Function Relationships in Middle Ears

Project Staff

Professor William T. Peake, Dr. John J. Rosowski, Michael E. Ravicz

In cooperation with scientists at the Harvard Museum of Comparative Zoology, we have written two manuscripts which analyze the ear structures of a 200 million year old fossil, *Morganucodon,* considered by some to be the earliest known mammal. The first manu-

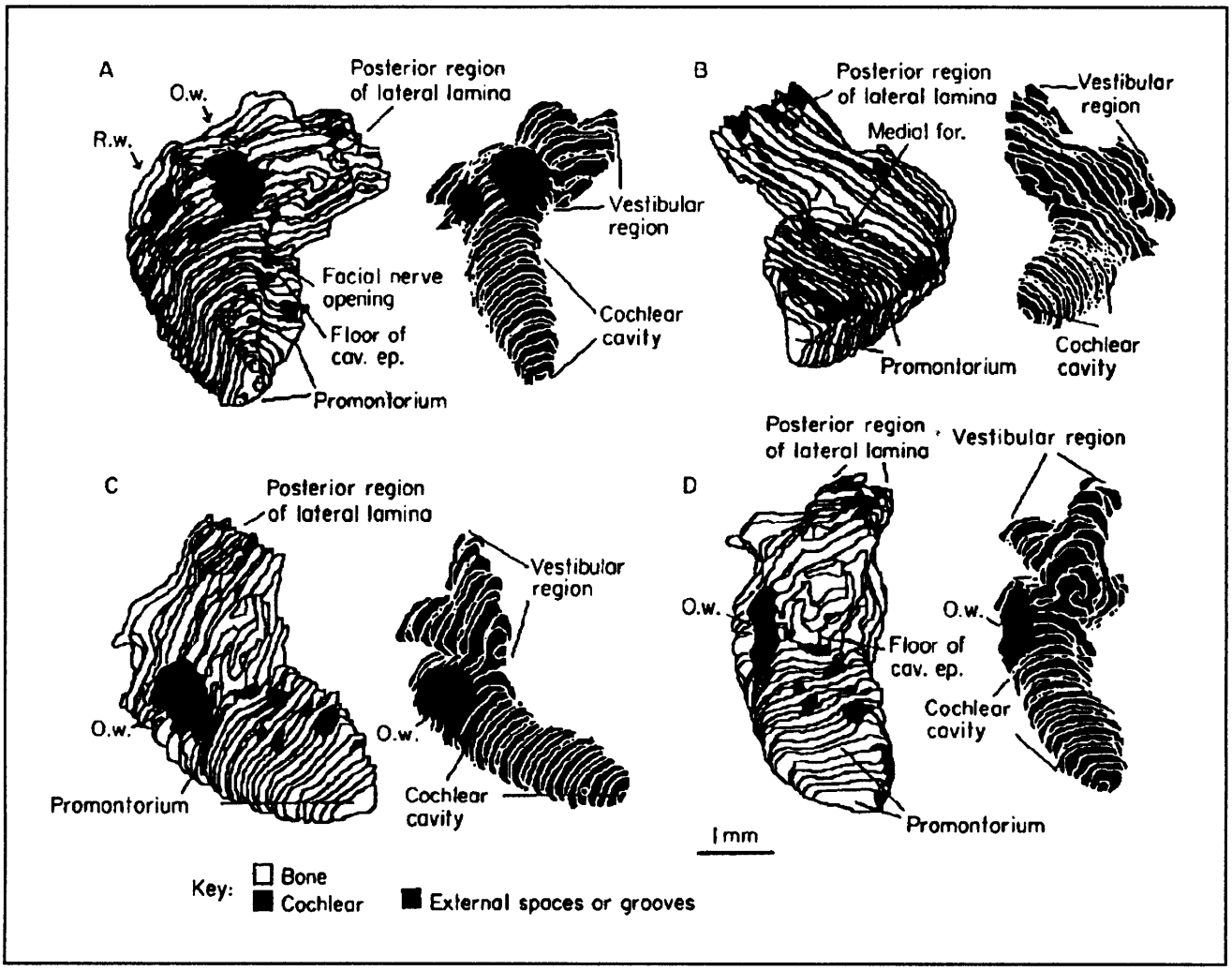

Figure 1. Reconstructions of the right inner ear of *Morganucodon* in four views. A, ventrolateral; B, anteromedial; C, lateral, and D, dorsoanterior. Each quadrant A-D shows two reconstructions: the left is a simultaneous reconstruction of the bone, cochlear cavity and the external spaces or grooves; the right is a reconstruction of the cochlear cavity. The side-by-side representation of the two types of reconstructions shows how the cochlear cavity is oriented within the bone. (Abbreviations: o.w. = oval window; r.w. = round window; cav. ep. = cavum epiptericum) After Graybeal et al., 1989.

script[1] describes the boney structure of the auditory inner-ear in this beast (see figure 1). The second manuscript[2] analyzes the middle-ear structures in this early mammal and suggests that its hearing was similar to that observed in modern mice and shrews.

This year, Michael Ravicz submitted his master's thesis to the Boston University Department of Bio-Medical Engineering describing the measurements of the impedance of the middle and external ears of gerbils.[3] The results indicate that the size of the gerbil auditory structures plays a role in defining

---

[1] A. Graybeal, J.J. Rosowski, D.R. Ketten, and A.W. Crompton, "The Inner-Ear Structure of *Morganucodon*, An Early Jurassic Mammal," *Zool. J. Linn. Soc.* 96: 107-117 (1989).

[2] J.J. Rosowski and A. Graybeal, "What Did *Morganucodon* Hear?" submitted to *Zool. J. Linn. Soc.*

[3] M.E. Ravicz, *The Acoustic Impedance of the Gerbil Ear,* S.M. thesis, Dept. of Bio-Med. Eng., Boston University, 1990.

these impedances; smaller ear dimensions result in larger acoustic impedances. Another significant finding is that small diameter ear canals place large restrictions on the power available to the ear.

We also participated in several scientific conferences. Talks detailing the action of the middle-ear cavities in cat and human[4] along with a simple model for auditory nonlinearities observed in the alligator lizard[5] were presented at the conference celebrating the sixtieth birthday of Professor Nelson Kiang. Manuscripts of these talks are being prepared for publication. Dr. Rosowski was also invited to address the November Symposium on Noise-Induced Hearing Loss organized by the Committee on Hearing, Bioacoustics and Biomechanics of the National Research Council. This presentation reviewed work on the flow of sound power through the external and middle ear and argued that the external and middle ear play a large role in defining the strength of noxious acoustic stimuli. A manuscript describing this work has been submitted for publication.[6]

1.2.2 External and Middle Ears

Project Staff

Professor William T. Peake, Dr. John J. Rosowski, Kathleen M. Donahue

Our work on development of a cadaver model for study of the human middle ear was presented to the American Otological Society (San Francisco, April 4, 1989), and a companion manuscript accepted for publication.[7] This paper noted that measurements of the middle-ear input impedance in cadaver ears are indistinguishable from similar measurements made in living subjects. The cadaver-ear preparation was used in a series of experiments by Kathleen Donahue to describe the motion of the human malleus.[8] The results indicate that at frequencies below the middle-ear "resonant" frequency, the malleus rotates about a fixed axis. At higher frequencies, the measurements suggest that the malleus motion is more complex and perhaps dependent on the load of the ossicular chain.

Publications

Donahue, K.M. *Human Middle-Ear Mallear Motion: Models and Measurements.* S.M. thesis. Dept. of Elec. Eng. and Comput. Sci., MIT, 1989.

Graybeal, A., J.J. Rosowski, D.R. Ketten, and A.W. Crompton. "The Inner-Ear Structure of *Morganucodon,* an Early Jurassic Mammal." *Zool. J. Linn. Soc.* 96: 107-117 (1989).

Peake, W.T., J.J. Rosowski and T.J. Lynch III. "The Cat's Middle Ear: Measurements, Models and Predictions." Paper presented at the Symposium in Honor of N.Y.S. Kiang, Dedham, Massachusetts, July 5-7, 1989.

Ravicz, M.E. *The Acoustic Impedance of the Gerbil Ear.* S.M. thesis. Dept. of Bio-Med. Eng., Boston University, 1990.

Rosowski, J.J. "The Effects of External- and Middle-Ear Filtering on Auditory Thres-

---

[4] W.T. Peake, J.J. Rosowski, and T.J. Lynch III, "The Cat's Middle Ear: Measurements, Models and Predictions," paper presented at the Symposium in Honor of N.Y.S. Kiang, Dedham, Massachusetts, July 5-7, 1989.

[5] J.J. Rosowski, W.T. Peake and N. Yang, "A Simple Model for Level-dependent Growth Rates of Auditory Distortion," paper presented at the Symposium in Honor of N.Y.S. Kiang, Dedham, Massachusetts, July 5-7, 1989.

[6] J.J. Rosowski, "The Efects of External- and Middle-Ear Filtering on Auditory Threshold and Noise-induced Hearing Loss," submitted to *J. Acoust. Soc. Am.*

[7] J.J. Rosowski, P.J. Davis, S.N. Merchant, K.M. Donahue, and M.D. Coltrera, "Cadaver Middle-Ears as Models for Living Ears: Comparisons of Middle-Ear Input Immittance," *Ann. Otol., Rhinol., Laryngol.,* forthcoming.

[8] K.M. Donahue, *Human Middle-Ear Mallear Motion: Models and Measurements,* S.M. thesis, Dept. of Electr. Eng. and Comput. Sci., MIT, 1989.

hold and Noise-induced Hearing Loss." Submitted to *J. Acoust. Soc. Am.*

Rosowski, J.J., P.J. Davis, S.N. Merchant, K.M. Donahue, and M.D. Coltrera. "Cadaver Middle-Ears as Models for Living Ears: Comparisons of Middle-Ear Input Immittance." *Ann. Otol., Rhinol., Laryngol.* Forthcoming.

Rosowski, J.J., and A. Graybeal. "What Did *Morganucodon* Hear?" Submitted to *Zool. J. Linn. Soc.*

Rosowski, J.J., W.T. Peake, and N. Yang. "A Simple Model for Level-dependent Growth Rates of Auditory Distortion." Paper presented at the Symposium in Honor of N.Y.S. Kiang, Dedham, Massachusetts, July 5-7, 1989.

1.3 Cochlear Mechanisms

Project Staff

Professor Thomas F. Weiss, Professor Lawrence S. Frishkopf, Dr. Dennis M. Freeman, Farzad Ehsani, Donna K. Hendrix

We completed a paper[9] that describes a theoretical study of the degradation of timing information in the cochlea. Results of this study suggest that three hair-cell processes, each acting as a first-order lowpass filter process, contribute to the degradation of timing information in the cochlea. These are: (1) the charging of the membrane capacitance; (2) the kinetics of opening of calcium channels; and (3) the time course of accumulation of calcium in intracellular compartments.

We have submitted for publication a manuscript[10] that describes methods used to construct an accurate, three-dimensional, plastic model of the cochlea of the alligator lizard. The model, which consists of three pieces (representing the otic capsule, the cochlear duct, and the posterior branch of the VIIIth nerve), is based directly on histological sections of the cochlea.

We have submitted for publication[11] the results of theoretical studies of the mechanical stimulation of the hair bundles of hair cells.

We have completed a study[12] whose goals were to develop an *in vitro* preparation of the cochlear duct of the alligator lizard and to evaluate the effects of placing the duct in different solutions. The technique is to dissect the duct and place it in an artificial lymph solution. The vestibular membrane is opened, and a cement (derived from mussels) is used to attach the duct to a glass slide at the bottom of a chamber. Microspheres (1 μm and 3 μm diameter polystyrene) are added and allowed to settle onto the duct. The chamber is perfused with an artificial lymph solution, and the duct is observed through a compound microscope with interference contrast (Nomarski) optics. Three different types of iso-osmotic lymph solutions have been tested: an artificial perilymph (AP), artificial endolymph (AE), and a tissue culture medium (L-15). Results show that the microspheres on the endolymphatic surface of the duct move in characteristically different ways in the three iso-osmotic lymphs, suggesting that the tissue swells in AE and changes rather little in AP and in L-15. Most of the measure-

---

[9] R.C. Kidd and T.F. Weiss, "Mechanisms That Degrade Timing Information in the Cochlea," *Hear. Res.*, forthcoming.

[10] D.M. Freeman, "Anatomical Model of the Cochlea of the Alligator Lizard," *Hear. Res.*, forthcoming.

[11] D.M Freeman and T.F. Weiss, "Superposition of Hydrodynamic Forces on a Hair Bundle," *Hear. Res.*, forthcoming; D.M Freeman and T.F. Weiss, "Hydrodynamic Forces on Hair Bundles at Low Frequencies," *Hear. Res.*, forthcoming; D.M Freeman and T.F. Weiss, "Hydrodynamic Forces on Hair Bundles at High Frequencies," *Hear. Res.*, forthcoming; D.M Freeman and T.F. Weiss, "Hydrodynamic Analysis of a Two-dimensional Model for Micromechanical Resonance of Free-standing Hair Bundles," *Hear. Res.*, forthcoming.

[12] D.K. Hendrix, *Development of an in vitro Preparation of the Alligator Lizard Cochlear Duct,* S.M. thesis, Dept. of Electr. Eng. and Comput. Sci., MIT, 1990.

ments of microsphere displacement versus time could be fit acceptably with exponential time functions. The time constants were of the order of 10^2 minutes. Comparison of the motion of microspheres at different locations in the duct does not reveal any systematic dependence of motion on location. We conclude that the methods we have developed provide a simple tool for determining the artificial lymph compositions that result in osmotic stability of the cochlear duct. Based on our present results, on the physical appearance of the cochlear duct, and on the work of other investigators, we believe that a medium consisting of L-15 of appropriate osmolarity will prove to be superior to either AE or AP in maintaining the viability of an *in vitro* preparation of the alligator-lizard cochlea.

Publications

Freeman, D.M. "Anatomical Model of the Cochlea of the Alligator Lizard." *Hear. Res.* Forthcoming.

Freeman, D.M., and T.F. Weiss. "Superposition of Hydrodynamic Forces on a Hair Bundle." *Hear. Res.* Forthcoming.

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Forces on Hair Bundles at Low Frequencies." *Hear. Res.* Forthcoming.

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Forces on Hair Bundles at High Frequencies." *Hear. Res.* Forthcoming.

Freeman, D.M., and T.F. Weiss. "Hydrodynamic Analysis of a Two-dimensional Model for Micromechanical Resonance of Free-standing Hair Bundles." *Hear. Res.* Forthcoming.

Hendrix, D.K. *Development of an in vitro Preparation of the Alligator Lizard Cochlear Duct.* S.M. thesis. Dept. of Electr. Eng. and Comput. Sci., MIT, 1990.

Kidd, R.C., and T.F. Weiss. "Mechanisms That Degrade Timing Information in the Cochlea." *Hear. Res.* Forthcoming.

1.4 Regeneration of Primary-Auditory Neurons in vitro

Project Staff

Dr. Robin L. Davis

The regenerative capacity of primary-auditory neurons was studied in a tissue culture system that permits single goldfish primary-auditory neurons to be maintained *in vitro* for up to one or two months.[13] Following placement in tissue culture, only very few of these neurons regenerate their processes. These cells are, however, physiologically active as evaluated with intracellular and single-channel recordings.[14] Focal crush lesions made to the goldfish primary-auditory nerve one and two days prior to removal for tissue culture increased the amount of neurite outgrowth observed *in vitro*.[15] The rate, extent and pattern of this growth response is being characterized for individual neurons and will be compared to the effects of known neurotropic factors added to the medium.

---

[13] R.L. Davis, E.A. Mroz, and W.F. Sewell, "Isolated Auditory Neurons in Culture," *Abstr. Assoc. Res. Otol.* 11: 240 (1988).

[14] R.L. Davis, E.A. Mroz, and W.F. Sewell, "Single Channel Properties of Goldfish (Carassius auratus) Auditory Neurons *in vitro*," *Society for Neuroscience Abstr.* 14 (Part 2): 798 (1988).

[15] R.L. Davis, "Conditioning Lesions Promote Primary-Auditory Neurite Regeneration *in vitro*," submitted to the Association of Research for Otolaryngology, St. Petersburg, Florida, February 4-8, 1990.

Publications

Davis, R.L. "Conditioning Lesions Promote Primary-auditory Neurite Regeneration *in vitro*." Submitted to the Association of Research for Otolaryngology, St. Petersburg, Florida, February 4-8, 1990.

Davis, R.L., E.A. Mroz, and W.F. Sewell. "Isolated Auditory Neurons in Culture." *Abstr. Assoc. Res. Otol.* 11: 240 (1988).

Davis, R.L., E.A. Mroz, and W.F. Sewell. "Single Channel Properties of Goldfish (*Carassius auratus*) Auditory Neurons *in vitro*." *Soc. Neurosci. Abstr.* 14 (Part 2): 798 (1988).

1.5 Stimulus Coding in the Auditory Nerve

Project Staff

Dr. Bertrand Delgutte, Jenny S. Yu

During the past year, a report of earlier experiments on physiological mechanisms of psychophysical masking was submitted for publication and accepted.[16] In these experiments, masked thresholds of auditory-nerve fibers were measured for tone signals of different frequencies in the presence of 1-kHz tone maskers. Physiological masking patterns were obtained by selecting the lowest masked threshold for each signal frequency among many fibers with different characteristic frequencies (CF) and spontaneous rates of discharge. These physiological masking patterns resemble psychophysical masking patterns in that they show rapid growth of masking with masker level for signal frequencies above the masker. A correlate of the psychophysical phenomenon of off-frequency listening was found in that fibers with the lowest masked thresholds were not tuned to the signal frequency in quiet, but had their CF's slightly on the opposite side of the masker frequency with respect to the signal frequency. Comparison of simultaneous and nonsimultaneous masked thresholds showed that two-tone rate suppression plays an important role in masking, particularly for signal frequencies well above the masker.

In order to study physiological mechanisms of masking for a broader range of stimulus conditions than would be practical in physiological experiments, a phenomenological model of responses of auditory-nerve fibers was developed. This model simulates discharge rate responses of an array of auditory-nerve fibers for arbitrary steady-state stimuli defined by their frequency spectrum. The model produces two-tone rate suppression by having the output of a suppression filter modify the tuning of an excitation filter resembling tuning curves of auditory-nerve fibers. The model qualitatively predicts responses of auditory-nerve fibers to many stimuli, including single tones, two tones, broadband noise, and synthetic vowels, and produces masking patterns resembling those measured in auditory-nerve fibers. With the model, simulations of masking experiments show that suppression plays a complex role in masking, depending on stimulus conditions. Specifically, suppression among different frequency components of a complex masker can result in the unmasking of a tone signal in nonsimultaneous masking. Under certain conditions, tone signals can be detected because they suppress the response to broadband maskers. This effect was not found for narrowband maskers. Off-frequency listening plays a significant role in signal detection for intense signals, but not for low-level signals. These modeling results have been presented at several conferences.[17]

---

[16] B. Delgutte, "Physiological Mechanisms of Psychophysical Masking: Observations from Auditory-Nerve Fibers," *J. Acoust. Soc. Am.*, forthcoming.

[17] B. Delgutte, "Physiological Mechanisms of Masking and Intensity Discrimination," paper presented at the 117th Meeting of Acoustical Society of America, Syracuse, New York, May 22-26, 1989; B. Delgutte, "Does Suppression Result in Masking or Unmasking?" paper presented at the Symposium for Basic Research in a Clinical Environment, Dedham, Massachusetts, July 5-7, 1989; B. Delgutte, "Two-tone Suppression in Auditory-nerve Fibers: a Model and its Psychophysical Implications," paper presented at the 13th Meeting of the Association for Research in Otolaryngology, St. Petersburg Beach, Florida, February 4-8, 1990.

In fitting model parameters to physiological data, we made use of earlier data on the two-tone rate suppression in auditory-nerve fibers. A new analysis of these data showed that the rate of growth of suppression with the level of the suppressor tone depends on both the CF of auditory-nerve fibers and the frequency separation between the suppressor and the CF. For suppressors in the vicinity of the CF, the rate of growth decreases markedly with increasing suppressor frequency. However, the rate of growth reaches a plateau for suppressor frequencies well below the CF. The rate of growth in this plateau region increases slowly with increasing CF. These results pose difficulties for existing models of two-tone suppression. A report of these findings has been submitted for publication.[18]

Publications

Delgutte, B. "Physiological Mechanisms of Psychophysical Masking: Observations from Auditory-nerve Fibers." *J. Acoust. Soc. Am.* Forthcoming.

Delgutte, B. "Two-tone Rate Suppression in Auditory-nerve Fibers." Submitted to *Hear. Res.*

Delgutte, B. "Physiological Mechanisms of Masking and Intensity Discrimination." Paper presented at the 117th Meeting of Acoustical Society of America, Syracuse, New York, May 22-26, 1989.

Delgutte, B. "Does Suppression Result in Masking or Unmasking?" Paper presented at the Symposium for Basic Research in a Clinical Environment, Dedham, Massachusetts, July 5-7, 1989.

Delgutte, B. "Two-tone Suppression in Auditory-nerve Fibers: a Model and its Psychophysical Implications." Paper presented at the 13th Meeting of the Association for Research in Otolaryngology, St. Petersburg Beach, Florida, February 4-8, 1990.

1.6 Middle-Ear Muscle Reflex

Project Staff

Dr. John J. Guinan, Jr., Dr. James B. Kobler, Dr. Sylvette Vacher, Michael P. McCue

We aim to determine the structural and functional basis of the middle-ear reflexes. During the past year, we have published papers describing the course of stapedius motor axons within the brainstem,[19] and the correlation between the locations of stapedius-motoneuron cell bodies and their responses to sound.[20] These results are consistent with the idea that the stapedius motoneuron pool is divided into subgroups that are spatially segregated in the brainstem in terms of their patterns of input from the two ears. Continuing this work, we have traced to their endings in the muscle five physiologically-identified stapedius motor axons which were labeled with horseradish peroxidase (from the cells labeled in Vacher et al., 1989). The results are interesting in that one axon innervated only one muscle fiber (in most muscles, each axon innervates tens or hundreds of muscle fibers), but in two cases, one axon innervated muscle fibers spread throughout the stapedius muscle (this demonstrates that the innervation of the stapedius is not restricted to several non-overlapping zones, as had been thought). Thus, although stapedius motoneurons appear to be functionally segregated in the brainstem, the available evidence suggests that there is not a corresponding segregation in the muscle.

We have recently published a commentary on the function of muscle and reflex partitioning

---

[18] B. Delgutte, "Two-tone Rate Suppression in Auditory-nerve Fibers," submitted to *Hear. Res.*

[19] J.J. Guinan Jr., M.P. Joseph, and B.E. Norris, "Brainstem Facial-Motor Pathways from Two Distinct Groups of Stapedius Motoneurons in the Cat," *J. Comput. Neurol.* 289: 134-144 (1989).

[20] S.R. Vacher, J.J. Guinan Jr., and J.B. Kobler, "Intracellularly Labeled Stapedius-Motoneuron Cell Bodies in the Cat are Spatially Organized According to Their Physiologic Responses," *J. Comput. Neurol.* 289: 401-415 (1989).

in the stapedius.[21] In this commentary, we point out ways in which the organization of the stapedius motor system does not fit with a leading current theory on the organization of mammalian neuromuscular systems.

During the past year, work has been done to prepare for publication results in two areas: (1) data which demonstrate "unmasking" produced by stapedius contractions, and (2) data on the responses to sound and axon conduction velocities of stapedius motoneurons (these data provide the basis for the division of stapedius motoneurons into response-type groups).

This past year we have made progress on our project to determine whether there are systematic differences in motor-unit strengths and time courses across the different functional groups of stapedius motoneurons. To facilitate the work of this project, we have upgraded our experimental facility with a new data acquisition system centered around a MacIntosh II computer and National-Instruments input, output and direct-memory-access boards. Progress has also been made on many experimental issues, such as finding a location at which stapedius motor axons can be intracellularly recorded and stimulated without the electrode being dislodged by muscle motion, and developing a reliable paradigm for stimulating impaled stapedius motor axons and determining that the axon has responded. We plan to obtain measurements of the effects of individual stapedius motor units as monitored by the changes produced in middle-ear transmission and middle-ear input impedance.

Publications

Guinan, J.J., Jr., M.P. Joseph, and B.E. Norris. "Brainstem Facial-Motor Pathways from Two Distinct Groups of Stapedius Motoneurons in the Cat." *J. Comput. Neurol.* 289: 134-144 (1989).

McCue, M.P., J.J. Guinan Jr., J.B. Kobler, and S.R. Vacher. "Acoustic-Reflex Partitioning in the Stapedius." *Behav. Brain Sci.* 12: 663-665 (1989).

Vacher, S.R., J.J. Guinan Jr., and J.B. Kobler. "Intracellularly Labeled Stapedius-Motoneuron Cell Bodies in the Cat are Spatially Organized According to Their Physiologic Responses." *J. Comput. Neurol.* 289: 401-415 (1989).

1.7 Cohlear Efferent System

Project Staff

Dr. John J. Guinan, Jr.

In this project, we aim to understand the physiological effects produced by medial olivocochlear (MOC) efferents which terminate on outer hair cells. To test the hypothesis that efferent activity and two-tone suppression might affect the cochlear amplifier at different sites but produce similar effects, we compared effects of these agents on stimulus-frequency otoacoustic emissions (SFOAEs) in cats. Measurements were made of ΔP, the vector change in ear-canal sound pressure relative to the pressure with a probe tone alone. As a first approximation, ΔP is the removal of part of the probe SFOAE. Changes due to two-tone suppression (ΔPs) or efferent stimulation (ΔPoc) could be measured over a very wide range of probe frequencies (0.2–30 kHz). As the level of a suppressor tone was increased, ΔPs often had a constant phase and a monotonically increasing magnitude, but under certain conditions the relationship was strongly non-monotonic (e.g. showed a sharp dip and an abrupt phase change). With efferent stimulation, we did not find similar abrupt changes in ΔPoc. With both efferent stimulation and a suppressor tone, the resulting ΔPoc's ranged from vector addition of the separate effects to a result which was more like a mean than an addition. The results suggest that efferent and suppressive effects are not identical and that at least two different mechanisms produce suppressive effects.

---

[21] M.P. McCue, J.J. Guinan Jr., J.B. Kobler, and S.R. Vacher, "Acoustic-Reflex Partitioning in the Stapedius," *Behav. Brain Sci.* 12: 663-665 (1989).

During the past year, we have prepared a manuscript on previously unpublished experimental results on the physiology of the medial nucleus of the trapezoid body (MNTB).[22] There has been a renewed interest in MNTB principal neurons as possible sources of inputs to olivocochlear neurons and as sources of inputs to neurons of the lateral superior olivary nucleus. By orthodromic and antidromic stimulation of MNTB principal neurons, we have shown that there is usually one-to-one transmission from each calyx of Held (a very large presynaptic ending) to the contacted MNTB principal neuron. In addition, we demonstrated that the smaller, non-calyceal, synapses can also excite MNTB principal neurons. Finally, we found some evidence of inhibition, possibly recurrent inhibition, in MNTB principal neurons. Our data firmly establish that there is fast, secure spike transmission from calyces of Held to MNTB principal neurons and suggest that under some circumstances there is additional signal processing in MNTB principal neurons.

Publications

Guinan, J.J., Jr., and R.Y.S. Li. "Signal Processing in Brainstem Auditory Neurons which Receive Giant Endings (calyces of Held) in the Medial Nucleus of the Trapezoid Body of the Cat." *Hear. Res.* Forthcoming.

1.8 The Generators of the Brainstem Auditory Evoked Potential

Project Staff

Professor Nelson Y.S. Kiang, Jennifer R. Melcher

When a punctate sound is presented to the ear, a time-varying potential can be recorded from electrode pairs on the surface of the head. The potential waveform at short latencies (<10 msec following the stimulus) is distinguished from the potential at longer latencies by a characteristic series of deflections, each about one msec in duration. Similar waveforms have been measured in every mammalian species in which recordings have been attempted. It is believed that the short-latency potential is generated by cells in the auditory nerve and brainstem. Thus, it is called the brainstem auditory evoked potential (BAEP).

The goal of Jennifer Melcher's thesis[23] is to gain a better understanding of which cells generate the different components of the BAEP. In previous years, progress has been made along two lines: (1) a model for BAEP generation was developed, and (2) a series of lesion experiments were begun. The model relates the activity of individual cells in the auditory pathway to the BAEP and has served as a guide for designing and interpreting the experiments. The lesion experiments involve injecting a neurotoxin into different parts of the cat brainstem and correlating the resulting cell loss with changes in the BAEP. Preliminary experimental results suggested that different cell populations generate different components of the BAEP.

Further results of the past year are qualitatively consistent with the preliminary data and also support the hypothesis that one particular BAEP component is generated by a particular population of cells. In order to stabilize that interpretation, we have begun comparing data from many experiments to look for a quantitative relationship between the amplitude of the BAEP component and the number of cells eliminated from the population. To do this, we have developed a method for quantifying lesions that involves counting and characterizing individual cells. A quantitative description of a lesion is obtained by comparing the number of cells with particular characteristics in the experimental (lesioned) brainstems with the number in a normal brainstem. We plan to

---

[22] J.J. Guinan Jr. and R.Y.S. Li, "Signal Processing in Brainstem Auditory Neurons which Receive Giant Endings (calyces of Held) in the Medial Nucleus of the Trapezoid Body of the Cat," *Hear. Res.*, forthcoming.

[23] J. Melcher, *Generators of the Brainstem Auditory Evoked Potentials,* Ph.D. diss., work in progress, Dept. of Electr. Eng. and Comput. Sci., MIT.

complete the experiments and quantitative lesion analysis during the next year.

1.9 Cochlear Implants

1.9.1 Models of Current Spread and Nerve Excitation During Intracochlear Stimulation

Project Staff

Dr. Donald K. Eddington, Dr. Jay T. Rubenstein

The basic function of a cochlear prosthesis is to elicit patterns of activity on the array of surviving auditory nerve fibers by stimulating electrodes that are placed in and/or around the cochlea. By modulating these patterns of neural activity, these devices attempt to present information that the implanted subject can learn to interpret. The spike activity patterns elicited by electrical stimulation depend on several factors: the complex, electrically heterogeneous structure of the cochlea, the geometry and placement of the stimulating electrodes, the stimulus waveform, and the distribution of excitable auditory nerve fibers. An understanding of how these factors interact to determine the activity patterns is fundamental (1) to the design of better devices and (2) to the interpretation of the results of experiments involving intracochlear stimulation of animal and human subjects. As a first step towards this understanding, the goal of this project is to construct a software model of the cochlea that predicts the distribution of potential produced by the stimulation of arbitrarily placed, intracochlear electrodes and use these potential distributions as inputs that drive models of auditory nerve fibers.

As reported over the last two years, a three-dimensional, finite element model of the human cochlea has been developed that predicts the potential distribution produced in this structure by electrical stimulation of model electrodes of arbitrary position and geometry. For a scala tympani/far-field electrode pair, the model predicts that potential along the scala tympani falls monotonically from the electrode toward the base while, from the electrode to the apex, the potential falls initially and then plateaus. These potential distributions indicate that current spreads more toward the base than it does toward the apex. Measurements of potential at unstimulated electrodes made in five human subjects implanted with intracochlear electrodes confirmed the asymmetric potential distributions predicted by the model in all five subjects. Psychophysical measures of the interaction between two electrodes stimulated simultaneously also exhibited asymmetries in these five subjects that were consistent with those predicted by the model.

This year we have continued to make measurements of scala tympani potentials and psychophysical measures of interaction in additional subjects. The results from these additional subjects are consistent with those of last year. We are currently preparing a paper that describes our work in this area.

We have also begun work to integrate the model of potential distribution with linear and nonlinear models of extracellular excitation of myelinated and unmyelinated nerve fibers (which have been developed this year).

1.9.2 Psychophysical Measures and Their Correlation with Speech Reception

Project Staff

Dr. Donald K. Eddington

One striking aspect of speech reception measurements made with subjects using cochlear implants is the wide range of performance. This project is designed to identify basic psychophysical measures that correlate with the subject's speech reception ability. Such correlations should help us both to identify basic performance deficits that might be overcome with alternative processing schemes and to relate correlations found between pathology and psychophysical measures in experimental animals to their potential effect on speech reception.

Last year we reported correlations of speech reception with four psychophysical measures [threshold ($r = -0.80$), dynamic range ($r = 0.78$), interaction ($r = -0.90$), and place pitch ($r = 0.83$)] in an initial set of eight

subjects. This year we have extended these measures to sixteen subjects and are preparing a paper that describes these results.

1.9.3 Cues Used by the Brain to Assign Pitch Based on Electrode Position

Project Staff

Dr. Donald K. Eddington

Subjects with intracochlear electrodes provide a unique opportunity to elicit activity patterns in the array of auditory nerve fibers that cannot be elicited in normal hearing individuals using acoustic stimuli. This opportunity to present novel inputs to the brain and to determine how human subjects perceive them provides a powerful tool to probe the processing mechanisms of the "central processor." I have been using this tool to identify cues that the brain uses to determine the relative pitch of perceptions produced by two electrical stimuli that are temporally but not spatially equivalent. Preliminary results in three subjects indicate that the subjects use the apical boundary of excitation when assigning relative pitch to these stimuli.

1.10 Anatomical Basis for the Relationships between Binaural Hearing and Brainstem Auditory Evoked Potentials in Humans

Project Staff

Dr. Jill C. Gardner, Dr. Robert A. Levine, Dr. Miriam Furst, Dr. Barbara Fullerton, Patricia A. Cuneo

Previous studies have shown that brainstem auditory evoked potentials and some lateralization phenomena are closely related in both normal subjects and subjects with multiple sclerosis (MS). We are currently investigating several features of binaural processing, in normal and MS subjects, in order to determine the regions of the brainstem that are critical for sound localization and the evoked potentials. Our objective is to localize lesions in the brainstem, using magnetic resonance (MR) imaging, and to relate the location of the lesions to the subject's disturbances in auditory function.

During the past year, our primary focus was the development of a procedure to determine if an MS lesion, as detected by MR imaging, involved the brainstem auditory pathway. Toward that goal we: (1) constructed a model (atlas) of the auditory pathway in the human brainstem; and (2) developed an algorithm to map a specified section from the atlas to a corresponding section of an MR scan. The atlas was constructed from 40 mm, serial section histology of two adult human brainstems.[24]

The locations of the nuclei and fiber tracts of the auditory pathway were determined with light microscopy and the data were digitized (see figure 2) for visualization. Outlines of each section and the auditory pathway were entered into a computerized anatomy system, which allows "resectioning" of the atlas in any plane.

An algorithm was developed to estimate the location of the auditory pathway in the MR scans from the computerized atlas (1) as follows. First, for each MR section a corresponding section (same plane, thickness, and distance from the midline) is generated from the atlas. Second, a few well defined landmarks appearing in the two corresponding sections are selected, so that a search procedure can be employed (from regions between adjacent landmarks, it finds points that most closely correspond). By using these two sets of points and a linear fitting procedure, a transformation matrix is derived which superimposes a section from the atlas onto the corresponding MR scan. In the last step, this same transformation is applied to the auditory pathway that lies within the atlas section. This transformed auditory pathway is then superimposed on the MR section to

[24] Part of this work was done in collaboration with John Sundsten and Jeff Prothero at the University of Washington, Seattle, Washington.

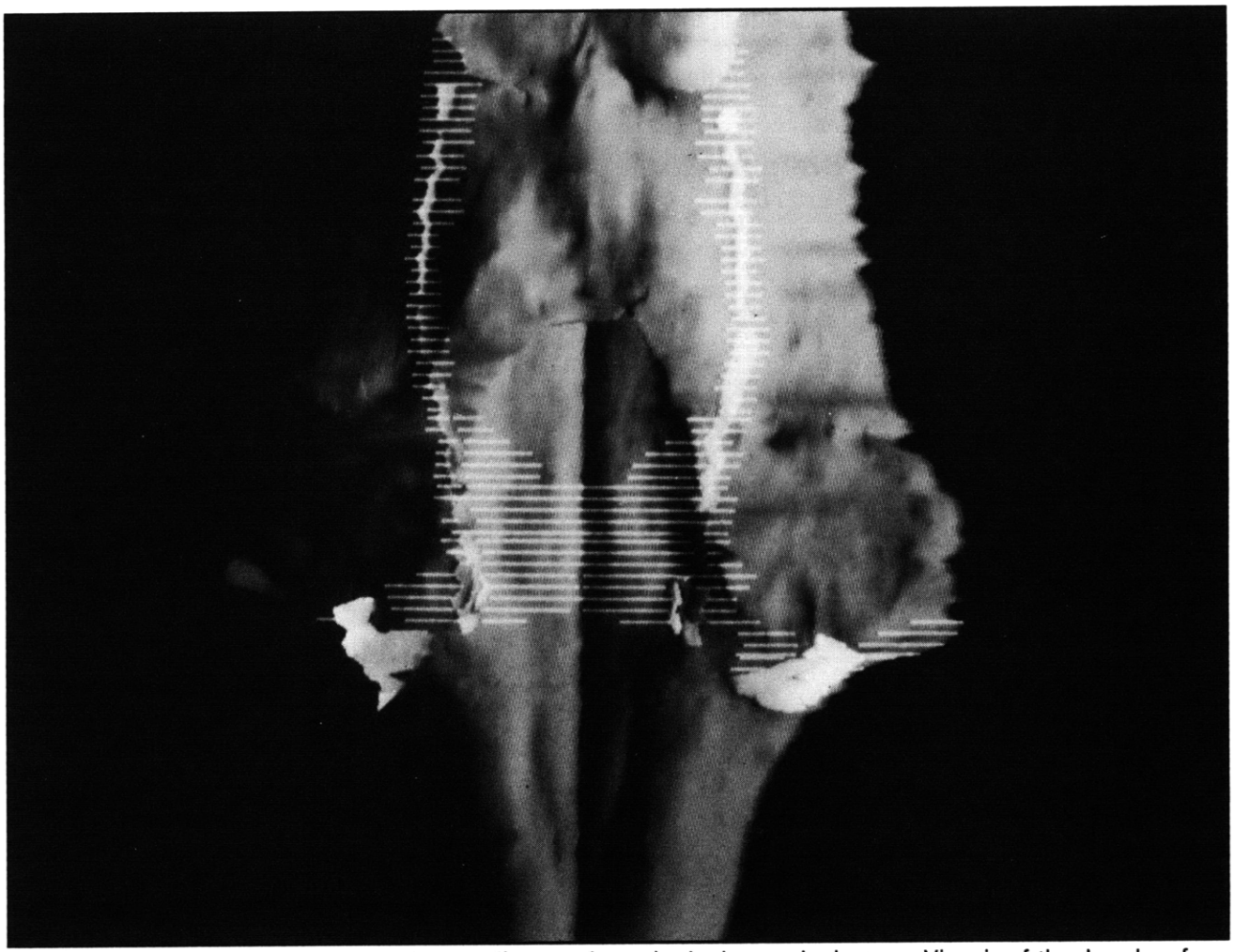

Figure 2. Computer reconstruction of the auditory pathway in the human brainstem. View is of the dorsal surface. Auditory nuclei and fiber tracts are shown as solid regions or broken lines.

give an estimate of the auditory pathway's location (see figure 3).

Publications

Furst, M., J.C. Gardner, R.A. Levine, B. Fullerton, and P. Cuneo. "Localizing the Brainstem Auditory Pathway in Human Magnetic Resonance Images: an Algorithm Matching MR Scans to a Computerized Anatomic Atlas." Paper presented at the Association for Research in Otolaryngology, midwinter meeting, St. Petersburg Beach, Florida, February 4-8, 1990.

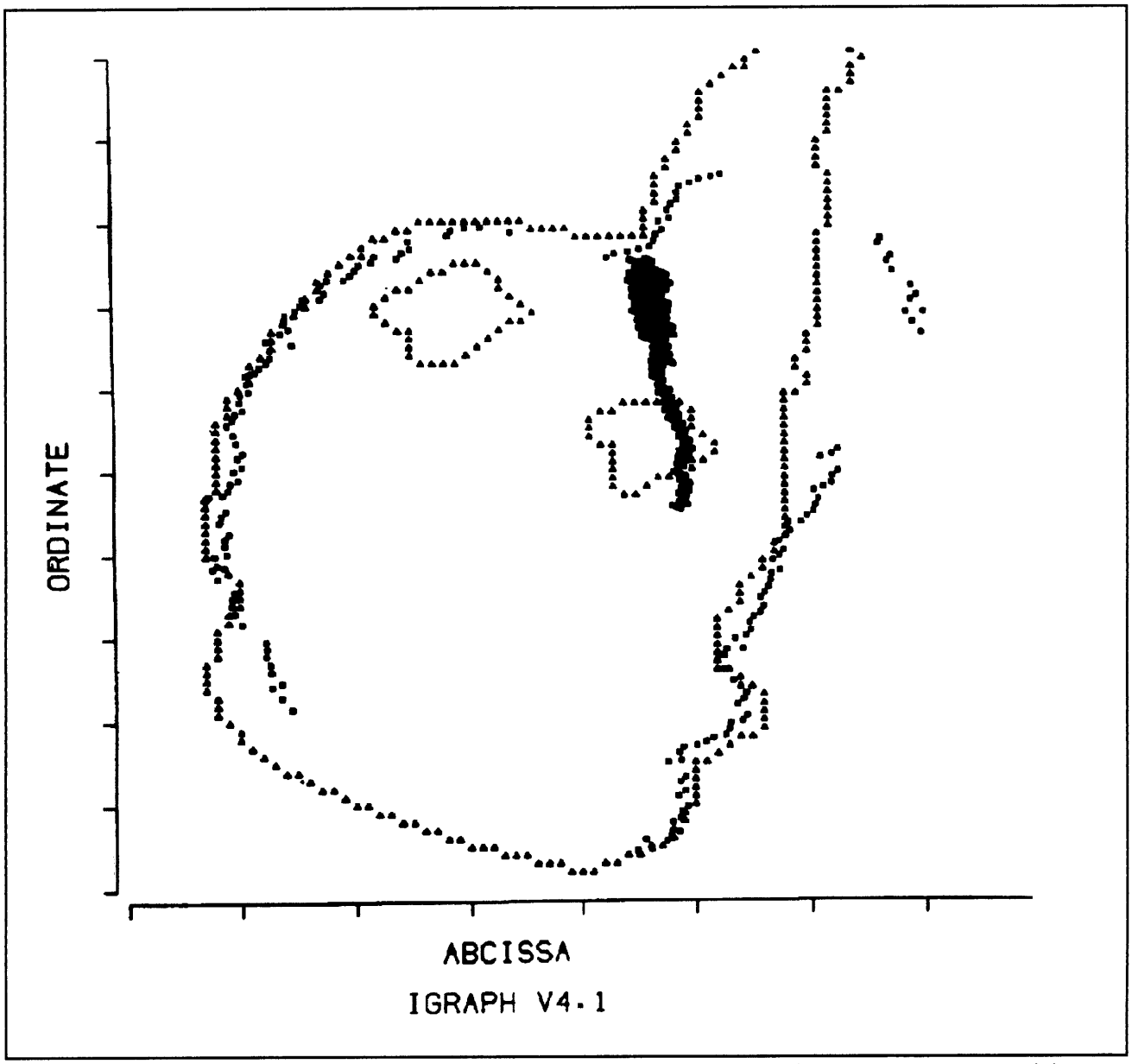

Figure 3. Results of the mapping algorithm. The outline of a sagittal magnetic resonance scan containing two multiple sclerosis lesions, is shown with triangles. A corresponding section from the anatomic atlas is represented with squares. The projection of the lateral lemniscus (dark area) of the auditory pathway overlaps one of the MS lesions.