THE DISTRIBUTION OF DIRECT CURRENT RESPONSES EVOKED BY SOUNDS IN THE AUDITORY CORTEX OF THE CAT

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INTRODUCTION

The evoked responses recorded with a direct current (D.C.) amplifier from the auditory cortex of the cat have been shown to be different from and generally more complex than those recorded with capacity coupled amplifiers (Gumnit and Grossman 1961). If the stimulus used is a continuous sound (*e.g.*, a pure tone or white noise lasting more than half a second), a change occurs in the potential difference between the cortical surface and a distant point. This change (hereafter for brevity called a shift), develops in approximately 100–150 msec and is maintained for the duration of the stimulus period (Köhler *et al.* 1955; Gumnit 1960). The shift, with which the cortical surface potential becomes more negative relative to a distant point, emerges from the second positive deflection of the initial triphasic evoked response. It is accompanied by an acceleration and enhancement of the background EEG (Bremer 1943), and is followed by a sharp return to the baseline when stimulation ceases (Köhler *et al.* 1955). The studies already cited also provided some information about the effect of click repetition rate and of temperature and anesthesia on the development of the D.C. shifts (see Discussion).

The purpose of this report is to present the results of a survey of the distribution and localization of these shifts and of the effects of changes in intensity, frequency and rise time of the stimulus. The relation between the shifts and the physiology of the auditory cortex will then be discussed.

METHODS

The data discussed in this paper were collected from 44 experiments with 37 cats. Details of the methods employed have been previously published (Gumnit 1960).

Briefly, plexiglas plugs were implanted in the skull providing access to the dura over the auditory area and a catheter was placed in the external jugular vein. On a subsequent day experiments were carried out under very light thiopental anesthesia. The electrical activity of the brain was led off via saline-agar salt bridges to calomel electrodes (Beckman type 270) and recorded with a chopper stabilized D.C. amplifier and ink-writer (Grass 5P1 pre-amplifiers and P5 polygraph). The amplifiers were differential in all cases, the animals were ungrounded and in a shielded cage. Signals from an audio oscillator, white noise generator or pulse generator (for 0.7 msec clicks) were fed into a loudspeaker via a calibrated attenuator and an electronic switch which permitted a choice of rise-decay times. The loudspeaker was positioned directly over the cat's head. Intensity was usually about 80 dB (above 0.0002 dynes cm^2), measured at the level of the external auditory meatus with a General Radio sound level meter.

An area of cortex 6–8 mm in diameter could be carefully surveyed through each plug and one or two plugs were used in each experiment. Relevant locations were marked by coagulation with an electro-surgical unit using a fine needle. The brains were fixed and subsequently examined for electrode location and damage. In the large majority of the experiments the salt bridges were placed on the dura, which was left intact to help maintain a warm, moist and undamaged cortex. In a few experiments which were performed with the dura removed, the recorded activity was similar in every respect, although the voltages recorded were generally somewhat higher. A polyethylene catheter filled with an agar-saline gel was inserted through the plexiglas plug and

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a slit in the dura in order to probe the depth of the cortex. The effective contact surface was flush with the end of the walls and had a diameter of about 0.8 mm. Such a large catheter significantly distorted the normal geometry of the cortex, so that only a very crude estimation of depth within the cortex (superficial, middle and deep) was possible. The catheter was inserted at a point from which D.C. shifts to sound had been recorded. The second electrode of the recording pair rested upon another responsive point 5 mm distant.

In all illustrations, an upward deflection indicates that the active electrode (G_1) has become negative with respect to a distant reference electrode (G_2). Unless otherwise indicated this reference electrode was on the bone overlying the frontal sinus.

RESULTS

1. *Responsive areas of the cerebral cortex*

The middle, anterior and posterior ectosylvian, suprasylvian, lateral (marginal), anterior and posterior sylvian gyri were systematically examined to determine the extent of cortex from which D.C. shifts could be recorded in response to auditory stimulation. The area from which shifts were recorded (stippled in Fig. 1) is in very close agreement with the primary auditory area as determined by click and shock evoked response techniques (Ades 1959). The oblique shading in the same Fig. outlines the areas sampled from which no shifts were recorded. The solid dot indicates an aberrant point from which a definite shift was obtained on one occasion. No shifts were observed along the length of the supra-sylvian or lateral gyri. This strongly suggests that the D.C. shifts to sound are limited to the auditory area and are not widespread throughout the cerebral cortex.

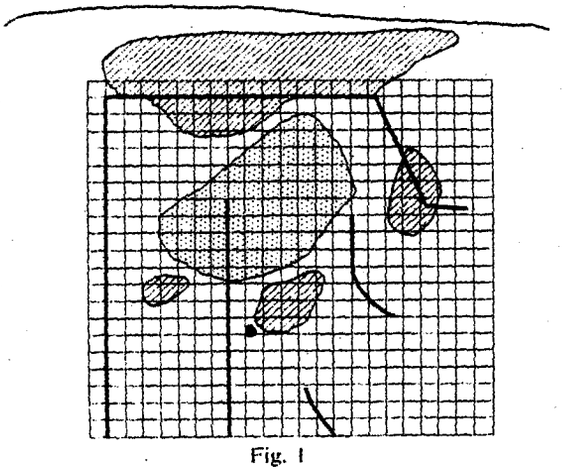

Fig. 1

Map of the middle ectosylvian gyrus and surrounding areas responding and not responding with a D.C. shift to sound. Schematized map of the auditory area (modified from Hind 1953). The lateral, supra-sylvian, posterior and anterior ectosylvian and pseudo-sylvian sulci are shown as heavy lines. The grid represents 1 mm divisions. The area from which shifts were regularly obtained is stippled; non-responsive areas are outlined by oblique shading; blank areas were not examined. The lateral and suprasylvian gyri were similarly sampled and found unresponsive. See text.

The shifts were very susceptible to habituation effects and careful control of anesthesia level and temperature was necessary for success in recording them (*cf.* Gumnit 1960). False negative results were ruled out by basing the description of the non-responsive areas only on those experiments in which multi-channel recording demonstrated not only the absence of a shift at the point being investigated, but also the presence of an unequivocal shift of at least average amplitude in the previously established area of responsiveness.

2. *Effects of changes in the frequency of the stimulating tone on the distribution of the D.C. shifts*

The frequency of the stimulating tone was varied over a range of 100–8000 c/sec in an attempt to demonstrate tonal localization. Although variations in responsiveness of particular points within the auditory area were found in individual experiments, no clear cut tonotopic representation was found. It was noted that one point would respond to a wide range of tones whereas a second responded to a smaller range, and that two such points were very often separated by only 3 mm (Fig. 2). Because this was the closest placement of electrodes permitted by the techniques used, it is possible that shifts may at times be restricted to even smaller patches of cortex. At no time was double dissociation of responsiveness found. That is, no pair of points was found in which one point responded to a high pitched tone and not to a low pitched

tone while the second would respond to a low pitched tone but not to a high pitched tone.

3. *Effects of changes in the intensity of the stimulus on the distribution and amplitude of the D.C. shifts*

Change in the intensity of the stimulating tone had a similar effect to change of frequency ordinarily was associated with little change in the amplitude of the shift at any given point. That is, the amplitude of the response to a sound 30 or 40 dB louder than a sound which caused a just noticeable response was rarely more than half as much again as large. The shift might become larger and more definite with each increase of 10 dB over a range of about 20 dB

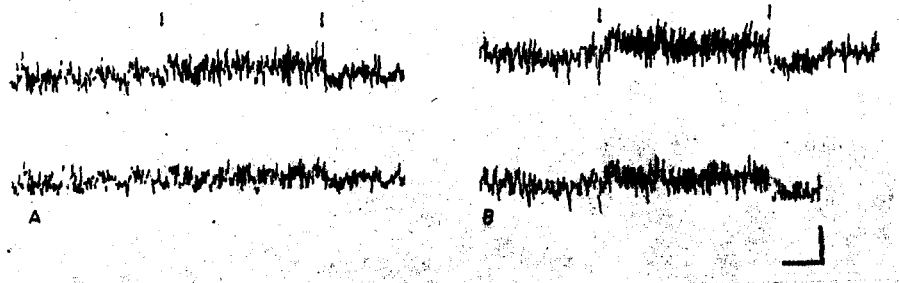

Fig. 2
Effect of frequency of tone on localization of D.C. shifts to sound. Upper and lower channels record the activity on the middle ectosylvian gyrus from two points separated by 3 mm. *A*, in response to a tone of 1.5 kc/sec, *B*, in response to 2.5 kc/sec. Note that one point responds to both tones, while the other responds only to 2.5 kc/sec. Note also that the shifts may be localized to within 3 mm. Calibration: 1 sec and 200 μV.

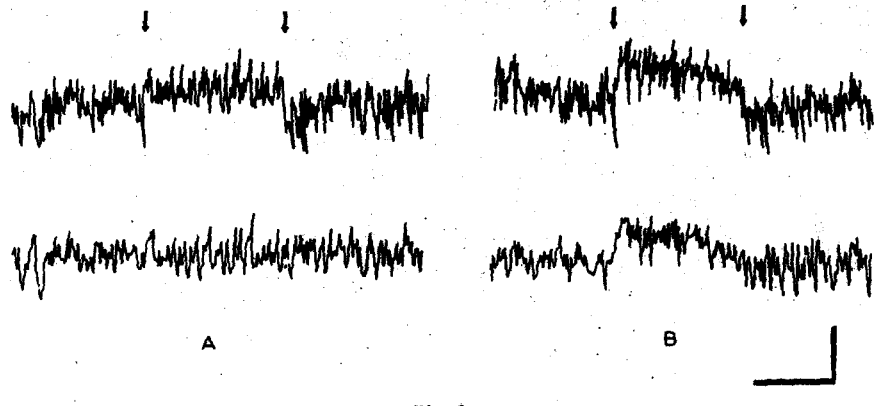

Fig. 3
Effect of increase in intensity of sound on localization of D.C. shifts to sound. Upper and lower channels record from two points on the middle ectosylvian gyrus separated by 3 mm. *A*, in response to a 2 kc/sec tone at 80 dB; *B*, to the same tone at 90 dB. Note that one point responds only to the higher intensity sound and that the other point responds to both intensities, but with a greater amplitude to the louder tone. Again it is seen that the shifts may be localized to within 3 mm. Calibration: 1 sec and 200 μV.

on the localization of the shifts (Fig. 3). It was common for one point within the auditory area to respond strongly and consistently at low and high intensities of stimulation while a second responded only at higher intensities.

Increase in intensity of the stimulating sound (Fig. 3), but further increases in loudness had no effect, or might even result in a decrement (Fig. 4).

4. *Effect of changes in the rise and decay times of the stimulus on the time course of the D.C. shifts*

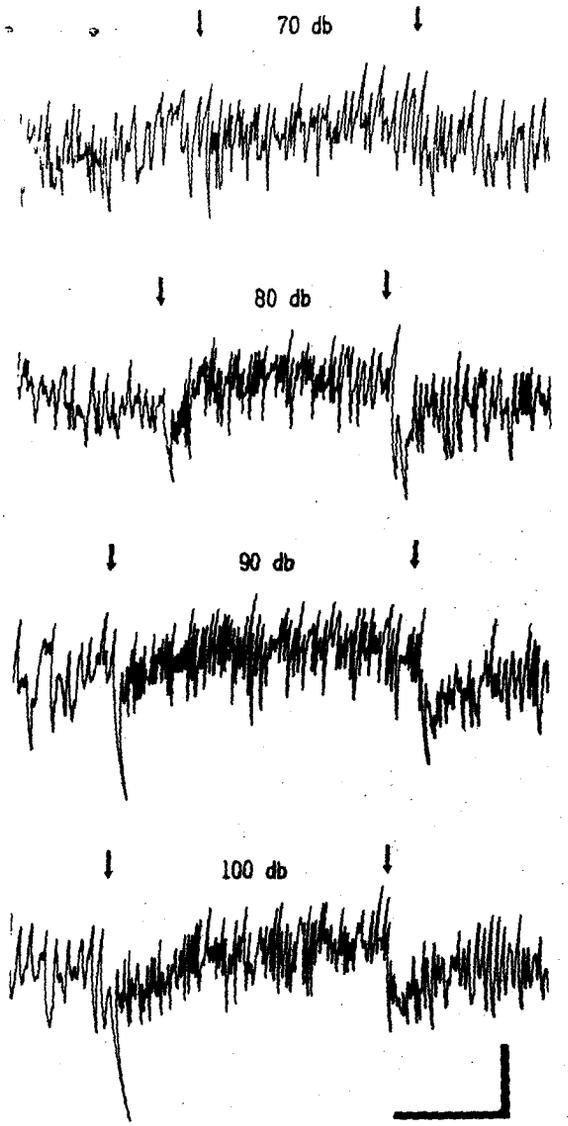

Fig. 4
Effect of increase of intensity of sound on amplitude of shift. Four consecutive responses to a tone of 4 kc/sec with 10 dB increments in intensity. Note that the shift first becomes clearer and larger, but that with further increases in intensity there is no parallel increase in amplitude; indeed, a decrement takes place. Calibration: 1 sec and 200 μV.

When the continuous sound was turned off, the shift characteristically returned abruptly to the baseline. This "off" response had a configuration resembling that of the click evoked response. In order to determine if the shift did in fact end abruptly, or if the prompt return was due to a response evoked by a click at the end of the stimulus, an electronic switch with a rise-decay time of 100 msec was used to shape the onset and end of the sounds. With click transients eliminated, an abrupt return was still seen (Fig. 5). This "off" response consisted of a sharp re-

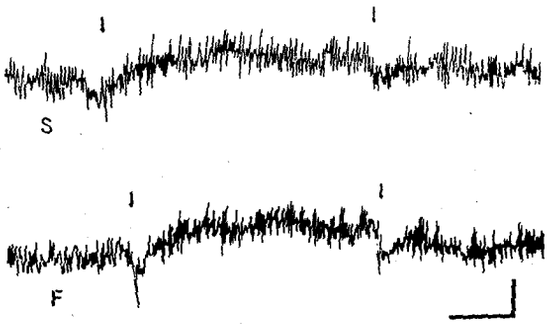

Fig. 5
Effect of shaping rise and decay of stimulating tone on the shape of the D.C. shift. *F*, fast rise-decay time of 0.5 msec. *S*, slow rise-decay time of 100 msec eliminating click transients at beginning and end of stimulus. Note that even with a slow rise and fall of the tone an evoked response and an abrupt "off" response is seen. Calibration: 1 sec and 200 μV.

turn to the baseline within 100–150 msec, usually with a small overshoot.

5. *Location of neural elements giving rise to shifts in response to sounds*

Depth recording demonstrated that the source of the EMF giving rise to the shifts to sound lies between the outer surface of the pia-arachnoid and the lower third of the cortex (Fig. 6). The reversal of sign of the initial wave of the evoked response in channel B (Fig. 6, II) shows that the probe is in the lower portion of the cortex (*cf.* Albe-Fessard 1957). Note that the amplitude of the shift recorded between the surface and the depth electrodes (channel D) is almost twice as large as the response recorded with a distant reference electrode (channel A). This indicates that the depth probe is near the source of EMF but on the opposite side of the dipole (*cf.* Bishop 1950). Further confirmation of this is obtained from Fig. 6, III. Here the depth probe has been advanced further, deep into the sub-adjacent white matter. Note that the background EEG in channel B is considerably flatter, that the positive shift is hardly evident, and that

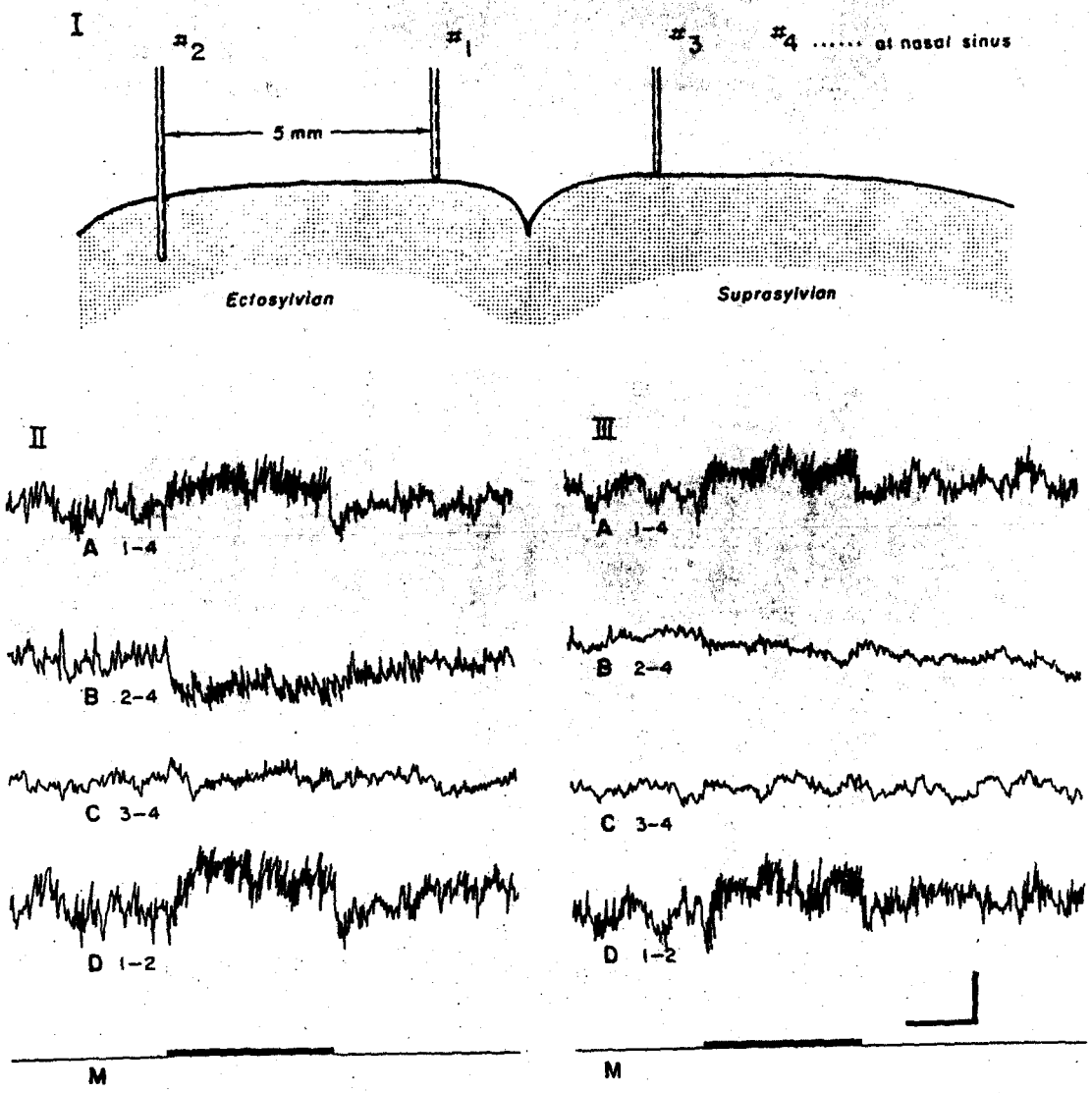

Fig. 6

Depth recording to locate elements giving rise to D.C. shifts.

I: sketch showing relation of electrodes to each other and to cortex.

II: clicks presented at a rate of 50/sec. Signal marker, channel M. Note that the first grid of channels A and D are connected to the same electrode on the cortical surface, and that the second grid of channel D is connected to the active electrode of channel B. Upward deflection indicates that G_1 is relatively more negative. See text.

III: The same experiment as in II but now the probe (electrode 2) has been pushed beneath the cortex deep into the white matter. The drift in channel B is caused by injury potentials, the probe having been advanced only a few minutes previously. See text. Calibration: 1 sec and 200 μV.

the response recorded between the surface and the depth is only slightly larger than that recorded between the surface and the nasal sinus. This indicates that the depth probe is now at a considerable distance from the source of EMF.

DISCUSSION

Data have been presented which indicate that there are D.C. shifts to sound which are an exclusive response of the auditory area and are

not a response widespread throughout the entire cerebral cortex. Such shifts, therefore, are clearly a separate class of response from the widespread changes in D.C. level associated with arousal or reticular stimulation (Arduini *et al.* 1957; Brookhart *et al.* 1958; Vanasupa *et al.* 1959; Caspers 1960). In the present study, no definite tonotopic localization was found. This negative finding may have been the result of the relatively crude recording techniques. It should be noted, however, that the tonal localization found by Tunturi (1950) in the dog was not found by Hind (1953) in the cat, and that both of these studies were performed in deeply anesthetized animals. The results from those experiments in which changes in frequency and intensity of the auditory stimulus produced a change in the points responding with a D.C. shift, make it clear that these shifts may be quite local phenomena within the auditory cortex and are not a response of the auditory cortex as a whole. The shifts may be present at one point in the auditory cortex and absent 3 mm away.

The experiments reported here make it probable that the neural elements giving rise to the shifts are within the upper or middle portion of the auditory cortex. Since the pia-arachnoid had to be left intact, one cannot rule out the possibility that the shifts are the result of impedance changes produced by localized changes in blood flow or that they are generated in the walls of blood vessels in the pia-arachnoid. However, the temporal characteristics of the shifts, their prompt rise and abrupt fall and the close relationship between characteristics of the shifts and the characteristics of the stimulus make this unlikely. Such responses are more characteristic of neural tissue than of slowly responding vascular structures.

Summary of available information about D.C. shifts to sound

The following points appear well established and present a coherent picture.

(*a*) The shifts are not an artifact of anesthesia. They are present in the *encéphale isolé* preparation (Gumnit 1960) and in animals implanted with chronic electrodes (Gumnit and Grossman 1961). Although movement of the animal or of the electrode against the cortex can cause D.C. artifacts, the shifts are present in paralyzed animals (Gumnit 1960) and in animals with rigidly fixed implanted electrodes (Gumnit and Grossman 1961). The D.C. shifts are not caused by eye movement. They are present in the paralyzed animal, the enucleated preparation (Köhler *et al.* 1955) and the source of EMF has been located in the cortex.

(*b*) The shifts are very sensitive to the effects of anesthesia and cooling of the cortex. They can only be recorded in the anesthetized preparation when the animal is nearly awake, able to struggle purposely and follow the experimenter with its eyes, and when the cortex is warm (over 37.5°C) and moist (Gumnit 1960).

(*c*) The D.C. shifts to sound display the phenomenon of habituation much more strongly than the click evoked response (Gumnit 1960; *cf.* Hernández-Peón *et al.* 1957; Galambos *et al.* 1956). They are very closely linked to the temporal characteristics of the stimulus, developing gradually with clicks repeated at 5–15/sec. At higher repetition rates the shift develops abruptly, and this is also the usual case in response to tones or white noise (Gumnit 1960). The shifts end abruptly with the end of the stimulus.

(*d*) The amplitude of the change in D.C. level is correlated with the intensity of the sound stimulus only over a very narrow range. This is similar to the behavior of the click evoked response at the cortex (*cf.* Rosenblith 1950). Tonotopic localization of the D.C. shifts has not been demonstrated.

(*e*) The D.C. shifts to sound are restricted to the auditory cortex. Depending on the type of auditory stimulus, they may be quite localized within the auditory area. The elements involved in the genesis of the potential change are within the cortex or the overlying pia-arachnoid; it is probable that they are neural in nature and located within the upper or middle third of the cortex.

The relation between the D.C. shift to sound and the functioning of the auditory cortex

On the basis of the facts just summarized, it seems justifiable to conclude that the D.C. shifts to sound are related to the functioning of the auditory cortex. With a gross electrode and capacity-coupled amplifiers, two electrical events

are generally accepted as signs of evoked activity in the (relatively) non-depressed primary auditory cortex: the click evoked response, and the "fast" after discharge which is prolonged if the auditory stimulus is continuous (*cf.* Bremer 1958). However, when the gross electrode is non-polarizable and the amplifier direct coupled, a third sign is revealed, the D.C. shift to a continuous sound. If the click evoked response is the sign of a very abrupt, transient change in state of activity of the auditory cortex, then the D.C. shift may be considered an expression of a more persistent change in state. Therefore, in order to examine all of the electrical activity during persistent events, the recording system must be capable of revealing D.C. changes.

SUMMARY

1. The D.C. shifts to auditory stimulation are limited to auditory cortex and are not a widespread response of the entire cortex, nor are they a massive response of the auditory cortex. They can be present at one point and absent 3 mm away.

2. No definite tonal or intensity localization of the shifts was found.

3. The shifts arise with the stimulus and cease abruptly with the end of the stimulus. They do not continue after the end of the stimulus as do the widespread D.C. shifts with arousal.

4. Evidence is presented which suggests that the shifts are generated by neural elements located within the upper or middle third of the cortex.

5. It is concluded that the D.C. shift to sound is a sign of functioning of the auditory system. While the click evoked response expresses brief transient changes in the activity of the auditory system, the D.C. shift is a sign of a more persistent change in state of the activity of the auditory system.

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