The occurrence of ATLL in a patient with HAM is extremely uncommon and has been described in only three other patients.[4-6]

It has been shown that the viruses isolated from patients with HAM and ATLL are identical in their genomic composition. The HTLV 1 carrier rate has been estimated to be 15% in the general population in Japan, and 5% in the Caribbean. The lifetime risk of developing ATLL if infected with HTLV 1 is 2% to 5% with an interval of about 30 years between acquiring the infection and developing symptoms. On the other hand the lifetime risk of developing HAM/TSP has been estimated to be 0·25%. Familial clustering of both ATLL and HAM is well recognised but the occurrence of both the conditions in the same family is extremely uncommon. Shoji *et al.*[7] describe the case of a 37 year old Japanese female patient with HAM, whose father had previously died of ATLL.

Why the two diseases, although caused by the same virus, do not occur in the same person, or for that matter in the same family, is not clear. The magnitude of the immune response in patients with HAM tends to be higher, as evidenced by the higher titres of the anti-HTLV 1 antibodies in the serum as well as the CSF. By contrast the titres tend to be lower in controls as well as in patients with ATLL. The degree of immune responsiveness is related to host genetic influences and the existence of HAM associated haloptypes and ATLL associated haplotypes has been suggested. Moreover, in vitro studies in patients with HAM have shown a high lymphocyte proliferation rate, spontaneously as well in response to stimulation by mitogens and HTLV 1 viral antigens, compared with asymptomatic carriers or patients with ATLL. Also, the virus integration site into the host genome in HAM is random, whereas it integrates at a very specific locus in ATLL. The monoclonal integration of proviral DNA in ATLL consists of the long terminal repeat 5'3' "tax" gene, the product of which induces interleukin 2 receptor expression and T cell proliferation.

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MATTERS ARISING

Magnetic resonance spectroscopic study of parkinsonism related to boxing

We read with interest the paper by Davie *et al* reporting a study of proton magnetic resonance spectroscopy (MRS) in three exboxers with parkinsonism.[1] They report a significant reduction in the absolute concentration of N-acetyl-aspartate (NAA) in the putamen and globus pallidus in the boxers with a parkinsonian syndrome compared with patients with idiopathic Parkinson's disease and controls. They speculate that the reduced NAA may result from neuronal loss in the corpus striatum secondary to head trauma. In support of this hypothesis reference is made to their previous study in which it was reported that NAA is reduced in the lentiform nucleus in patients with striatonigral and olivopontocerebellar variants of multiple system atrophy compared with patients with idiopathic Parkinson's disease and controls.[2]

This interpretation may be too simplistic. We have carried out a pilot study using MRS in 10 patients with idiopathic Parkinson's disease with motor response fluctuations on chronic levodopa treatment (satisfying the United Kingdom Brain Bank criteria for diagnosis of idiopathic Parkinson's disease) and seven healthy age matched controls using a voxel size of 4 ml centred on the putamen and one cerebellar hemisphere.[3,4] We found a consistent and striking reduction in NAA/creatine and NAA/choline ratios in the putamen in patients with idiopathic Parkinson's disease but not in controls. The choline/creatine ratios between controls and idiopathic Parkinson's disease in the putamen and cerebellum were unchanged suggesting that the changes seen were due to changes in MR-visible NAA itself. Repeat studies in two patients three months later, with regions of interest centred on the putamen bilaterally, showed similar reductions in the observed NAA signal.

These findings contrast with the results reported by Davie *et al*[1] and raise several questions about the importance of localised changes in brain NAA in idiopathic Parkinson's disease and related disorders.[2] Firstly, the exact positioning of the region of interest and voxel size are both likely to be crucial. The spectra analysed by Davie *et al*[1,2] were obtained from a voxel centred on the globus pallidus and striatum, whereas ours was restricted to the putamen. Striatopallidal degeneration is a feature of multiple system atrophy, but not (so far as is known) of idiopathic Parkinson's disease.[5] The findings of Davie *et al* thus may reflect the pathological changes in the pallidum rather than in the putamen. Certainly, it is not possible to conclude from the study of Davie *et al*[1] that striatal NAA concentration is unchanged in idiopathic Parkinson's disease compared with multiple system atrophy and other related disorders.

Similarly, in the study of Holshouser *et al* in which there were no significant differences in "striatal" NAA/creatine ratios between patients with idiopathic Parkinson's disease and normal controls (but a significant reduction in NAA/choline ratios in patients with idiopathic Parkinson's disease between 51 and 70 years of age compared with controls), the region of interest was centred wholly on the globus pallidus, not in the putamen and a much larger voxel size (8 ml) was used.[6] Furthermore, Holshouser *et al*[6] reported that choline/creatine ratios in idiopathic Parkinson's disease and controls were in the normal range and it is surprising, therefore, to note that they found significant reduction in NAA/choline and not NAA/creatine ratios in idiopathic Parkinson's disease. Thus at present conclusions on the relevance of changes in NAA concentration or NAA/creatine ratios in the "striatum" in idiopathic Parkinson's disease, multiple system atrophy, and other neurodegenerative disorders such as progressive supranuclear palsy or parkinsonism in boxers are premature.[1,7] Our finding of reduced NAA/creatine and NAA/choline ratios in the putamen could reflect a functional change, loss of nigrostriatal dopamine terminals, or loss of intrinsic striatal neurons, or a combination of these factors. Diagnostic error is another possibility as the present diagnostic criteria of idiopathic Parkinson's disease has an accuracy of 82% but the reduction in NAA/creatine ratios were consistent in most of our patients diagnosed with the disease.[8]

Further work is needed to establish the best paradigms for acquiring spectra in idiopathic Parkinson's disease and related disorders to decide whether striatal (putaminal) NAA really is reduced, and to understand what this means diagnostically and in terms of neuronal dysfunction and pathology.

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