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Received October 16, 1958. P.S.E.B.M., 1958, v99.

Suppression of Acoustic Input by Thalamic Stimulation.* (24496)

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Studies by Hernandez-Peon and others(1,2) on conscious cats with chronically implanted electrodes have shown that voltage of the response evoked in the cochlear nucleus by a standard sound decreases reversibly when the animal's attention shifts from acoustic to other sense modalities. It so appears that irrelevant information can be prevented from entering the brain further than the first relay nucleus on the afferent path. The centrifugal pathways thrown into operation under such circumstances and which must convey the influence of higher levels of the nervous system to the gating process are unknown. The suggestion is currently put forward that the brainstem reticular formation, which is known to regulate the excitatory state of the cerebral cortex(3), might also exert a direct control over sensory input(*e.g.* 4). We feel however that a good case can be made for distinguishing the neurophysiological processes underlying attention and perceptual selectivity from the reticular arousal mechanism, the latter being non-specific in its intrinsic operation. Direct evidence in favor of such a dissociation has been provided by acute experiments on cats showing that cochlear nucleus response to sound could be suppressed by brainstem stimulation(5,6). The anatomical distribution of electrode locations from which such inhibitory effects were observed was quite restricted, and it was certainly not coextensive with the reticular formation. Indeed the positive points were situated laterally to the accepted limits of the reticular formation and in the close vicinity of the lateral lemniscus and inferior colliculus(6). The structures stimulated in these experiments apparently represent links on a very specific acoustic descending inhibitory pathway which, as shown in the present paper, can be traced further cephalad in the diencephalon.

Methods. The experiments were made on adult cats immobilized with decamethonium or flaxedil (gallamine) and artificially ventilated. The initial surgical preparation was performed under ether anesthesia. Skin incisions were infiltrated with procaine. Electrical stimulation of deep structures in the brain and recording from the cochlear nu-

* This work was supported by grants from Rockefeller and Lekime Foundations and from the U. S. Air Force.

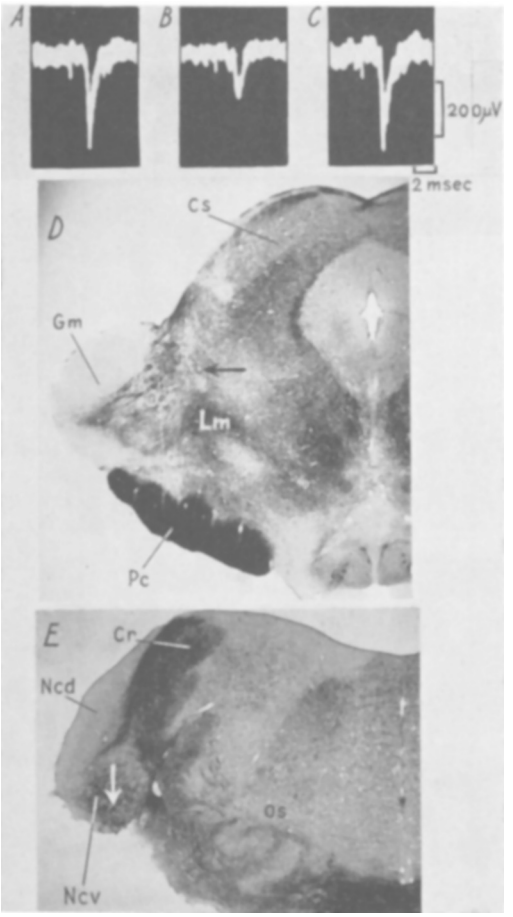

FIG. 1. Cat A 84, 3.2 kg. *A*, *B* and *C*, cathode-ray oscillograms of responses of right ventral cochlear nucleus to a near-threshold click. Four to 5 sweeps have been superimposed in each record to eliminate random fluctuations in response amplitude. Negativity of active recording electrode drives the trace upward. *A*, before, and *B*, during stimulation of inhibitory point in right diencephalon with shocks of 0.5 msec., 6 volts at 150/sec. *C*, just after faradization. *D*, frontal section in an oblique 45° plane (sec 7). Spielmeyer method for myelin. Arrow points to trace of stimulating electrode. *E*, frontal section in 45° oblique plane through posterior part of ventral cochlear nucleus to show location of recording electrode (arrow). Spielmeyer method.

Abbreviations. Bci, brachium colliculi inferioris. Ci, colliculus inferior. Cr, corpus restiforme. Cs, colliculus superior. Gm, nucleus geniculatus medialis. Lm, lemniscus medialis. Ncd, nucleus cochlearis dorsalis. Ncv, nucleus cochlearis ventralis. Os, oliva superior. Pc, pedunculus cerebri.

cleus were effected with bipolar stainless steel needles oriented stereotaxically. These electrodes tapered to about 50 μ and were insulated to the tip with varnish. The electronic equipment included Grass stimulator model S4C, differential preamplifier and DuMont oscilloscope. Monaural acoustic stimulation was performed with click emitted by a PDR-10 earphone. The sound was directed to the ear-drum through a short rubber tube and the hollow ear-bar of the stereotaxic instrument. Precise anatomical control of electrode positions was facilitated by depositing iron electrolytically from the electrode tip at critical points. After completion of experiment, the cat's head was perfused with 10% formaline, ferrocyanide being added to give a prussian blue reaction with the iron. Serial sections were prepared from each brain and stained with the Nissl and Spielmeyer methods.

Results. In our current electroanatomical study of acoustic centrifugal pathways, we try to delimit for each frontal level in the brain, the regions, stimulation of which will suppress acoustic input recorded at the first relay nucleus. The test used is the potential wave evoked in the ventral cochlear nucleus by a near-threshold homolateral click (Fig. 1,A). No attempt is made to isolate cochlear units in the records. Then trains of electrical stimuli at 100-200/sec are delivered to a separate electrode inserted (vertically in the present series) into the diencephalon. This electrode is moved in millimeter steps to explore the region systematically until an inhibitory effect on cochlear nucleus response to click is recorded (Fig. 1,B). As a rule inhibition is not observed after a single shock. It appears during faradization and dissipates quickly when stimulation is withdrawn (Fig. 1,C). Another similar experiment on a different cat is illustrated (Fig. 2, A to C) to show that clear-cut suppression of acoustic input can be consistently produced by repetitive stimulation of a critically-localized area in the posterior diencephalon. This area (Figs. 1,D and 2,D) does not correspond to a readily definable anatomical structure and it certainly includes fiber tracts and cell components which remain to be elucidated. It is situated on the mesial aspect of the nucleus geniculatus medialis and dorso-laterally to the lemniscus medialis and to the rostral reticular formation. The region is very restricted and does not belong to the classical auditory pathway in the sense that clicks generally evoke no potential from it.

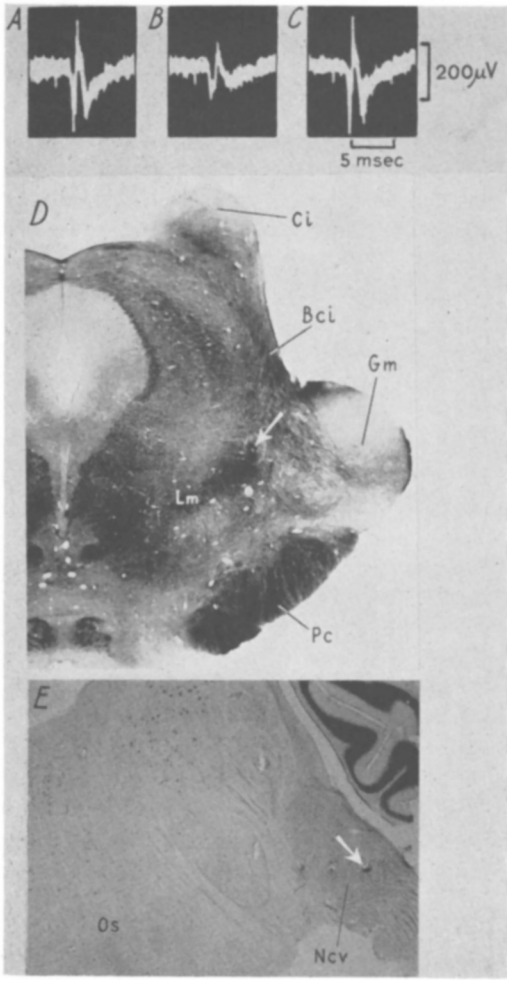

FIG. 2. Cat A 99. 2.8 kg. *A*, *B* and *C*, oscillograms of 4-5 superimposed responses of left ventral cochlear nucleus to a near-threshold click. *A*, before, and *B*, during faradization of inhibitory point in left diencephalon with shocks of 0.5 msec, 7 volts at 150/sec. *C*, just after faradization. *D*, frontal section in 45° plane showing trace of stimulating electrode (arrow). Spielmeyer method. *E*, frontal section in 45° plane through middle part of ventral cochlear nucleus showing trace of recording electrode (arrow). Toluidine blue stain.

By contrast, when the thalamic electrode is inserted more laterally in the same frontal plane, acoustic responses can be recorded (in the nucleus geniculatus medialis) but faradization of these points has not suppressed cochlear response.

That the phenomenon recorded in these experiments is genuine inhibition and not occlusion by possible antidromic stimulation of cochlear axons is indicated by the last-mentioned results showing that points stimulated are close to, but not within the ascending auditory pathway. Moreover a single shock applied to these points evokes no antidromic potential in cochlear nuclei, which in fact do not seem to project fibers further cephalad than the midbrain.

As found previously(6) repetitive stimulation of an inhibitory point situated on any one side of the brain suppresses the acoustic potential recorded both in right and left cochlear nuclei. The centrifugal pathway thus possesses commissural connections which enable it to control simultaneously acoustic input from both ears.

Comment. Little is known about how sensory messages are translated into conscious perception, but a promising start has been made in this direction by analyzing how the brain deals with messages according to its interest in them. Clearly irrelevant stimuli can be screened out at quite early stages in the afferent pathway(1,2) and the sensory information is only handed over to the cerebral cortex after having been subjected to a sort of "editing which emphasizes the important items and sets the unimportant aside" (8).

The present experiments relate to the problem because they provide the first physiological evidence for a specific descending inhibitory pathway, the function of which is presumably to modulate acoustic input to the brain. The descending pathway has been traced at the level of midbrain(6), of the posterior diencephalon (this paper) and further cephalad (to be published). It seems very restricted and the stereotaxically oriented electrodes have to be placed at critical points to produce the effect. In some experiments no inhibition was seen although the preparation seemed in good condition; in many of these cases anatomical study of the brain showed subsequently that the stimulating electrode had narrowly missed the critical region and had been inserted somewhat more medially or laterally.

The evidence indicates consistently that we are dealing with a quite specific descending pathway which seems to be operated by higher levels of the brain. It does not sub-

stantiate the hypothesis that the brainstem reticular formation might control acoustic input through direct reticulo-cochlear fibers.

Summary. 1. Electrical responses to clicks were recorded from the ventral cochlear nucleus in curarized cats, and the effect thereon of brain stem repetitive stimulation was investigated (stereotaxic method). 2. Clear-cut inhibition of the cochlear nucleus response to click was recorded when a critically-localized region of the posterior diencephalon was stimulated. 3. These and previous results provide the first physiological evidence for a specific extra-reticular descending pathway, presumably enabling higher levels of the nervous system to control acoustic input.

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Received October 17, 1958. P.S.E.B.M., 1958, v99.

Paper Electrophoresis of Duodenal Fluid from Patients with Cystic Fibrosis of Pancreas. (24497)

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Farber(1) suggested that the basic pathology in patients with cystic fibrosis of the pancreas resulted from abnormal mucous secretion. In patients with meconium ileus, a common manifestation of cystic fibrosis, the meconium has been demonstrated chemically by Rapoport and Buchanan(2) to contain an abnormal mucoprotein and electrophoretically by Green, Clarke, and Shwachman(3) to have an abnormal protein component. Recently di Sant' Agnese *et al.*(4), using precipitation with a benzene-alcohol mixture, have demonstrated an abnormal mucoprotein in the duodenal fluid in children with cystic fibrosis.

In our studies, samples of duodenal fluid from children with cystic fibrosis were examined by paper strip electrophoresis and the results compared with those observed in control children.

Methods. Ten children with cystic fibrosis were studied, 6 with this diagnosis considered but ruled out by laboratory studies, and 2 normal children. Following intubation, in most instances with fluoroscopic or x-ray verification of the position of the duodenal tube, duodenal fluid was collected in an ice bath. After centrifugation the fluid was frozen until used for electrophoretic study. A volume of .04 cc of the fluid was applied to Schleicher and Schuell (No. 2043A-mgl) filter paper strips in Spinco Model R electrophoresis cell. A veronal buffer of pH 8.6 and ionic strength 0.075 was used with constant current of 2½ ma applied for 16 hours. Following electrophoresis the strips were dried at 120°C for 30 minutes, fixed in absolute methanol for 6 minutes, stained with Bromphenol Blue Dye (Spinco) in alcoholic solution for 30 minutes, rinsed 3 times in 5% acetic acid, dried at 120°C for 15 minutes, and placed in ammonia fumes for 15 minutes-4 hours to enhance color development. Then they were read immediately with Spinco RA Analytrol, utilizing 1½ mm slit, 500 mu interference filters, and a B-5 cam.

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