Effect of Undernutrition in Early Life on Glutamate Decarboxylase Activity in the Adult Brain

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Rats were undernourished during the foetal and suckling periods by restriction of maternal food intake (Adlard & Dobbing, 1972). At weaning (25 days of age) undernourished animals were divided into two groups: (a) rats fed *ad libitum* from weaning (rehabilitated group); (b) rats whose diet was further restricted until 12 weeks of age (chronically undernourished group), when they weighed about 60g (controls weighed about 360g). Those animals of the latter group not killed at 12 weeks were fed *ad libitum* until 44 weeks of age. Animals well-nourished throughout life served as controls.

At 12 weeks of age forebrain and cerebellar acetylcholinesterase activities (Ellman *et al.*, 1961) (per g wet wt.) were significantly ($P < 0.01$) higher both in rehabilitated and in chronically undernourished animals compared with controls. These changes, in support of previous findings (Adlard & Dobbing, 1971a,b), were in the range 10–15%, but were not apparent in 44-week-old animals.

At 44 weeks of age glutamate decarboxylase activity (Tapia & Awapara, 1969) (per g wet wt.) was significantly ($P < 0.05$) increased in each group of previously undernourished animals compared with controls. Results [mean $\pm$ s.d. (n)] for forebrain were as follows: control, 38.1 ± 1.0 (9) $\mu\text{mol/h per g}$; rehabilitated, 39.3 ± 1.3 (8) $\mu\text{mol/h per g}$; chronically undernourished, 40.4 ± 2.4 (9) $\mu\text{mol/h per g}$. Corresponding results for cerebellum were: control, 22.7 ± 1.2 (9) $\mu\text{mol/h per g}$; rehabilitated, 24.6 ± 1.8 (8) $\mu\text{mol/h per g}$; chronically undernourished, 24.7 ± 2.2 (8) $\mu\text{mol/h per g}$. In contrast, total glutamate decarboxylase activity (per region) was not affected by undernutrition.

Histochemical studies have shown that glutamate decarboxylase and the product of its reaction, namely γ -aminobutyrate, which is a putative inhibitory neurotransmitter compound, are concentrated in certain nerve fibres and terminals in the mammalian central nervous system (Fonnum, 1972). Glutamate decarboxylase activity is enriched in the synaptosomal fraction of brain homogenates, and there is kinetic evidence for the existence of a compartment that has metabolic properties compatible with those of a ' γ -aminobutyrate-nerve-terminal compartment'

(Balázs *et al.*, 1972); a high proportion of the total γ -aminobutyrate flux is associated in this compartment with a small proportion of total glutamate. A possible interpretation of the present results is therefore that nerve endings are relatively spared after undernutrition in early life.

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- Adlard, B. P. F. & Dobbing, J. (1971a) *Brain Res.* **30**, 198–199
 Adlard, B. P. F. & Dobbing, J. (1971b) *Proc. Nutr. Soc.* **30**, 67A–68A
 Adlard, B. P. F. & Dobbing, J. (1972) *Brit. J. Nutr.* **28**, 139–143
 Balázs, R., Machiyama, Y. & Patel, A. J. (1972) in *Metabolic Compartmentation in the Brain* (Balázs, R. & Cremer, J. E., eds.), Macmillan, London, in the press
 Ellman, G. L., Courtney, K. D., Andres, V. & Featherstone, R. M. (1961) *Biochem. Pharmacol.* **7**, 88–95
 Fonnum, R. (1972) in *Metabolic Compartmentation in the Brain* (Balázs, R. & Cremer, J. E., eds.), Macmillan, London, in the press
 Tapia, R. & Awapara, J. (1969) *Biochem. Pharmacol.* **18**, 145–152

Aminopyrine Demethylase Activity in Normal and Vitamin E-Deficient Male Rats

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Aminopyrine is demethylated by the rat liver microsomal mixed-function oxidase system, first to monomethylaminopyrine, then to 4-aminoantipyrine, with the production of formaldehyde at each step (La Du *et al.*, 1955).

Microsomal fraction was prepared from the livers of rats given an adequate diet for 3–4 months, and also from rats given the vitamin E-deficient diet and the vitamin E-and-Se-deficient diet (Diplock *et al.*, 1971), and another 10%-casein vitamin E-and-Se-deficient diet. Further experiments were carried out with microsomal fraction from deficient rats re-fed with vitamin E for 6 days (3mg of DL- α -tocopherol/day orally in 0.1 ml of olive oil).

The apparent K_m and V_{max} for the overall two-stage reaction were obtained by measuring the formaldehyde production by the method of Nash (1953). Microsomal fraction from the vitamin E-deficient animals exhibited abnormal kinetics: the apparent V_{max} fell 15–20% below normal values (from 4.4 to 3.7 $\mu\text{mol/h per g}$ of protein), whereas the K_m increased threefold from 2.5×10^{-4} to 8.7×10^{-4} M. Similar results were obtained with microsomal fraction from the vitamin E-and-Se-deficient animals.

This lowered activity was not due to a decrease in cytochrome P-450 concentration, which, measured by