A. L. Benton, *Neurology* **19**, 525 (1969); E. De Renzi and G. Scotti, *Cortex* **5**, 53 (1969)]. However, for some tactile-spatial tasks, such as the perception of direction of brief tactile stimulation to the hands, even unimanual stimulation may yield perceptual asymmetry [A. L. Benton, H. S. Levin, N. R. Varney, *Neurology* **23**, 1248 (1973)].
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17. The particular test used involved free recall of series of three dichotic pairs of digits, presented at the rate of two pairs per second. On such tests, accuracy is greater for material presented to the right than to the left ear in adults [for example (*14*)] and in children [for example (*3*, *4*)], which is considered to reflect left hemisphere specialization for linguistic processing.
18. The total number of subjects in each sex group for this test is less than 100 due to the exclusion of those subjects whose audiometric testing indicated depressed or differential ear acuity.
19. Although some studies with adult men and women [for example, S. Weinstein, in *The Skin Senses*, D. R. Kenshalo, Ed. (Thomas, Springfield, Ill., 1968), pp. 195–222] indicate greater pressure sensitivity for the left fingers and palm, whereas other studies report no laterality difference [for example, A. Carmon, D. E. Bilstrom, A. L. Benton, *Cortex* **5**, 27 (1969)], the one study with children reports greater left sensitivity in girls by the age of 6, but in boys only by the age of 11 [L. Ghent, *J. Comp. Physiol. Psychol.* **54**, 670 (1961)]. In contrast, in my study boys as young as age 6 showed a left-hand superiority for shape discrimination; girls did not, in spite of possibly greater left-finger sensitivity.
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21. The study of Braille reading by Rudel *et al.* (*9*) suggests greater participation of the right hemisphere on this task in boys by the age of 11 years but not in girls even by the age of 13. The late appearance of left-hand superiority in boys in this study may be related to the verbal component in the particular task used, and, by inference, to left hemisphere processing. One study using a "conflict drawing test" [A. W. H. Buffery and J. A. Gray, in *Gender Differences: Their Ontogeny and Significance*, C. Ounsted and D. C. Taylor, Eds. (Churchill Livingstone, London, 1972), pp. 128–157] suggests the opposite hypothesis, that boys develop right hemisphere specialization for spatial functioning later than girls. However this interpretation does not follow unequivocally from their data.
22. Although Knox and Kimura (*8*) found that overall (left plus right) accuracy for recall of environmental sounds was greater for boys than girls, superiority of the left ear occurred as early and was of the same magnitude in girls as in boys. Entus (*5*) also found no sex differences.
23. No data indicative of sex differences in speech representation are reported in studies of acquired aphasia in children. Many studies using verbal dichotic tests in normal children analyzed performance of the sexes separately, and most found no sex difference in age of onset, incidence, or magnitude of superiority of the right ear [for example, Kimura (*3*); Knox and Kimura (*8*); C. I. Berlin, L. F. Hughes, S. S. Lowe-Bell, H. L. Berlin, *Cortex* **9**, 393 (1973); Entus (*5*)]. A few studies did find no superiority of the right ear in some age-sex groups: in some cases for girls, in others for boys, and sometimes at age levels beyond those for which significant ear asymmetry was obtained [for example, Kimura (*14*); M. Nagafuchi, *Acta Oto-Laryngol.* **69**, 409 (1970); Ingram (*4*)]. These data do not provide evidence of a sex difference in lateralization of language functions in children.
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31. F. Nottebohm [*Science* **167**, 950 (1970); *J. Exp. Zool.* **179**, 35 (1972)] reports that lateralization of neural control for bird song is fixed and plasticity is no longer possible by the end of song learning, and that termination of the critical period for normal full song development is postponed by reduced early testosterone concentrations. Therefore, reduced testosterone may prolong the period of latent neural plasticity.
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Susceptibility of Mice to Audiogenic Seizures Is Increased by Handling Their Dams During Gestation

Abstract. *Fetal mice treated on days 10, 11, and 12 of gestation by injecting the mothers with (i) 50 milligrams of β-2-thienylalanine, (ii) solvent, or (iii) sham injection had identical frequencies of audiogenic seizures when tested 23 days after birth; these frequencies were significantly higher than those of an unhandled control group. Results of the sham treatment suggest that maternal stress induced by handling, rather than the nature of the substance injected, increased the susceptibility of the offspring to seizures.*

Riley has reported that C3H/He mice that had been routinely handled developed mammary tumors earlier than mice reared under conditions designed to minimize what he called "environmental stress factors" (*1*). He interpreted his observations and those of others as showing that stress is associated with "subtle modulating factors" in the environment and described the effects of such stress.

We now report that inducing even transient mild stress in the pregnant mouse increased the frequency of audiogenic seizures among the progeny. The experiments were originally designed to clarify an ambiguous result on seizure frequency after prenatal treatment with the phenylalanine analog β-2-DL-thienylalanine (*2*). In those experiments, the frequency of audiogenic seizures induced 23 days after birth following a priming sound stimulus at 21 days (*3*), while highest among animals treated with thienylalanine, was not significantly higher in that group than in the control mice treated with solvent. Both groups of mice showed seizure frequencies significantly higher than those of unhandled controls.

Our investigation was a repetition of the earlier study with minor variations in methodology and with the addition of a group of sham-treated subjects. The mice were the 23rd and 24th generation of a cross of C57BL/Gr, CBA/Gr, C3H/C-Hw, and A/Gr strains maintained by maximum outbreeding, and were designated as CBHA-C (*4*). A subgroup was subjected to brother-by-sister mating in generation 23. The sexes were housed separately, four or five females in a cage adjacent to a cage containing a single male. Females were placed with the male in late afternoon or early evening; they were checked for a vaginal plug as evidence of mating and removed to their own pens the following morning. The date the plug was found was considered day 0 of pregnancy. Mated females were assigned to one of four treatment groups. Treatments were randomized over males and cages. Mice were isolated during the 17th or 18th day of gestation. Litters were reduced where necessary to seven pups to minimize the influences of variation in litter size and of crowding (*5*). All mice had free access to food and water and were housed in the same room with 18 hours of light in 24 hours (LD 18 : 6). Treatments and sound stimuli were presented between 11 a.m. and 1 p.m.

Treatments consisted of intraperitoneal injection, on days 10, 11, and 12 of gestation, of either (i) 50 mg of β-2-DL-thienylalanine in 1 ml of 0.5*N* NaOH, 0.5*N* HCl, and 0.9 percent NaCl (1 : 1 : 5), (ii) solvent alone, or (iii) a sham treatment, in which a needle was inserted into

Table 1. Responses of CBHA-C mice to sound stress 23 days after birth following a primary sound stimulus 21 days after birth. Entries are percentages ± standard error of the means. A clonic seizure is mild or incomplete, and a tonic seizure is severe or one in which the animal becomes cataleptic following a series of convulsive movements. Frequencies are calculated as the number in the class divided by N, times 100. Frequencies are not substantially different if calculated as mean litter percentages. Chi-square of homogeneity results, with no response, wild running, clonic seizure, and tonic seizure incidence as columns, and varying combinations of thienylalanine-treated (Th), solvent-treated (So), sham-treated (Sh), and unhandled (Un) groups as rows, were as follows. Overall: χ^2 (Th versus So versus Sh versus Un) = 29.1, d.f. = 9, $P < .001$. All treatments combined: χ^2 (Th + So + Sh versus Un) = 24.48, d.f. = 3, $P < .001$. Each treated contrasted with control: χ^2 (Th versus Un) = 11.4, d.f. = 3, $P < .01$; χ^2 (So versus Un) = 22.3, d.f. = 3, $P < .001$; χ^2 (Sh versus Un) = 14.3, d.f. = 3, $P < .006$. Each treatment contrasted with each other: χ^2 (Th versus So) = 4.5, d.f. = 3, $.50 > P > .20$; χ^2 (Th versus Sh) = 0.7, d.f. = 3, $P > .50$; χ^2 (So versus Sh) = 2.3, d.f. = 3, $P = .50$.

Treatment group	Individuals (No.)	Litters (No.)	Frequency of response						Percent of tonic seizures that are fatal
			No response	Wild running	Clonic seizure	Tonic seizure			
						Recovered	Fatal	Total	
Thienylalanine	96	17	21.9 ± 4.2	7.3 ± 2.7	25.0 ± 4.4	17.7 ± 3.9	28.1 ± 4.6	45.8 ± 5.1	61.4 ± 7.3
Solvent	103	17	14.6 ± 3.5	13.6 ± 3.4	19.4 ± 3.9	15.5 ± 3.6	36.9 ± 4.8	52.4 ± 4.9	70.4 ± 6.2
Sham	104	19	22.1 ± 4.1	9.6 ± 2.9	22.1 ± 4.1	15.4 ± 3.5	30.8 ± 4.5	46.2 ± 4.9	66.7 ± 6.8
Unhandled	120	20	39.2 ± 4.5	10.8 ± 2.8	23.3 ± 3.9	6.7 ± 2.3	20.0 ± 3.7	26.7 ± 4.0	75.0 ± 7.7

the abdomen and held in place with nothing injected. A fourth group served as unhandled control subjects.

Litters were weaned 21 days after birth, at which time mice were weighed and placed, individually or in groups of three, into a galvanized wash tub to which was attached a 4-inch bell (1 inch = 2.54 cm); the tub was suspended in an illuminated sound deadening chamber with a plexiglass lid to permit observation (*2, 6*). After the mice were acclimatized to the chamber for 30 seconds, the bell was rung for 60 seconds; during this time the mice were observed and their seizure responses (*7*) were scored. On day 23, the mice were subjected to the sound stress in the same order and according to the same procedure. Almost no responses to sound stress occurred at 21 days. Responses at 23 days lay on a continuum from wild running through clonic (spasmodic and partial) seizures followed by recovery, or to tonic (rigid and complete) seizures. All seizures were preceded by wild running. Fully two-thirds of the tonic seizures resulted in death of the animal (Table 1).

Chi-square analysis for homogeneity (*8*) revealed that each group under treatment differed significantly from controls, and the three groups under treatment were identical to one another. The same situation obtains when one compares the elicitation of any response (wild running, clonic and tonic seizures combined) with the failure of the sound stress to elicit any response at all. Thus any of the three treatments applied to pregnant mice increased audiogenic seizure susceptibility to the same extent relative to control treatment. It thus seems that the act of manipulating the pregnant mouse, rather than the test substance, produced sufficient stress to cause the behavioral differences in the progeny.

Whether an animal had been subjected to the sound stress individually or as part of a group of three made no difference in any experiment, although this parameter does affect other lines of mice (*9*). Similarly, the proportion of tonic seizures from which animals failed to recover was the same in all experiments. In all but the sham-treated group, chi-square analysis suggested differences in animals from brother-sister matings contrasted with those from continuously outbred populations. But the directions of the differences varied, and an overall test of heterogeneity of pooled data from all four experimental groups revealed no significance ($\chi^2 = 7.71$, d.f. = 3, $P < .06$). There was considerable variation in response between litters in all experiments. Analyses of variance (*10*) in which responses were scaled from 1 (no response) to 4 (tonic seizure) revealed significant litter effects among all four groups. Mortality of pups before weaning was approximately 4 percent in all groups.

Reports of postnatal effects on progeny of handling or otherwise mildly stressing the dam during gestation are frequent (*11*). The subjects have usually been rats, and the effects observed have been on normal behaviors. There are comparable reports in which sham injection of dams (or injection of distilled water, saline, or other control fluids) influences behavior, body weight, or adrenal function of their progeny (*12*). Similar postnatal effects of handling during gestation are known also in mice (*13*). Handling of dams during gestation may, in fact, result in increased embryo mortality (*14*). So profound an influence of a mild maternal stress on susceptibility to audiogenic seizures serves as a caution to investigators using audiogenic seizures as a measure and to those attempting to assess postnatal effects of prenatal treatments.

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Reticulocyte Transfer RNA and Hemoglobin Synthesis

Smith (*1*) has suggested that transfer RNA (tRNA) availability may regulate hemoglobin synthesis in reticulocytes. Central to this argument is the finding that the level of leucine tRNA ($tRNA^{Leu}$) in rabbit reticulocytes is relatively low: only 34 pmole per A_{260} unit, or 220 molecules of $tRNA^{Leu}$ per leucine residue in