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GABA metabolism in Venezuelan Equine Encephalomyelitis virus infection. Preliminary communication.

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Abstract. Mice infected with Venezuelan equine encephalomyelitis virus showed a significant decrease in GABA content of cerebral hemispheres. Activity of the enzyme which synthesizes GABA, glutamic acid decarboxylase, is also reduced in whole cerebral hemispheres, caudate nucleus, and frontal cortex of infected animals, as compared to values obtained from the same regions of control mice.

Metabolismo de GABA en la infección producida por el virus de la Encefalitis equina venezolana.
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Resumen. En ratones infectados con el virus de la encefalomielitis equina venezolana, se observó un descenso significativo en la concentración de GABA en los hemisferios cerebrales. La actividad de la enzima responsable de la síntesis de GABA (decarboxilasa del ácido glutámico) también se encuentra reducida en los hemisferios cerebrales, núcleo caudado y corteza frontal de los animales infectados.

INTRODUCCION

Some workers believe that viral encephalitis is the major cause of Parkinson's disease (3). This disease, in turn, is characterized by a degeneration of the nigrostriatal dopaminergic pathway with the consequent depletion of dopamine and homovanilic acid in the substantia nigra and striatum (4, 6). A consistent decrease in glutamic acid decarboxylase (GAD) activity in the substantia nigra, caudate nucleus, putamen, and globus pallidus with no corresponding change in gamma-aminobutyric acid (GABA) concentration has also been found in post-mortem brain of Parkinsonian patients.

Recent reports suggested that viral infections can produce chan-

ges in the turnover of brain monoamines. These changes are characterized by increased concentrations of the acid end-products, homovanilic acid (HVA) and 5-hydroxyindolacetic acid (9-11). A rise in dopamine (DA), HVA and serotonin in Venezuelan equine encephalomyelitis (VEE) virus-infected brains has also been reported (1, 2).

The present work was undertaken in order to investigate the functional state of the GABA-ergic neurons in VEE virus infection. We now report studies which indicate that in this experimentally induced encephalitis there is a dysfunction of brain GABA metabolism.

MATERIAL AND METHODS

Swiss albino mice, 21-28 days old, were inoculated intraperitoneally with 0.03 (containing 100 LD50) of the Guajira strain of VEE virus (14) suspended in 0.75% bovine albumin phosphate-buffered saline solution (BAPS), pH 7.4 (7). Control animals were injected with 0.03 ml of BAPS and killed simultaneously with the diseased animals. On the sixth day after inoculation, when paralysis of the limbs was evident, the mice were sacrificed by cervical dislocation, the brains immediately removed and analysed for GABA content (5) and GAD activity (12). None of the animals survived the infection after the seventh day of inoculation.

RESULTS AND DISCUSSION

The data shown on Table I demonstrated a significant decrease in GABA concentration in cerebral hemispheres of mice infected with VEE virus. A decrease in GAD activity was observed in whole cerebral hemispheres, frontal cortex and caudate nucleus (Table II). As shown in the present report the changes in GABA function seen in VEE virus infection are not identical to those reported in Parkinson's disease. As stated, in the latter disease there is a reduction in the activity of GAD in the striatum, but concentrations are normal (8).

Viral infections and the dysfunction of monoamine metabolism have both been considered to be respon-

TABLE I

GABA CONTENT IN CEREBRAL HEMISPHERES OF MICE INFECTED WITH VEE VIRUS. DATA REPRESENT MEANS ± S.E. OF 8 DUPLICATED EXPERIMENTS

Groups	GABA concentration (n moles/mg wet tissue)
Control	1.75 ± 0.15
Infected	0.84 ± 0.10
P	< 0.001

TABLE II

ACTIVITY OF L-GLUTAMIC ACID DECARBOXYLASE IN DISCRETE BRAIN REGIONS OF CONTROL AND VEE VIRUS INFECTED MICE. ENZYMATIC ACTIVITY EXPRESSED AS N MOLES CO_2 MIN/G WET WT. RESULTS ARE GIVEN AS MEANS ± S.E. OF DUPLICATED OBSERVATIONS, FIGURES IN PARENTHESES REPRESENT THE NUMBER OF EXPERIMENTS

Groups	Cerebral hemispheres	Caudate nucleus	Frontal cortex
Control	441.61 ± 26.11 (6)	544.22 ± 37.26 (8)	435.88 ± 30.16 (8)
Infected	318.88 ± 37.40 (6)	315.65 ± 30.16 (8)	274.84 ± 12.78 (7)
P	< 0.01	< 0.0001	< 0.0001

sible for the development of psychiatric and neurological diseases. In our laboratory we have noted that mice infected experimentally with VEE virus showed excitation and hypermotility followed by hipomotility, paralysis, coma, and death. Episodes of emotional and conductual disturbances as well as psychotic behaviour are common in human cases of VEE viral infections (13).

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