Arginase deficiency and phenylketonuria

Hyland et al. report clinical similarities between arginase deficiency and phenylalanine hydroxylase deficiency, two inborn errors causing progressive neurological damage. The similarity in the changes of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5HIAA) levels in cerebrospinal fluid and plasma of the deficient patient reported was striking.

We have measured the dihydropteridine reductase (DHPFR) activity in rats loaded with phenylalanine and rats loaded with arginine. Inborn DHPFR deficiency is responsible for the “atypical” phenylketonuria (PKU) which unlike its classical variant is not controllable by strict dietary regimes. The effect on the brain and blood DHPFR activity of loading phenylalanine or arginine was in both cases a similar dramatic reduction.

Brain tyrosine can be synthesised from phenylalanine by tyrosine hydroxylase. Lowered brain tyrosine of untreated PKU is therefore not explicable by amino acid competition for brain entry. We suggest that the action of hyperargininaemia and hyperphenylalaninaemia on catecholamine and serotonin metabolism may be indirectly due to a reduction in DHPFR activity.

References


AMP directly, and indirectly through inhibition of noradrenergic locus coeruleus mechanisms. Thus the net result of opioid action would be expected to reduce neuronal metabolic demand. Indeed, opiates are known to reduce CMRO2 by 85% with a lesser reduction of CBF. In addition, areas rich in opioid receptors have shown to have their oxygen consumption specifically decreased by low-dose morphine. Thus it is quite conceivable that the dramatic increases in the release of beta-endorphins during ischaemical act teleologically to decrease neuronal activity and oxygen consumption. This may possibly represent an extension of a physiological modulatory role of the intrinsic opioids during periods of metabolic stress.

References