Physiol. Res. 43: 387–389, 1994

SHORT COMMUNICATION

Protective Effect of Carnitine on Lipoperoxide Formation in Rat Brain

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Received June 10, 1994
Accepted October 18, 1994

Summary

Carnitine administration (by intraperitoneal injection) to 21-day-old-rats prevents the increase of thiobarbituric acid-reactive substances (index of lipid peroxidation and free radical damage) induced by 30 min hypobaric hypoxia in four different parts of the brain (cerebral cortex, subcortical structures, medulla oblongata and cerebellum).

Key words

Brain (Rat) – Hypobaric hypoxia – Lipid peroxidation – Carnitine

Hypobaric hypoxia followed by reoxidation increases the level of lipoperoxides in brain tissue (Koudelová *et al.* 1992). In our previous paper we found that rats aged 21 days show the lowest resistance to a lack of oxygen such as anoxia, hypoxia and ischemia (Koudelová and Mourek 1991, Koudelová and Mourek, 1992). A significantly higher content of thiobarbituric acid-reactive substances (TBARS) which is the most frequently used index of lipoperoxide level was found in the brain of 21-day-old animals after hypobaric hypoxia (Koudelová *et al.* 1992) as well as after increased pO_2 (Koudelová and Mourek 1994).

During the past decade numerous data have demonstrated the protective effect of carnitine in different physiological and pathological processes (Ferrari *et al.* 1992). It was recently found that propionyl-carnitine decreases the lipoperoxide formation in the rat heart during ischaemia-reperfusion injury (Packer *et al.* 1992). It seems that carnitine protects cell energy metabolism but the exact mechanism of this protection is not yet elucidated.

The aim of our study was to evaluate to what extent the administration of carnitine to 21-day-old-rats can decrease the level of TBARS produced in different parts of the brain during hypobaric hypoxia and reoxidation.

Table 1

The increase of plasma carnitine of 21-day-old rats 60 min after intraperitoneal administration (80 mg/ 100 g weight).

μmoles carnitine /l of plasma			
Control animals	%	Injected animals	%
42.4±2.9 (n=6)	100	317.4±13.9 (n=5)	48

Data are means ± S.D. The number in brackets indicates the number of experiments.

The experimental animals were 21-day-old Wistar rats of both sexes. These animals received an intraperitoneal injectionof carnitine (generous gift of Sigma Tau, Italy) in the amount of 80 mg per 100 g of

body weight and its plasma concentration was determined after 60 min as described by Cejka and Kithier (1992). The lipid peroxide content was measured by determinating TBARS according to Ohkawa *et al.* (1979) in the cerebral cortex, subcortical structures, medulla oblongata and cerebellum. The TBARS content in the whole tissue was expressed as nnanograms ofmalondialdehyde per gram of wet weight. In our experiments we used the thiobarbituric acid test for malondialdehyde determination which is the most popular procedure for assessing lipid peroxidation in spite of its lack of chemical specifity. Some other substances (e.g. sugars, amino acids, urea, biliverdin, pharmaceuticals, glyoxal, furfuraldehyde) may also form complexes with thiobarbituric acid (Esterbauer *et al.* 1991). The results were statistically analyzed by variance analysis (ANOVA) in the Biocybernetics Section of the Department of Physiology.

Table 1 documents the high increase of plasma carnitine concentration carnitine administration. We found no differences between males and females.

Table 2
Level of TBARS in different parts of the brain of 21-day-old control rats, after carnitine administration, rats exposed to acute hypobaric hypoxia and after carnitine administration exposed to acute hypobaric hypoxia.

Males

Tissue	Controls	Controls + carnitine	9 000 m	9 000 m + carnitine
Cortex	12.6±2.1	13.0±1.6	15.4±1.9**	12.0±2.2^{++}
Subcortex	13.8±3.4	12.1±2.3	16.3±2.3**	11.5±2.2^{++}
Medulla	11.6±1.5	11.5±3.6	15.9±2.3**	11.0±2.3^{++}
Cerebellum	9.3±2.8	11.1±3.1	13.9±4.3**	9.9±3.4^{+}

Females

Tissue	Controls	Controls + carnitine	9 000 m	9 000 m + carnitine
Cortex	10.5±2.5	12.3±2.1	16.2±4.1**	11.0±1.8^{++}
Subcortex	11.0±1.3	12.7±2.3	17.2½±.3**	11.0±2.5^{++}
Medulla	10.2±2.6	11.1±2.3	15.8±2.3**	10.3±1.4^{++}
Cerebellum	8.8±2.5	8.8±2.2	14.0±3.6**	9.3±1.8^{++}

*Data are means ± S.D. TBARS (thiobarbituric acid-reactive substances) content was expressed as ng malondialdehyde per g of wet tissue. The number of measurements in the individual groups was at least 10. ** - significantly different ($p<0.001$), $^{+}$, $^{++}$ - significant effect of carnitine for $p<0.01$ and $p<0.001$, respectively.*

Table 2 shows no significant differences between control animals and animals after carnitine administration. When acute hypobaric hypoxia (stimulating an altitude of 9000 m with pO_2 6.4 kPa) was applied for 30 min, a significant increase of TBARS was found in all parts of the brain studied. When carnitine was administered 60 min before the hypoxia, no increase in TBARS occcurred. We found similar results in males and females.

Our experiments showed that carnitine can decrease the production of TBARS in different brain regions and so protect the brain tissue against the destructive effects induced by lipoperoxides. In the literature, several possibilities have been proposed about the protective role of carnitine. One hypothesis is connected with the role of carnitine in lipid metabolism especially with the maintenance of a high energy potential in the cell and acceleration of recovery processes after anoxia which may affect a leak of electrons and oxygen radical formation. Packer *et al.* (1991) mentioned the second hypothesis that carnitine can act through another unspecific mechanism, e.g. as a chelating factor decreasing the concentration of cytosolic iron which plays a very important activatory role in oxygen eradical formation.

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Reprint Requests

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