Alpha Tocopherol Levels in Various Regions of the Central Nervous Systems of the Rat and Guinea Pig

G.T. VATASSERY, Neurology Research and Geriatric Research, Education and Clinical Center, V.A. Hospital, Minneapolis, Minnesota 55417 and the Departments of Biochemistry and Neurology, University of Minnesota, and **R. YOUNOSZAI**, Department of Anatomy, University of Minnesota, Medical School, Minneapolis, Minnesota 55455.

ABSTRACT

The alpha tocopherol contents of various discrete anatomical regions in the central nervous system of adult rats and guinea pigs were assayed using a liquid chromatographic method. All parts of the guinea pig nervous system had lower alpha tocopherol contents per gram wet, dry or lipid weights than the corresponding areas in the rat. In both animals the distribution of alpha tocopherol did not correspond to the distribution pattern of total lipid. There was also a rostral to caudal concentration gradient with respect to alpha tocopherol content; gray matter from cerebral hemisphere has the highest concentration and cervical spinal cord the least. In both animals alpha tocopherol contents per gram dry weight or lipid weight were higher in gray matter areas when compared with white matter areas. The low concentration of alpha tocopherol in spinal cord could make this region more susceptible to damage from deficiency than the rest of the central nervous system.

INTRODUCTION

A deficiency of vitamin E in animals is known to result in several pathological changes in the central nervous system. A detailed morphological study of the effect of vitamin E deficiency on the nervous systems of various laboratory animals was done by Einarson and Telford (1). They found from their study of suckling rats, adult rats, mice, guinea pigs, rabbits and monkeys that the nerve cells undergo pathological changes as a result of vitamin E deficiency.

Several investigators have observed the occurrence of neuroaxonal dystrophy in the brains of rats deficient in vitamin E (1-4). In the adult rat, both demyelination and axonal lesions were observed in the posterior fasciculi. The accumulation of lipofuscin pigment in the neurons of vitamin E deficient rats is also a well known phenomenon (1). The mechanism of production of such pathological changes and a potential role for vitamin E in nervous system function is still unknown. One of the initial steps in understanding the neurochemistry of vitamin E is to determine the distribution of the substance in various areas of the nervous systems of different species of experimental animals. This paper reports results of studies on the steady state levels of alpha tocopherol, the most active of all the naturally occurring tocopherols, in different areas of the central nervous systems of adult rat and guinea pig.

MATERIALS AND METHODS

Male Sprague-Dawley rats were raised on normal control diets. Four rats weighing 350-400 g were sacrificed by decapitation after overnight fasting, and the brains were carefully removed. The following regions were dissected out as described by Glowinski and Iversen (5): cerebellum, medulla oblangota including the pons, thalamus and subthalamus plus caudate (head). After these regions were removed under a dissecting microscope, the corona radiata was followed and the white matter removed from the cerebral hemispheres. A sample of the remainder of the cortex was taken as gray matter. A sample of cervical spinal cord also was obtained. Brain and cervical spinal cord samples from four adult guinea pigs raised on normal guinea pig diet were similarly dissected out.

The dissected nervous tissue samples were immediately frozen in liquid nitrogen and kept frozen at -70 C. All analyses were conducted within 3 weeks. Each sample was divided into two roughly equal parts. One portion was used for determination of the alpha tocopherol content, and the other was used for the determination of water content by dessication of the samples to constant weight under vacuum (6). Alpha tocopherol levels were determined by a liquid chromatographic procedure developed in this laboratory (7). Using corresponding samples from similar adult rats and guinea pigs, total lipid contents were determined gravimetrically after chloroform-methanol extractions of the tissue samples (8).

RESULTS AND DISCUSSION

The alpha tocopherol content of the various

TABLE I

Alpha Tocopherol Levels in Various Areas of the Central Nervous Systems of the Rat[a] and Guinea Pig[a] Expressed as Micrograms Per Gram Wet, Dry and Lipid Weights

Areas analyzed	Micrograms alpha tocopherol/gram					
	Wet weight		Dry weight		Lipid weight	
	Rat	Guinea pig	Rat	Guinea pig	Rat	Guinea pig
	mean ± S.E.	mean ± S.E.	mean ± S.E.	mean ± S.E.	mean ± S.E.	mean ± S.E.
Gray matter from cerebral hemispheres	13.2 ± 0.2 (13.0 – 13.6)[b]	9.4 ± 0.3 (8.8 – 10)[b]	64 ± 0.4 (63 – 65)[b]	48 ± 1.3 (45 – 51)[b]	169 ± 1.7 (165 – 174)[b]	141 ± 3.9 (131 – 150)[b]
Thalamus plus head of caudate nucleus	12.1 ± 0.3 (11.5 – 12.6)	9.4 ± 0.2 (8.9 – 9.8)	53 ± 0.9 (51 – 55)	42 ± 1.0 (40 – 45)	116 ± 2.3 (111 – 121)	119 ± 2.5 (113 – 124)
Cerebellum	9.2 ± 0.1 (9.0 – 9.5)	7.0 ± 0.1 (6.8 – 7.3)	42 ± 0.7 (41 – 44)	31 ± 0.6 (30 – 33)	97 ± 1.2 (95 – 100)	86 ± 1.3 (84 – 90)
White matter from cerebral hemispheres	13.4 ± 0.2 (13.1 – 13.9)	9.5 ± 0.5 (8.3 – 10.6)	50 ± 0.8 (48 – 52)	32 ± 1.1 (29 – 35)	104 ± 1.5 (102 – 108)	76 ± 3.8 (66 – 85)
Medulla plus pons	12.4 ± 0.2 (11.8 – 12.8)	8.2 ± 0.3 (7.9 – 8.9)	44 ± 0.7 (42 – 45)	30 ± 1.2 (29 – 34)	79 ± 1.5 (76 – 82)	69 ± 2.1 (66 – 75)
Cervical spinal cord	11.1 ± 0.2 (10.8 – 11.4)	5.4 ± 0.2 (5.0 – 5.7)	32 ± 0.9 (30 – 34)	17 ± 0.6 (16 – 18)	53 ± 0.7 (52 – 55)	34 ± 1.1 (31 – 36)

[a]Tissues from four animals were used.

[b]The values within brackets give the range of results obtained.

TABLE II

Statistical Analysis of the Difference in Mean Alpha Tocopherol Concentrations in Micrograms per Gram Dry Weight Among Some of the Areas in the Central Nervous Systems of the Rat and Guinea Pig

Neuroanatomical areas compared	P value for rat	P value for guinea pig
Gray vs White	<0.005	<0.005
Gray vs thalamus and caudate	<0.005	Not significant
Gray vs cerebellum	<0.005	<0.005
Gray vs medulla and pons	<0.005	<0.005
Gray vs spinal cord	<0.005	<0.005
White vs thalamus and caudate	Not significant	<0.01
White vs cerebellum	<0.01	Not significant
White vs medulla and pons	<0.02	Not significant
White vs spinal cord	<0.001	<0.005
Thalamus and caudate vs medulla and pons	<0.01	<0.005
Thalamus and caudate vs cerebellum	<0.005	<0.005
Thalamus and caudate vs spinal cord	<0.001	<0.005
Medulla and pons vs spinal cord	< 0.001	<0.005
Cerebellum vs medulla and pons	<0.05	Not significant
Cerebellum vs spinal cord	<0.001	<0.001

areas of the central nervous systems of rats and guinea pigs expressed as micrograms per gram wet, dry and lipid weights are given in Table I. In both animal species, there is a roastral to caudal gradient in alpha tocopherol levels. Results of statistical comparisons of mean alpha tocopherol levels per gram dry weight of different areas of the central nervous systems of rat and guinea pig are given in Table II. Similar comparisons of alpha tocopherol levels per gram lipid showed significant differences in all cases except white matter vs. medulla pons in the guinea pig.

An examination of Table I reveals that there is no neuroanatomical region in either the rat or guinea pig which has a particularly high concentration of alpha tocopherol with respect to the rest of the brain. This contrasts with the levels of a transmitter substance like dopamine, which is highly concentrated in the striatum (9). The wide spread distribution pattern of alpha tocopherol in the central nervous systems of these animals suggests that the compound is functionally involved with the general metabolic integrity of brain.

Vitamin E deficiency results in a wide spectrum of pathological changes which are species specific (10). Myopathy, which is one of the most widely occurring changes due to vitamin E deficiency, responds to treatment with vitamin E to varying degrees depending upon species (11). Telford (11) points out that muscles of most animals regenerate quite readily following tocopherol therapy, whereas in man or adult rat, the myopathy is irreversible. The role of the nervous system in the pathogenesis of such nutritional myopathy has not been elucidated. Hence, a comparison of the regional distribution of alpha tocopherol in the central nervous systems of adult rats and guinea pigs was performed. In general, the patterns of distribution of alpha tocopherol in both species are very similar. In both species gray matter areas have higher levels of alpha tocopherol per gram dry weight than white matter areas. This observation is especially interesting since Einarson and Telford (1) found that nerve cells are primarily the site of pathology in the central nervous systems of vitamin E deficient animals, indicating that alpha tocopherol plays a functional role in maintaining the structural and/or metabolic integrity of the nerve cell body. In both rats and guinea pigs, gray matter from the cerebral hemispheres has the highest level of alpha tocopherol per gram dry weight or lipid weight. Levels of tocopherol in guinea pig brain are generally lower than those of rat brain, and the alpha tocopherol level in the guinea pig spinal cord is the lowest compared with all other central nervous system areas. Interestingly, Einarson and Telford (1) found that, in guinea pigs with pronounced vitamin E deficiency, the neuropathological changes which could be characterized as liquifaction or disso-

lution of the nerve cells were most marked in the cervical and lumbo-sacral enlargements of the spinal cord. Recent studies in this laboratory using human autopsy brain have shown that the spinal cord alpha tocopherol levels are the lowest among all the central nervous system regions examined (12).

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