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Authors

Starr, A
Wernick, JS

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Olivocochlear Bundle Stimulation: Effects on Spontaneous and Tone-Evoked Activities of Single Units in Cat Cochlear Nucleus

A. STARR AND J. S. WERNICK

Department of Neurology, Stanford Medical School, Palo Alto, California

THE OLIVOCOCHLEAR BUNDLE (OCB) is known to modify afferent auditory input at the cochlea. Electrical stimulation of the bundle in the floor of the IVth ventricle causes a suppression of neural response to clicks recorded at the cochlea (10), and a paradoxical enhancement of microphonics (8). Fex (8) and, more recently, Wiederhold (23) have shown that both spontaneous and tone-evoked activities of single units in the VIIIth nerve are similarly suppressed during such OCB stimulation. The purpose of the present study was to investigate the effects of OCB stimulation on spontaneous and tone-evoked activities of single units in cochlear nucleus, the first central auditory station receiving cochlear input. Rasmussen's finding that OCB collaterals terminate in cochlear nucleus (18), raises the possibility that this efferent system may have a central regulatory role as well. Our results indicate that OCB stimulation can modify cochlear nucleus units in a variety of ways. Although suppression of spontaneous activity was frequently observed, there were many units in which OCB stimulation affected an increase in spontaneous discharge rates. Furthermore, the effects of OCB stimulation on tone-evoked responses were found to vary with tone intensity in complex ways.

METHODS

Figure 1 is a block diagram of the stimulus and recording arrangement. Successful experiments were performed on 19 adult cats. The animals were anesthetized with a mixture of halothane (Fluothane, Ayerst), oxygen, and nitrous oxide (14), intubated, and placed in a stereotaxic apparatus with hollow ear bars. Anesthesia was maintained

while the carotid arteries were ligated, a trephine opening made in the skull, and decerebration performed with a blunt spatula lowered stereotaxically at A 2 on either side of the sagittal sinus. In 17 animals the right bulla was opened from a ventral approach and an electrode placed on the round window and cemented to the edge of the bulla. In 2 animals (10, 11), the right cochlea was destroyed by a rongeur, the contents aspirated by suction, and a recording electrode implanted on the left round window instead. Stereotaxic coordinates were used to locate both the cochlear nucleus and the crossing OCB fibers in the floor of the IVth ventricle in the first 9 animals. These structures were directly visualized after aspirating the cerebellum in the last 10 animals, 5 of which received 0.3 g/kg of urea solution (Urevert, Travinol) to reduce brain-stem edema. After surgery, anesthesia was discontinued and the animal moved in the stereotaxic frame into a sound-attenuating chamber. Gallamine triethiodide (Flaxedil, Abbott), 6 mg/kg, was injected intravenously and the animal's respiration maintained by a pump. Additional gallamine triethiodide was given every 60 min. Body temperature was monitored and maintained between 36.5 and 38 C by a heating pad. Parenteral fluids (5% dextrose and water) were given periodically throughout the course of the experiment. The physiological state of the animal was judged to be satisfactory if: 1) the pupils remained constricted, and 2) the amplitude of the neural response to click, recorded at round window, remained constant.

OCB stimulation

OCB stimulating electrodes consisted of three insulated and shielded, 175- μ , stainless steel wires. The tips were separated by 0.75 mm and were aligned in a rostrocaudal direction. The stimulus consisted of 0.1-msec pulses, presented at a rate of 200/sec, applied between any two of the electrodes through an isolation transformer. The duration of the stimulus train was 350 msec. The current strength, as measured by a current probe (Tek-

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FIG. 1. Block diagram of stimulus and recording apparatus. Insert in the lower right-hand side of the figure is a schematic representation of one stimulus trial.

tronix model 131), was varied between 20 and 300 μ a with 100 μ a used most frequently. A variable resistor, center tapped to ground (a Wagner ground), was placed across the stimulating electrodes to control the polarity and amplitude of the stimulus artifacts.

Sound stimulus

Sinusoidal voltages for tonal stimuli were generated by an audio oscillator, passed through an electronic switch for regulation of rise and decay times, attenuated, and presented to the animal by Telephonics (TDH 39) transducers. The response of this system with a 1-v rms input measured in a 1-cc coupler was 102 db SPL between 200 and 1,500 Hz, and then decreased at 20 db/octave above 1,500 Hz. Tone bursts of 200 msec with rise and decay times of 25 msec were routinely used. The tone's onset occurred 150 msec after the onset of OCB stimulation and both were terminated together (Fig. 1). Square-wave pulses 0.05 msec in duration were applied to the transducers to provide "click" stimuli during the placement of the OCB electrodes.

Electrophysiological data acquisition and processing

Electrical activity recorded by a stainless steel microelectrode with a tip diameter of 0.5–1 μ (13) was amplified by a unity gain cathode follower in series with a Grass P511A preamplifier and converted to digital information by a Schmidt trigger

circuit. Round-window responses were amplified by another Grass P511A preamplifier. The output of the Schmidt trigger was monitored on an oscilloscope along with unit activity to determine if triggering levels were correct, and then passed through an electronic switch to an electronic counter (Hewlett-Packard, model 522B) to determine the discharge rate of the unit under study. In the last 14 animals studied the data were also recorded on magnetic tape for subsequent computation of poststimulus time histograms (PSTH) and interspike-interval histograms (ISIH) and for photographic display using a technique of converting each unit discharge to a discrete dot on the oscilloscope (22).

Procedure

In the first nine animals round-window responses to clicks were monitored on the oscilloscope, while the OCB electrodes were advanced in 0.5-mm steps. The location of the stimulating electrodes was considered satisfactory if a current of 200 μ a or less caused: 1) a decrease in the amplitude of the N_1 response equivalent to at least a 10-db decrease of click intensity, and 2) an increase in the amplitude of the microphonic response. The same criteria were also used when the stimulating electrodes were placed on the floor of the IVth ventricle under direct visual control. The bipolar stimulating pair that effected the largest attenuation of round-window neural responses

was selected for the remainder of the experiment.

The microelectrode was advanced into the cochlear nucleus while tone bursts were presented. When a unit was found that was either spontaneously active or responsive to tones, its location along the tract was noted from the micrometer drive and the following parameters were defined: 1) the lowest intensity tone evoking an increase in discharge rate (the "best" frequency), 2) spontaneous discharge rates with and without OCB stimulation, 3) discharge rates evoked by different frequency tones presented at a single intensity (65 db SPL) with and without OCB stimulation, 4) discharge rates to a single tone presented at different intensities with and without OCB stimulation, 5) discharge rates during contralateral tonal stimulation with and without OCB stimulation. "Best" frequency was defined by standard audio-visual monitoring techniques.

Discharge rates were determined by gating the input to the electronic counter for a 200-msec period once every 2 sec for a total of 10 trials. The 200-msec periods sampled coincided with the tone burst and the last portion of the OCB stimulus train (see insert, Fig. 1). For spontaneous discharge rates with and without OCB stimulation a minimum of 2 and a maximum of 10 separate counts were made. For tone-evoked activity with and without OCB stimulation, usually only 1 count at each intensity level was made. Unit activity was sampled both during insertion and withdrawal of the microelectrode and up to 4 penetrations were made in each animal. At the end of the experiment anodal current was passed through the microelectrode at a defined position along the final electrode track and through the cathodal pole of the OCB stimulating electrodes. The animals were perfused with a dilute solution of potassium ferricyanide in 10% formalin, the brain removed, and the completeness of decerebration verified. The brain stem was sectioned histologically (52- μ frozen sections) and the position of the electrode tips determined by the presence of the Prussian blue reaction (13). Successful reconstruction of the electrode track was accomplished in 12 of the experimental animals. In the other 7 animals there was either histological evidence or direct visualization of the electrode's passage through cochlear nucleus, but insufficient definition of electrode tip location.

Classification of units

The effect of OCB stimulation on unit activity was classified by the following criteria. For spontaneous activity, when only two sets of determinations had been made, a difference in the discharge rate of at least 50% was needed to consider the change in unit discharge rate significant. If three determinations had been made, this difference needed to be at least 20% in each of the trials to

TABLE 1. *Spontaneous activity during olivocochlear bundle stimulation: relation to spontaneous discharge rate*

	Percentage of Units			
	No effect	Decrease	Increase	N
All units	51	31	18	121
Spontaneous rate/sec				
0	100	0	0	28
1-25	53	29	18	38
26-50	24	35	41	34
>50	29	67	4	21

N = number of units.

be considered significant. If four or more determinations had been made, a simple sign test was used to evaluate the differences found. A difference in discharge rate was considered significant at the $P = .05$ level. The effects of OCB stimulation on tone-evoked activity was defined by examining the curves relating discharge rate to tone intensity.

RESULTS

OCB stimulation and spontaneous activity

The effects of OCB stimulation on spontaneous activity of 121 units in the cochlear nucleus were determined by comparing the number of discharges during a minimum of 20 trials of OCB stimulation with activity in a comparable period in the absence of such stimulation. Spontaneous activity was unchanged by OCB stimulation in 51% of the units, decreased in 31%, and increased in 18% (Table 1). The distribution of these effects varied with spontaneous discharge rate. Units without spontaneous activity were all (28 units) unaffected by OCB stimulation, as they did not discharge during the stimulus train. Slightly more than one-half of the units with low rates of spontaneous activity (1-25/sec) were similarly unchanged by OCB stimulation (20 of 38 units). In contrast, most of the units with spontaneous discharge rates greater than 25/sec were modified during OCB stimulation (40 of 54 units); those with rates greater than 50/sec were, in general, decreased (14 of 21 units), whereas the different modifications of spontaneous activity occurred with equal probability in units with intermediate discharge rates (26-50/sec).

FIG. 2. Poststimulus time histograms of spontaneous activity during and after stimulation of the OCB. Duration of the OCB stimulus is indicated between the arrows at bottom of the figure. Amplitude calibration is 5 unit discharges. Each bin is 5 msec in duration. Number of stimulus trials sampled ranged from 10 to 50.

Unit	Spontaneous Activity Discharges/Sec	Trials for Histogram
A 18-1	7	50
B 19-2	52	10
C 12-1	120	20
D 12-2	35	50

There were four general types of discharge patterns evoked by OCB stimulation (Fig. 2): 1) a decrease of activity during OCB stimulation followed by a gradual return to prestimulus rates (Fig. 2A), 2) a decrease of activity during OCB stimulation followed by a rebound acceleration of activity to greater than prestimulus rates (Fig. 2B), 3) an increase of activity during OCB stimulation followed by gradual return to prestimulus rates (Fig. 2C), and 4) an increase of activity during OCB stimulation followed by a rebound depression of activity to below prestimulus rates (Fig.

2D). Spontaneous activity was affected after a latent interval, and the changes persisted well beyond the end of the stimulus train. Thus, in eight units with a decrease in discharge rate during OCB stimulation without rebound aftereffects, the latency from the onset of the stimulus train to the time of maximal spontaneous activity modifications varied from 20 to 90 msec, and spontaneous activity did not return to normal rates for up to 500 msec after the end of the OCB stimulus train. In units with an increase of activity during OCB stimulation the latency from the onset of the stimulus train to the appearance of spontaneous activity modifications varied from 5 to 150 msec.

In one unit there was an increase of activity during the initial 50 msec of OCB stimulation followed by a suppression of activity for the remainder of the stimulus train (Fig. 3). Though this sequence was found in only one unit of the population examined, it indicates that OCB regulation of cochlear nucleus activity may be quite complex.

There was no correlation between the occurrence of a particular response pattern and

FIG. 3. Representation of spontaneous activity in unit 9-5 with (B) and without (A) OCB stimulation. Each dot represents a unit discharge, and each line represents a 500-msec period that commences with the onset of the OCB stimulus. Stimulus period is indicated between the arrows. Note that the unit discharges several times at the onset of the stimulus, and then is suppressed.

the strength of stimulus or location of the stimulating electrodes on the floor of the IVth ventricle. Thus, units located within a few hundred microns of one another along a single microelectrode penetration could be affected in very different ways by the same OCB stimulus (Fig. 4). Furthermore, in nine units tested with OCB currents ranging from 20 to 300 μ a, the type of response pattern elicited at threshold currents also appeared in response to supramaximal currents. Stimulus strength was a factor, however, in determining the extent of spontaneous activity modifications with maximal effects occurring when current intensities were two- and threefold above threshold levels.

The distribution of intervals between adjacent discharges of a unit during the last 200 msec of OCB stimulation was computed for 11 units and compared with the distribution of intervals of their spontaneous activity (Fig. 5). In 8 of the units, differences in the histograms of spontaneous and OCB activities could be attributed to the differences in discharge rates in the 2 experimental conditions. By adjusting the analysis to correct for this factor, the histograms became comparable (the standard binwidth in milliseconds times the ratio of the spontaneous discharge rate/ the discharge rate during OCB stimulation (17)).

There were three units in which changes in the interspike-interval histograms during OCB stimulation could not be attributed solely to changes in discharge rate. These units had interval periodicities corresponding approximately to the periodicity of the stimulus train (i.e., 5 msec). Thus, for unit 12-5 in Fig. 6, discharges occurred preferentially at intervals of 5, 10, 15, and 20 msec, indicating that the unit was discharging at a fairly constant latency following some of the pulses of the stimulus train. The latency of response of these units to single OCB pulses was 3-8 msec (Fig. 6C). It is unlikely that these units were antidromically activated by spread of current to the acoustic stria, which traverses the brain stem ventral to the stimulating electrodes. First, the response latencies of 3-8 msec were considerably longer and more variable than typical antidromic latencies of 0.5-1 msec measured in a separate experiment, in which the stimulating electrodes were located in the trapezoid body. Second, units were unable to respond to every OCB stimulus even when

FIG. 4. Tracing of the microelectrode tract through cochlear nucleus in animal 9. Location of the units and their protocol numbers are depicted to the right of the brain section. Effects of OCB stimulation on evoked and spontaneous activity is shown in the following table.

Unit	Spont Activity Discharges/Sec		Evoked Activity	
	Control	+OCB	Best freq, kHz	OCB effect
7	45	49	1.2	Complex
5	16	5	.7	Decrease
8	0	0	.6	Decrease
6	21	40	.3	Increase

presented at rates as slow as 1/sec, whereas antidromically evoked activity from stimulating the trapezoid body followed stimulus frequencies in excess of 200/sec.

OCB effects on spontaneous activity after destruction of cochlea

Thirty-three single units in the cochlear nucleus were studied in two animals after destruction of the cochlea ipsilateral to the cochlear nucleus examined. Changes in spontaneous activity during OCB stimulation in these animals cannot be attributed to the action of the OCB at the receptor, but would have to be due to its influence on the cochlear nucleus itself. None of these units were activated by sounds presented to the ipsilateral ear. During stimulation of the OCB, 42% of the units had an increase in their spontaneous discharge rate, 15% had a decrease, and 43%

FIG. 5. Poststimulus time histograms (*A*) and interspike-interval histograms (*B*, *C*, *D*) of two units affected in opposite ways by OCB stimulation. In *A* the period of stimulation is indicated between the arrows. Histograms are derived from 30 stimulus trials in unit 12-1 and 20 stimulus trials in unit 15-3. Time calibration is 200 msec, and amplitude calibration refers to 5 unit discharges. Binwidth is 5 msec. Interspike-interval histogram of the last 200 msec of stimulus period is shown in *B*, and a control histogram (spontaneous

activity without OCB stimulation) is shown in *C*. *D* is the interspike-interval histogram of activity during the last 200 msec of the stimulus period after adjustment for the change in discharge rate produced by OCB stimulation. Ordinate is expressed in percent probability.

Unit	Spontaneous Activity	+OCB
12-1	120/sec	159/sec
15-3	77/sec	47/sec

were unchanged. Poststimulus time histograms were very similar to those described for units sampled from animals with intact cochleae.

OCB stimulation and sound-evoked activity

Eighty-four percent of the 121 units tested in these experiments responded to tone stimuli. Those units unaffected by tones may have

FIG. 6. Interspike-interval histogram (A), poststimulus time histogram (B) and responses to single OCB stimuli (C) for unit 12-5. Interspike-interval histogram is calculated from activity during the last 200 msec of the OCB stimulus train. The poststimulus time histogram is based on 20 stimulus trials and OCB stimulation is indicated between the arrows. Latency of unit responses to single OCB shocks presented at 1/sec is shown in upper trace of C. Lower trace is the output of current probe indicating 200 μ a. Responses to 15 trials are superimposed on the photograph. Amplitude calibration in B is 5 unit discharges and in C is 100 μ v. Time calibration is 200 msec in B and 2 msec in C.

had best frequencies higher than the capabilities of the sound system employed, or were insensitive to the slow rise times of the tonal stimuli used. Table 2 summarizes the changes produced by OCB stimulation of the evoked discharge rate of 91 units tested with different tone intensities at their best frequency, and representative examples of each category are graphed in Fig. 7. OCB stimulation had no effect on tone-evoked activity of 18% of the units (Fig. 7A). Units in which tone-evoked activity was decreased by OCB stimulation (37%) were of three general types: 1) those in which the intensity function was simply shifted (Fig. 7B), 2) those in which the decrease of activity at higher sound intensities deviated from a uniform shift of the intensity function (Fig. 7C), and 3) those in which there was a decrease of activity only at intensities near threshold (Fig. 7D). Units with an increase of tone-evoked activity during OCB stimulation (27%) were of two types: 1) those in which the increase occurred at all intensities (Fig. 7E), and 2) those in which the increase occurred with tone intensities 20 or more db above that particular unit's threshold

(Fig. 7F). Finally, there are 20 units in which OCB stimulation had complex effects, causing a decrease or an increase in evoked activity as a function of tone intensity (Fig. 7G, H, I). In every instance a decrease of activity was associated with intensities close to the threshold, whereas an increase of activity was always associated with higher intensities. In 5 of these units the effect of OCB stimulation was, in fact, equivalent to a shift in the intensity function (Fig. 7H). There was a non-monotonic relation between discharge rate and tone intensity in these units, and the response modifications accompanying OCB stimulation were equivalent to those that would have occurred had the intensity of the tone simply been reduced. The effects of OCB stimulation on the other 15 units with complex response modifications differed from that of a simple shift of the intensity function (Fig. 7G, I).

The influence of OCB stimulation on tone-evoked activity was also evaluated by determining: 1) the pattern of unit discharges evoked by tones (18 units), 2) the distribution of intervals between adjacent discharges

TABLE 2. *Tone-evoked activity during olivocochlear bundle stimulation*

	Percentage of Units				N
	No effect	Decr	Incr	Complex	
All units	18	37	23	22	91
Threshold, db SPL					
<30	3	51	15	31	33
30-70	16	32	16	36	19
>70	47	29	18	6	17
Best frequency, kHz					
<1	20	33	20	27	15
1-3	9	39	27	25	33
>3	13	48	19	20	31
Inhibitory surround					
Present	0	16	37	47	19
Not present	29	29	29	13	14
Intensity function					
Monotonic	18	50	23	9	22
Nonmonotonic	0	32	18	50	28

N = number of units.

(11 units), and 3) the latency of evoked activity (9 units). Poststimulus time histograms indicated that OCB stimulation changed the over-all level, but not the pattern of unit firing in response to tones (Fig. 8), and when OCB stimulation resulted in an increase in firing rate in response to tones there was an increase in the number of unit events appearing at the mode interval characteristic of the interspike-interval histogram to tone alone (Fig. 10). Finally, OCB stimulation affected the latency of tone-evoked activity in 8 of the 9 units in which this parameter was measured. The change in latency was the inverse of the change in discharge rate (Fig. 9).

Measurements were made in 10 units of OCB effects on responses evoked by tones differing from the best frequency. In 7 of these units response modifications were similar to those found at the best frequency (2 of these units are shown in Fig. 11 *A, B*), whereas significant differences with tone frequency were found in 3 units. In 1 of the latter units (Fig. 11*C*), OCB stimulation during the pres-

entation of a tone at its best frequency (0.735 kHz) was accompanied by a decrease of activity at threshold intensities, and by an increase of activity at higher sound levels. For frequencies in the inhibitory surround (0.3, 1 and 6 kHz), OCB stimulation effected only a further decrease or no change of activity over the entire intensity range. In another unit (Fig. 11*D*) OCB stimulation was associated with a shift in the intensity function at 0.58 kHz, whereas at 1 kHz there was both a decrease of discharges at threshold intensities and an increase at higher intensities.

The effects of OCB stimulation on tone-evoked activity were evaluated with respect to the unit's threshold, best frequency, presence of an inhibitory surround, and the shape of the intensity function (monotonic or non-monotonic; Table 2): 1) Units with low thresholds (below 70 db SPL) were more likely to be affected by OCB stimulation (48 of 52 units) than were units with high thresholds (above 70 db SPL, 8 of 17 units). 2) Of the units affected by OCB stimulation those with thresholds below 70 db SPL were more likely (17 of 52 units) to show complex changes than were units with thresholds above 70 db SPL (1 of 17 units). This difference may be due to the fact that the detection of complex response modifications depended on the ability to measure unit activity at many intensities. Units with high thresholds could only be evaluated over a limited intensity range (30 db) with the sound system employed, whereas units with low and medium thresholds were tested over a much more extended range (up to 100 db). 3) The only trend evident between the effects of OCB stimulation and best frequency was that almost all of the units, in which OCB stimulation caused only an increase in tone-evoked activity, had best frequencies below 4 kHz (19 of 21 units). The other response modifications were uniformly distributed with regard to best frequency. 4) Units with an inhibitory surround were more likely to have either an increase in discharge rate or complex response changes with OCB stimulation (16 of 19 units) than were units without inhibitory surrounds (6 of 14 units). 5) Units with non-monotonic intensity functions were more likely to have complex response modifications with OCB stimulation (14 of 28 units) than were units with monotonic intensity functions (2 of 22 units).

FIG. 7. Effects of OCB stimulation on tone-evoked activity tested with the unit's best frequency (indicated in upper left-hand corner of each graph) at different intensities. Ordinate of the graphs is the number of discharges occurring during 2 sec of tone stimulation (ten 200-msec tone bursts), and abscissa represents the attenuator setting re 1-v rms into earphones. Numbers just above the best frequency notations are the protocol listing for each of the units. Bars in the lower left-hand corner of each graph indicate mean spontaneous discharge rate. No bar indicates the unit was not spontaneously active.

Interactions between OCB stimulation and contralateral tones

Pfalz (16) has shown that a contralateral acoustic stimulus may inhibit spontaneous discharges of units in cochlear nucleus. The inhibition is thought to involve pathways distinct from OCB, since it persists following section of OCB in the floor of the IVth ventricle, but is abolished after trapezoid body section (7). Results from the present experiments indicate, in addition, that OCB stimulation and a contralateral tone can have opposite effects on spontaneous activity of single units in cochlear nucleus. In seven units in which a contralateral tone elicited a decrease of spontaneous activity, OCB stimulation increased spontaneous activity in four, had no effect in

one, and decreased discharge rates in two. Furthermore, the effects on spontaneous activity of pairing a contralateral tone and OCB stimulation could be additive.

Correspondence between OCB modifications of spontaneous and tone-evoked activities

The effects of OCB stimulation on spontaneous activity were compared with its effects on tone-evoked responses (Table 3): 1) Most of the units that were not spontaneously active showed a decrease in tone-evoked responses during OCB stimulation (18 of 26 units). These units were all unaffected by OCB stimulations in the absence of tonal stimuli. 2) Units with a decrease of spontaneous activity during OCB stimulation had, in

FIG. 8. Poststimulus time histograms of tone-evoked activity with (○-----○) and without (●——●) OCB stimulation. Period of tone presentation is represented between the arrows of the lower row. Histograms were computed at the points indicated by letters *A*, *B*, and *C* on graphs on the left side of the figure from 10 stimulus trials. Amplitude calibration at bottom of the figure is equivalent to 10 unit discharges. Each bin is 2.5 msec in duration. Spontaneous discharges, when present, are indicated by bars in the graph.

FIG. 9. Comparison of effects of OCB stimulation on the latency of tone-evoked activity (*A*) with the effects on discharge rate (*B*). Abscissa for both *A* and *B* and ordinate for *B* are similar to Fig. 7. Asterisks in the ordinate of latency graph for units 17-6 and 18-1 indicate that no measure was possible. Data are the mean of 10 stimulus trials, unless otherwise indicated.

FIG. 10. Interspike-interval histogram of tone-evoked activity with (+OCB) and without (control) OCB stimulation. Ordinate is expressed in percent probability. Unit activity from 10 200-msec trials was used to calculate the histogram.

FIG. 11. Effects of OCB stimulation on tone activities tested with a range of frequencies at many intensities. The ordinate and abscissa of graphs are similar to Fig. 7. *A*, unit 4-2; *B*, unit 12-5; *C*, unit 18-1; and *D*, unit 9-8. Mean spontaneous discharge rate, when present, is indicated by bars.

TABLE 3. *Relation of spontaneous and tone-evoked activities during olivocochlear bundle stimulation*

Evoked	Spontaneous			
	Percentage of units affected			
	No effect		Decr	Incr
	No spontaneous activity	Spontaneously active		
No effect	19	32	9	9
Decrease	69	26	47	0
Increase	7	26	0	64
Complex	5	16	44	27
N	26	19	23	22

N = number of units.

general, a corresponding decrease in their tone-evoked responses (11 of 23 units). An increase in evoked activity was restricted to tones at least 30 db above threshold as part of that unit's complex response change. 3) Units in which spontaneous activity was increased by OCB stimulation were also likely to have an increase in tone-evoked activity (14 of 22 units). Any decrease in discharge rate was limited to threshold intensities as part of that unit's complex response change. 4) If a unit's spontaneous activity were modified by OCB stimulation it was almost certain that its evoked activity would be modified as well (41 of 45 units). 5) The converse, however, was not true. More than two-thirds of the

units in which spontaneous activity was not modified by OCB stimulation had changes in evoked responses (13 of 19 units).

Anatomical location of units studied

The relation between effects of OCB stimulation on spontaneous and tone-evoked activity and the location of the units within cochlear nucleus (anteroventral, dorsal, and posteroventral) are shown in Table 4. All of the various effects of OCB stimulation were found in each of the subdivisions of the cochlear nucleus. The only trend evident was that units with an increase of spontaneous activity during OCB stimulation were encountered rarely in the anteroventral subdivision. In this division suppression of spontaneous activity occurred most frequently.

Relation of changes in cochlear nucleus activity to stimulation of OCB

There are five lines of evidence indicating that stimulation of the floor of the IVth ventricle in these experiments affected discharge rates of cochlear nucleus units by activating the OCB. 1) Histological sections of the brain stem in the 19 animals studied showed the cathodal pole of the stimulating electrodes to be from 0.5 to 2.0 mm rostral to the facial genu in the area known to contain crossing OCB fibers (18). 2) Stimulation of this region produced changes in round-window responses to clicks of the type known to accompany activation of the OCB: neural responses were attenuated, and microphonics were increased (8, 10). 3) The parameters of

TABLE 4. *Relation of olivocochlear bundle effects to location of units within cochlear nucleus*

	Percentage of Units					
	Spontaneous			Evoked		
	AVCN	DCN	PVCN	AVCN	DCN	PVCN
No effect	64	48	58	15	9	35
Decrease	32	32	21	50	37	30
Increase	4	20	21	15	21	0
Complex				20	33	35
N	25	41	14	20	24	7

AVCN = anteroventral cochlear nucleus; DCN = dorsal cochlear nucleus; PVCN = posteroventral cochlear nucleus. N = number of units.

the stimulating currents needed to elicit changes in discharge rates of single units in the cochlear nucleus were comparable to those needed to elicit changes in round-window responses. 4) If the stimulating electrodes were displaced 1.5 mm rostral or caudal to the region of the OCB, stimulation with previously effective current levels no longer produced changes in discharge rates of single units in cochlear nucleus. Increasing the current strength at the new site to a level effective in modifying round-window responses to clicks resulted in the reappearance of effects on discharge rates of single units in the cochlear nucleus. 5) The possibility that middle ear muscle contractions contributed to the changes in unit activity was unlikely, since the animals were immobilized with gallamine triethiodide, rendering the middle ear muscles inactive. Furthermore, stimulation in the floor of the IVth ventricle was accompanied by an increase in cochlear microphonics, whereas middle ear muscle contractions would have resulted in an attenuation of microphonics (2).

DISCUSSION

These experiments show that stimulation of the OCB can modify both spontaneous and tone-evoked activities of single units in cochlear nucleus. The changes encountered were more complex than those reported in single afferent VIIIth nerve fibers during similar OCB stimulation. Fex (8), and more recently Wiederhold (23), found that the rate of both spontaneous and tone-evoked activities of almost all of the VIIIth nerve fibers studied decreased during OCB stimulation; the only exceptions were units which were unaffected by the stimulation. No increase in activity was found. In contrast, in the present study 18% of the units examined in the cochlear nucleus had an increase in their spontaneous discharge rate during OCB stimulation, and tone-evoked activities were even more frequently enhanced. Furthermore, studies on single afferent VIIIth nerve fibers have shown the effects of OCB stimulation to decrease as tone intensity is raised (23). In contrast, interactions between OCB stimulation and tone intensity were much more varied in cochlear nucleus. In some units OCB stimulation caused a decrease in unit

activity evoked by threshold intensities and facilitated the same unit's response to tones 20–30 db more intense. There were other units in which OCB stimulation enhanced activity evoked by all tone intensities, and still others in which evoked responses were attenuated as a function of tone intensity similar to VIIIth nerve units.

Some of the differences between the effects of OCB stimulation on VIIIth nerve activity and on cochlear nucleus activity may be related to the distribution of OCB fibers. Rasmussen (18) has shown that the OCB projects both to cochlear nucleus, terminating in the granular cell layer of the ventral subdivision, and to the cochlea. The ability of OCB stimulation to modify activity at the cochlea has been well documented (3, 4, 8, 10), and results from the present experiments suggest there are direct effects of OCB stimulation on cochlear nucleus as well. In two animals with the cochlea surgically ablated, OCB stimulation was still capable of modifying spontaneous discharge rates in more than 50% of the cochlear nucleus units sampled. It is likely that some of the complex changes of cochlear nucleus activity found in animals with intact cochleas were the result of an interaction between OCB effects at the cochlea and at cochlear nucleus.

Spontaneous activity

Koerber et al. (15) have shown that spontaneous discharges in units located in both dorsal and posteroventral subdivisions of cochlear nucleus persist after destruction of the cochlea, whereas spontaneously active units in ventral cochlear nucleus were rarely encountered after this procedure. These authors propose that spontaneous activity in ventral cochlear nucleus depends upon input from the cochlea, whereas the sources of spontaneous activity for units in dorsal and posteroventral cochlear nuclei are independent of peripheral input. The results from the present experiments in two animals with their cochleae acutely destroyed are in agreement with these authors' findings, as spontaneously active units were encountered only in dorsal and posteroventral subdivisions of cochlear nucleus. The ability of OCB stimulation to modify spontaneous discharges of these units raises the possibility that this efferent pathway may be one of the sources

contributing to spontaneous activity in cochlear nucleus.

Tone-evoked activity

The major effect of OCB stimulation on evoked activity was to change the relationship between the unit's rate of discharge and tone intensity. In many units there was a simple shift of the intensity function (see Fig. 7 *B, H*) similar to the shift of the intensity function found in primary afferent VIIIth nerve fibers (23). There were other units, however, in which changes in tone-evoked activity during OCB stimulation could not be attributed solely to peripheral mechanisms. In these units OCB stimulation during low-intensity tones was associated with a decrease in unit activity, whereas the same OCB stimulus in the presence of high-intensity tones facilitated evoked activity. Since no instances of an increase of tone-evoked activity have been found in primary VIIIth nerve fibers during OCB stimulation, it is likely that these complex response modifications originated within the cochlear nucleus itself. Furthermore, the occurrence of complex response changes was most likely in units having either an inhibitory surround or a nonmonotonic intensity function, both characteristic of units in cochlear nucleus (12, 19).

Basis of OCB effects on cochlear nucleus

Fex (9) has presented experimental evidence that the crossed OCB is inhibitory in nature, and that it attenuates the transduction of acoustic energy into neural impulses at the cochlea by hyperpolarizing the hair cells. Also strychnine, which blocks some inhibitory transmitter effects, blocks OCB actions (3). There are four possibilities that might account for the ability of OCB stimulation to increase single-unit activity in cochlear nucleus, while it is inhibitory at the cochlea. First, an increase of cochlear nucleus activity would occur if the transmitter substance released by OCB at cochlear nucleus were excitatory rather than inhibitory. This possibility is unlikely if the OCB fibers terminating in cochlear nucleus were collaterals of OCB axons destined for the cochlea, since just one transmitter substance is apparently produced by each cell (Dale's principle). Second, an increase in unit activity with OCB stimulation might result if the membrane characteristics of cochlear nucleus cells

caused them to discharge in response to a nominally inhibitory transmitter. Such a phenomenon has been observed in single cells of *Aplysia* (21). Third, an increase of unit activity in the cochlear nucleus could occur if OCB stimulation inhibited inhibitory interneurons in this structure. The relatively long latency of the excitatory effects and the finding that some spontaneously active units in animals with unilateral cochlea destruction had a decrease in firing rate during OCB stimulation lend support to this possibility. Fourth, some of the OCB fibers terminating in cochlear nucleus could be excitatory in nature if they were distinct from those destined for the cochlea. Shute and Lewis (20) have proposed that the OCB is, in fact, not homogeneous, since there are a number of fibers in the crossing bundle that do not stain for cholinesterase.

Relation to acoustic discrimination

Recent experiments have indicated that the OCB may play a role in both frequency discrimination (1) and detection of signals in noise (5, 6). Three attributes of the OCB appear relevant for these auditory functions. 1) Individual OCB fibers project to a limited portion of the cochlea (8), 2) the OCB inhibits discharges in primary afferent VIIIth nerve fibers (8, 23), and 3) the degree of inhibition varies with tone intensity (23). The first two characteristics could provide a means for selectively attenuating receptor responses to particular portions of the acoustic spectrum. Frequency selection might be enhanced centrally if the distribution of OCB fibers within the cochlear nucleus corresponded to its distribution at the cochlea. The loss of such selective efferent controls may explain the impairment of frequency difference limens in monkeys after section of the crossing fibers of the OCB (1). The complex effects of the OCB on cochlear nucleus units with changes in tone intensity may reflect a neurophysiological mechanism useful in enhancing the detection of signals in background noise. However, it is necessary to be cautious in relating the data obtained from the present experiments to acoustic discriminations. The OCB was activated by tetanic electrical stimulation producing a pattern of activity quite unlike that occurring naturally. Moreover, the acoustic signals used were relevant for evaluating the effects of

OCB stimulation on intensity functions, and other parameters such as the shape of the tuning curve, the response to noise, etc., were not examined.

SUMMARY

These experiments examined the effects of stimulating the OCB at its point of decussation in the floor of the IVth ventricle on both spontaneous and tone-evoked activities in 121 single units in cochlear nucleus of unanesthetized, decerebrate cats.

Spontaneous discharge rates were unaffected in 51% of the units, decreased in 31%, and increased in 18%. The effects on spontaneous activity persisted beyond the period of OCB stimulation and were often followed by rebound aftereffects.

OCB stimulation did not affect tone-evoked responses in 18% of the units, decreased response rate in 37% of the units, and increased response rate in 23%. In the remaining 22% of the units OCB stimulation had complex effects on tone-evoked responses, causing a decrease in activity evoked by tones near threshold intensity and an increase in activity

to tones of higher intensity. The occurrence of these different effects could be correlated with the units' intensity function (monotonic or nonmonotonic), presence of an inhibitory surround, and the changes in spontaneous activity induced by OCB stimulation. There was little correlation of OCB effects with the location of the unit in cochlear nucleus complex or with the unit's best frequency.

OCB stimulation was still effective in modifying spontaneous activity in cochlear nucleus units after destruction of the cochlea ipsilateral to the recording site. This finding suggests that OCB has a direct effect on cochlear nucleus.

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Present address of J. S. Wernick: Communication Sciences Laboratory, University of Florida, Gainesville, Fla.

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