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ORIGINAL PAPER

Low Tryptophan and Protein in the Diet During Development Increase the Susceptibility to Convulsions in Adult Rats

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Abstract Tryptophan (TRY) is the precursor for serotonin (5-HT) synthesis. Common maize has low protein content with low concentration of TRY and lysine. A diet based on two strains of corn differing in their TRY content were given to adult female rats, prior mating, during pregnancy and lactation. Same diets were offered to their male offspring after weaning until reaching 60-days old. The pattern and severity of the convulsive phenomenon induced by monosodium glutamate (MSG) in a well established model of *Status epilepticus* were evaluated in comparison with data from animals of two control groups: (a) rats fed a hypoproteic (8% protein) diet, and (b) rats fed a normal Purina chow diet (23% protein). Significant increased susceptibility to convulsions was observed in both groups of rats fed the corn-based diets. However, the animals fed the common corn-based diet (8–9% protein; 0.058% TRY) showed a higher susceptibility to convulsions than what was registered in animals fed a Quality Protein Maize (QPM)-based diet (8–9% protein; 0.1% TRY). It is concluded that low TRY concentration in the diet during development, produces lower rate of brain 5-HT synthesis, affecting development and maturation of GABAergic inhibitory cortical interneurons, with alteration of cortical excitability, contributing in part, to the increased susceptibility to convulsions, as shown in the experiments here reported.

Keywords Corn-diet · Convulsions · Monosodium glutamate · Tryptophan · Hyperexcitability · Malnourished rats

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Introduction

Nutritional insults early in life have a profound and often permanent effect on the development of the central nervous system (CNS), resulting in various anatomical, biochemical and physiological disturbances [1–4]. Employing an animal model for malnutrition characterized by substantial reduction in the brain levels of tryptophan (TRY), serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) [5–8], we have reported a reduction in the number of GABAergic [9] and serotonergic [10] nerve cells in cerebral cortex and raphe nuclei, respectively. Corn protein is among the most deficient in TRY and lysine of all proteins normally ingested by humans. Administering this diet to rats determines low brain concentration of 5-HT and 5-HIAA levels, which might at least partially reflect a

decrease in 5-HT formation as result of its substrate deficiency [5, 7, 8], probably altering the postnatal development of brain microneurons. In these conditions, the circuit formation and function which are essential to establish the delicate balance between inhibitory and excitatory activities in critical brain structures, such as dentate gyrus of the hippocampal formation, cerebellar and cerebral cortices are thus altered.

A direct relationship between malnutrition and epilepsy has not been well established; however, numerous animal studies suggest that malnutrition may have detrimental effects on the brain predisposing the animals to develop seizures [11].

Monosodium L-glutamate (MSG) a common food additive produces motor disorders manifested as epileptiform seizures when parenterally administered to rats [12–16]. Such effects are similar to those produced by intracisternal injection of L-glutamate [17] and the various episodes of the convulsive phenomenon can be easily monitored. The glutamate carrier at the blood-brain barrier (BBB) is virtually saturated under physiological conditions, and the glutamate passage from blood to brain is much lower than its efflux from the brain [18]. However, when administered in a hyperosmolar solution its massive entry through opening of the BBB may produce signs of hyperexcitability affecting the physiology of various brain systems [15–19].

The aim of the present study was to investigate whether the neurochemical changes induced by TRY and protein restriction in rats fed with a diet based on two strains of corn differing in their TRY content determines more susceptibility to seizures induced by monosodium glutamate (MSG) in a well established model of experimental *Status epilepticus.*

Experimental Procedures

Malnutrition Induction Paradigm

Twenty eight 60-day-old female Wistar rats were divided into four groups of 7 rats each and fed with the various diets: (a) corn group (CORN) fed a common corn-based diet, (b) a group fed a quality protein maize-based diet (QPM), (c) a group fed a hypoproteic diet (HYP) containing 8% protein on a chow-Purina base, and (d) a control group (CTRL) fed Purina chow diet, containing 23% protein (Table 1). The rats were given free access to their respective diets and to water, during 6 weeks; after this time the animals were caged with healthy males overnight, and pregnancy was determined by identifying sperm cells in the vaginal smears. Pregnant rats were kept in individual cages, at 23 ± 1°C and 45–55% relative environmental humidity, under controlled light-darkness cycles (12 h light; 12 h darkness). The food intake was similar during gestation in CTRL, QPM and HYP groups of rats, whereas it was non significantly lower in the CORN group, as seen in previous works [6, 20]. At birth, all litters in all groups were adjusted to 8 male pups per group. The pups were fed with mothers with each diet during lactation. Animals in each litter were fed the same diet at weaning until reaching 60-days old. Postnatal body weight was registered in animals from all groups.

Table 1 Composition of diets (g/100 g diet)

Components	Groups			
	CTRL	HYP	CORN	QPM
Chow Purina	98.00	34.04	–	–
Corn mixture	–	–	86.00	86.00
Dextrose	–	19.00	–	–
Sucrose	–	20.10	–	–
Dextrin	–	12.67	–	–
Vegetal oil	2.00	3.13	4.00	4.00
Mineral mixture[a]	–	1.00	4.00	4.00
Vitamins mixture[a]	–	1.00	1.00	1.00
Cellulose fiber[b]	–	9.06	6.90	6.90
Total protein	23.00	8.00	8.00	9.00
Kilocalories per 100 g	350.00	350.46	348.50	350.00
Tryptophan (g/100 g of diet)	0.30	0.15	0.058	0.10

[a] Obtained from ICN Biochemicals, Inc.

[b] Obtained from Instituto de Madera, Celulosa y Papel, University of Guadalajara

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

Procedure for Seizures

MSG was intraperitoneally (i.p) administered to male rats from the 4 groups according the diets received (see Tables 1 and 2) at doses varying from 4.5 to 5.2 mg/g (26.10 to 30.16 mmol/kg) from a 50% aqueous solution of the compound. Total volume injected ranged between 0.1 and 1.0 ml. Control rats of ages similar to those of the experimental groups for each diet group, were injected with either a sodium chloride solution (NaCl) equimolar to that of MSG (eqNaCl), or physiological saline solution (PSS) in proportional volumes to those employed for the MSG-injected animals. No rat was used more than once in any experiment, and the housing, feeding, cleanliness, ventilation, care and treatment of laboratory animals were carefully observed according the Mexican Federal law for protection of animals [21], which is in accordance with the National Institutes of Health Guide for Care and Use of Laboratory Animals [22].

Table 2 Effect of diets deficient in tryptophan and protein on the postnatal body weight of rats from all groups studied

Postnatal age (days)	CTRL	HYP	CORN	QPM
1	12.0 ± 0.8	11.4 ± 0.9	11.0 ± 6.1	11.8 ± 0.9
10	48.1 ± 1.9	37.1 ± 2.45	17.9 ± 1.1	25.3 ± 3.6
20	61.3 ± 3.4	41.2 ± 3.8	24.3 ± 0.9	32.5 ± 4.6
30	86.0 ± 5.4	56.2 ± 4.5	25.3 ± 1.1	40.8 ± 5.8[a]
40	115.4 ± 6.1	75.03 ± 6.1	28.0 ± 1.8	52.7 ± 5.4[a]
50	162.1 ± 7.3	92.1 ± 7.6	37.4 ± 2.9	76.2 ± 6.0[a]
60	210.3 ± 5.2	100.7 ± 10.1	42.0 ± 3.8	83.3 ± 6.2[a]

Values are expressed in grams and represent the mean from 8 male rats per each postnatal age in the four groups of animals ± SEM

[a] Significantly different from data obtained from the CORN group at $P < 0.01$

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

Table 3 Effect of diets deficient in tryptophan and protein on the latency to stereotyped movements in the model of experimental *Status epilepticus* induced by i.p. injection of various doses of monosodium L-glutamate to adult rats

Doses of MSG (mg/g)	CTRL	HYP	CORN	QPM
4.5	–	–	28.7 ± 2.6[a]	–
4.8	27.3 ± 4.7	26.7 ± 3.5	20.5 ± 4.0	24.2 ± 3.1
5.0	25.3 ± 2.6	26.1 ± 2.2	18.0 ± 2.5	20.0 ± 2.6
5.2	21.1 ±	19.6 ± 1.9	16.7 ± 2.5	17.5 ± 2.0

Values are expressed in minutes and represent the mean from 7 animals per MSG dose in each group ± SEM

[a] Significantly different from data of CTRL, HYP and QPM groups at $P < 0.01$

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

In all animals, the incidence of convulsive episodes and deaths, as well as the duration and characteristics of motor disorders were visually recorded during a period of 8 h on blind bases.

Intensity of Seizures

Severity of the seizure period was graded according the following criteria [13]:

Grade 1. Animals presented clonic seizures of forelimbs and some tonic jerks of hindlimbs.
Grade 2. Animals showed tonic-clonic seizures with clearly defined interictal episodes.
Grade 3. Animals showed tonic-clonic seizures reaching *Status epilepticus*, characterized by long lasting episode of convulsive activity, usually ending in a tonic hyperextension of all limbs with further recovery.
Grade 4. Animals reached *Status epilepticus* with very short or absent interictal periods and death.

Statistical Analysis

The non parametric Chi-square test was used to evaluate the significance of differences in incidence of seizures induced by MSG at the various doses, whereas the Newman–Keuls test was employed to compare the mean values of the parameters recorded in all groups at the various MSG doses administered.

Results

Rats with chronic malnutrition induced by feeding a corn-based diet and a QPM-based diet showed a significant diminution in the weight gain curve compared to what was seen in animals fed a hypoproteic (8% protein diet) and a normal Chow Purina diet (23% protein). However, significant difference was found when both corn-based diets were offered to the animals, with higher body weight gain in the QPM group than in the common corn-based group (Table 2).

Most animals injected with MSG, especially at high doses corresponding to the 4 types of diet showed convulsive activity. On the other hand, all animals from the 4 groups injected with the corresponding doses of eqNaCl solution or with PSS did not show convulsions or signs of hyperexcitability.

Five parameters were evaluated as the effects of MSG injection in all groups studied: (a) latency period for stereotyped movements, (b) latency period for convulsions, (c) duration of the convulsive period, (d) frequency of convulsions, and (e) severity of the convulsive episodes. Neither convulsions nor stereotyped movements were registered in the animals from CTRL, HYP and QPM groups when MSG was i.p. injected at a dose of 4.5 mg/g, whereas both, stereotyped movements and convulsions induced with MSG i.p. injection at that dose were seen in animals from the CORN group (Tables 3 and 4).

Latency Period for Stereotyped Movements

The latency period was defined as the time elapsed from MSG injection to the appearance of non-directed automatic motor manifestations typical of the species, such as biting and cleaning face movements. During this period, the animals appeared quiet, sleepy and slow responsive to environmental acoustic stimuli.

Table 4 Effect of diets deficient in tryptophan and protein on the latency to convulsions in the model of experimental *Status epilepticus* induced by i.p. injection of various doses of monosodium L-glutamate to adult rats

Doses of MSG (mg/g)	CTRL	HYP	CORN	QPM
4.5	–	–	50.1 ± 4.6[a]	–
4.8	54.1 ± 4.1	48.3 ± 6.1	58.6 ± 3.8	51.2 ± 4.6
5.0	58.3 ± 6.0	47.6 ± 4.8	48.1 ± 5.2	48.5 ± 4.8
5.2	50.2 ± 5.6	46.9 ± 6.2	41.6 ± 5.7	45.1 ± 5.1

Values are expressed in minutes and represent the mean from 7 animals per MSG dose in each group ± SEM

[a] Significantly different from data of CTRL, HYP and QPM groups at $P < 0.01$

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

Latency period for stereotyped movements progressively decreased at MSG doses of 4.8 to 5.2 mg/g in animals of the CTRL group. No significant differences were seen in this parameter, between data registered in the HYP group compared to those seen in the CTRL group at all MSG doses administered. However, in the CORN group that reduction of this latency period was more evident when MSG was i.p. injected at doses of 4.8 to 5.2 mg/g when compared to data from the other three groups (Table 3).

Latency Period for Convulsions

This period was considered from the time of MSG injection to the occurrence of the first convulsive episode, varying in each group at the various doses employed. Thus, statistically significant differences were seen when values from the HYP, CORN and QPM groups were compared to those obtained in animals from the CTRL group at MSG doses of 4.5 to 5.2 mg/g (Table 4). Motor hyperactivity and some flexo-extension and lateral movements of the head were occasionally seen a few seconds before the first convulsive episode in animals from all groups.

Duration of Convulsive Period

The convulsive period was considered as the time elapsed from the first to the last convulsive episodes. The average time in CTRL, HYP and QPM groups at MSG dose of 4.8 mg/g was 60 min increasing when 5.0 and 5.2 mg/g were injected , shortening at the highest dose employed in the CORN group due to severity of convulsions and death of some animals (Table 5). Animals from the CORN group showed convulsions with MSG dose as low as 4.5 mg/g the duration of this period varied between 70 and 85 min drastically decreasing at the highest MSG dose due to severity of convulsions and death of animals (Tables 5 and 6).

Frequency of Seizures

Convulsive activity in all groups was characterized by tonic-clonic seizures for 2 to 4 min with interictal periods of 2 to 5 min when stereotyped movements and vegetative responses were seen (sialorrhea, urination, piloerection).

Seven convulsive episodes per hour in average were observed in animals from the CORN group at the MSG dose of 4.5 mg/g, whereas 14 to 17 convulsive episodes per hour were registered in animals from the CORN and QPM groups at MSG doses between 4.8 and 5.2 mg/g, being these data significantly different from those from CTRL and HYP groups (Tables 5 and 6).

Severity of the Convulsive Period

Table 6 shows the data distribution per group according the severity of convulsive period at the various MSG doses used for animals from the 4 groups of diet employed. Grouping grades 1 and 2 as *mild*, and 3 and 4 as *severe* permitted us to clearly see the response differences among the groups studied at the various MSG doses used. Animals from all groups reaching Grade 4 of severity of the convulsive period died in *Status epilepticus*; it was in a tonic convulsion with hyperextension of head, limbs and tail with a cyanotic aspect.

Table 5 Effect of diets deficient in tryptophan and protein on the duration of the convulsive period in the model of experimental *Status epilepticus* induced by i.p. injection of various doses of monosodium L-glutamate to adult rats

Doses of MSG (mg/g)	CTRL	HYP	CORN	QPM
4.5	–	–	73.3 ± 5.6[a]	–
4.8	60.4 ± 4.8	64.1 ± 5.8	68.2 ± 6.1	62.3 ± 3.7
5.0	70.9 ± 6.1	80.2 ± 4.1	79.4 ± 5.2	77.4 ± 5.3
5.2	75.9 ± 6.9	85.9 ± 4.3	50.3 ± 9.6[a]	80.5 ± 2.5

Values are expressed in minutes and represent the mean from 7 animals per MSG dose in each group ± SEM

[a] Significantly different from data of CTRL, HYP and QPM groups at $P < 0.01$

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

Table 6 Effect of diets deficient in tryptophan and protein on the frequency of the convulsions in the model of experimental *Status epilepticus* induced by i.p. injection of various doses of monosodium L-glutamate to adult rats

Doses of MSG (mg/g)	CTRL	HYP	CORN	QPM
4.5	–	–	7.3 ± 2.6	–
4.8	7.8 ± 2.6	7.3 ± 2.0	15.1 ± 2.2[a]	14.3 ± 1.9[a]
5.0	10.3 ± 3.1	15.7 ± 4.8	16.0 ± 2.0	16.7 ± 3.2
5.2	13.7 ± 4.0	14.8 ± 3.2	13.6 ± 2.6	16.5 ± 4.1

Values are expressed in number of convulsive episodes per hour and represent the mean from 7 animals per MSG dose in each group ± SEM

[a] Significantly different from data of CTRL and HYP groups at $P < 0.01$

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

Five out of 7 animals showed severe convulsive period with the MSG dose of 4.5 mg/g injected to rats from the CORN group, whereas none from the other groups manifested severe convulsive episodes at this MSG dose. Correspondingly, 6 out of 7 (86%) rats from the CORN group injected with MSG at a dose of 4.8 mg/g showed severe convulsive episodes, whereas 14%, 28% and 28% of the animals from CTRL, HYP and QPM groups, respectively, showed severe convulsive episodes. The highest severity degree of the convulsive period was registered in animals from the CORN group when data obtained with MSG dose of 5.0 and 5.2 mg/g were compared to corresponding values obtained from CTRL HYP and QPM groups (Table 7 and Fig. 1).

Discussion

The present work evaluated the effects of two corn-based diets over the pattern and severity of the convulsive phenomenon induced by various MSG doses in a well established experimental model of *Status epilepticus* in adult rats [12–16]. The basic difference between the composition of both corn-based diets was their proportion of TRY, as the total amount of protein was similar in both diets. Previous communications from our laboratory have shown that the low concentration of TRY in the diet offered to adult female rats determines a reduction of brain 5-HT synthesis in their progeny when healthy rats are fed this diet since pre-mating, during pregnancy and nursing periods, and from weaning till progeny reaches 60 postnatal days [6, 20]. Although various parameters related to central nervous system structure and function have been communicated in these works and by other authors [7–9], no studies have been designed to explore seizure susceptibility.

The differences in the curves of postnatal body weight gain can be explained in part, in terms of the differences in protein content among all diets, and particularly the TRY proportion, being evident when the gain curve of QPM group was compared to that of the CORN group. In addition to acting as a precursor in 5-HT synthesis, TRY stimulates liver protein synthesis [23] and pituitary secretion of growth hormone (GH) [24]. Also, the regulatory role of 5-HT in the release of GH is well documented [25, 26].

The trophic role of 5-HT during CNS development on the prenatal and immediate postnatal stages, contributing to the integration and differentiation of various neurotransmitter systems, especially on those events related to proliferation of different neuronal populations, and synaptogenesis is well known [27–29]. The aforementioned has an effect on the maturation of the neurotransmission systems, basically the inhibitory ones, so that when there is an interference on 5-HT metabolism, an unbalance between excitatory and inhibitory systems occur, affecting cerebral excitability. When cerebral excitability increases, an increment on the epileptogenic agents sensitivity with an increment of susceptibility to convulsions shall be attained [30]. It is in keeping with what Datiche et al. have communicated in relation to the association between a diminution of 5-HT during development, and a reduction of GABAergic neurons in cerebral cortex [31]. All this correlates with data obtained in our laboratory with the chronic malnutrition model feeding the animals with a common corn-based diet showing a significant decrease on the pups cerebral cortical GABAergic neurons, employing immunohistochemical techniques [9], possibly leading towards an unbalance of those mechanisms regulating cerebral excitability. This became evident in the present work by noticing that those animals fed a corn-based diet clearly showed a greater susceptibility to convulsions than those fed a normal Purina Chow diet. Furthermore, when the animals were fed a diet based on a quality protein maize (QPM) containing double the amount of TRY than that of the common corn, a significant reduction in the susceptibility to convulsions employing a well established model of experimental *Status epilepticus* in rats was seen.

Inasmuch as the corn-based diet employed for this work is an isocaloric diet containing a low proportion of protein (8%) [6, 7], a group of animals fed a hypoproteic diet was included as a matched group to the proportion of protein in the corn-based diets. This, as well as the difference on the TRY content in this HYP group (one third of the TRY content in the Purina Chow diet) explain the outcome differences since this group of animals showed a greater susceptibility to convulsions than the one disclosed by the animals in the CTRL group. Nevertheless, those

Table 7 Effect of diets deficient in tryptophan and protein on the severity of the convulsive episodes in the model of experimental *Status epilepticus* induced by i.p. injection of various doses of monosodium L-glutamate to adult rats

Groups	MSG dose (mg/g)	GRADE 1	GRADE 2	GRADE 3	GRADE 4	Mild (Grades 1 + 2)	Severe (Grades 3 + 4)
CTRL	4.5 (7)	1	–	–	–	1 (14%)	–
	4.8 (7)	–	3	1	–	3 (42%	1 (14)
	5.0 (7)	–	2	1	1	2 (28%)	2 (28)
	5.2 (7)	–	1	2	4	1 (14%)	6 (86%)
HYP	4.5 (7)	–	1	–	–	1 (14%)	–
	4.8 (7)	–	2	2	–	2 (28%)	2 (28%)
	5.0 (7)	–	2	2	3	2 (28%)	5 (72%)
	5.2 (7)	–	–	2	5	–	7 (100%)
CORN	4.5 (7)	–	2	5	–	2 (28%)	5 (72%)
	4.8 (7)	–	1	5	1	1 (14%)	6 (86%)
	5.0 (7)	–	–	1	6	–	7 (100%)
	5.2 (7)	–	–	–	7	–	7 (100%)
QPM	4.5 (7)	–	1	–	–	1 (14%)	–
	4.8 (7)	–	3	2	–	3 (42%)	2 (28%)
	5.0 (7)	–	1	3	3	1 (14%)	6 (86%)
	5.2 (7)	–	–	2	5	–	7 (100%)

Data represent the number of animals grouped in grades of the convulsive period and its severity (mild = 1 + 2 grades; severe = 3 + 4 grades)

Numbers in parentheses at the doses column represent the number of animals per group at the various MSG doses employed

Proportion of animals corresponding to moderate and severe convulsive period induced by the various MSG doses in each group appear in parentheses

CTRL = control group; HYP = group fed a hypoproteic diet; CORN = group fed a corn meal diet; QPM = group fed a quality protein maize

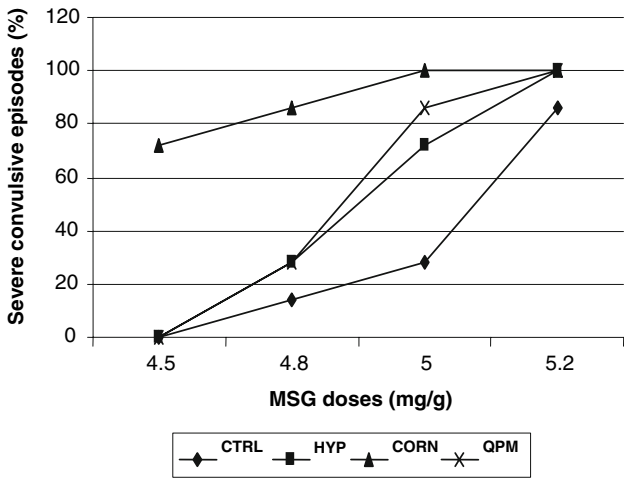

Fig. 1 Graphic representation of the proportion of severe convulsive episodes (grades 3 + 4) in the 4 groups studied (CTRL = control; HYP = hypoproteic; CORN = common corn; QPM = quality protein maize). Increased susceptibility to convulsions induced experimentally by injecting various doses of monosodium L-glutamate (MSG) to animals from the CORN, HYP and QPM groups is observed in comparison with data from the CTRL group. Significant reduction of this susceptibility is depicted at MSG doses of 4.5, 4.8 and 5.0 mg/g i.p. injected to animals from QPM group compared to corresponding data obtained from the CORN group

differences observed in terms of susceptibility to convulsions among animals from CORN and HYP groups, seem to be directly related to the differences on TRY content in both diets (HYP group diet contains twice as much quantity of TRY in relation to the common corn-based diet). This is further supported by the data obtained for all parameters evaluated in the QPM group of animals. This is an improved variety of *Zea maize L* which contains protein of higher quality than that of common corn, and the hybrids have been selected by conventional methods and characterized with the use of molecular markers [32]. QPM-based diet contains similar TRY and protein proportion to that of the diet offered to animals of the HYP group (see Table 1) [33, 34].

Animals from CORN, QPM and HYP groups showed a greater susceptibility to convulsions than those from the CTRL group which were fed a Purina Chow diet containing 23% of protein and nearly five times the TRY quantity than that of the common corn-based diet. However, such effect was much greater in rats from the CORN group, which was evidenced by a lesser latency for stereotyped movements and convulsions and by the severity of the convulsive period as well. Duration of the convulsive period and convulsive episodes frequency progressively decreased in animals from all groups. The greatest susceptibility to convulsions reflecting an increased cerebral excitability determines a reduction of the convulsive period because animals die in a shorter period of time than less susceptible animals. Similarly, convulsive episodes frequency is reduced (Table 3), because when the events are more severe, each convulsive episode is longer.

Both, MSG and eqMSG solutions are hyperosmotic; however, only signs of hyperexcitability and convulsions were observed after MSG administration, suggesting –as it has been discussed in previous works [12, 13, 35–37] that because of the solution hyperosmolarity, the BBB is opened and the glutamate ions massively penetrate into the brain parenchyma, exerting their excitatory effect [15, 19].

Cerebral alterations experimentally produced by malnutrition conditions are related to the duration of malnutrition, diet characteristics, and the brain developmental stage when malnutrition is established [2–4]. In the present work, the animals were exposed to chronic malnutrition conditions with protein and TRY restriction during prenatal and immediate postnatal stages, which are critical for the CNS development [6, 20, 29]. It is concluded that low TRY concentration in the diet during development, produces lower rate of brain 5-HT synthesis, affecting development and maturation of GABAergic inhibitory cortical interneurons, with alteration of cortical excitability, contributing in part, to the increased susceptibility to convulsions, as shown in the experiments here reported. It is possible that other experiments designed with TRY supplementation to the corn-based diets employing a similar experimental paradigm as the one used for the present work, would show some improvement of the seizure susceptibility here reported. Also, other studies using ketogenic or other nutritional schemes in malnourished animals to test seizure susceptibility are needed.

Present results support the theory that humans with chronic malnutrition may have some brain damage, particularly related to systems regulating brain excitability, making the subjects more susceptible to some forms of convulsive or non-convulsive epilepsy [9, 38, 39].

The malnutrition model used for the present work might represent, to a certain point, the feeding conditions of a large human population in the rural areas of countries in the process of development, where corn is the basic food and in some cases, the only nutrient source. Even though, there are reports about the frequency and prevalence of the various types of epilepsy within low socio-economic level rural zones, further research with systematic studies trying to correlate these data with the nutrition conditions in those areas and with their diet nutrient characteristics is needed.

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