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EFFECT OF ASCORBIC ACID ON GLUTAMINE SYNTHESIS AND ON THE AMIDATION OF THE BRAIN PROTEINS AND DISTURBANCE OF THESE PROCESSES IN VITAMIN C DEFICIENCY

Chair of Biochemistry
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ВЛИЯНИЕ ВИТАМИНА С НА СИНТЕЗ ГЛЮТАМИНА И АМИДИРОВАНИЕ БЕЛКОВ МОЗГА И НАРУШЕНИЕ ЭТИХ ПРОЦЕССОВ ПРИ С-АВИТАМИНОЗЕ

На английском языке

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The rational use of vitamins in nutrition as well as in therapy presupposes the knowledge of the biochemical mechanism of their functioning as biocatalysts of metabolism. The effect of vitamins, in particular that of vitamin C, on the metabolism of the central nervous system in connection with the functional state of the latter has been studied rather insufficiently. Nevertheless, vitamin deficiency reveals itself in a number of general symptoms of disturbances in the functional state of the brain.

As a number of investigations by E.A.Vladimirova and others have shown, ammonia is one of the biochemical factors which are closely connected with the functional state of the brain. Previous experiments carried out by E.Martinson and I.Fetisenko on an isolated liver established the stimulating effect of ascorbic acid on urea synthesis, i.e. on the detoxication of ammonia in the liver (1937). Later on it was confirmed by us (1955) in conditions of the accumulation of ammonia in the organism in drug-induced sleep which brought about a disturbance of urea synthesis.

In the present report we have studied the effect of vitamin C on the process of binding ammonia locally in the brain itself.

Our experiments showed that when the solution of ammonium chloride was subcutaneously administered to guinea-pigs along with ascorbic acid, the ammonia concentration in the brain increased to a considerably smaller extent than after administering ammonium chloride alone (Fig.1).

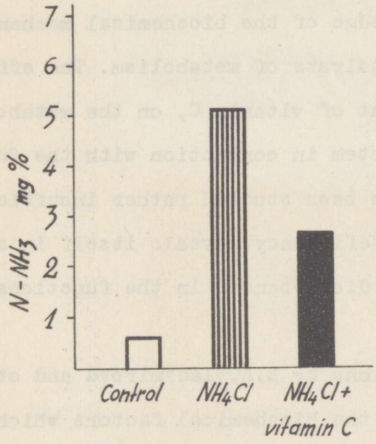

Fig.1. Changes in ammonia content in the brain after administration of ammonium chloride alone and along with vitamin C.

At the same time the rise of the ammonia level in the blood was markedly lower in the case of administering ammonia to an animal along with ascorbic acid. This, however, does not only result from the stimulation of urea synthesis in the liver. It was simultaneously accompanied by a rise of the glutamine content in the blood. Obviously, ascorbic acid intensifies the binding of ammonia in the organs in the form of glutamine, which enters the blood (Fig.2). Indeed, our analyses showed that in a number of cases there proceeded a marked increase in the values of free glutamine in the brain, but not in all the cases (Fig.3).

However, in all the cases we observed a significant increase in the binding of ammonia by the brain proteins in the form of protein-bound, amide nitrogen (Fig.4). Apparently vitamin C stimulates the amidation of the proteins in the brain. This is confirmed by a decrease in the amide nitrogen bound in the brain proteins of the guinea-pigs, which had been suffering from vitamin C deficiency caused by scorbutic diet (Fig.5).

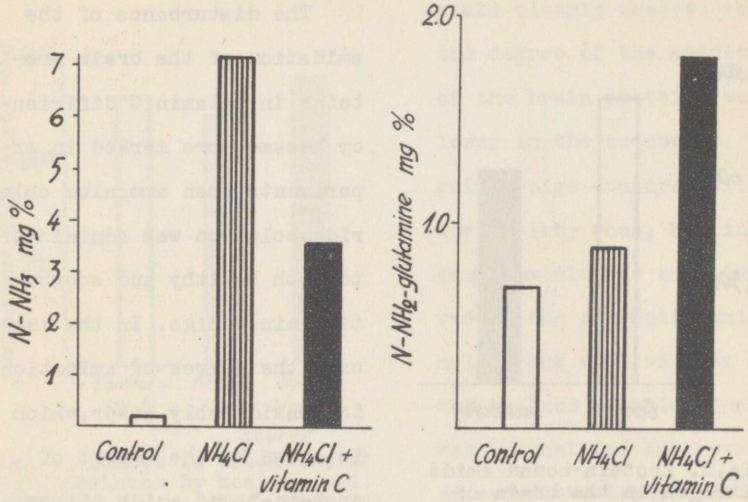

Fig.2. Changes in ammonia and glutamine content in the blood after administration of ammonium chloride alone and along with vitamin C.

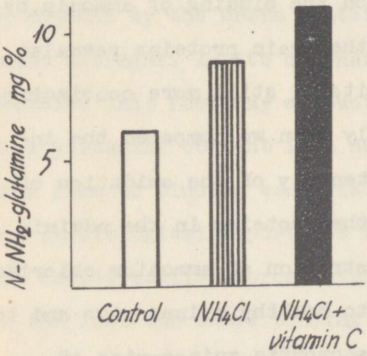

Fig.3. Changes in glutamine content in the brain after administration of ammonium chloride alone and along with vitamin C.

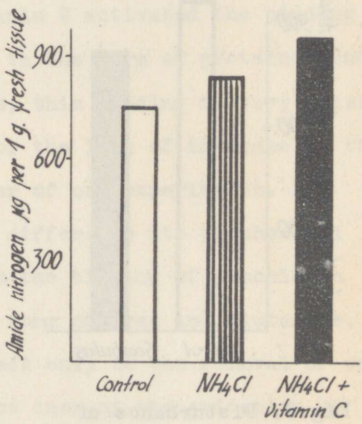

Fig.4. Changes in protein-bound amide nitrogen content in the brain after administration of ammonium chloride alone and along with vitamin C.

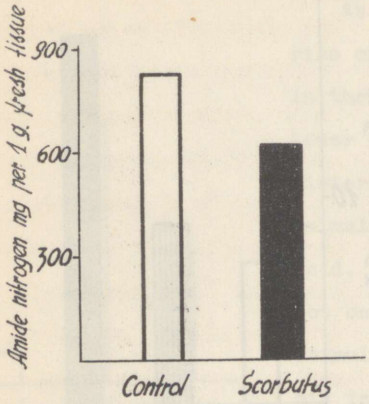

Fig.5. Protein-bound amide nitrogen in the brain of healthy and scorbutic guinea-pigs.

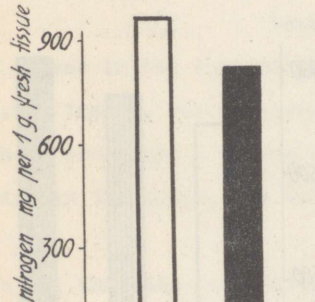

Fig.6. Disturbance of amidation of brain proteins by scorbutus after administration of ammonium chloride.

The disturbance of the amidation of the brain proteins in vitamin C dificiency became more marked in experiments when ammonium chloride solution was administered to both healthy and scorbutic guinea-pigs. In the last case the degree of amidation is considerably lower, which is shown by the amount of protein-bound amide nitrogen (Fig.6).

And lastly, the stimulating effect of ascorbic acid on the binding of ammonia by the brain proteins revealed itself still more convincingly when we compared the intensity of the amidation of the proteins in the administration of ammonium chloride to healthy guinea-pigs and to scorbutic guinea-pigs of which some received no vitamin C and the others were given vitamin C (Fig.7). We

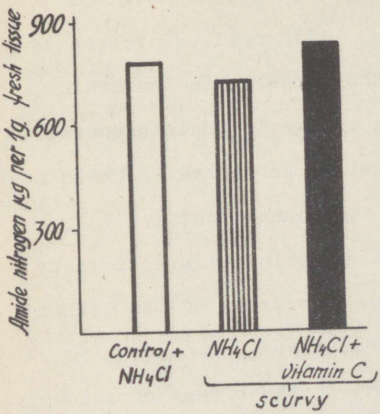

Fig.7. Changes in amidation of brain proteins by healthy and scorbutic guinea-pigs after administration of ammonium chloride alone and along with vitamin C.

could clearly observe that the degree of the amidation of the brain proteins was lower in the scorbutic guinea-pigs compared with the healthy ones, but in case ammonia was administered to the scorbutic animals along with vitamin C, the process of amidation was intensified and even exceeded the degree of amidation of the healthy animals.

It may be concluded that vitamin C activated the binding of ammonia by the brain proteins in the form of protein-bound amide nitrogen. In its dimensions, this binding is very considerable. This fact may account for the lack of increase in the free glutamine content in a number of our experiments. But this form of binding essentially differs in its biochemical and physiological importance from the binding of ammonia in the freely mobile micromolecular form of urea and glutamine. In the last two cases binding leads only to the removal of ammonia as a toxic substance. In the case of the amidation of the macromolecular proteins structurally fixed in the cells there proceeds, in addition, a change in their physico-chemical state. The binding by ammonia of free carboxylic groups

of the proteins in the amide form reduces the total number of its free negative electric charges, but this, as was shown by our previous reports (E.Martinson, L.Tähepõld), involves a change in the macrostructure of the proteins in the brain.

This must be accompanied by a change in their biochemical properties which, in its turn, must be reflected in brain metabolism and, hence, also in its functional state.

This makes vitamin C indicated in clinical practice not only as a means of intensifying the processes of the detoxication of ammonia (e.g. in liver diseases), but also gives a reasonable foundation for the study of the effect of ascorbic acid in the pathology of the central nervous system on the macromolecular level.