S U M M A R Y

SUMMARY

From the foregoing it is evident that brain is more vulnerable to nutritional stress during the critical periods of development. Brain development is very rapid during the suckling period and is highly vulnerable to undernutrition during this period. Marasmus is one of the most commonest form of malnutrition afflicting millions of infants in the developing countries during the postnatal period.

Besides a significant reduction in body and brain weight and decreased activity of some of the enzymes of glucose metabolism was observed. A significantly decreased activity of pyruvate kinase may be indicative of a decreased glycolytic rate in the undernourished rat brain during the suckling period. Decreased glycolytic activity in brain due to undernutrition during suckling period have been reported. Decreased activities of pyruvate dehydrogenase and succinate dehydrogenase, key mitochondrial enzymes denote retarded energy metabolism in the brain of undernourished animal. As glucose is an obligatory substrate for energy metabolism of brain, a significant reduction in the oxidative metabolism of glucose may decrease the neuronal output of the brain. NADP-isocitrate dehydrogenase is an important enzyme linking Krebs cycle intermediates with amino acid synthesis which is particularly active in immature brain. A retarded conversion of glucose carbon into amino acids reported in postnatal undernutrition seems to support this view. This assumes greater significance due to the fact that brain assumes functional maturation during this period of rapid conversion of glucose carbon into amino acids. A significant reduction in the glucose metabolism and its consequent effect on amino acid formation in the undernourished brain may perhaps explain the poor mental development reported in children due to postnatal undernutrition (Winick et al, 1975; Lien et al, 1977).

However, mature brain is resistant to severe undernutrition and moderate protein deficiency. Though there was significant decrease in body and brain weight, there was no reduction in the rate of glucose metabolism as judged by the activity of the enzymes of glucose metabolism. Thus, unlike preweaning undernutrition, postweaning nutritional deficiencies did not have any effect on the metabolic activity of the brain. Thus it is the time of implementation of undernutrition that matters as far as its effects on brain metabolism is concerned. Adult animals are found to register growth even in severe undernutrition. This adaptive mechanism may be achieved by reducing the basal metabolic rate and thereby permitting to save more energy for growth.

Though brain could successfully resist a moderate protein deficiency in the postweaning period, a severe dietary protein deficiency in the immediate postweaning period had its telling effects on brain energy metabolism. As expected, a near protein deprivation and severe protein deficiency induced a negative growth rate, presumably due to a negative nitrogen balance. Brain weight was also significantly reduced. Though the glycolytic rate in the brain of protein deficient animal was comparable with that of the control animal, the energy metabolism was severely depressed in the brain of protein deprived and severely protein deficient animals. These are in agreement with the earlier observation on protein energy malnourished children (Mehta et al, 1977; Mehta and Nain, 1982). A near normal glycolytic rate in the brain of protein malnourished animals may signify the adaptive capability of mature brain even in adverse nutritional circumstances to provide energy for more fundamental functions of the brain.

As pyruvate dehydrogenase plays a pivotal role in energy metabolism of brain, a significant reduction in its activity may denote a decreased rate of energy metabolism. Further, a significant decrease in the activity of succinate dehydrogenase, a key mitochondrial enzyme might be further strengthening this view. As malnourished brain had comparable hexokinase activity the influx of glucose into malnourished brain can be expected to be at the rate of the control animal (Cremer et al, 1981). As discussed earlier, a marked reduction in the activity of NADP-isocitrate dehydrogenase in the brain of protein malnourished animal may signify a decreased rate of formation of amino acids.

Kwashiorkor is a disease due to severe deficiency of both protein and energy in the diet. It is more prevalent among the children in the postweaning age in developing countries. A vast majority of children in the developing countries have access to only poor weaning

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foods. Besides, poor sanitation and frequent bouts of diarrhea pushes them to the clinical condition of kwashiorkor. Poor learning capacity and mental development are well documented among these children in the preschool age. This makes their task of learning at school more difficult.

As many of the neurotransmitter substances are amino acids, there may be decreased availability of these transmitter substances in the context of a severe protein deficiency in kwashiorkor. Besides a substantial quantity of energy metabolism of brain takes place in the neurones. A large share of the energy is used in the conduction of neuronal impulses. Hence a retarded energy metabolism may impair the neuronal communication in protein energy malnutrition. This perhaps may explain the poor learning performance reported in protein malnourished children. Poor nerve conduction velocity has already been reported in protein malnutrition (Stern et al, 1983).

Nutritional deficiencies are more prevalent among the elderly. A chronic protein deficiency did neither affect brain weight nor any of the enzymes of glycolysis and energy cycle studied. It seems the protein requirement of the elderly is much less in comparison to the young adult. Brain seems to be resistant to a chronic protein deficiency in the adult age. This may perhaps be due to a lower metabolic demand of the brain in the elderly. However, there is a general decrease in most of the enzymes of glycolysis and energy cycle. This confirms the earlier report of a decreased metabolic rate as age advances.

Vitamin A deficiency is one of the most important public health problems of the tropics. It is also significant to take into consideration of its association with protein deficiency. Field surveys have established the prevalence of the deficiency of the vitamin in kwashiorkor children. Although, the nutritional importance of vitamin A is widely known, its exact metabolic role in relation to its physiological function is not yet fully understood. The requirement of the vitamin increases when dietary intake of protein increases. This is because the vitamin promotes growth. Hence there is an appreciable reduction in the rate of growth in the high protein fed vitamin deficient animal.

There are quite a number of reports regarding the role of the vitamin in myelin formation. Neurological symptoms due to the deficiency of various water soluble vitamins are well known (Rajalakshmi, 1981). As discussed, early, vitamin A though not stored, is transported into brain. There are cellular retinol binding of protein in brain. All these points to some metabolic role of the vitamin in brain function. Vitamin A has been implicated in the maintenance of catalytic activity of some of the membrane bound enzymes. Vitamin deficiency resulted in significant reduction of both body and brain weight in the high protein fed animals. It is significant that the deficiency symptoms were observed quite early in the high protein fed animals. The content of vitamin A in these animals are self explanatory in this regard. Vitamin A deficiency resulted in significant decrease in the activity of some of the key enzymes of glycolysis such as phosphofructokinase and aldolase in brain. This may lead to an impaired glycolysis in the brain of the vitamin deficient animal. A link between impaired glycolysis and retarded myelination in the deficiency of the vitamin cannot be ruled out.

Although reports on the effect of nutritional deficiencies in early life on subsequent development of brain, behavior and mental faculties are equivocal, it is generally accepted that children malnourished early in life, even after rehabilitation, still show retardation in the development of neuromotor coordination, speech and learning (Wiggins, 1982). Hence priority should be given to studies on the effect of nutritional deficiencies on brain development.

It is well known that brain is a heterogenous organ and hence different area will show wide difference in the metabolic rate depending on its functional demand. Although the present study shows deleterious effect of preweaning energy and postweaning deficiencies of protein and vitamin A on brain metabolism, it may be more appropriate to study these effects on energy metabolism of various regions of the brain. The study on whole brain might have a net diluting effect. Besides, metabolic study on different regions may be able to identify the type of structure involved and hence the specific function affected in different nutritional deficiencies.

A major share of human population suffer from chronic malnutrition (Stern et al, 1983). However, one has to take into consideration that good nutrition alone cannot guarantee a normal development of brain.

Proper environment also has an equal influence on the mental development of the child (Dobbing, 1981; Jamison, 1986).

There are quite a few objections in using animal models, especially the rat in nutritional studies and extrapolating them to human conditions. However, one has to bear in mind that our present understanding on human physiology as well as its molecular basis is based on the use of animal models. Animal models have also been used in understanding diseases and its treatment. A good number of nutritional studies have been conducted using rat as an animal model (Fischer and Turkewitz, 1984). Rat has very much resemblence with the developmental features of human brain (Dobbing and Sands, 1973; Booth et al, 1980; Wiggins, 1982). Nevertheless, the results on animal models may not be able to be translated to human nutritional deficiencies. Surely, they function as warning signals to take precautionary measures.