are members of the large desert-adapted *repleta* species group to which also *D. pachea* originally had been assigned (*1*). However, a more recent evaluation by L. Throckmorton on the basis of internal anatomy shows that *D. pachea* is more closely related to *D. nannoptera*, a desert-inhabiting species from southern Mexico. The *nannoptera* species group, which is monotypic, is considered phylogenetically older than the *repleta* group (*14*). *D. pachea*, therefore, apparently has had ample time to evolve into and become dependent upon a niche which supplies it with a unique sterol. This niche in the Sonoran Desert is secured from competitors by the presence of another substance which is toxic in varying degrees to other species of local *Drosophila* and to which *D. pachea* has evolved a tolerance. Our results indicate that the alkaloid fraction of the cactus contains this material.

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Background and Evoked Activity in the Auditory Pathway: Effects of Noise-Shock Pairing

Abstract. *Unanesthetized cats with electrodes permanently implanted along the auditory pathway were presented first with sustained "white" noise stimuli and then with the same noise paired with subcutaneous electric shocks. Pairing noise with shock decreased both background and noise-evoked activity in the inferior colliculus, and, in some cats, also in the cochlear nucleus, trapezoid body, and at the round window. No changes occurred in medial geniculate or auditory cortex recordings. The effects in the inferior colliculus do not depend on changes in the degree of arousal of the animal, on changes in the medullary auditory areas, or on the actions of the middle-ear muscle.*

It is well known that perceptions are influenced by expectations, purposes, and past experience (*1*). The neurological mechanisms underlying these effects have traditionally been assigned to "associative" or "integrative" areas of the brain; the sensory systems were thought to simply relay information about the physical characteristics of the stimulus from receptor to primary cortex (*2*). However, neuroanatomists have demonstrated descending tracts in parallel with the classical ascending sensory pathways, and electrical stimulation of these descending systems modifies evoked potentials in the sensory nuclei (*3*). Therefore, it seems possible that past experience may affect perception by acting on sensory signals very early in the input pathway (*4*).

In order to investigate the plasticity of the subcortical auditory areas, cats were presented first with sustained noise stimuli and then with the same noise paired with subcutaneous electric shocks. Background and noise-evoked activity were recorded with permanently implanted electrodes. Sustained noise was used instead of the conventional click or tone pips, because Starr and Livingston (*5*) showed that the sustained response to sustained noise is limited to the classical auditory pathway, while click-evoked responses are widespread in the unanesthetized brain. This report describes the changes in electrical activity observed under these conditions.

Multiple electrodes were implanted in nine adult male cats, at the round window (RW), cochlear nucleus (CN), lateral trapezoid body (Trz), superior olive (SO), inferior colliculus (IC), medial geniculate (MG), and primary auditory cortex (AI) (Table 1). All electrode placements were verified histologically (*6*). The electrodes were made of 36- or 32-gauge insulated stainless steel wire with only the cut ends bare. The electrodes for RW were monopolar spirals (*7*); all other electrodes were bipolar, with tips 0.5 to 2.0 mm apart. Electrodes for delivery of conditioning shocks were implanted subcutaneously on the cat's back. The middle-ear muscles of all animals were

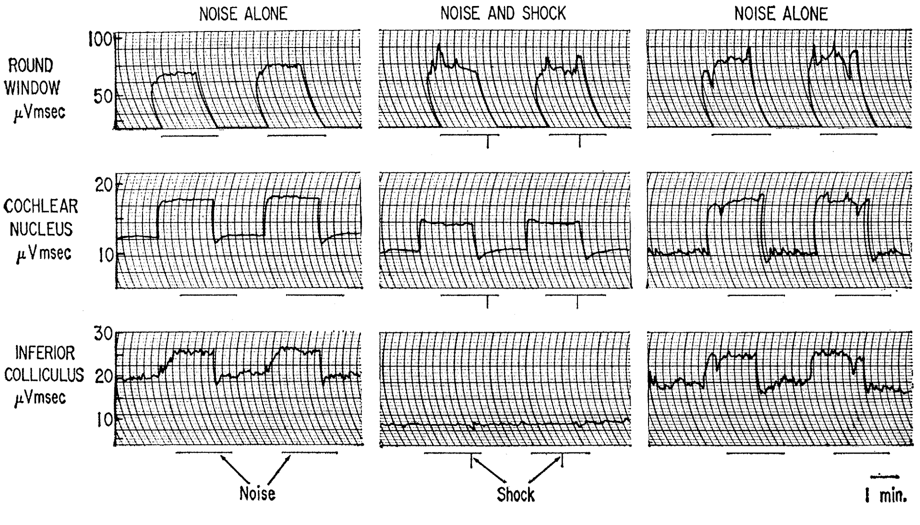

Fig. 1. Simultaneous "integrator" recordings from RW, CN, and IC. Samples from the 15th day on which noise was presented alone, the 2nd day on which both noise and shock were presented, and the 27th day of the second "noise-alone" period. Noise presentations (70 db) indicated by horizontal bars. Subcutaneous shocks indicated by vertical markers. Noise-shock pairing decreases background and evoked activity at IC although RW response is unchanged. The decrease in CN background persists after CN evoked activity has returned to the control level.

left intact; the middle ears were examined post mortem and were found free of infection. The animals were allowed to recover for at least 3 weeks after surgery. The a-c amplified signals (0.2 to 10,000 cy/sec) from four electrode sites were displayed on an oscilloscope and also delivered to four "integrating" circuits (*5*). The "integrator" output is a d-c voltage proportional to both the amplitude and frequency of the conventional recording, and can be thought of as a moving average over periods of 3 seconds or as an approximation to the integral of the a-c signal. This technique is very useful for observing background activity and events with a time course of minutes. The units of "integration" are microvolt-milliseconds; that is, the a-c signal is expressed in terms of a d-c voltage lasting 1 msec. At the IC and below, where very little slow-wave activity is recorded, the "integrated" record reflects the amount of fast activity (individual action potentials and fast summated post-synaptic potentials).

The cats were unrestrained in a chicken-wire cage (50 by 50 by 75 cm) in the center of a sound-attenuating room. Background sound pressure level (SPL) relative to 0.0002 dyne/cm^2 was 50 to 53 db. A "white" noise (20 to 20,000 cy/sec), projected from a speaker mounted about 1 m above the cat's head, varied no more than ± 1.5 db within the cat's range of movement. In each daily session, 20 to 40 presentations of "white" noise, each lasting 1 to 2 minutes, were separated by silent periods of 1 to 2 minutes. Noise intensity was constant for each animal from day to day. Intensities of 65 to 75 db were used with different animals.

Three variables were studied in the oscilloscopic and "integrator" records: (i) *absolute level* of background activity (the "resting" or "spontaneous" activity before each noise presentation); (ii) *absolute level* of sustained noise-evoked activity; and (iii) evoked response *amplitude* (the difference between evoked and background levels).

Noise alone was presented for up to 40 days in control sessions. Then noise and shock were paired for 7 to 21 days. Subcutaneous shocks were delivered at irregular intervals during each noise presentation, and never without noise. The stimulating current was monitored continuously. After the noise-shock sessions, noise was presented alone again. Recordings were made during all sessions, and all periods of background activity and evoked responses were analyzed (Table 1).

Recordings from 8 of 11 IC electrodes (six of nine cats) showed systematic changes with noise-shock pairing. Typically, sustained "white" noise alone produced an increase in activity above the background level (*5*). After the noise had been paired with shock, the *background activity* decreased by as much as 50 percent and remained low for weeks; even against the reduced background, the noise now evoked little or no increase in activity. Subsequently, after many more "noise-alone" sessions, both background and evoked activity returned approximately to control values (Figs. 1 and 2).

All changes were independent of the degree of alertness. Simultaneous recordings from the RW, CN, Trz, and SO showed that the decreases in IC activity did not depend on decreases at lower stations, or on acoustic or nonacoustic contractions of the middle-ear muscles (*8, 9*).

Figure 2 shows the entire time course of the changes in the electrical activity in the brain of one cat. The cat's behavior was reflected more clearly by the absolute levels of background and evoked activity than by the response amplitude. At the start of the control period, when the cat appeared apprehensive, both background activity and noise-evoked activity were low (top and middle curves, Fig. 2). As the cat relaxed during the first control days, both background and evoked activity increased. As background and evoked levels rose, the difference between them (that is, the response amplitude) remained constant. Thus in contrast to the absolute levels, the response amplitude did not reflect the gross change in the cat's overt behavior as he gradually relaxed (bottom curve, Fig. 2).

When electric shock was introduced during the noise presentations, the animal again appeared frightened, and again both the background and evoked levels decreased (Fig. 2, top and middle; Fig. 1, bottom). This decrease was not immediate, but occurred after only four noise-shock pairings. Although the absolute level of evoked activity remained below the control values, the response amplitude on individual noise

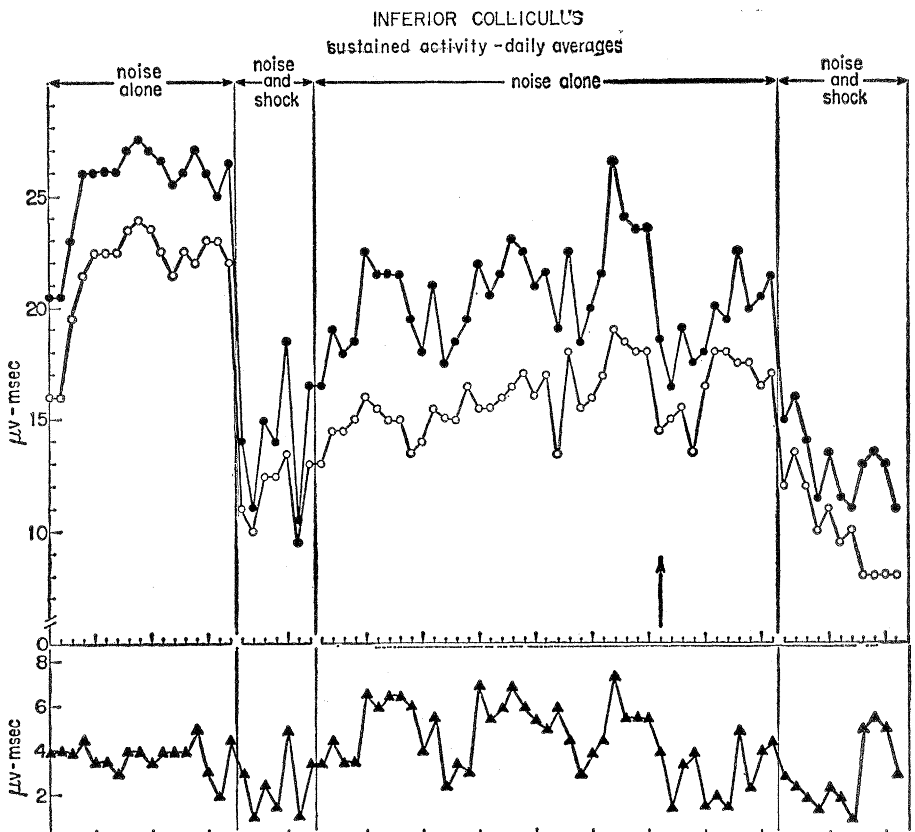

Fig. 2. Daily average values of "integrator" recordings from IC of one cat (same animal as in Fig. 1). Open circles, background activity; solid circles, evoked activity; solid triangles, amplitude of evoked response (difference between background and evoked levels). Vertical arrow indicates 7-day interruption in second "noise-alone" period.

Table 1. Summary of electrode placement and results. The recordings were classified by comparing all trials of the last 3 days of the initial noise-alone period, of the noise-shock period, and of the second noise-alone period. A record was said to show changes clearly related to the noise-shock pairing if the values of the background or evoked activity in the shock period did not overlap the values in the initial noise-alone period, and if they returned toward the initial levels in the second noise-alone period. Some recordings which could not meet this strict criterion of no overlap nevertheless contained many individual trials which were beyond the control range, and were classified as showing suggestive changes.

Locus	Total	Changes		
		Clear	Suggestive	None
RW	6	1	4	1
CN	3	1	2	0
Trz	4	2	1	1
SO	1	0	0	1
IC	11	8	2	1
MG	6	0	0	6
AI	2	0	0	2

trials varied from zero to above the control values (bottom curve, Fig. 2). This variability was typical.

During the second noise-alone period, background and evoked activity returned toward control values. However, the evoked activity returned faster than the background activity, and, consequently, the response amplitude was greater than in the first noise-alone period (bottom curve, Fig. 2). The second noise-alone period was unavoidably interrupted for 7 days (arrow, Fig. 2). When noise-alone trials resumed, another decrease in both background and evoked activity was seen, similar to the decrease at the start of the control period and when shock was introduced. Background and evoked activity still had not reached control levels after 41 days of the second noise-alone session (covering 2 months). Noise-shock pairing was resumed, and both background and evoked activity decreased again. There was no consistent correlation between either the background level or response amplitude and the animal's state of arousal. The IC record was the same during the noise-shock pairing whether the cat crouched and hissed or lay relaxed with his head on his paws. In contrast to cortical and thalamic recordings, the integrated level of activity in the IC and CN varies very little with changes from sleep to waking as monitored by electroencephalograph and recorded from the neck muscle by electromyograph (*10*).

Three cats showed a decrease or complete abolition of the IC response to noise after 4 or 5 days of noise-shock pairing, but showed no change in background activity.

Although the IC seemed to be the area most consistently and most markedly affected by pairing noise and shock, suggestive decreases were seen at Trz, CN, and even RW in some of the animals which showed decreases at IC. Some of these changes were marked and long lasting (Fig. 2, CN background activity). Both acoustic and nonacoustic contractions of the middle-ear muscles were monitored by recording the microphonic potentials at the RW (*8*, *9*). Contraction of the middle-ear muscles can attenuate the sound delivered to the receptor even if the sound delivered to the tympanic membrane is held constant (for example, with earphones). In two of the six RW recordings, the noise-evoked sustained response decreased by the equivalent of a 10- to 15-db decrease in SPL after the noise had been paired with shock. The RW response to the onset of noise (before the acoustic reflex contraction) was also decreased, indicating that the middle-ear muscles were tonically contracted in the silent intervals before and between noise presentations.

Recordings from two electrode placements in the AI cortex and six placements in the MG showed no changes when the noise was paired with shock.

Previous studies of subcortical sensory activity in behavioral situations have been criticized because of inadequate control of sound (or light) stimuli, ear-muscle (or pupil) effects, movement, or degree of arousal (*8*, *11*). These factors were accounted for in the present experiment. The results show that the animal's experience modifies the evoked neural activity along the auditory pathway, particularly at the IC. Even the receptor response may not be a simple function of the physical characteristics of the sound stimulus. The most striking finding was that the background activity is also modified by the animal's experience. Background activity is often ignored or treated as "noise." The present observations show that the background must be considered in evaluating evoked activity, and also as a significant physiological variable in itself.

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Lactate Dehydrogenases in Trout

To Goldberg's report of the discovery of nine lactate dehydrogenase isozymes in the speckled trout [*Science* **148**, 391 (1965)] I can add that at least nine LDH isozymes are also present in the rainbow trout, *Salmo gairdnerii*. Using the electrophoretic method of S. Raymond [*Ann. N.Y. Acad. Sci.* **121**, 350 (1964)], I have separated a tenth LDH fraction from the blood plasma of this trout. I have not as yet found the tissue of origin. These results support Goldberg's belief that a third genetic locus is involved in the synthesis of LDH and perhaps other proteins.

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