What can be said in relation to this case is that a tendency towards lowered seizure threshold with tricyclic antidepressants is not necessarily an indicator of ECT responsiveness.

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Alzheimer's disease and Lewy body dementia

SIR: The study by Förstl *et al* (*Journal*, March 1993, **162,** 385–392) highlights the current problems regarding the nosological status of cortical Lewy body pathology (CLBP) in people with co-existent Alzheimer-type pathology. They suggest that in a patient presenting with a combination of Alzheimer-type dementia together with severe Parkinsonian rigidity and a pattern of accentuated frontal lobe atrophy on computerised tomographic scan, the differential diagnosis should include a diagnosis of 'Lewy body dementia variant of Alzheimer's disease'. Thus, it is appropriate to review the evidence that examines whether Alzheimer's disease (AD) and Lewy body dementia (LBD) are indeed aetiologically distinct entities, or whether the variations in neuropathology seen represent a single disease process with a broad range of phenotypic expression.

Recent studies strongly support the aberrant processing of β-amyloid precursor protein (β-APP) and consequent deposition of β-amyloid protein (β-AP) as the primary pathological event in AD. If LBD and AD are different phenotypic presentations of a single nosological entity, it would be logical to surmise that β-AP deposition is the central feature in both conditions. One would therefore expect to find similar patterns of β-AP deposition in both AD and LBD.

In addressing this important point, Förstl and co-workers found that for patients who had CLBP, densities of cored (classic) and un-cored (diffuse) β-AP plaques in the cortex were slightly lower compared with cases who had AD pathology alone. However, the data supporting this statement is not presented. Moreover, the study examined only eight cases and used a silver staining technique to visualise the plaques, which often fails to show all the diffuse amyloid deposits present in the section.

In a larger fully quantitative immunohistochemical study, using a monoclonal antibody to β-AP, we found no significant difference between AD and LBD, in either the total β-AP load (Gentleman *et al*, 1992) or in the density or relative proportions of classic and diffuse plaques (McKenzie *et al*, 1993).

A further point is the finding of cortical Lewy bodies (LBs) in a familial case of AD which has a mis-sense mutation (Val-Ile) in codon 717 of APP and in the absence of genetic data would be classified as a form of LBD (Lantos *et al*, 1992). Other mutations at this codon (e.g. Val-Gly) have failed to result in Lewy body pathology (Mann *et al*, 1992). Mutations within a single gene are generally regarded as a single nosological entity despite variability in phenotypic presentation, as seen in prion disease (Roberts & Harrison, 1991).

Förstl *et al* noted that tangle densities in the frontal lobe and parahippocampal gyrus were significantly lower in the patients who had LBs; they also stated that these same two regions were the sites of great LB density. It has been proposed that the LBs themselves represent a form of modified neurofibrillary tangle (NFT) and in this context it is the total number of inclusion bodies (NFTs and LBs) that may be important. Therefore, an individual may exhibit a preponderance for either NFTs or for LBs, reflecting a common underlying aetiological process of neuronal damage due to β-AP deposition.

In summary, we suggest that the available evidence indicates that LBD represents part of the wide spectrum of clinico-pathological consequences of β-AP deposition. In such circumstances it seems inappropriate, at present, to propose a series of discrete subtypes of β-amyloid dementia.

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