metabolites, and receptors in the striatum and medial frontal cortex. These changes have been related to cognitive disorders and depression in patients with both these disorders.

**Cholinergic system**

Repeatedly reported shrinkage and depletion of cholinergic neurons in the magnoellular part of the basal nucleus of Meynert are accompanied by decreased choline acetyltransferase activity in the neocortex by 86% to 91%. In Parkinson's disease, cell loss averages 30% to 40% without correlation with age or duration of illness, and is much higher in demented parkinsonian patients in whom it approaches the values in Alzheimer's disease (50% to 70%) than in non-demented patients (0% to 40%) who show neuronal losses only slightly higher than normal aged controls. Even more severe depletion of the basal nucleus of Meynert with 75% to 80% loss or large cholinergic neurons has been found in Lewy body dementia which correlates well with recent biochemical data. The heterogeneity of degeneration of cholinergic neurons in the basal forebrain and the variability in nucleus basalis cell depletion and loss of cholinergic markers in the neocortex and hippocampus in the respective of cortical Lewy body or Alzheimer type pathology, suggest a primary degenerative process of the cholinergic forebrain system in Parkinson's disease, while secondary retrograde degeneration proposed for Alzheimer's disease has been confirmed by defective retrograde transport of nerve growth factor to the basal nucleus in the brains of patients with Alzheimer's disease.

In conclusion, there are still some conflicting data on the neurochemical and pathological basis of behavioural changes in dementia disorders, the elucidation of which will be a major task for modern neuro-sciences.

**Esiiri replies to Jellinger and Caplan**

I am grateful to Jellinger for adding supplementary information to that presented in my editorial. I was necessarily selective in such a condensed account of a complicated subject and largely limited my comments to findings that related to behavioural disturbances in dementia. I would emphasize the importance of my colleagues and I to attaining a better understanding of the relationship between cholinergic changes for the future. The studies of the cholinergic system referred to by Jellinger, while of interest, have not specifically examined the relevance of cholinergic changes for behaviour in dementia, an area that certainly deserves attention.

The comments that Caplan makes about the desirability of subdividing my depressive category of behaviour into apathy and depressed mood, as reflected in evident unhappiness or crying, are well taken. I was intending only to indicate broad categories of behavioural change but agree that it is best to avoid assumptions about which individual types of behaviour go together, particularly in demented subjects who are often unable to give a direct account of subjective feelings. In searching for neurochemical correlates of the changes in dementia we have tried to avoid making assumptions about which types of behaviour are related, although analysis of detailed, prospectively acquired data suggest that there are some constellations of symptoms that cluster together (T Hope, unpublished data).

I would agree that there are some conflicting data on the neurochemistry of behavioural change in dementia. In such a complex area of investigation it would be surprising if there were not. The important point is that prospective studies are being undertaken that are likely to resolve the differences and uncover new findings that have a direct bearing on the optimal way to manage the difficult behavioural problems that people with dementia suffer from.

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