bral grey matter was normal. The posterior borders of these lesions were formed by the caudate nuclei, the anterior parts of the internal capsules being spared. The lesions reached the parietal periventricular areas. The necrotic areas were characterised by extensive loss of myelin with myelin laden gitter cells. On both sides a substantial number of neurons in the ventromedial parts of the putamen and in the nuclei accumbens showed central chromatolysis. No signs of neuronal degeneration were found in the rostralateral parts of the putamen or in the caudate nuclei on both sides.

The extensive coagulative necrosis of central white matter with spongiosis, sparing the U fibres, is in agreement with the diagnosis of delayed necrotising leukoencephalopathy.¹ The presence of gitter cells and reactive gliosis is compatible with onset of the disease about six to eight weeks before the patient's death. The absence of CSF pleiocytosis at the onset of delayed necrotising leukoencephalopathy suggests that a CNS leukaemic relapse was not important in its evolution.

In the present case all symptoms of anterior cingulate syndrome as described by Cummings² were present, but the clinical picture did not deteriorate to the most severe form of anterior cingulate syndrome—that is, the akinetic mutism strikingly characterised by Cairns *et al* as “a state of motionless, mindless wakefulness”.⁴ In our patient verbal communication remained possible by writing and reading excluding global aphasia as the cause of his mutism.

In children mutism is a rather non-specific symptom, which may occur in a wide variety of neurological diseases.⁵ The present finding suggests that in children with anterior cingulate syndrome mutism is associated with an extreme loss of initiative. This selectively affects the modalities of communication of which spontaneous speech and spontaneous writing seem to be the most vulnerable ones.

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Unilateral auditory hallucinations in a boy with ipsilateral conductive hearing loss

Unilateral auditory hallucinations in adults and adolescents are associated with con-

tralateral CNS lesions and ipsilateral peripheral lesions.¹

A nine year old boy was admitted to the child psychiatric inpatient unit after exhibiting self destructive and aggressive behaviour for two weeks at school. He attempted to burn himself on a radiator and to jab a pencil into his hand. He banged his head, punched one teacher, and threw a chair at another without provocation.

Four years before admission he had tried to set a tree on fire. Two years before admission he had tried to strangle a cat and to set his bedroom on fire. He often shoplifted from the neighbourhood store and often fought siblings and peers. One month before admission his mother's intoxicated boyfriend hit him hard on the chest, leaving marks.

He was conceived when his father raped his mother. The umbilical cord was tightly wrapped around his neck at birth. His Apgar scores were 6 and 8. At birth he had a cleft soft palate, hyperbilirubinaemia, and sepsis with *Streptococcus viridans* and *diphtheroids*. At two and a half years of age his cleft palate was repaired and bilateral myringotomy tubes were placed to treat multiple episodes of otitis media. At four years of age a right hydrocele was repaired. At four and a half years of age audiological evaluation disclosed a mild left conductive hearing loss and a mild to moderate right conductive hearing loss. Both parents used street drugs. His father is a violent, abusive man who has not been involved with the family for many years. His mother was abandoned by her own mother and was raised in orphanages. His mother had psychiatric admissions to hospital beginning in childhood, resulting in treatment with dopamine receptor blocking drugs. No other family member was reported to have a hearing loss.

On mental status examination he had a moderately severe articulation deficit. He heard the voices of devils outside his head at night and during the day telling him to jump off the building and to kill himself. He heard the voices only in his right ear. He saw faces of devils, a rag doll that his mother had given him, Jason, a character in a horror movie, cockroaches that turned into red devils, and hell that looked like a fire surrounded by cockroaches.

His right myringotomy tube was disimpacted from the cerumen and was removed. His left myringotomy tube was patent and in place. The visual and auditory hallucinations continued unabated. Audiograms showed normal left hearing and a mild right conductive hearing loss at 1 kHz and 4–8 kHz and improved to normal hearing at 1.5–3 kHz. His EEG was normal.

The visual and auditory hallucinations and suicidal and homicidal ideation stopped a few days after starting treatment with the antipsychotic drug molindone (5 mg twice daily). He denied having visual or auditory hallucinations during subsequent treatment with molindone and, later, with haloperidol. His discharge diagnoses were brief reactive psychosis and conduct disorder.

This case report is reminiscent of the occurrence of schizophrenia in elderly people with peripheral auditory disease. Typically, unilateral hearing loss is associated with auditory hallucinations in adults with severe sensorineural hearing loss. Our case is novel because the patient is a child with a mild conductive hearing loss affecting only a portion of the acoustic frequencies which are significant in speech perception.

The disappearance of auditory hallucinations in our patient coincided with the resolution of his psychosis when he received antipsychotic medication.

The occurrence of hallucinations has been considered to be caused by (1) stimulatory phenomena in the CNS—for example, electrical excitation by electrodes, seizures,² schizophrenia,³ and pharmacological agents,⁴ or (2) release of inhibitory phenomena on sensory neurons—for example, sensory deprivation,⁵ the visual hallucinations in blindness (the Charles Bonnet syndrome), and the phantom limb hallucinations after damage to peripheral nerves in amputees.² We propose that mild conductive hearing loss, even if limited to only a portion of the acoustic frequencies which are significant in speech perception, may predispose vulnerable children to develop ipsilateral auditory hallucinations during psychotic episodes.

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MATTERS ARISING

Low dose interferon- α is safe in patients with myasthenia gravis

Piccolo and colleagues¹ have recently reported that interferon- α (IFN α) could induce myasthenia gravis in a patient with hepatitis C virus infection and briefly reviewed the incidence of patients with myasthenia gravis induced by IFN α . The therapeutic efficacy of IFN α treatment in myasthenia gravis has been shown in experimental studies.² We performed a prospective study that aimed to evaluate the efficacy of IFN α (Roferon-2b, (3 mu subcutaneously three times a week, for six months)) in seven myasthenic patients. No appreciable clinical deterioration or myasthenic crisis was noted during the IFN α treatment; clinical grading according to modified myasthenia gravis scoring showed improvement in four, no significant change in two patients, and the score was worse than that before treatment in one patient. Findings from single fibre

electromyography (SFEMG) showed improvement in all but one patient. Concentrations of AChR antibody decreased in four, increased mildly in two, and increased twofold in one patient who showed improvement according to clinical and SFEMG changes. However, changes in concentrations of AChR antibody were not correlated with clinical grading or SFEMG 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.

IFN α has been used in the treatment of many diseases including the autoimmune diseases, rheumatoid arthritis, lupus erythematosus, and multiple sclerosis. However, Rönnblom *et al*² published that patients with malignant carcinoid tumours, especially when autoantibodies were present, could develop an autoimmune disease during treatment with IFN α . Furthermore, it has been reported that five patients developed myasthenic symptoms and AChR antibody positivity during IFN α treatment for malignancy and for HCV infection. Batocchi *et al*³ supposed that IFN α 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 lactate concentrations, 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 after bone marrow transplantation. IFN α down regulates mitochondrial gene expression within four hours with the maximal inhibition achieved at a concentration of 1000 u/ml, and mitochondrial dysfunction would be expected after 24–48 hours. Thus if the myopathy were related to IFN α , as Batocchi *et al* suggested, three months would be considered to be late. In addition, whether the serum concentration of IFN α 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 and whether AChR antibodies persisting for two years without any symptomatology in a patient with malignancy could be attributed to IFN α 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. Therefore, in the patient with HCV reported by Piccolo *et al*,¹ high dose IFN α could have induced myasthenia gravis, although their finding could be coincidental. Consequently, a possible contribution of underlying malignancy to myasthenic symptoms as well as certain clinical conditions that might lead to false positive AChR antibodies should be consid-

ered in patients with myasthenic symptoms induced by IFN α . We presume that IFN α may act through different mechanisms in myasthenia and in malignancy or HCV infection. Our impression, from a limited number of myasthenic patients, is that low dose IFN α is safe in myasthenia gravis and does not aggravate the disease.

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Habitual snoring, sleep apnoea, and stroke prevention

I read with interest the recent review articles on stroke prevention by Khaw¹ 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 3.3.³ 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 The link between snoring and stroke seems to be particularly strong when habitual snoring is associated with symptoms or signs suggestive of sleep apnoea. In a study of 177 stroke victims and 177 age and sex matched controls, habitual snoring was found to be an independent risk factor for stroke with an odds ratio of 2.1.⁶ The relative risk increased, however, to 8.0 in patients in whom habitual snoring was associated with a history of nocturnal apnoea, hypersomnia, and obesity. In a series of 59 patients with acute cerebrovascular events sleep apnoea was present in > 50%.⁷

Several physiological aberrations associated with obstructive apnoeas including hypoxaemia, cardiac arrhythmias, and pronounced variations in blood pressure and cerebral blood flow may contribute to the increased risk of stroke in patients with disordered sleep breathing.

Although it is not known if treatment of sleep apnoea reduces the risk of stroke, it seems to reduce vascular morbidity and mortality.^{8,9} As sleep apnoea is a treatable condition, sleep apnoea and habitual snoring should be included in discussions of modifiable risk factors of stroke.

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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 noradrenergic, serotonergic, and cholinergic transmission.¹ 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:

Noradrenalin

Despite substantial neuronal loss in the noradrenergic locus coeruleus in Parkinson's and Alzheimer's diseases,^{2,3} markers of noradrenalin 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*,⁴ whereas most other authors demonstrated significantly decreased noradrenalin values ranging from 29% to 52% of controls in the striatum, hypothalamus, and several cortical areas.^{5–9} In non-cortical projection areas there was no evident decrease in noradrenalin concentration.⁹

On the other hand, Zubenko *et al*¹⁰ found a specific and pronounced loss of noradrenalin 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 serotonergic systems in both Alzheimer's and Parkinson's disease results from neuronal losses in the dorsal raphe nuclei ranging in Alzheimer's disease from 10 to 76%, most severe in caudal parts containing many neurofibrillary tangles that may involve up to 90% of the neurons¹¹; cell depletion in Parkinson's disease averages 20 to 40%.¹² This correlates well with a reduction of 5-HT and 5-HIAA in some cortical and hippocampal regions of Alzheimer disease brain ranging from 54% to 77%,⁸ and a reduction of 5-HT, its