however, no changes in gonadotrophins or TSH were seen in relation to magnetic stimulation. The changes in PL, GH and cortisol were most likely due to non-specific stress, as similar patterns were seen during test and control periods, and in many instances the rise in hormone concentrations began before stimulation. The concomitant increase in cortisol, PL and GH seen in two subjects is further evidence that the hormone changes are related to a stress response. Earlier studies have shown the effects of various forms of stress on hormone concentrations, with marked variation between individuals. The increment in GH that occurred during the post-stimulus period was in a young female subject, and was most likely due to a spontaneous physiological pulse of GH (these occur more commonly in younger women).

The only previous published report showed a fall in PL with magnetic stimulation, but we were unable to confirm this finding.

No changes in the EEG were seen in the half hour following stimulation, confirming previous reports. It is interesting that no long term changes are seen in those subjects who had undergone electrical stimulation 18 months before, particularly since that technique produces higher current densities in the cortex than magnetic stimulation.

We conclude that there are no changes in plasma levels of pituitary hormones occurring as a direct or specific consequence of transcranial magnetic stimulation as used in clinical practice. The absence of EEG changes is also encouraging evidence of the safety of the technique.

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Association of amyotrophic lateral sclerosis, Holigae’s syndrome and residence in Guam

Anaphylaxis is a form of generalised trauma and trauma itself has long been suggested to have a role in precipitating amyotrophic lateral sclerosis (ALS). We report a case of ALS which appeared to be precipitated by an acute anaphylactic reaction to penicillin.

The patient was a 32 year old male right handed married black American. He worked as a welder in the American navy and in 1971 he was stationed on the island of Guam for one year. Six years later he received four intramuscular injections of penicillin for gonorrhoea. After the second injection he had a severe reaction with dizziness, chest pain, numbness in the left arm and leg, muscle spasms, nausea, throbbing pain in the neck radiating to the occipital region, diplopia, black and white flashes, hot flushes, buzzing in the ears, a choking sensation, intense anxiety and panic. These symptoms occurred almost every other day for several weeks and lasted 10–15 minutes each time. They were not related to exertion. There were no aggravating or relieving factors. Physical examination was entirely normal. Repeat electrocardiograms and electroencephalograms during these attacks and a brain computerised tomography (CT) scan were all normal. A diagnosis of conversional reaction and fatigue neurosis was made and treatment with diazepam, breathing into a paper bag and psychotherapy was started but without any effect.

Three months after his initial presentation the patient became anorexic and began to lose weight. He then became aware of difficulty in speaking and was conscious of very poor tongue movements. A few months later his legs and then his arms became progressively weak.

He had mumps and measles as a child and also mild concussion playing football in high school. At the age of 19 years he was involved in an automobile accident during which his head went through the windscreen. He had also been treated for venereal disease six or seven times. He did not smoke and drank alcohol occasionally. His only medication was diazepam 5 mgs twice daily. He was allergic to penicillin. His mother and brother were hypertensive, but there was no family history of neuro-psychiatric disorders.

On neurological examination three months after the initial presentation there was no intellectual impairment but he was moody at times and emotionally labile. The cranial nerves were intact except for a small spastic tongue and an exaggerated jaw jerk. Wide-spread fasciculations were present in all four limbs and there was severe wasting of the intrinsic muscles of the hands and moderate wasting around the shoulder girdle. Muscle tone was spastic in all limbs, the legs being affected more than the arms. There was mild proximal and moderate distal weakness in the upper limbs but there was no weakness in the legs. The tendon reflexes were brisk in all limbs and both plantar responses were extensor. There was a non-sustained clonus of the left ankle. He walked with a broad-based spastic gait. There were no abnormal sensory or cerebellar signs detected. His pulse was 110/minute and regular. Blood pressure was 110/70. The rest of the general physical examination was unremarkable.

Routine blood tests and plasma noradrenalin levels were normal. Serological tests for
syphilis were negative in the blood and the cerebrospinal fluid (CSF). He was HIV negative. CSF protein was 0.25 g/l and there were no cells or oligoclonal bands. Serum creatine phosphokinase was raised at 199 IU/L. Muscle stretch reflexes were absent and sensory conduction velocities, fibrillation and fasciculation potentials and positive sharp waves. Voluntary units were generally small in amplitude and there was gross excess of non-specific units. The patient was started on a full or slightly reduced interference pattern in all muscles tested. The findings were consistent with the diagnosis of ALS.

There were no delays in the progression and a road traffic accident in our patient 17 and 13 years before clinical presentation with ALS. Although a history of mechanical trauma or surgical operations was found to be two to three times more common in patients with MND than in matched controls, it is unlikely that trauma had played an important role in this patient because of the long latent period between his injuries and the onset of ALS. ALS itself may be preceded by a bizarre intermittent illness which at the beginning was thought to be psychiatric in origin. However, the patient did not have a past or family history of psychiatric disease nor did he have a personality disorder. Furthermore, these symptoms did not respond to adequate psychiatric measures including treatment with anxiolytics, breathing into a paper bag and psychotherapy. The patient's symptoms were therefore almost certainly organic in nature and are probably a hypersensitivity reaction to penicillin. In fact, intermittent symptoms lasting weeks or months which may be noticed in those in our patient occasionally result from penicillin hypersensitivity and they are known as pseudosalergic reactions or Hoigne's syndrome. Our patient almost certainly had Hoigne's syndrome which was followed by ALS two to three months later.

The association between MND and anaphylaxis has not been reported before. However, we are aware of another patient who had developed ALS shortly following a severe anaphylactic shock (J Lewis, personal communication). Other neurological disorders are sometimes precipitated by hypersensitivity reactions. We have observed two cases of extrapyramidal disease following insect stings. Demyelinating diseases and peripheral neuritis also have also been reported following anaphylactic reactions. Like trauma, these may be more common in ALS or alternatively, accelerate the progression of latent disease. A recent study has demonstrated that non-specific injury outside the CNS, for example, transection of a peripheral nerve, induces strong expression of MHC class 1 and to a lesser extent class 2 antigens in CNS neurons. One can postulate a similar mechanism for the role of anaphylaxis in ALS.

Fatigue and melanin in Parkinson's disease

Fatigue is a major, although often neglected symptom of Parkinsonism. This is influenced to some extent by circadian factors, including sleep benefit, diurnal changes in levodopa metabolism, dopamine receptor sensitivity, and monoamine oxidase activity.1

In normal subjects, one of many factors that influences fatigue may be changes in melatonin rhythmicity.2 The use in Parkinson's disease of the decarboxylase inhibitor benserazide, which reduces 5-hydroxytryptamine and melatonin concentration in the rodent pineal3 may therefore indirectly affect fatigue mechanisms. We have investigated Parkinsonian disability, plasma melatonin levels and urinary 6-hydroxy-melatonin sulphate (aMT6s) as an index of the evening melatonin rise in untreated subjects and following levodopa and benserazide treatment.

Eighteen subjects with idiopathic Parkinson's disease were studied, 11 males, seven females, aged 42–81 (mean 64 years) with a mean duration of symptoms of nine years (range 2–30). None had on/off fluctuations. Twelve had a stable response across the day, six progressive fatigue. Six subjects were studied untreated and one week following benserazide 50 mg orally four times daily, the remaining taking levodopa 500 mg daily and levodopa 1700 mg daily plus benserazide 380 mg daily (n = 7).

Samples for plasma melatonin assay were obtained by indwelling venous catheters at three hourly intervals over a 24 hour period. Four, six hourly consecutive urinary collections were carried out during the same 24 hour period. Plasma melatonin concentration (natural urinary 6-hydroxy-melatonin sulphate) was assayed by radioimmunoassay as described by Fraser et al. and Arendt et al. respectively.

Peak plasma melatonin concentrations in six untreated subjects with Parkinson's disease showed wide interindividual variation
Association of amyotrophic lateral sclerosis, Hoigne's syndrome and residence in Guam.

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