ficient neonatal animals. At 24h later the saturation of glutamate decarboxylase and γ -aminobutyrate transaminase with coenzyme returned to normal, as did γ -aminobutyrate concentrations.

The dramatic effect of pyridoxine deficiency on the development of the γ -aminobutyrate shunt, reported here, is very likely to be associated with some of the characteristic neurological signs of the deficiency. However, a direct relationship cannot be claimed.

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Effects of Portocaval Anastomosis on the Metabolism of [$1\text{-}^{14}\text{C}$]Acetate and on Metabolic Compartmentation in Rat Brain

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The cerebral disturbances in chronic liver disease have been attributed to the high blood ammonia concentration (Bessman & Bessman, 1955). Portocaval anastomosis in man leads to similar cerebral disturbances (McDermott & Adams, 1954), and in the rat it reproduces the changes in astrocyte morphology found constantly in human chronic liver disease (Cavanagh & Kyu, 1971a,b). Further, a rise in glutamine concentration related to plasma ammonia concentration occurs regularly in the rat brain in these circumstances (Williams *et al.*, 1972). Most brain glutamine is normally formed from a small pool of glutamate that is preferentially labelled by certain precursors, such as [$1\text{-}^{14}\text{C}$]acetate (Berl & Clarke, 1969). To investigate this model system further the cerebral metabolism of [$1\text{-}^{14}\text{C}$]acetate was therefore studied in rats with portocaval anastomosis.

Six experimental animals 6 weeks after the operation (Kyu & Cavanagh, 1970) and six weight-matched controls were injected subcutaneously with [$1\text{-}^{14}\text{C}$]acetate ($20\mu\text{Ci}/100\text{g}$ body wt.; specific radioactivity $59\text{mCi}/\text{mmol}$) and decapitated 10min later. The basal grey areas of the brain (caudate nucleus, thalamus and hypothalamus) were studied because they show the most conspicuous astroglial changes.

Fractionation of tissue and separation of amino acids were done as described by Patel & Balázs (1971).

Portocaval anastomosis had no marked influence on the tissue weight, water content or concentrations of RNA and protein, but [$1\text{-}^{14}\text{C}$]acetate metabolism was significantly affected. Thus the tissue contained 50% less ^{14}C per g than did that of the controls, and the utilization of [$1\text{-}^{14}\text{C}$]acetate in biosynthetic reactions was severely inhibited. The proportion of total tissue ^{14}C in the lipid fraction was decreased from 20 ± 0.5 to $6.5\pm 0.49\%$, and in the protein fraction from 2.8 ± 0.20 to $1.8\pm 0.31\%$. Although the percentage conversion of [$1\text{-}^{14}\text{C}$]acetate into 'tricarboxylic acid-cycle' amino acids was only little affected, the distribution of ^{14}C among the various amino acids differed markedly from that in the controls.

The concentration of glutamine increased by 400% and that of glutamate by 20%, whereas that of aspartate did not change significantly from the control value. The specific radioactivities of glutamate and glutamine, adjusted to a total ^{14}C content of $1\times 10^5\text{d.p.m./g}$, were significantly diminished, and those of aspartate were increased. Hence the aspartate/glutamate specific-radioactivity ratio increased from 0.77 ± 0.03 to 1.42 ± 0.03 , indicating that a new type of metabolic compartmentation had developed. On the other hand, the glutamine/glutamate specific-radioactivity ratio decreased from 2.86 ± 0.20 to 1.17 ± 0.09 . Nevertheless the results showed that the overall rate of glutamine synthesis was increased; relative to the specific radioactivity of glutamate, 75% more ^{14}C was incorporated into glutamine per g wet wt. in the experimental than in the control animals.

The mechanism of these effects is not yet clear. The chronic influx of ammonia into the brain may lead to an accumulation of glutamine at sites that are relatively metabolically inactive, and this 'inert' glutamine would mask the accelerated synthesis of glutamine at the active sites. Alternatively, the rates of acetate oxidation and glutamine synthesis may be increased in metabolic compartments that are normally relatively inactive.

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