Noise-Induced Hearing Loss Can Alter Neural Coding and Increase Excitability in the Central Nervous System

Abstract. *Responses of auditory neurons in the inferior colliculi of mice were studied longitudinally before and shortly after each animal was exposed to intense noise. Noise exposure caused expected losses in auditory sensitivity, but in 31 percent of the neurons studied, unexpected alterations of temporal patterns of action potentials were observed: certain suprathreshold stimuli that had evoked only transient "onset" responses or inhibition of spontaneous discharges prior to noise exposure came to elicit sustained excitation after exposure. Thus, noise-induced hearing loss can be associated with increases in neural responsivity and alterations of normal neural coding processes.*

The effects of noise exposure on hearing sensitivity have been studied primarily in the peripheral auditory system. Noise can impair the function of cochlear structures, resulting in temporary or permanent hearing loss (*1*). Little is known, however, about the consequences of this reduced peripheral sensitivity on the activity of neurons in the auditory areas of the central nervous system (CNS), where the ultimate coding processes take place for perceptual experiences such as pitch and loudness. Such perceptual experiences are often altered after noise exposure (*2*).

One way to approach this problem is to record the activity of single neurons immediately before and after noise exposure to determine the resulting alterations in response properties. Only one neuron can be studied in a given animal—once the animal has been exposed to intense noise, the sensitivity of its auditory system is reduced (*3*). We have used mice as subjects to study changes of discharge patterns of individual neurons that indicate increased excitability and alterations of coding after exposure to noise.

The temporal pattern of neuronal discharges (action potentials) during acoustic stimulation is thought to play a key role in the coding of sounds (*4–6*), and central auditory neurons can display one or several of a variety of patterns. The discharge pattern is presumed to reflect the interplay of excitatory and inhibitory neuronal processes (*4–6*): sustained (repetitive) firing of action potentials during the presentation of stimuli thus indicates the predominance of excitatory processes with little influence of inhibitory processes; "onset" responses (at the beginning of stimulation only) or inhibition of spontaneous neural discharges by sound reflect inhibitory influences. Since peripheral auditory nerve fibers respond to sounds with sustained responses only, the occurrence of onset or inhibitory responses in the CNS indicates suppression of neural excitation by inhibitory processes. Changes in discharge patterns for a given neuron under particular stimulus conditions would imply an alteration in the interplay of excitatory and inhibitory processes and, consequently, interference with normal coding. Thus, in evaluating the effects of noise on coding, we focused our attention on discharge patterns.

Seventy inbred C57BL/6 mice were studied, with data being obtained from one neuron in the inferior colliculus (IC) of each (*7*). The IC is a higher-order auditory nucleus whose neuronal responses reflect synaptic input from numerous other auditory centers in the brain. Extracellular responses were obtained from individual neurons of lightly anesthetized, tranquilized mice (*8*). Tone stimuli (200 msec long, 5-msec rise-fall, one stimulus per second, series of ten stimuli) were presented at frequency-intensity combinations throughout the neuron's frequency response range, and frequency threshold curves (FTC's) (response threshold as a function of frequency) were obtained. The mouse was then exposed to white noise [95- or 110-dB sound pressure level re 0.0002 dyne/cm^2 (20 μN/m^2)] for 30 seconds (Fig. 1). Immediately after noise exposure, responses were again recorded.

Noise exposure of either intensity caused statistically significant mean threshold elevations, most prominently at high frequencies (*9*); changes in suprathreshold response properties will be described elsewhere (*10*).

Twenty-two of the 70 neurons showed noise-induced increases in response rates associated with the addition of sustained discharges to onset or inhibitory patterns (*11*). In all cases, the changes in response patterns occurred only at some frequencies. Figure 1 presents data from two neurons that demonstrate the addition of sustained discharges to the onset patterns that existed before noise exposure at certain frequencies. The number of discharges at 27.2 kHz increased after noise exposure despite a severe threshold elevation (Fig. 1A). Increased responsiveness caused a decrease in the threshold at 35.4 kHz (Fig. 1B). Although discharge rates at all intensities of stimulation are not shown, the addition of sustained discharges occurred at other suprathreshold intensities as well (but were not seen at any intensities before exposure). The changes in discharge pattern were observed mainly (14 neurons) in the high-frequency portions of the neurons' response areas, but were sometimes found in low- or mid-frequency ranges (four neurons each), and occurred in 16 of 41 neurons of mice exposed to 95-dB noise and in 6 of 29 neurons after 110-dB noise. Most of these neurons were located near the center of the central nucleus of the IC (Fig. 1, E and G).

These data indicate that after noise exposure, neuronal discharge patterns can undergo significant changes. Thus, noise exposure can alter neural coding in ways previously unappreciated. The question of whether these effects are caused by noise exposure or are perhaps an aspect of normal response variability must be addressed. Several points argue that noise exposure is responsible. (i) The time interval between recording and rerecording was short, from 1 to 15 minutes, reducing the likelihood of general changes in the state of the animal. (ii) Control experiments, in which one neuron or a small cluster of neurons were monitored over comparable time periods but without noise exposure, showed a high stability of patterns (*12*). (iii) Previous work with this preparation (*8*) and the work of other investigators using other preparations, indicate that IC response patterns are generally stable for a given stimulus condition (*13*). This is even true of unanesthetized behaving animals (*6*) in which variability might be expected to be greater than in our anesthetized preparation. (iv) Finally, recordings were obtained from several neurons at additional temporal intervals after the noise (that is, on several retests). Threshold sensitivity recovered somewhat, and additions of sustained discharges that appeared shortly after noise exposure tended to disappear with time as the pattern returned to its original form (*10*).

How could a reduction of auditory sensitivity cause changes in discharge patterns and increases in the excitability of central auditory neurons? Although excitability can increase in pathological cochleas (*14*), interplay among excitatory and inhibitory synaptic inputs to CNS neurons must also be considered. Re-

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sponse patterns of auditory neurons in the IC and elsewhere are often changed by variations of frequency, intensity, or other properties (*4–6*). Presumably different combinations of acoustic properties activate different peripheral elements, which in turn activate different combinations of excitatory and inhibitory circuits. After noise-induced hearing loss, a stimulus may initiate an abnormal set of neural events, resulting in altered interactions among excitatory and inhibitory processes. Thus, a variety of functional changes could be induced by hearing loss, depending on the particular array of synaptic inputs that a neuron receives and how these inputs are activated by various stimuli. If inhibitory input to a neuron were especially impaired by noise exposure, the relative effectiveness of excitatory inputs could increase, resulting in observations such as ours. Thus, it is of interest that (i) most of the increases in responsiveness were observed at high frequencies; (ii) mouse IC neurons are most likely to receive inhibitory input from high-frequency stimulation (*8*); and (iii) the noise exposures used impaired high-frequency sensitivity most (*9*).

Whether an auditory neuron responds to a particular sound with an onset or a sustained response must determine the ability of its action potentials in coding. After noise exposure some neurons that responded to certain sounds with onset responses came to respond with sustained responses (and vice versa) (*11*), at least temporarily. Thus, exposure to noise (at levels not uncommon in our environment) not only reduces hearing sensitivity, but can also affect neural coding processes in the brain. These observations may help to explain why hearing loss (resulting from noise or other causes) often causes perceptual problems, even when sounds can be readily heard.

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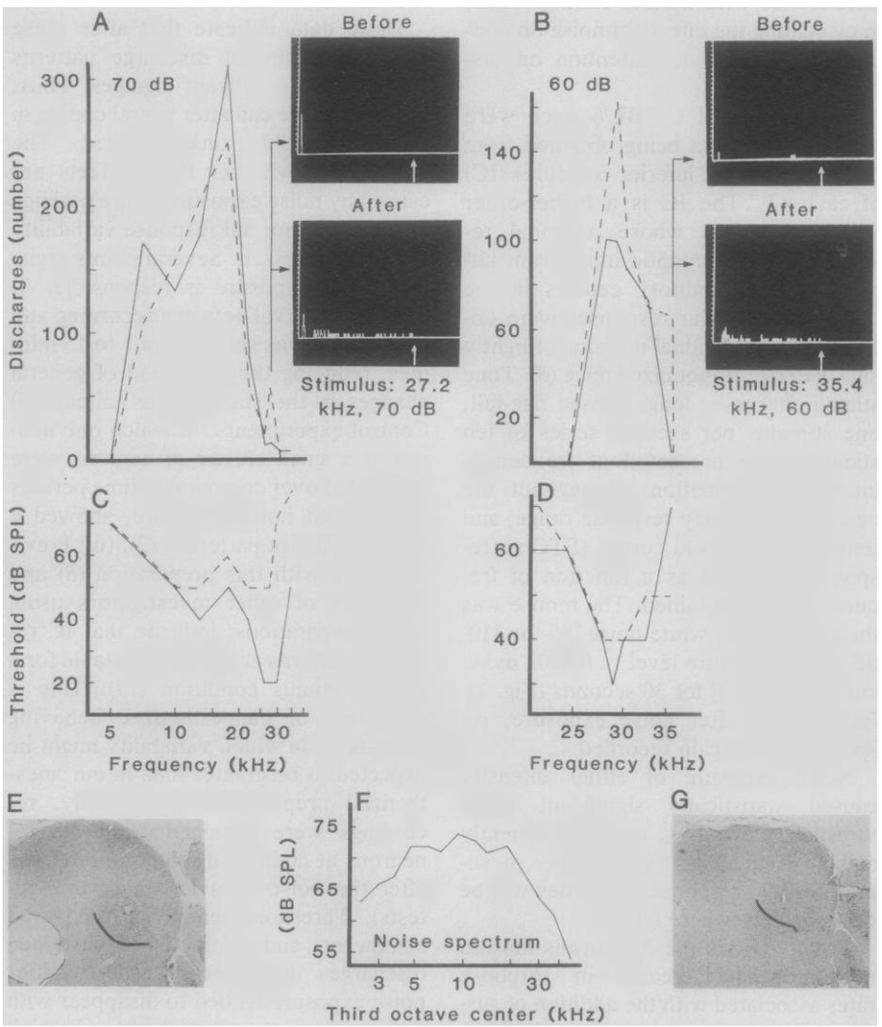

Fig. 1. Noise-induced changes in response areas of two IC neurons. (A and B) Number of discharges per ten-stimulus series at one suprathreshold intensity before noise exposure (solid lines) and after noise exposure (dashed lines). Histograms (black background) show discharge patterns and represent sums of ten responses, each evoked by a 200-msec tone. White arrow indicates termination of tone. Only onset responses were evoked by high-frequency tones; after noise exposure, the same stimuli also evoked sustained discharges. (C and D) Frequency threshold curves. (E and G) Locations of the two neurons are shown by lesions in Nissl-stained coronal sections; the curved black lines show the ventromedial border of the central nucleus of the IC. (F) The spectrum of the white noise as a function of sound pressure level per third-octave band is also shown for 95-dB intensity. The shape was similar for 110-dB noise, with sound pressure levels elevated somewhat.

References and Notes

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7. Animals in two age ranges, 16 to 18 days and 28 to 30 days, were pooled for this analysis.
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9. Mean unit threshold elevations as a function of test-tone frequency were, for 95-dB exposures: 3.5 dB, < 5 kHz; 2.0 dB, 5 to 10 kHz; 3.1 dB, 10 to 20 kHz; 12.6 dB, 20 to 40 kHz [$t(27) = 4.5$, $P < .001$]; and 1.3 dB, > 40 kHz. For 110-dB exposures (t's = 2.4 to 8.9, d.f.'s = 10 to 22, P's < .05): 9.1 dB, < 5 kHz; 12.6 dB, 5 to 10 kHz; 21.8 dB, 10 to 20 kHz; 38.7 dB, 20 to 40 kHz; and 37.2 dB, > 40 kHz].
10. S. M. Lu and J. F. Willott, in preparation.
11. An "increase" or "decrease" was based on actual discharge variability, and it was required that a change exceeded 3 standard errors of the mean ($P < .0025$) [J. F. Willott *et al.*, *Exp. Neurol.* **65**, 625 (1979)]. Many neurons showed a pattern change opposite that discussed here, as sustained discharges were eliminated after noise exposure.
12. Control experiments concentrated on discharge patterns near the upper frequency limits of neuronal response areas. A total of 94 neurons demonstrating onset-inhibitory responses and 15 demonstrating sustained responses were recorded from repeatedly without noise exposure. No instances of pattern changes were observed.
13. Although discharge pattern stability is not usually evaluated formally, figures or text of published reports usually suggest that patterns are stable for given sets of stimulus conditions [J. Moller, G. Neuweiler, H. Zoller, *J. Comp. Physiol.* **125**, 217 (1978); G. D. Pollack, D. S. Marsh, R. Bodenhamer, A. Souther, *J. Neurophysiol.* **40**, 926 (1976); M. S. Silverman and B. M. Clopton, *ibid.*, p. 1266; (5)].
14. R. A. Schmeidt, J. J. Zwislocki, and R. P. Hamernick [*J. Neurophysiol.* **43**, 1367 (1980)] reported interference with peripheral two-tone inhibition; B. L. Lonsbury-Martin and M. B. Meikle [*ibid.* **41**, 987 (1978)] found increased nonevoked eighth nerve discharges; and N. Y. S. Kiang, M. C. Liberman, and R. A. Levine [*Ann. Otol. Rhinol. Laryngol.* **75**, 752 (1976)] showed hypersensitivity of eighth nerve FTC "tails."

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