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11. Supported by NIDR special postdoctoral fellowship 5-F3-DE-28, 947-02 and PHS grant AI-07970. We thank Dr. Sun Lee for his demonstration of kidney grafting in rats.

20 May 1968; revised 9 July 1968

Mice Unilaterally Sensitized for Audiogenic Seizures

Abstract. *Strain SJL/J mice exposed to loud bell-ringing (primed) with one ear blocked do not convulse, but are susceptible to audiogenic seizures 48 hours later when stimulated only through the ear open at priming. Mice stimulated through the ear blocked at priming do not convulse, but are convulsible when retested on the opposite ear. The site of sensitization appears to be either in the ear or in those portions of the auditory system receiving input only from one side.*

Henry (*1*) demonstrated that "seizure-resistant" C57BL/6J mice can be made highly susceptible to audiogenic seizures by exposing them to the sound of a bell during a sensitive period, which includes portions of the 2nd and 3rd weeks after birth. Similar dependence of the induction of audiogenic seizure upon prior sensitization has been found in SJL/J mice by Fuller and Collins (*2*). In this strain, convulsibility develops 30 to 36 hours after a priming exposure to bell-ringing at 3 weeks of age. Repeated exposures to bell-ringing at 6-hour or 12-hour intervals following priming, but not at 18-hour intervals, interfere with sensitization. Once sensitized, an SJL/J mouse remains convulsible for more than 20 weeks. Sensitization becomes progressively less predictable with age, and by 8 weeks it is demonstrable in 10 percent, or less, of subjects. Attempts in our laboratory to prevent sensitization following priming exposure to the bell or to induce sensitization by other procedures have been unsuccessful, although a wide variety of agents, including general anesthetics, anticonvulsant drugs, electroconvulsive shock, and food deprivation, have been used. The stability of the process in the presence of these diverse treatments led us to suspect that the site of sensitization might be relatively localized, possibly in the ear itself.

To test this possibility, mice were exposed to bell-ringing for the first time (priming exposure) with one ear blocked, and were tested for susceptibility to audiogenic seizure by a second exposure with either the ipsilateral or contralateral ear blocked. Failure to elicit convulsions when the contralateral ear was blocked would be evidence for a peripheral locus of sensitization. Forty-two SJL/J mice, 3 weeks old, from the production colony of the Jackson Laboratory (*3*) were exposed to the sound of an electric bell (sound level, approximately 95 db above 0.0002 dyne/cm^2) for 30 seconds, half with the right ear and half with the left ear blocked by flooding the external auditory canal with glycerine. This procedure, performed bilaterally, had been shown to protect against seizures in known convulsible mice and to prevent sensitization in 3-week-old mice exposed to a normally adequate sound stimulation. Immediately following priming the contralateral ear was also blocked to insure that both ears would have similar prior treatment at the time of testing.

Forty-eight hours after priming each mouse was exposed to the same bell-ringing for 60 seconds or until it convulsed. In half the mice, the same ear was blocked as at priming (group I, ipsilateral) and in the other half, the opposite ear (group C, contralateral). Twenty out of 22 mice in group I convulsed; one out of 20 in group C (chi square, 27.5; $P < .0001$). Motor patterns in all seizures were bilaterally symmetrical, and no correlation was observed between the direction of the running phase of the seizures and the ear that was blocked either at priming or at test.

A further demonstration of the unilateral nature of sensitization in these mice, and the dependence of convulsibility upon conditions at priming and not upon a history of previous convulsibility, was obtained by retesting all subjects 24 hours after the first test. At this time group I was subdivided into groups II and IC, with the second letter designating the blocked ear in relation to conditions at priming. Similarly group C was subdivided into groups CI and CC. The ratios of convulsions to numbers tested were: group II, 7:12; group CI, 9:10; and combined ipsilaterals, in second test, 16:22. In the combined contralateral groups IC and CC, during the second test, there was one convulsion in 20 mice tested (chi square, 17.2; $P < .0001$). Groups II and CC responded similarly on tests 1 and 2, except for a slight reduction of seizures in group II which we attribute to a postictal refractory state observed in other experiments. Groups IC and CI showed reversed susceptibility between tests, but in opposite directions.

The site of sensitization, therefore, resides either in the ear itself or in parts of the auditory system which receive input solely or chiefly from one side. Delimitation of the location of the process will permit better direction of research on the nature of sensitization. The possibility must be considered also that genetic differences among mouse strains in audiogenic seizure susceptibility are based upon variations in the areas within which sensitization has been demonstrated to occur.

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3. Standards of laboratory animal care as prescribed by the National Society for Medical Research are followed in this laboratory.

4. Supported by PHS grant MH-11327 and by an allocation from an American Cancer Society institutional grant, IN-19. We thank Frank H. Clark, Jane L. Harris, Helen D. Geils, and Geddes W. Simpson, Jr., for assistance.

23 September 1968