THE EFFECT OF ASCORBIC ACID DEFICIENCY ON BRAIN CATECHOLAMINES AND MONOAMINE OXIDASES

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Sir,

In vitamin C deficient animals, ascorbic acid levels are reduced in various parts of brain but dopamine levels are raised in striatum (3). Further experiments were performed to assess the effect of vitamin C deficiency on regional brain catecholamines as well as monoamine oxidase (MAO) activity.

Vitamin C deficiency was induced in guinea pigs (250-300 g) according to the method of Ginter et al. (4). The animals were sacrificed by stunning and the brain was rapidly removed. The cerebrum, cerebellum, medulla oblongata, striatum and midbrain were homogenized in appropriate media at 4°C as described by Glowinski and Iversen (6).

Ascorbic acid and catecholamines contents of tissues were determined by the method of Roe and Kuether (8) and by Anton and Sayre (1), respectively. The mitochondrial fractions were prepared as described by Clark and Nicklas (2); the integrity of the mitochondrial preparations was established by electron microscopy. The protein content was estimated by the method of Gornall et al. (5).

The activity of MAO was assayed by measuring the $O_2$ uptake by the mitochondrial preparation using benzylamine and 5-HT substrates. The rate of $O_2$ uptake was measured with a Gilson GME Oxygraph connected to a Sargent SR recorder.

Prolonged vitamin C deficiency had no significant effect on the weight of various parts of the brain in comparison with control animals. Table I shows the level of ascorbic acid and noradrenaline in control and vitamin C deficient animals. While the deficiency of ascorbic acid caused a decrease in noradrenaline content in all other regions of the brain there was no such rise in striatum; the amount of dopamine also was increased in this tissue (5.040 ± 0.92 to 7.450 ± 0.88 µg/g of tissue, n=6). The dopamine levels remained unaltered in other regions of the brain.
The activity of Type A-MAO (nanoatoms of O\textsubscript{2} consumed/min/mg of the protein ± SE) was significantly depressed in the brain mitochondria of scorbutic guinea pigs (controls, 3.16 ± 0.06; scorbutic animals, 1.28 ± 0.177; P<0.001, n=9). However, there was no appreciable difference in the activity of Type B-MAO in mitochondrial preparations from the brains of scorbutic and control animals. Addition of ascorbic acid (8 x 10\textsuperscript{-4} M) in vitro significantly increased the activity of mitochondrial Type A-MAO from scorbutic guinea pigs (1.28 ± 0.177 to 3.16 ± 0.06).

It was confirmed that under the conditions of vitamin C deficiency, the level of ascorbic acid diminishes markedly in all regions of the brain particularly the cerebrum and midbrain regions. Apparently various parts of the brain were differentially affected. Simultaneously there was a significant decline in the concentration of noradrenaline in most of the tissues except the striatum, where the noradrenaline content was not altered. This region also had higher content of dopamine as reported earlier (3).

Tyrosine hydroxylase is a rate limiting enzyme in the normal synthesis of dopamine (7). Scorbutic animals have been reported to have a much lower activity of tyrosine hydroxylase and ascorbic acid has been demonstrated to be directly involved in the synthesis of this enzyme. Our present results show that the levels of dopamine in various regions of the scorbutic brains were not reduced suggesting that during vitamin C deficiency, dopamine might be synthesised via an alternate pathway.

The lower levels of noradrenaline in all the non-striatal tissues could be attributed to the decreased rate of its formation from dopamine because of depressed activity of dopamine \(\beta\)-hydroxylase in avitaminosis C.
The present investigation also reveals that vitamin C deficiency selectively influences the activity of Type A-MAO.

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B.S. BHARAJ*, S.N. NDUATI* AND B.V. TELANG**

Department of Biochemistry*
and
Division of Pharmacology** (Department of Medicine),
University of Nairobi, P.O. Box 30197, Nairobi (Kenya)

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