Matters Arising
decreased electromyography showed improvement in all but one patient. Concentrations of AChR antibody decreased twofold and increased twofold in one patient who showed improvement according to clinical and SFE MG changes. However, changes in concentrations of AChR antibody were not correlated with clinical grading of SFE MG findings. Cytotoxic activity of NK cells, CD4/8 ratio, and the CD4+ T lymphocyte count increased during the treatment but not significantly. No side effects were detected by laboratory tests including complete blood count, erythrocyte sedimentation rate, peripheral smear, urine analysis, electrolytes, liver, renal, and thyroid function tests, rheumatoid factor, ANA, anti-DNA, and antimitochondrial antibodies; nevertheless, a flu-like syndrome in six and nausea in three patients were noted at the beginning of the therapy.

IFNγ has been used in the treatment of many diseases including the autoimmune diseases, rheumatoid arthritis, lupus erythematosus, and multiple sclerosis. However, Batocchi et al.5 reported that patients with malignant carcinoid tumours, especially when autoantibodies were present, could develop an autoimmune disease during treatment with IFNγ. Furthermore, it has been reported that five patients developed myasthenic symptoms and AChR antibody positivity during IFNγ treatment for malignancy and for HCV infection. Batocchi et al.6 supposed that IFNγ could induce myasthenia gravis or simply manifest a preclinical disorder in two patients, one with bladder carcinoma and one with non-Hodgkin’s lymphoma. Nevertheless, increased serum levels of muscle-specific, myopathic changes in EMG, and ragged red fibres in muscle biopsy that were compatible with mitochondrial myopathy raise some doubts about the diagnosis of myasthenia gravis in their first patients. Moreover, antibodies to AChR and myasthenia gravis are found occasionally in patients with motor neuron disease, epilepsy, other autoimmune diseases, aplastic anaemia, and acute lymphocytic leukaemia.9-11 Secondary or autoimmune myopathy may be in question in such patients. IFNγ down regulates mitochondrial gene expression within four hours with the maximal inhibition achieved at a concentration of 1000 U/ml. A 30% concentration of IFNγ would be expected after 24-48 hours. Thus if the myopathy were related to IFNγ, as Batocchi et al suggested, three months would be considered to be late. In addition, whether the serum concentration of IFNγ was high enough to lead to this effect is unclear. d-Penicillamine induced myasthenia gravis and AChR antibody positivity disappears after the drug is discontinued, but AChR antibodies persisting for two years without any symptomatology in a patient with malignancy could be attributed to IFNγ treatment is debatable. In addition, autoimmunity associated with HCV is noteworthy, and activation of CD19/CD5+ cells, a subset of lymphocytes associated with human autoimmune disorders has been detected in more than half of the patients infected with HCV. Thus, the patient in the HCV reported by Piccolo et al.,1 high dose IFNγ could have induced myasthenia gravis, although their finding could be considered. Consequently, a probable contribution of underlying malignancy to myasthenic symptoms as well as certain clinical conditions that might lead to false positive AChR antibodies should be considered in patients with myasthenic symptoms induced by IFNγ. We presume that IFNγ may act through different mechanisms in malignancy or HCV infection. Our impression, from a limited number of myasthenic patients, is that low dose IFNγ is safe in myasthenia gravis and does not aggravate the disease.


Habitual snoring, sleep apnoea, and stroke prevention

I read with interest the recent review articles on stroke prevention by Klaw and Bronner et al.2 and was surprised that snoring and sleep apnoea were not mentioned as risk factors for stroke. Several cross-sectional and case-control studies have shown that habitual snoring represents an independent risk factor for stroke, with odds ratios ranging from 2.1 to 3.5.3 Based on a 10%-30% prevalence of habitual snoring and a 2%-4% prevalence of sleep apnoea4 the risk of stroke associated with habitual snoring may be of the same magnitude as the risk associated with diabetes mellitus and dyslipidaemia.5 Several physiological alterations associated with obstructive apnoeas including hypoxaemia, cardiac arrhythmias, and pronounced variations in blood pressure and cerebral blood flow may contribute to the increased stroke risk in patients with disordered breathing.

Although it is not known if treatment of sleep apnoea reduces the risk of stroke, it seems to reduce vascular morbidity and mortality.6,7 As sleep apnoea is a treatable condition, sleep apnoea and habitual snoring should be included in discussions of modifiable risk factors of stroke.


The basis for behavioural disturbances in dementia

In her editorial, The basis for behavioural disturbances in dementia, Esiri reviews some possible neurochemical and pathological correlates of behavioural changes in dementia with particular reference to alterations in monoaminergic, serotonergic, and cholinergic transmission.7 These data, offering some pathophysiological explanations for behavioural disorders in demented subjects are of great current interest but unfortunately, this review is not complete and even presents some incorrect impressions that deserve the following comments:

Noradrenaline

Despite substantial neuronal loss in the noradrenergic locus coeruleus in Parkinson’s and Alzheimer’s diseases,2 markers of noradrenaline metabolism in brain tissue are reported to be unchanged or increased.1 A non-significant increase in Alzheimer type senile dementia has been reported by Yates et al., whereas most other authors demonstrate a significant decrease in noradrenaline values ranging from 29% to 52% of controls in the striatum, hypothalamus, and several cortical areas.4 In non-cortical projection areas there was no evident decrease in noradrenaline.

On the other hand, Zubenko et al.8 found a specific and pronounced loss of noradrenaline in the middle frontal area, superior temporal cortex, and hippocampus (90% to 95%) in demented patients with major depression along with a relative preservation of choline acetyltransferase activity in several subcortical regions. These data in patients with Alzheimer’s disease suggest that dysfunction of the noradrenergic system is also related to mental changes and depression in parkinsonian patients.9

Serotonin

Degeneration of serotoninergic systems in both Alzheimer’s and Parkinson’s disease results from neuronal losses in the dorsal raphe nuclei ranging in Alzheimer’s disease from 20% to 76%, most notable in the caudal parts containing many neurofibillary tangles that may involve up to 90% of the neurons10; cell depletion in Parkinson’s disease average to 40%.11 This correspondingly, and cholinergic reduction of 5-HT and 5-HIAA in some cortical and hippocampal regions of Alzheimer disease brain ranging from 54% to 77%,12 and a reduction of 5-HT, its...
Habitual snoring, sleep apnoea, and stroke prevention.

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