CHAPTER IV

GENERAL DISCUSSION AND RECAPITULATION

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Thus the present studies confirm previous observations of the effects of protein deficiency on brain glutamate dehydrogenase and decarboxylase. They underline the possibility that metabolic parameters may be affected even in the absence of changes on the composition of the brain with regard to protein, lipids etc. However, as enzyme concentrations do not necessarily reflect substrate or product concentration, further studies are needed on amino acid composition and turnover in the brain with protein deficiency.

The observation that enzymes whose maturation is completed before or shortly after weaning are nevertheless affected by protein deficiency during the postweaning period needs comment. Enzymes are proteins which have to be constantly renewed and it is perhaps not surprising that during an age when the rat is still growing rapidly their synthesis and turnover are affected by nutritional deficiency. It must also be pointed out that the brain continues to grow, albeit slowly, even after weaning.

Similar observations have been made on the effects of postweaning deficiency in dogs on histological changes in the brain (Platt and Stewart, 1968). Barnes and his associates have found postweaning protein deficiency to affect psychological performance in rats (Barnes et al, 1966) and pigs (Barnes et al, 1968).

In this connection, in man although the maturation of the brain is said to be complete by the age of 4-5 years (Dobbing and Sands, 1973) brain changes have been found in children dying of severe malnutrition at the age of 9 years (Bachhawat, 1972). Although it is conceivable that malnutrition had earlier onset in such cases, it is unlikely to have been of more than 2-3 years of duration as children generally die or recover from serious deficiency within a year or so.

It is also interesting to note that in man central nervous system effects are less evident in neonatally undernourished children (belonging to upper class) than in those subjected to severe protein deficiency during the postweaning period (Rajalakshmi and Ramakrishnan, 1972). In the studies reviewed earlier (Table 5, page 31) brain deficits appeared to be more in some cases in the older child. This could be because of differences in the nature of deficiencies generally occurring during the neonatal and postweaning periods.

Some of the other points that emerge from these investigations are discussed below.

The level of dietary protein needed for preventing brain enzyme changes during the postweaning period is only about half that needed for achieving optimum growth. This is consistent with expectation as the brain is the last organ to be affected by nutritional deprivation and the changes in the brain are generally less than those in other organs. As pointed out

earlier this gives room for hope regarding the future development of children subject to mild or moderate deficiency during the postweaning period while at the same time emphasizing the urgent need for the prevention and treatment of such deficiency.

It is interesting to note that the effects of protein deficiency on brain enzymes are fully reversed by dietary rehabilitation with adequate protein. Similar observations have been made by Platt. et al,(1964) on dogs subjected to protein deficiency in early life. Some investigators have reported the effects of protein deficiency in early childhood on EEG patterns to be reversible (Valenzuela, et al, 1959) but others have not found this to be the case (Engel, 1956). It is, however, not possible to ascertain to what extent the dietary rehabilitation of these children was adequate. Most children who have managed to recover from kwashiorkor and marasmus are chronically undernourished and malnourished subsequently as well. Many of them are found to come back to the hospital with a recurrence of disease (Rajalakshmi, 1973). More extensive studies with adequate monitoring of nutritional rehabilitation are needed.

Reports have been made on the irreversibility of psychological retardation in children subject to episodes of kwashiorkor or marasmus in early life (Stoch and Smythe, 1963;

Cravioto and Robles, 1965; Cravioto, 1966; Stoch and Smythe, 1967). However, the nutritional rehabilitation may not have been complete in these studies. Further, the home environment appears to have been far from satisfactory in the case of children studied by Stoch and Smythe (1963). In one of the studies of Cravioto (Cravioto and Robles, 1965) the children were separated from the mothers and hospitalized for a long period and this can be expected to have influenced their subsequent development. The effects of maternal deprivation on the development of the child have been well documented (Bowlby,1960) and the importance of maternal stimulation demonstrated in animal studies (Novakova, 1966).

Reports have also been made of the reversibility of the effects of kwashiorkor on psychological status (Patel, Jain, Amdekar, Desai, Mankodi, Patel and Singhal, 1972).

In the absence of more extensive and consistent information on this aspect social action should be guided by the possibility of the complete recovery of children suffering from kwashiorkor rather than by a pessimistic attitude regarding their future status. On the other hand the possibility of incomplete recovery emphasizes the need to institute urgent measures for the proper nutritional care of children during the postweaning period. It is encouraging that governments and agencies such as the UNICEF and WHO are becoming increasingly aware of this need.

It is also necessary to ensure a proper psychological environment for these children. In studies carried out in Baroda the difference in I.Q.'s between rural and urban children belonging to the low income group of comparable nutritional status was much more than that between "fed" and control children of same social status (Rajalakshmi, unpublished observations). Such observations underline the need for organizing play centres and day-care centres along with supplementary feeding programmes. It must be mentioned in this context that children in rural areas are not only poorly nourished but also poorly cared for. They are often left either alone or in the care of a not much older sibling who is also apathetic and malnourished. In the coastal areas of Kerala fisher folk are sometimes found to leave the children to themselves on the seashore to await their return after several hours (the mother is busy with other chores). Such children being severely apathetic 'stay put' till they are picked up by the parents (Rajalakshmi, 1973).

The question arises how far results obtained on small animals such as the rat can be extrapolated to man with a different pattern of maturation and far greater complexity of the brain. It is however relevant to consider that at weaning the development of the human brain is more advanced than that of the rat or the pig. This should lead us to expect an even greater reversibility of the effects of deficiency in man than

in experimental animals. This encouraging prospect should stimulate more social effort towards the alleviation of malnutrition. However the possibility exists that psychological deprivation caused by the extreme apathy of the kwashiorkor child during critical stages of development may produce a permanent impact.

It is also interesting to note that the level of protein needed for reversing the effects of previous deficiency is somewhat higher than that needed for preventing deficiency. This is consistent with expectation and with observations in severely malnourished and undernourished children. Such children are found to need about 150-200 calories and 3-5g of protein per kg. of body weight per day as compared to 100-120 calories and 2-3g of protein in normal children (Waterlow, 1961).

The observation that whereas body weights varied with the severity of deficiency the activities of brain enzymes did not necessarily follow the same pattern is of interest. Similarly progressive deficits in brain weight with more severe degrees of deficiency are not associated with increasing deficits in brain enzymes which reach a certain minimal level and do not decrease further. This underlines the fact that the composition and metabolic activity of the brain show less variation than those of other organs.

The results also underline the differential effects of protein deficiency and complete protein deprivation. This raises the question how far the effects of a protein free diet found by Lehr and Gayet (1963) or Mandel and Mark (1965) would be comparable with those of a low protein diet.

The observation that the effects of protein deficiency are evident with three weeks of treatment and are not increased by a longer period of treatment is also of interest. In other studies liver glutathione was reduced within a week of deprivation. This suggests that the effects on the brain appear at a later stage than those on other aspects of metabolism, as might be expected.

The small decrease in brain weight with the progress of protein deprivation raises questions regarding the factors responsible. Atrophy of the brain in severely malnourished children has been noted by Udani (1962). Further studies are needed on the lipid composition of the brain with deprivation. However, the decrease was only of the order of 4-5%.

It must be mentioned in this context that the differential effects of protein and calorie deficiencies are also to be inferred from the studies of Platt et al (1964). In these studies an additional control group of animals was fed the stock diet in restricted amounts so that their food intake matched that of the deficient animals. This group was not found to show the changes found with protein deficiency.

Similarly, Barnes and his associates found protein deficiency but not undernutrition to impair psychological performance in rats and pigs (Barnes et al., 1966, 1968).

That the effects of neonatal undernutrition should be different from those of postweaning undernutrition is not surprising in view of the general pattern of development in the brain and similar observations on brain lipids (e.g. Dobbing, 1968b; Rajalakshmi, Nakhasi and Ramakrishnan, 1974). Also it is interesting to note that these effects are reversible. The development of the brain during the neonatal period in the rat is comparable to the prenatal period in man.

As pointed out earlier, these observations raise questions regarding the effects of fetal growth retardation associated with maternal malnutrition and placental insufficiency (Rajalakshmi, 1971). Conflicting observations have been made on the development of babies with low birth weights. While a greater incidence of psychological retardation has been reported by Knobloch and Pasmanick (1963) no such phenomenon was observed either in the studies of Ghosh et al (1972) or in previous studies in this laboratory. The possibility of phylogenetic difference in the relative vulnerability of the brain to malnutrition cannot also be ruled out because of differences in the rate of development and also because of the location of the species on the evolutionary ladder. The brain

increases in size and complexity as we go higher up the scale and the question arises as to whether it also enjoys a greater protection from the effects of deficiency. The situation is also complicated by the fact that in man the type of deficiency occurring during the neonatal period is generally different from that occurring during the postweaning period.

The observation that brain weight deficits occur independently of changes in metabolic activity is of greater interest. Thus both undernutrition and protein deficiency were found to result in brain weight deficits but only the latter was associated with enzyme deficits. In other studies in this laboratory in animals fed low and high protein diets and the former supplemented with glutamic acid, animals fed the low protein diets with or without glutamic acid were found to have slightly decreased brain weights and body weights, but the glutamate supplemented animals showed normal activities of brain enzymes (Rajalakshmi et al, 1969). These observations underline that differences in brain weight may occur in the absence of differences in chemical make up or metabolic activity and that metabolic activity may differ in animals with comparable brain weights. They caution against the use of brain weight as a criterion of brain function. The lack of consistent correlations among head circumference, brain weight and intelligence has been pointed out earlier.

The observation that the effects of postweaning undernutrition are modified by the nutritional status of the animal during the neonatal period is of great interest. In man, most children of poorly nourished mothers develop normally during the first few months of life and become undernourished only during the postweaning period. Similarly children with low birth weights show more than the normal increase in weight during the neonatal period (260% increase in body weight as against 140% in children of average birth weights) (Rajalakshmi, 1971). However, occasionally, children with low birth weights may fail to develop normally during the neonatal period as well. Similarly some children fail to develop satisfactorily prior to weaning. If such children continued to be undernourished and malnourished during the postweaning period as well they may suffer from more serious consequences. In studies carried out by this department in Kerala the children admitted for kwashiorkor and marasmus were reported by the mothers to have developed quite well during the first 8-12 months of age if not till later so that such a combination of prenatal, neonatal and postweaning undernutrition may be rare. It is also possible that such a combination ends fatally so that they do not come in the purview of hospital practice.

The observation that the ratio of brain weight to body weight is higher in nutritional deficiency and that this ratio continues to be somewhat greater than normal even after

rehabilitation is fairly widespread (e.g. Winick and Noble, 1966; Dobbing, 1968b) although a lone report has been made to the contrary (Dobbing and Sands, 1972). The question arises as to how far the permanent stunting observed with nutritional deficiencies in early life is due to the operation of an adaptive mechanism designed to maintain this ratio. This may also account for the higher rate of basal metabolism in undernourished and rehabilitated animals observed in some studies as the brain may account for a greater share of metabolism not reflected by body size or surface area in these animals.

The observation that animals continue to grow in spite of severe undernutrition points to the operation of biological adaptations.

The observation that postweaning undernutrition has no effects on brain enzymes or learning performance should not obscure the possibility of other effects. For instance, skeletal development is found to be affected by such undernutrition. Animals undernourished in early life also show in subsequent life hoarding behaviour, an increase in purposeless activity and a decrease in exploratory activity (Bronfenbrenner, 1968; Frankova and Barnes, 1968b; Latz, Widdowson and McCance, 1961). The effects of chronic hunger and feeding frustration in early life can be expected to have

some effect on the personality development of the child, particularly his feelings of security. Even some adults subjected to severe deprivation for a prolonged period show feelings of insecurity and apprehension that food would not be available in the face of generous supplies (Keys et al, 1950).

Finally the lack of effects of nutritional deficiency in later life on the structure and metabolism of the brain has rightly led to the emphasis on the need for the prevention of nutritional deficiency in early life. This has led some people to question the wisdom of school lunch programmes and the like. First of all, the case for a well-fed society should not rest on whether or not the brain is affected. There is no disputing the fact that undernutrition at any stage affects the motivation, well-being and function of the individual. Poorly nourished adolescent boys (10-12 years) show greater height, weight, and bone-age deficits than younger children (6-10 years) because of their rapid growth and greater nutritional requirements (Rajalakshmi and associates,unpublished). They also show a greater response to nutritional supplementation. For instance, in studies on the effects of the CARE lunch programme in Gujarat, adolescent boys of the fed group were found to weigh 4-5 kg more than controls. The corresponding figure was 1.5-2.5 kg. in the case of younger children. Further

the emotional satisfaction of an individual does not depend necessarily on whether a situation affects the metabolic activity of the brain.

In conclusion, the present studies demonstrate the effects of nutritional deficiencies in early life on selected metabolic parameters in the brain. They confirm the general impression that the effects of deficiency depend on the age of the animal and the type, severity and duration of deficiency.