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Changes in Brain Levels of NE and 5-HT are Not Responsible for Attenuation of Audiogenic Seizures by Spinal Cordotomy

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WILLOTT, J. F., C. E. LINTS AND L. H NENJA. *Changes in brain levels of NE and 5-HT are not responsible for attenuation of audiogenic seizures by spinal cordotomy.* PHARMAC. BIOCHEM. BEHAV. 10(6) 957–958, 1979.—Spinal cord transection affords protection from audiogenic seizures (anterior to paralysis) in 21 day-old DBA/2J mice. To test the possibility that altered brain levels of NE or 5-HT are involved in mediating this effect, whole brain levels of these amines were assayed in cordotomized and control DBA/2J mice, aged 21 days. The assay revealed no significant differences between cordotomized and control mice. Therefore, cordotomy protects mice from seizures by mechanisms other than altering brain levels of NE or 5-HT.

Audiogenic seizures Spinal cordotomy Norepinephrine 5-Hydroxytryptamine

DBA/2J MICE are susceptible to audiogenic seizures from approximately 15–30 days of age, with maximum susceptibility around 21 days [7,8]. Spinal cordotomy has been shown to reduce the incidence and severity of audiogenic seizure activity manifested anterior to paralysis by about 45% in the maximally susceptible 21-day old mice but not in less susceptible 16 or 28–30 day-olds [8]. Since there is some evidence that whole-brain levels of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) are reduced in 21 day-old DBA/2J mice [4,7], it is possible that the age-dependent effects of cordotomy on audiogenic seizure activity could involve altered brain levels of one or both of these amines. That is, cordotomy could conceivably protect mice of this age from seizures by elevating brain levels of NE and/or 5-HT, since elevation of either amine has been reported to attenuate audiogenic seizures [5]. This could involve influences on aminergic pathways in the brain or generalized effects of spinal cord trauma, which has been shown to elevate cerebrospinal fluid levels of 5-HT [3]. The present study investigated the role of NE and 5-HT levels in the protective effects of cordotomy by comparing whole-brain levels of both amines in cordotomized and noncordotimized 21-day-old DBA/2J mice.

METHOD

Animals were DBA/2J mice, the offspring of stock obtained from the Jackson Laboratory. At 20 days of age, littermates were assigned to either a control or cordotomized group. The latter (N = 7) were given midthoracic cordotomies under ether anesthesia as described in detail elsewhere [8]. Control mice (N = 7) were treated in an identical manner, but cordotomies were not made.

Monoamine Assay

The animals were sacrificed by decapitation on the day following surgery, when they were 21 days old. Their brains were quickly removed, blotted, weighed, frozen in liquid nitrogen and stored in a freezer until assay within one week. Each tissue sample was then assayed for levels of NE and 5-HT using a modification of the procedure reported by Maickel, Cox, Saillant and Miller [6] which included substituting iso-octane for purified heptane [1] and washing the aliquot of homogenate to be assayed for 5-HT with borate buffer (pH 10.1) to remove the acidic indoles [2]. The concentrations of each monamine were determined as ng/g tissue (wet weight).

RESULTS AND DISCUSSION

As can be seen from Table 1, there were no significant differences between the cordotomized and control (noncordotomized) mice with respect to mean whole-brain levels of NE and 5-HT, as well as mean brain weight. In spite of the fact that the data were pooled from two assays, the variability within both groups is similar. If protection from audiogenic seizures afforded by cordotomy were mediated by an increase in brain levels of either or both amines, then the degree of protection afforded would be expected to be reflected in either elevated brain levels or within-group variability.

One may speculate as to mechanisms that are consistent with the negative findings of the present study. Increased turnover of one or both transmitters could be responsible for the attenuation of seizures by cordotomy (see [4]), or another transmitter system could be involved. It has also been

TABLE 1

WHOLE BRAIN NE AND 5-HT LEVELS OF CORDOTOMIZED AND CONTROL 21 DAY DBA/2J MICE

Treatment Group	N	Brain Weight (mg)	5-HT (ng/g)	NE (ng/g)
Control	7	344 ± 4	383 ± 22	441 ± 16
Cordotomized	7	338 ± 8	402 ± 26	412 ± 16

Each value is the mean ± SEM of data pooled from 2 assays.

suggested that interruption of spinal cord pathways results in a reorganization of central patterns of neural activity which interferes with seizures [9]. In any event, protection from audiogenic seizures produced by cordotomy can not be explained by elevations of whole brain levels of NE or 5-HT.

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