Viruses, Parkinsonism and Alzheimer's disease

SIR,—The possibility that certain chronic degenerative diseases of the CNS, such as Alzheimer's disease and idiopathic Parkinson's syndrome, might have a viral aetiology, became attractive when it was shown[1] that another such condition, Jakob-Creutzfeldt disease, could be transmitted to other primates. Because of its propensity to produce latent infections of the CNS, herpes simplex virus (HSV) has been thought of as a likely infectious agent; a suggestion strengthened by findings of raised serum HSV antibody levels in Alzheimer's disease[2] and Parkinsonism.[3 4] We have examined cerebral tissue of patients with Alzheimer's disease and Parkinson's syndrome, for presence of HSV specific antigen, using an immunoperoxidase technique.[5]

Twelve brains were obtained from patients dying with a diagnosis of dementia and a further six, with Parkinsonism of no obvious predisposing cause. Histological examination of the former group showed widespread cortical plaques and nerve cells containing neurofibrillary tangles, while in the latter, there was severe cell loss from substantia nigra and locus caeruleus, with many of those remaining containing Lewy inclusion bodies. These 18 cases were grouped as Alzheimer's disease and idiopathic Parkinson's disease respectively. A further eight brains from patients of similar age, but dying without neurological and psychiatric disease showed only slight cerebral softening or senile changes or both, and were taken as controls. Cortical biopsies of temporal lobe were obtained at diagnostic craniotomy from 10 other cases of Alzheimer's disease and from five other controls, where tumour of the temporal lobe was suspected. A single case of herpes simplex encephalitis was used as positive control. Tissue samples of temporal cortex in the Alzheimer's disease cases and also of substantia nigra and locus caeruleus in the Parkinsonism cases, were stained for HSV surface antigens using the unlabelled antibody-enzyme (PAP) method.[5]

Excluding the positive control, in only a single other case was an area of positive immunoperoxidase reaction product observed. This was in a biopsy case of Alzheimer's disease staining being localised to neurones and astrocytes in a small focal region of about 0·5 mm in diameter All other 40 cases were negative. These findings are consistent with other studies which have failed to demonstrate (in levels above controls) HSV viral antibodies in CSF,[4] degree of HSV nucleic acid hybridisation,[6 7] HSV surface antigens (by immunofluorescence), in brain tissue.[8] Disease transmission to primates,[9 10] in both Parkinsonism[4 6 8 9] and Alzheimer's disease[7 10] has also not been shown. Furthermore it has not been possible to show that any significant relationship might exist between idiopathic Parkinsonism and any other viral infections, including arboviruses,[6 11 12] cytomegalus,[4] Epstein-Barr,[13] or varicella Zoster[13] viruses.

Despite this wealth of negative evidence, the as yet unconfirmed findings of HSV genome in brain tissue of some psychiatric patients[14] (including ones of Alzheimer's disease), and the observation[15] that an extract of brain from cases of Alzheimer's disease can induce the formation of paired helical filaments (neurofibrillary tangles) in cultured neurones, means that a role for viruses in the aetiology of the disease processes of these two conditions cannot, at present, be definitely ruled out.

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