PART IV

C H A P T E R V

SUMMARY

S U M M A R Y

In previous studies in this laboratory on rats, protein deficiency during the immediate postweaning period was found to decrease brain glutamate dehydrogenase and glutamate decarboxylase but not GABA-Transaminase. Similar decreases were found with diet of poor quality protein.

The present investigations were concerned with an extension of these studies on the relation between diet and brain enzymes and were concerned with the following aspects:-

I. the comparative effects of calorie restriction and protein deficiency.

II. the effects of differences in protein quality.

III. the effects of glutamic acid supplementation to diets varying in protein content and of different doses of such supplementation.

IV. the effects of vitamin A deficiency in relation to the protein content of the diet.

Additional studies were carried out on the partial purification and characterization of glutamate dehydrogenase from brain and liver.

Animals fed the low protein diet were found to show decreased activities of brain glutamate dehydrogenase and glutamate decarboxylase but not of GABA-transaminase. These decreases were not found in high protein animals pair fed with the low protein groups suggesting that the effects of a low protein diet are not due to calorie restriction.

Animals fed a poor quality protein such as kodri were found to have decreased levels of brain glutamate dehydrogenase and glutamate decarboxylase. Supplementation of kodri with lysine improved the protein quality and increased the activities of brain glutamate dehydrogenase and glutamate decarboxylase. A deficit in the brain glutamate dehydrogenase was found when the animals were fed only maize. This was restored to the normal values on the supplementation of maize with bengal gram and fenugreek leaves. In the case of wheat the deficit in brain glutamate dehydrogenase fell short of statistical significance.

In spite of the decreased food intake and body weight, glutamic acid supplementation at the level of 2 per cent or more was found to restore brain enzyme activities to normal levels in the low protein animals.

The poor acceptability of glutamic acid resulted in decreased food intake and weight gain even when the protein content of the diet was high. Glutamic acid supplementation resulted in restoring to normal levels the activities of brain glutamate dehydrogenase and glutamate decarboxylase in animals fed 3 per cent and 5 per cent protein diets, but supplementation of 8 per cent and 20 per cent protein diets was without effect.

Vitamin A deficiency resulted in decreased food intake, weight gain and poor utilization of food for tissue gain. With the period of treatment used these effects were found only with high protein diets. The high protein animals fed the deficient diet showed the clinical-symptoms of deficiency. The most interesting observation however was the decrease in brain glutamate dehydrogenase and glutamate decarboxylase with vitamin A deficiency in animals fed the HP diets. The LP animals did not show clinical evidence of vitamin A deficiency either with 11 weeks of treatment or 17 weeks of treatment. When the high protein fed animals were fed the deficient diet for 11 weeks and a diet adequate in vitamin A for six weeks, the growth was restored and the clinical symptoms disappeared completely. In the case of brain

enzymes, however, the restoration of activity did not appear to be complete.

PURIFICATION STUDIES

The optimum pH for brain and liver glutamate dehydrogenases were found to be 8.0 and 7.5; km values for 2-oxoglutarate were 7.3×10^{-4}M and 1.3×10^{-3}M. A high concentration of $NADH_2$ was inhibitory in both cases. Stability on storage, heat lability and the inhibition with metals like copper, mercury, and zinc were found to be identical and AMP, ADP and ATP were found to activate the enzyme in both cases.

It was found that liver glutamate dehydrogenase was inhibited with iron whereas brain glutamate dehydrogenase was not, even at a high concentration. The brain enzyme was found to be more sensitive to inhibition by silver than that of liver. Certain tranquilisers which are centrally acting drugs were found to inhibit the brain glutamate dehydrogenase and have either a smaller effect as in the case of fluphenazine dihydrochloride and chlorpromazine or no effect as in the case of trifluprom azine and hydroxyzine on the liver enzyme.

It is necessary to purify these enzymes further and carry out detailed studies on their characteristics with special reference to active sites etc. to understand the preferential effect of nutritional and other stress on brain and liver glutamate dehydrogenase.