Letters

The effect of age on tetrahydrobiopterin metabolism in the human brain

Sir: The availability of the hydroxylase cofactor, tetrahydrobiopterin, is a regulatory factor in catecholamine biosynthesis.[1] BH_4 levels are maintained in the cell by de novo synthesis from guanosine triphosphate (GTP) and a salvage pathway requiring dihydropteridine reductase (DHPR).[2] The biosynthetic pathway requires three enzymes: GTP cyclohydrolase, phosphate eliminating enzyme and sepiapterin reductase in that order.[3,4]

It has been reported that biopterin levels in CSF decrease with age[5] suggesting that BH_4 metabolism is altered in the CNS in normal ageing. We now report diminished BH_4 synthesis and DHPR activity in the ageing brain.

Human brain samples from the frontal cortex (Brodmann area 9) and temporal cortex (Brodmann areas 20/21) obtained at necropsy were supplied by courtesy of Dr Reynolds and his colleagues at the Brain Bank, Cambridge, and Dr Altmann at the London Hospital, Whitechapel, London. High speed supernatants of tissue homogenates were prepared in 0·107 M Tris buffer pH 7·6 and used in all assays. BH_4 synthesis[6] and DHPR activity[2] were determined for the frontal cortex and temporal cortex. GTP cyclohydrolase activity[7] and sepiapterin reductase activity[8] were determined in the temporal cortex. All activities were measured on a protein base-line using the Biuret method for protein determination. Pearson correlation coefficients were calculated for age and enzyme activity.

BH_4 synthesis significantly declines with age in the frontal cortex ($r = 0·590$, $p < 0·05$) and temporal cortex ($r = 0·523$, $p < 0·05$) (table). DHPR activity significantly declines with age in the frontal cortex ($r = 0·722$, $p < 0·01$) and temporal cortex ($r = 0·575$, $p < 0·01$). Sepiapterin reductase activity and GTP cyclohydrolase activity show no correlation with age in the regions examined.

BH_4 levels in the CNS decline in normal ageing.[5] We find that BH_4 synthesis and DHPR activity are reduced in the ageing brain suggesting that decreased cofactor availability may limit noradrenergic activity in the ageing brain. It may be argued that reduced BH_4 metabolism is the result of the neuron loss which occurs in the locus coeruleus with age.[9] However, GTP cyclohydrolase activity and sepiapterin reductase activity show no correlation with age. Therefore we propose that the salvage pathway and biosynthetic pathway are diminished in the ageing brain and further suggest that the lesion in BH_4 synthesis is at the level of phosphate eliminating enzyme.

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Table *Correlation between enzyme activity and age in the frontal cortex and temporal cortex*

	Age Range Years	*n*	*r*	*p*
BH_4 synthesis				
frontal cortex	40–87	14	−0·590	0·05
temporal cortex	40–87	16	−0·523	0·05
Dihydropteridine reductase				
frontal cortex	40–87	14	−0·722	0·01
temporal cortex	40–89	19	−0·575	0·01
GTP cyclohydrolase				
temporal cortex	40–85	9	–	ns
Sepiapterin reductase				
temporal cortex	40–85	8	–	ns

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T cell subsets in AIDS: relationships between peripheral blood and cerebrospinal fluid

Sir: A profound deficiency in immune function underlies the ongoing epidemic of the acquired immune deficiency syndrome (AIDS). A major feature of the immune deficiency in AIDS is a lowering of the ratio of helper to suppressor T lymphocytes in the peripheral blood.[1] Neurological complications are observed in over 30% of the cases and the CNS may be frequently and early involved in AIDS.[2] CSF studies have revealed inflammatory features, such as pleiocytosis, raised IgG index and oligoclonal bands but quantitative changes in T helper or T suppressor lymphocytes have not yet been reported.

We have analysed T lymphocytes subsets in CSF and blood of three AIDS patients with central nervous system manifestations and one patient with AIDS-related complex. T-cell-surface phenotypes were performed with Leu-3a (Beckton Dickinson) to detect