Chemoconvulsive Thresholds in Mice of Differing Audioconvulsive Susceptibilities[1]

Much attention has been directed in recent years to the physiological mechanisms underlying the phenomenon of audiogenic seizure in animals[2]. FULLER and SMITH[3] have hypothesized that strains of mice susceptible to sound-induced convulsions possess more rapidly arousable excitatory processes of the brain than non-susceptible mice so that normal inhibitory processes cannot counterbalance the neural excitatory activity elicited by intense sound. This concept suggests that sound-susceptible mice should also be more sensitive to non-auditory convulsive stimuli, unless the postulated inhibitory influences were exerted only upon afferent auditory pathways. Results of studies comparing audioconvulsive susceptible and resistant mice for responsiveness to electrical[4] and chemical[5] convulsive stimuli imply a positive correlation between sensitivity to auditory and non-auditory convulsive stimuli. The present report provides a further test of this possibility.

Methods. Thresholds (as response latencies) for myoclonic jerk, clonic convulsion and tonic convulsion upon inhalation of hexafluorodiethyl ether[6] (HFE) were determined by the method of TRUITT et al[7]. Tests of audiogenic seizure susceptibility were conducted by the method of FINK and SWINYARD[8] in mice of the same age and source as those tested for chemoconvulsive threshold. Male mice of the DBA/2 and C57BL/6 strains (source: Texas Inbred Mice Co.) were compared as they have been in many earlier studies on audiogenic seizures[9]. Swiss mice inbred 16 generations for high audioconvulsive susceptibility were compared to random-bred Swiss controls (source: Flora O'Grady, 2336 Gunther Ave., New York City). Tests were conducted over a wider range of ages than in the earlier studies. All observations were made between 09:30 and 11:30 (light period 08:00 to 20:00) in view of diurnal changes in chemoconvulsive thresholds of mice[10]. Statistical evaluation was by means of the *t* test.

Results. Thresholds for myoclonic jerk and clonic convulsion were significantly lower in DBA/2 than in C57BL/6 mice at five weeks of age (Table, group I), when their susceptibilities to the audioconvulsive stimulus contrasted considerably (68% vs. 10% total responses). However, the strain difference in chemoconvulsive thresholds remained even at 11 and 30 weeks, while the difference in audioconvulsive susceptibility disappeared between 8 and 11 weeks as both strains became unresponsive. The inbred and random-bred Swiss strains did not differ in response to HFE at either 5 or 9 weeks (Table), while their susceptibilities to audiogenic seizures contrasted sharply – 83% and 84% total responses (maximal and sub-maximal) for the inbred mice vs. 4% sub-maximal responses for the controls. The low thresholds of DBA/2 mice for myoclonic jerk and clonic convulsion differed as much from those of the inbred Swiss mice ($p < 0.001$) as from the C57BL strain.

Discussion. These observations demonstrate that susceptibilities to auditory and chemical convulsive stimuli do not necessarily show a positive correlation. It may be concluded that determinants of chemoconvulsive sensitivity are not equivalent to determinants of audioconvulsive sensitivity. ABOOD and GERARD[11] found evidence that audioconvulsive susceptibility of DBA mice is related to deficient oxidative phosphorylation, the metabolic defect occurring only during the age span for audiogenic seizures and being absent in C57 mice. Further neurochemical study seeking an age-independent factor to explain the low threshold of DBA/2 mice to myoclonic jerk and clonic convulsion with HFE would be of interest.

Résumé. Les souris des lignées susceptibles et résistantes de la crise audiogène ont été étudiées à l'égard de seuil de sensibilité au convulsivant chimiques, l'éther hexafluorodiéthyle. Les sensibilités a la stimulation audiogène et chimique ne montre pas de correlation positive.

W. M. DAVIS and O. L. WEBB

College of Pharmacy, University of Oklahoma, Norman (Oklahoma, USA), December 9, 1963.

Thresholds of convulsive responses to hexafluorodiethyl ether in strains of audioconvulsive-susceptible and audioconvulsive-resistant mice

	Strains compared	Age (weeks)	No.	Response latency (sec) ± Standard error of the mean		
				Myoclonic jerk	Clonic convulsion	Tonic convulsion
I.	DBA/2	5	12	122 ± 5[a]	163 ± 13[a]	457 ± 9
	C57BL/6	5	12	218 ± 8	258 ± 14	489 ± 19
II.	DBA/2	11	10	105 ± 3[a]	168 ± 13[b]	435 ± 14
	C57BL/6	11	10	202 ± 4	249 ± 8	404 ± 12
III.	DBA/2	30	12	113 ± 14[a]	162 ± 10[b]	332 ± 34
	C57BL/6	30	12	175 ± 8	246 ± 13	384 ± 31
IV.	Audiosusceptible Swiss (O'Grady)	5	10	194 ± 16	236 ± 16	460 ± 20
	Control Swiss	5	10	189 ± 12	227 ± 15	431 ± 23
V.	Audiosusceptible Swiss (O'Grady)	9	12	179 ± 11	196 ± 10	403 ± 18
	Control Swiss	9	12	174 ± 8	222 ± 18	382 ± 12

[a] $p < 0.001$, [b] $p < 0.02$; all other values, p exceeds 0.05.

[1] This work was supported by Public Health Service Research Grants B-2250 (C2) and NB-02250 from the National Institute of Neurological Diseases and Blindness.

[2] Colloques Internationaux No. 112, *Psychophysiologie, Neuropharmacologie et Biochemie de la Crise Audiogène* (Centre National de la Recherche Scientifique, Paris 1963).

[3] J. L. FULLER and M. E. SMITH, Amer. J. Physiol. *172*, 661 (1953).

[4] M. HAMBURGH and E. VICARI, J. Neuropath. exp. Neurol. *19*, 461 (1962).

[5] R. G. BUSNEL and A. LEHMANN, J. Physiol. (Paris) *53*, 285 (1961).

[6] Hexafluorodiethyl ether (Indoklon) was generously supplied by the Ohio Chemical and Surgical Equipment Co. through the courtesy of Dr. A. H. NEELEY, Research Laboratories, Murray Hill (N.J.), and Dr. B. E. MCLAUGHLIN, Medical Research Foundation of Philadelphia.

[7] E. B. TRUITT JR., E. M. EBERSBERGER, and A.S.C. LING, J. Pharmacol. exp. Therap. *129*, 445 (1960).

[8] G. B. FINK and E. A. SWINYARD, J. Pharmacol. exp. Therap. *127*, 318 (1959).

[9] W. BEVAN, Psychol. Bull. *52*, 473 (1955).

[10] W. M. DAVIS and O. L. WEBB, Med. exp. *9*, 263 (1963).

[11] L. G. ABOOD and R. W. GERARD, in H. WAELSCH, *Biochemistry of the Developing Nervous System* (Academic Press, New York 1955), p. 467.