

to the lesions we documented. This means that, as far as can be judged from CT scan evidence, the lesion of our patients never encroached upon the arcuate bundle. As to the occipito-frontal bundle, it runs medially to the corona radiata at the level of the roof of the lateral ventricle, which it helps to form. Thus only damage appearing in the CT scan slices where the lateral ventricle is no longer visible bears a relationship to occipito-frontal interruption. In our patients the lesion never reached this level.

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## Glutamatergic Denervation in Alzheimer's Disease—A Cautionary Note

Sir: Sodium dependent binding of D-[<sup>3</sup>H] aspartic acid has been used<sup>1</sup> as a tool for identifying the degenerate neurons which Neary and colleagues consider important to the dementia of Alzheimer's disease.<sup>2,3</sup> However, a more suitable<sup>4</sup> marker of nerve endings of these cells in the human brain, sodium dependent uptake of D-[<sup>3</sup>H] aspartic acid into fresh tissue, has not hitherto been examined.

The brains of six cognitively impaired patients were obtained within 2 hours of death. One cerebral hemisphere was fixed for neuropathological examination and coronal sections (1 cm thick) of the other were transported to the neurochemical laboratory in an ice-cold physiological buffer. Other samples were obtained from patients undergoing surgical treatment for intracerebral tumour where the removal of apparently normal tissue was a necessary part of the procedure. The cerebral cortex from both types of sample was immediately processed to yield tissue prisms or "mini-slices", and the sodium dependent uptake of D-[<sup>3</sup>H] aspartic acid was then determined<sup>3</sup> with modifications for "mini-slices".<sup>5</sup> This approach has advantages<sup>6</sup> which include minimising the possibility that inappropriate subfractions are produced when disease-affected tissue is studied<sup>7</sup> but any influences of either other epiphenomena (for example, interaction between altered energy metabolism<sup>8</sup> and terminal coma) or glia have not been completely excluded.

Of the patients examined post-mortem, three had Alzheimer's disease with widespread senile plaque and neurofibrillary tangle formation (table) and three were found to have other causes of cognitive

Table Sodium-dependent uptake of D-[<sup>3</sup>H] aspartate in human brain

	D-[ <sup>3</sup> H] aspartate uptake (pmol/min/mg protein)		
	Alzheimer's disease (n = 3)	"Other dementias" (n = 3)	Neurosurgical specimens (n = 3)
Temporal cortex	11.0 (8.3–14.3)	27.6 (20.2–40.6)	24.2 (19.8–28.2)
Parietal cortex	7.5 (4.1–11.9)	17.7 (12.7–22.7)	ND
Occipital cortex	9.2 (5.2–11.5)	16.4 (13.8–18.4)	ND
Cingulate cortex:			
Anterior	9.9 (6.4–12.4)	22.8 (18.5–30.0)	ND
Posterior	12.4 (11.7–12.9)	15.5 (12.4–17.9)	ND

Values are means with the range in parentheses, ND—not determined. The mean age and necropsy delay of Alzheimer subjects (71 years, 1.8 hours) was similar to that of subjects with "other dementias" (71 years, 1.5 hours). Neurosurgical specimens were from patients with a mean age of 53 years.

impairment (Pick's disease, multi-system degeneration and depressive pseudo-dementia; "other dementias", table). While the neurosurgical specimens and "other dementias" had comparable uptake values in equivalent areas, Alzheimer's disease subjects had the lowest uptake values in almost all regions examined. Studies of the metabolism of previously frozen brain tissue<sup>8</sup> indicate that the mode of death of the patient may be a major factor affecting energy-dependent measures such as this. However, both groups included subjects with a short (under 1 hour) and a long (3 days) terminal coma, and there appeared to be no effect of a magnitude comparable to that of Alzheimer's disease.

It is now important to substantiate these findings in a larger series. However, glutamate release from the Alzheimer neurosurgical specimens<sup>2</sup> is not altered<sup>9</sup> and glutaminase immunoreactivity seems to mark all neurons which previous studies would predict use glutamate as neurotransmitter, with the exception of some supragranular pyramidal neurons.<sup>10</sup> Neurotransmitter candidates for these cells and excitatory cortical interneurons<sup>11</sup> are unknown but homocysteic acid has some characteristics of such a neurotransmitter.<sup>12</sup>

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AW PROCTER\*†  
AM PALMER\*  
DM BOWEN\*  
E MURPHY†  
D NEARY‡

\*Department of Neurochemistry,  
Institute of Neurology,  
London

†Department of Psychiatry,  
UMDS—Guy's Hospital,  
London

‡Department of Neurology,  
Manchester Royal Infirmary,  
Manchester

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