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STUDIORUM PROGRESSUS

Physiological Evidence for a Cochleo-Cochlear Pathway in the Cat[1]

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The identification of the places in the brain where functional interaction between the ears takes place constitutes one of the major problems of acoustic neurology. The known anatomical projection of the two ears through the nervous system affords many possibilities for interaction between them to occur. Each ear, as is well known, evokes electrical activity as early in the pathway as the trapezoid body and lateral lemniscus[3], and the presumption that interactions between them here and elsewhere are of importance for binaural (as opposed to monaural) phenomena is usually conceded.

The purpose of this communication is to demonstrate that one of the places where interactions occur may be the cochlea itself. The argument rests upon the observation that the earliest neural event recordable in the auditory pathway can be modified by a stimulus applied to the contralateral ear. It is supported by the fact that an electrical event, most likely the result of neural processes, can be recorded at the cochlea when a stimulus is delivered to the contralateral ear. The evidence to be presented is thus consistent with the concept that each cochlea projects to its mate on the opposite side, and that a cochleo-cochlear pathway does indeed exist.

Materials and methods

Observations were made on six cats in this study. They were anesthetized with dial-urethane (0·7 cm³/kg).

The stimuli employed were square pulses 0·1 msec in duration, transduced by Permoflux (PDR-10) earphones and delivered at a rate of 1 per second. An earphone was connected to each ear by plastic tubing 6 cm long inserted into the external meatus and tied securely in place. An attempt was made to have the sound systems deliver symmetrical stimuli to the two ears.

For recording, a grid-to-ground amplifier was used. The cochlear electrode consisted of a platinum or silver wire in contact with the round window or its niche. The ground lead was uniformly the head holder securing the animal. The potentials obtained were recorded photographically from the tube face of a DuMont 247 oscilloscope in the usual manner.

Results

Fig. 1*A* shows the response to a click as it was recorded at the round window of the cochlea. The stimulus artifact (*s*) marks the delivery of the electrical pulse to an earphone. Some 0·3 msec later—an interval accounted for largely by sound conduction to the eardrum—a deflection (*M*) most probably reflecting the activity of the hair cells (microphonic) begins. There then occurs a large negative deflection (N_1) described by DERBYSHIRE and DAVIS[1] as neural in origin, an interpretation that has not been seriously questioned since that time. It is a very early event in that about 1 msec separates its peak from the peak of the initial microphonic deflection. This latency can be increased by cooling the animal, and the deflection can be abolished by a sufficiently large reduction of temperature[2]. Its magnitude is cut down in the presence of masking noises (DERBYSHIRE and DAVIS, *op. cit.*) and after exposure to loud sounds[3]. Its electrical polarity is not changed (as is that of the microphonic) when the direction of the initial motion of the earphone diaphragm is reversed. It is the component of the round-window response most sensitive to anoxemia (unpublished data from this laboratory), and it is the first to disappear when the animal dies. These items of evidence point to the deflection labeled N_1 in Fig. 1*A* as related to the first neural event in the acoustic pathway.

The precise anatomical origin of the potential N_1 is as yet unsettled. It has been ascribed to action potentials in the dendritic processes of the auditory nerve (DERBYSHIRE and DAVIS, *op. cit.*), and more recently to the «cell bodies of the spiral ganglion within the modiolus»[4]. Regardless of its exact source, the deflection N_1 is generally assumed to indicate a synchronized discharge of the primary afferent neurons.

The experiment summarized in Fig. 1 illustrates the effect of a prior click delivered to the opposite ear upon the electrical events aroused by a click to the ear on which the electrode is located. To simplify the description of the experiment, the ear on which the electrode lies will hereafter be referred to as the *ipsilateral* ear, and its mate on the other side will be termed the *contralateral* ear.

In the experiment summarized in Fig. 1, we find the response evoked by an ipsilateral click in the normal animal (Fig. 1*A*) to be appreciably modified by a click delivered 1·25 msec earlier to the contralateral ear (Fig. 1*B*). The main difference between records *A* and *B* is in the remarkable reduction of N_1. Record *C* illustrates that the contralateral ear, when stimulated alone, may produce a potential recordable across the head, at the ipsilateral cochlea.

The records in the right-hand column of Fig. 1 were taken after the contralateral cochlea was destroyed by inserting a probe through its round window, cracking the cochlea open, and injecting formalin into the cochlear wound. Otherwise, conditions of stimulating and recording were unchanged. Fig. 1*D* shows that this

[1] This research was carried out at the Psycho-Acoustic Laboratory, Harvard University, under contract with the Office of Naval Research, U.S. Navy (Contract N5ori-76, Project NR142-201, Report PNR-97). Reproduction for any purpose of the U.S. Government is permitted.

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[3] J. E. HAWKINS, Jr., and M. KNIAZUK, Science *111*, 567 (1950). – W. A. ROSENBLITH, R. GALAMBOS, and I. J. HIRSH, Science *111*, 569 (1950).

[4] H. DAVIS, B. E. GERNANDT, and J. S. RIESCO-MACCLURE, J. Neurophysiol. *13*, 73 (1950).

operation had little effect upon the response to a click delivered to the intact ipsilateral ear. Record *E* demonstrates that the contralateral click no longer depressed N_1, and record *F* shows that a potential was no longer evoked by the contralateral click alone.

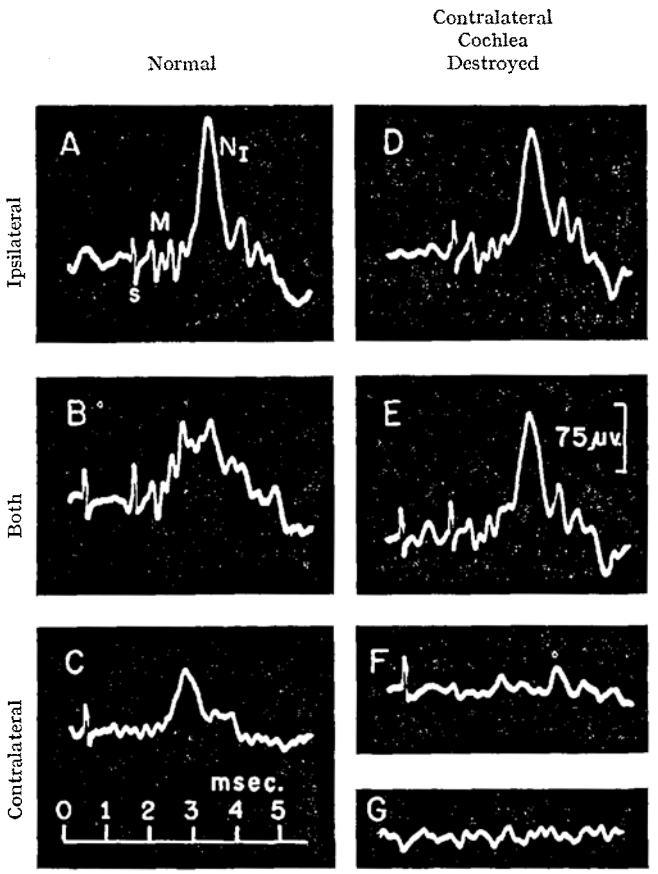

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Fig. 1. – Physiological evidence for a cochleo-cochlear pathway. Electrode on right round window throughout. In *A* the electrical response to an ipsilateral click is reproduced. A stimulus artifact (s) indicates the delivery of the electrical pulse to the earphone. The microphonic event (*M*) is succeeded by the first neural event in the acoustic pathway (N_1). In *B* a click delivered 1·25 msec earlier to the opposite ear (its artifact is at the left of the trace) is seen to reduce the magnitude of N_1. In *C* the click to the contralateral (left) ear gives rise to an electrical event at the electrode. This is the contralateral potential defined in the text. After the contralateral cochlea was destroyed, the stimulus conditions of *A*, *B*, and *C*, respectively, were repeated in *D*, *E*, and *F*. The response to an ipsilateral click remained unchanged (*D*). However, a contralateral click no longer caused a reduction of N_1 (*E*), and the contralateral potential no longer appeared (*F*). The noise level of the recording system is shown in *G*. The approximate intensities of the clicks used were: ipsilateral, 40 db above its threshold; contralateral, 60 db above its threshold. The two ears had approximately equal thresholds.

This experiment obviously suggests that neural events aroused by a contralateral click, and these alone, are responsible for both the depression of N_1 in the opposite ear and the small potential recordable there. We have examined this small potential (hereafter called *contralateral potential*) in an attempt to define its origins more adequately.

The contralateral potential disappears, as we have seen (Fig. 1 *C* and *F*), when the contralateral cochlea is destroyed. This has been demonstrated in a number of animals. It may also be abolished, and this time reversibly, simply by cooling the contralateral ear. (To cool the cochlea, ethyl chloride was sprayed into its bulla. A thermistor[1] located there showed in the experiment of Fig. 2 a temperature of 35° C before cooling, 11 to 12° C at the minimum point, and 35° C again 5 minutes after cooling began.)

The effects of local cooling of the cochlea are shown in Fig. 2. The electrical response of the cooled end organ to a click shows N_1 reduced.(Fig. 2 *B*); in other words, cooling has prevented the arousal of auditory nerve discharges on the cooled side. Approximately coincident with the reduction of N_1, the contralateral potential also is reduced (Fig. 2 *E*). Both potentials return when the cochlear temperature is restored to normal (Figs. 2 *C* and *F*), and they do so, to a first approximation, along the same time course. Since the only important effect of cooling the contralateral cochlea is to prevent neural discharges from originating within it, the conclusion that the voltage recordable in the opposite ear is a neural

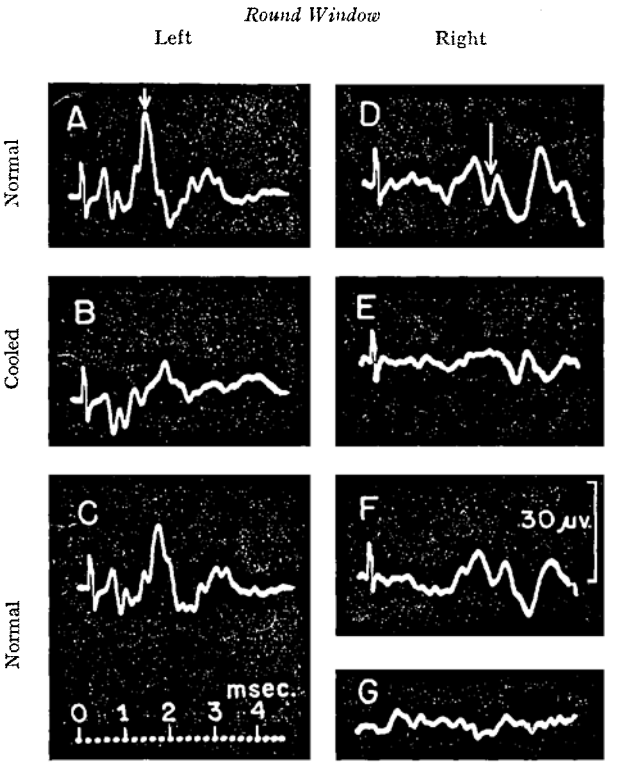

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Fig. 2. – The effects of temperature upon N_1 and the contralateral potential. Clicks delivered to the left ear throughout. The various deflections in *A* can be identified by consulting Fig. 1*A*. The contralateral potential shown in *D* is the event recorded at the right round window when the left ear is stimulated (compare with Fig. 1*C* where its configuration is different). When ethyl chloride was sprayed into the left bulla to cool the left cochlea, the neural event evoked by the click was sharply reduced (*B*) and so was the contralateral potential (*E*). Rewarming of the left cochlea resulted in a return of N_1 (*C*) and of the contralateral potential (*F*). The voltage gain in recording from the right round window was ten times greater than that for the left round window. The noise level for the right round window records is shown in *G*. The arrows in *A* and *D* indicate the points from which an estimate of the latencies of the ipsilateral (*A*) and contralateral (*D*) potentials can be made.

[1] J. A. Becker, C. B. Green, and G. L. Pearson, Electrical Engineering *65*, 711 (1946).

event appears inescapable. A comparison of the latencies of ipsilateral and contralateral potentials yields a figure of the order of 1 msec for the minimum neural conduction time from one cochlea to the other (e. g. Figs. 2 *A* and *D*).

The neural structures that generate the contralateral potential cannot as yet be specified. A peripheral location is indicated in order to explain the interaction at the level of the first neural event (Fig. 1 *B*); it would appear necessary to project the neural pathway from the opposite cochlea into the region of the cell bodies of Corti's ganglion or perhaps into the organ of Corti itself.

A few further facts about these phenomena may be mentioned here. In some experiments the depression of N_1 by a prior contralateral click is small enough to be easily missed unless it is specifically looked for; the depression pictured in Fig. 1 *B* is the best example thus far observed. The contralateral potential, similarly, shows considerably variability from animal to animal (compare Figs. 1 *C* and 2 *D*); but it was invariably identified when searched for. To abolish the contralateral potential, the contralateral cochlea must indeed be destroyed. Preliminary studies, finally, have shown that the prior contralateral click may have an effect upon the ipsilateral N_1 potential for several milliseconds.

While many points still remain to be settled, these experiments, taken together, provide a considerable weight of evidence for the following conclusions[1]:

(1) Each cochlea is connected by a neural pathway to its mate.

(2) This cochleo-cochlear pathway delivers impulses across the medulla and into the opposite cochlea in a time of the order of 1 msec.

(3) The cochleo-cochlear pathway enables the neural events aroused in one ear to interact with, and to modify, the eighth nerve discharge aroused by an acoustic stimulus applied to the opposite ear. This statement rests, of course, upon the assumption discussed earlier that N_1 reflects the activity at the first neuron in the auditory pathway.

Stimulus and recording conditions, while different for the experiments of Figs. 1 and 2, were unchanged within a given experiment.

The results and the experimental controls allow us, therefore, to reject three alternative explanations of the observed phenomena:

(1) The contralateral potential cannot be due to acoustic "leakage" of the contralateral stimulus around the head to the ipsilateral ear. If such cross-hearing were the explanation, there would still have been responses after the contralateral ear had been cooled or destroyed (Figs. 2 *E* and 1 *F*). Furthermore, in each experiment the threshold for cross-hearing was found to be substantially above the intensity that was used for the effective contralateral click.

(2) The contralateral potential can hardly be due to electrical spread of a potential generated on the other side of the head. Such spread would be essentially instantaneous; however, the contralateral potential occurs after activity has almost ceased in the ear to which the stimulus was delivered (compare Figs. 2 *A* and 2 *D*).

(3) Finally, simple algebraic summation of the potentials shown in Figs. 1 *A* and *C*, does not explain the depression of N_1 shown in Fig. 1 *B*.

The anatomical possibilities for a cochleo-cochlear pathway require brief mention. So far as is known, the efferents necessary to support the concept of a cochleo-cochlear pathway are not described as such by anatomists. Neurons passing to the cochlea have, however, been reported to exist, and recently the details of an efferent tract passing from the (contralateral) superior olive to the cochlea via the bundle of Oort have been admirably elucidated by RASMUSSEN[1]. These efferents take up a position within the cochlea identical with that of the internal spiral fibers (hitherto considered afferent in function), and some or perhaps all of them pass out to the region of the hair cells.

Whether this olivo-cochlear tract of RASMUSSEN is part of the cochleo-cochlear pathway required by the physiological evidence is, of course, neither supported nor denied by any of the information at hand. It is mentioned here merely to illustrate that a neural connection between the ears is by no means to be ruled out on anatomical grounds. The actual pathway involved, it should be pointed out, will meet the requirement of a minimum neural conduction time of the order of 1 msec.

Zusammenfassung

1. Wird eine Elektrode an das runde Fenster der Katzenschnecke gelegt und wird ein Knack entweder dem rechten oder dem linken Ohre zugeleitet, so werden in jedem Falle registrierbare elektrische Potentiale hervorgerufen. Ein Knack, der dem in Bezug auf die Registrierelektrode ipsilateralen Ohr zugeleitet wird, gibt den bekannten Komplex von Mikrophon- und Nervenpotentialen. Kontralaterale Knacke verursachen Potentiale, die zeitlich etwas nachhinken und auch kleiner sind.

2. Das durch kontralaterale Knacke hervorgerufene Potential verschwindet dauernd, wenn die kontralaterale Schnecke zerstört ist. Es läßt sich durch vorübergehende Abkühlung der kontralateralen Schnecke reversibel herabsetzen. Diese Maßnahme reduziert auch die Entladungen im kontralateralen achten Nerv. Aus diesen und verwandten Beobachtungen läßt sich folgern, daß zwischen dem einen und dem andern Ohr eine Nervenverbindung besteht (cochleo-cochleare Bahn).

3. Eine Funktion der cochleo-cochlearen Bahn wird erörtert. Ein vorausgegangener Knack, der dem kontralateralen Ohr appliziert wird, setzt die von einem ipsilateralen Knack zu erwartenden nervösen Vorgänge herab.

4. Die in Betracht kommenden Zeitverhältnisse machen eine minimale cochleo-cochleare Überleitungszeit von der Größenordnung von 1 msek. wahrscheinlich.

[1] Note added in proof. Conclusions one and two may be attenuated by certain recent observations. Preliminary experiments indicate that the contralateral potential may still be recorded after transsection of the ipsilateral auditory nerve. It is, however, abolished when the contralateral auditory nerve is cut. We await histological confirmation of the completeness of our nerve sections.

[1] G. L. RASMUSSEN, J. Comp. Neurol. *84*, 141 (1946); Anat. Rec. *106*, 69 (1950).