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EFFECT OF THALLIUM INTOXICATION ON THE AMINOACID CONCENTRATION OF DIFFERENT REGIONS OF THE RAT BRAIN

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Abstract

Rats were given thallous acetate (5 mg/kg) i.p. for one week. The brain was removed and the free aminoacid levels were estimated in three regions; cerebral hemispheres, cerebellum and brainstem. Whereas the concentrations of taurine, serine, glycine, glutamic acid, histidine, tryptophan and phenylalanine was significantly reduced in the cerebral hemisphere, the levels of taurine, aspartic acid, lysine, phenylalanine, glutamic acid, tryptophan, histidine and GABA were diminished in the brainstem. All the aminoacids tested exhibited significant reduction in the cerebellum except histidine. Taurine, glutamic acid and tryptophan levels were uniformly diminished but other aminoacids showed regional heterogeneity.

Introduction

THE toxicity of thallium was recognized in man and animals[1] shortly after its discovery by Crookes in 1861[2]. The cases of human thallium poisoning were first reported in the 1920s from Germany but others were subsequently reported from Holland and Belgium[3]. Reports of thallitoxicosis with varying presentation still appear sporadically[3-6]. The initial symptoms of thallium intoxication are frequently neurologic and include dysesthesia, neuropathy, choreoathetosis, psychoses, excitement, convulsions, hysterical laughter, nerve palsies, coma and death[4-7]. The patho-physiology of thallium intoxication is, as yet, not clearly understood. Significant diminution of aminoacid concentration of brain areas has recently been reported by several workers in cases of convulsive disorders, including drug-induced convulsions[8]. It would, therefore, be appropriate to investigate the effect of thallium on the free aminoacid content of different regions of the rat brain. The present study is the first attempt in this direction. In this paper, the effect of thallium intoxication on the concentration of taurine, GABA, glycine, phenylalanine, lysine, serine, aspartic acid, glutamic acid, histidine and tryptophan in the cerebral hemisphere, brainstem and cerebellum will be presented.

Experimental Procedure

Male albino rats weighing 150–200 g, were used. They were kept under standard laboratory conditions throughout the experiment. Thallous acetate and other chemicals of Analar grade were obtained from B.D.H. (England). The treated and control groups consisted of equal number of animals. Rats of the treated group were injected thallous acetate 5 mg/kg, i.p. (0·1 ml/100 g body weight of a 5 mg/ml solution) daily for 7 days. The control group was treated in a similar manner with 0·1 ml/100 g body weight of physiological saline. The rats were sacrificed by decapitation, the brains were removed within 15–20 seconds and blotted on filter paper. Cerebral hemispheres, brainstem and the cerebellum were dissected.

Assay of Aminoacids

The three different parts of the brain were weighed separately and homogenized in 80% ethyl alcohol. The homogenates were treated according to the method of Awapara[9] for the estimation of free aminoacids. Following storage for an hour on ice, the homogenates were centrifuged at 16,000 g on the International Refrigerated Centrifuge for 10 min. The precipitate was washed with 3–5 ml ethyl alcohol and the supernatant was evaporated to dryness on the water bath at 70°–90° C. To the residue was added 1 ml distilled water, 2 ml methyl alcohol and 2 ml chloroform and the resultant solution centrifuged for 20 min. The supernatant was obtained which was applied to chromatographic paper as recommended by Awapara[9]. The value of amino acids was calculated in μ mol/g, wet weight of brain tissue. The data were analysed statistically using student '*t*' test and significant differences between the means of the treated and the control groups and the '*p*' values calculated.

Results and Discussion

Following the administration of thallous acetate to rats, signs such as irritability, ataxia and at times convulsions were observed. After 5 days the rats usually became lethargic and the motor activity was considerably diminished.

Table I shows the effect of thallous acetate on en aminoacids in the cerebral hemisphere, cerebellum and brainstem. In the cerebral hemisphere, the concentration of taurine and histidine were most significantly reduced ($P < 0{\cdot}001$), followed by the serine level ($P < 0{\cdot}01$), glycine ($P < 0{\cdot}05$), glutamic acid ($P < 0{\cdot}01$), tryptophan ($P < 0{\cdot}05$) and phenylalanine ($P < 0{\cdot}05$). The reduction of GABA, lysine and aspartic acid levels was insignificant. All the aminoacids were significantly reduced in the cerebellum except histidine. This uniformity in the reduction of aminoacid concentration was, however, not observed in the brainstem. Whereas the levels of taurine, lysine, aspartic acid, phenylalanine, glutamic acid, histidine, tryptophan and GABA were significantly diminished in this region, the reduction in the concentration of serine and glycine was insignificant. The present investigation was carried out in three different areas of the brain to reveal the regional characteristics of thallium toxicity. Regional heterogeneity was, however, apparent in the distribution as well as in the thallium-induced reduction in the concentration of GABA, aspartic acid, lysine and histidine. Free aminoacids are of considerable interest as the source from which proteins and neurohumours are synthesized and to which end-products of their degradation return. They also participate in the regulation of metabolic homeostasis and are part of ionic environment[10]. Significant changes in the concentration of aminoacids, according to Modak *et al.*[11], must reflect changes in the underlying process of their synthesis,

Table I

Concentration of aminoacid (μmol/gm wet weight of brain tissue) in different regions of rat brain (mean ± S.E.)

Aminoacid	Cerebral hemisphere		Cerebellum		Brainstem	
	Control (N=8)	Experimental (N=8)	Control (N=8)	Experimental (N=8)	Control (N=8)	Experimental (N=8)
GABA	9·73±1·26	6·25±0·97	26·26±2·93	10·20±2·31*	14·64±1·55	4·77±0·87†
Aspartic acid	5·74±0·75	3·99±0·60	20·81±2·03	9·35±1·65**	15·12±2·33	4·53±0·97**
Taurine	3·74±0·32	1·54±0·24†	17·41±0·22	5·68±0·48†	11·22±1·44	3·63±0·16†
Serine	4·61±0·47	2·37±0·28**	13·70±1·52	5·66±1·04**	11·64±0·95	4·13±0·47†
Lysine	2·69±0·34	1·75±0·41	12·36±1·98	3·55±0·13**	9·20±0·95	3·08±0·54**
Ph. Alanine	1·95±0·15	0·92±0·11*	6·16±0·69	2·81±0·11**	5·97±0·52	1·88±0·11†
Glutamic acid	1·52±0·08	0·92±0·08**	3·91±0·33	2·03±0·25**	4·09±0·29	2·01±0·28**
Histidine	1·18±0·03	0·77±0·06†	3·43±0·41	2·15±0·41	4·11±0·23	2·41±0·25**
Tryptophan	0·98±0·06	0·65±0·06*	2·49±0·21	1·33±0·17*	2·22±0·12	1·50±0·11*
Glycine	17·35±1·13	10·03±1·26*	65·71±9·06	29·91±2·40**	31·75±3·06	11·51±1·33†

* Indicates $P < 0{\cdot}05$; ** $P < 0{\cdot}01$; † $P < 0{\cdot}001$.

uptake or degradation in different regions of the brain. Another possible reason for the decrease in the levels of aminoacids mentioned, could be their likely utilization for the production of energy in thallium-toxicosis. In the present study the level of taurine, but not those of GABA and aspartic acid, showed a significant reduction in the cerebral hemisphere, suggesting that the reduction in GABA and aspartic acid levels is small and highly discrete and the reduction in taurine level is large and widespread. The latter suggestion is further supported by the observation that the taurine levels have been significantly reduced in all the brain areas included in this study. Like taurine, also GABA and glycine are inhibitory transmitters[12]. On the principle that the brain very often functions through "inhibition of inhibition" or "disinhibition" a decrease in the level of inhibitory transmitters is likely to be associated with hyper-excitability of neuronal structures. An important pathway of tryptophan metabolism in animals is conversion to serotonin. Similarly, phenylalanine and tyrosine are precursors of epinephrine and norepinephrine in the rat[13]. Thus the known precursors of serotonin, norepinephrine and epinephrine are depleted in the case of thallium poisoning. It is apparent that thallium intoxication leads to a decrement in the concentration of aminoacids but this diminution is not uniform throughout the brain.

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AWARD OF RESEARCH DEGREES

Sri Venkateswara University, Tirupati, has awarded the Ph.D. degree in Chemistry to Sri Y. Seshasayi; Ph.D. degree in Mechanical Engineering to Sri K. Lakshminarayana Chetty; Ph.D. degree in Zoology to Sri D. Venkateswarlu; Ph.D. degree in Geology to Sri K. S. Sudhakar.

Karnatak University, Dharwar, has awarded the Ph.D. degree in Chemistry to Shri Shivasharan Siddappa Kaddargi; Ph.D. degree in Mathematics to Smt. Pushpavati; Ph.D. degree in Zoology to Shri Gangadhar Basalingappa Dodakundi; Ph.D. degree in Mathematics to Shri Shivashankar Sidramappa Chetty; Ph.D. degree in Botany to Shri Ulhas Damodar Bongale.

Utkal University, Bhubaneswar, has awarded the Ph.D. degree in Physics to Shri Narayan Chandra Das; Ph.D. degree in Mathematics to Shri Surendranath Bastia; Ph.D. degree in Botany to Shri M. P. Sinha.

Sambalpur University, Burla, Orissa, has awarded the Ph.D. degree in Chemistry to Sri Purna Chandra Roy.

The M.S. University of Baroda, has awarded the Ph.D. degree in Botany to Shri Jitendrakumar Jayantilal Dave; Ph.D. degree in Biochemistry to Shri M. N. Subba Rao; Ph.D. degree in Botany to Shri Sanjappa, Munivenkatappa; Ph.D. degree in Botany to Shri Rajendrakumar.