Letters

Is the loss of cerebral cortical choline acetyl transferase activity in Alzheimer's disease due to degeneration of ascending cholinergic nerve cells?

Sir: Although some of the marker enzyme choline acetyl transferase may be present in cholinergic neurons intrinsic to the cerebral cortex,¹ most is thought to reside within the terminals of ascending fibres whose nerve cell bodies are located within that area of brain known as the substantia innominata.^{1,2} Reductions in cerebral cortical choline acetyl transferase activity in Alzheimer's disease³⁻⁶ may therefore reflect dysfunction of these nerve cells. Alterations in the capacity to form proteins needed for physiological function are indicated⁷ by changes in nerve cell nucleolar volume and cytoplasmic RNA content.

We have measured⁸ these features in 60 nerve cells of the substantia innominata, in each of 12 demented patients dying with histologically verified Alzheimer's disease (mean age 81.2 ± 1.3 yrs; necropsy delay 32.9 ± 2.8 h) and in eight others (mean age 78.2 ± 1.7 yrs; necropsy delay 36.7 ± 3.1 h) with multi-infarct dementia. Findings are compared with those from a control group of eight patients (mean age 80.4 ± 1.3 yrs; necropsy delay 32.4 ± 4.0 h) dying without neurological or psychiatric disease and judged to be mentally preserved.

When compared with controls both nucleolar volume and cytoplasmic RNA content were significantly reduced in Alzheimer's disease by 34 and 32% respectively, whereas neither was altered in multi-infarct dementia (Table). Such changes in function in Alzheimer's disease are consistent with other findings⁹⁻¹¹ of neuronal degeneration and loss of choline acetyl transferase activity in this region of the brain, and indicate that the loss of cerebral cortical choline acetyl transferase activity in Alzheimer's disease,³⁻⁶ is probably mainly due to reduced levels of function within the perikarya of cholinergic neurons of the substantia innominata. The smaller decreases in cortical choline acetyl transferase activity reported in multi-infarct dementia^{3,4} most likely stem from tissue destruction caused by local circulatory deficits or the involvement of cholinergic synapses in the few senile pla-

Table

Group	Nucleolar volume (μm^3)	Cytoplasmic RNA content (Arbitrary units)
Control (n = 8)	31.6 ± 2.3	34.7 ± 1.6
Alzheimer's disease (n = 12)	$20.8 \pm 1.9^*$	$23.6 \pm 1.2^*$
Multi-infarct dementia (n = 8)	32.4 ± 2.5	35.8 ± 1.9

Values are means $\pm$ SEM

*p < 0.001, compared with control values

ques usually present in these patients.

The degeneration in Alzheimer's disease, but not in multi-infarct dementia, of other nerve cells which also give rise to ascending pathways, such as those of the locus caeruleus,¹²⁻¹⁵ vagus nerve nucleus,¹⁵ and hypothalamus,¹⁶ suggests that the cholinergic changes, in Alzheimer's disease, may be only one facet of a wider process of deprivation of cerebral input and may partly explain why the many therapeutic trials aimed at restitution of the cholinergic system alone, have, so far, met with little success.

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Insulin-induced hypoglycaemia does not abolish chorea

Sir: Pathological changes occur in the hypothalamus in Huntington's disease.¹ Insulin tolerance tests have been used to examine hypothalamic function in such patients, and mild abnormalities of growth hormone secretion have been described.²⁻⁴ In the course of such an investigation, Keogh *et al*² noted that chorea ceased some 30 min after the insulin injection and was not evident for the next 60 to 75 min in all of the twelve patients studied. They did not think that this dramatic change was due to