was completed, cognitive measures being repeated one month after completion.

On review, this patient reported no subjective change in his concentration or memory, although significant improvements in recall memory and new word learning were apparent on neuropsychological reassessment. Quite unexpectedly he declared that he no longer felt cold at all, the change having appeared briskly after about two weeks of treatment and persisting despite the discontinuation after one month. A further contact six months later, after the winter, disclosed that his temperature perception had remained normal without further treatment, although he had continued to take carbamazepine (which stimulates release of endogenous vasopressin) because it successfully controlled his episodic dyscontrol. Follow up 11 years later confirmed that the symptom had never recurred, despite his having discontinued carbamazepine some seven years earlier. (He had remained totally anosmic.) This permanent improvement after only a month's treatment parallels what was reported in earlier studies of Syntopressin in memory disorders, as well as our experience of those whose cognitive states improved in our own study.

Since this unexpected finding, I have seen a further 12 patients with the same symptom, 11 after severe traumatic brain injuries (coma range 3–70 days, mean 16·8, median 8, SD 17·8; post-traumatic amnesia 6–150, mean 58·1, median 42, SD 39·8 days) and one after carbon monoxide poisoning (coma 14 days, post-traumatic amnesia 150 days). In 10 of the 13, the patient or a relative spontaneously mentioned the symptom; in three with very poor communicative ability it was inferred from the consistent wearing of excessive clothing. All were slightly cool to the touch, but not cold. In no case was the sublingual temperature abnormally low. Three patients had thyroid function tests performed, the results being normal in each case. The patients were culled from three settings: three were from 659 seen in a general hospital head injury clinic (0·5%), five among 502 seen medicolegally (1%), and five from 167 treated in a residential rehabilitation unit (3%). The symptom thus seems to be quite rare. The relative frequencies, given the different kinds of populations, raise the possibility of an association with more severe injury, although they might simply reflect the greater opportunities for observation and comment with inpatients.

Nine patients were male, the male:female ratio of 2·25:1 being within the range typically seen in traumatic brain injury. There did not seem to be any uniformity in the patterns of injury or of residual disorders. Seven of the 13 were anosmic, three unilaterally, although two with bilateral anosmia recovered olfaction after 23 and 47 months and one with unilateral anosmia at nine months. Four had diabetes insipidus in the acute stage (three of them were anosmic), but in none of these did it persist. Ten had residual disabilities due to brainstem dysfunction. The only feature common to all 13 was that the acute brain injury was complicated by considerable global brain swelling identifiable on CT. Despite this, age at injury did not seem to be important, the range being 15 to 57 (mean 30·8, median 29, SD 12·4).

Of the 13 patients, 11 stopped feeling cold completely and permanently after one month's treatment with Syntopressin; one was much improved, but not to a normal level. One of two 15 year old girls (not anosmic) was unchanged. The duration of the symptom (3 to 88 months, mean 35·5, median 34, SD 21·4) did not seem to be a factor determining the response, the girl who did not respond being 33 months from injury. Indeed no specific aetiological or prognostic factors could be identified. (The occurrence of significant brain swelling in all patients suggests the possibility of compressive injury to the diencephalon, where vasopressin is produced, but this is unlikely to be a specific causal factor, as large numbers of patients with this complication do not develop the symptom.) In view of the earlier literature discussed above, it was interesting that four of the responders had previously been treated (for other reasons) with DDAVP, without any effect on the symptom of feeling cold. It has been argued that intranasal vasopressin might reach the base of the brain via nervous or lymphatic structures in the olfactory nerves, so it is of interest that traumatic anosmia clearly did not impede responsiveness.

Although vasopressin is known to be present in neurons distributed widely through the diencephalon and limbic areas, and to have effects on mechanisms of arousal and possibly learning that are distinct from its extracerebral effects on renal function,[10] no clear explanation of this effect on temperature perception is apparent. Nor is it easy to see how such short term treatment should produce lasting improvement, although there is a parallel with some effects of dopamine agonists on post-traumatic motivational deficits.[11 12]

PETER EAMES
Grafton Manor Brain Injury Rehabilitation Unit, Grafton Regis, Towcester, Northants NN12 7SS, UK

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Nerve growth factor concentrations in human cerebral blood vessels

The nerve supply to cerebral blood vessels plays an important part in migraine and cerebral vasospasm, via sympathetic fibres containing the vasoconstrictors noradrenaline and neuropeptide Y (NPY), and sensory fibres containing vasodilators substance P and calcitonin gene related peptide (CGRP). As evidence in rodents and humans supports the view that sympathetic fibres and sensory neuropeptides are dependent on nerve growth factor (NGF),[1] we have studied NGF concentrations in human cerebral vessels.

The circle of Willis was collected postmortem from subjects with no known neurological disorder (mean age 72 years, range 61 to 79 years; postmortem delay: mean 23 hours, range 18 to 28 hours), and dissected before storage at -70^{0}C. A specific enzyme linked immunoassay was used to measure NGF-like immunoreactivity, with recombinant human NGF as standard.[2] The table shows that NGF concentrations were lower in anterior than in posterior cerebral vessels in the circle of Willis, with a significant age related decline.

This is the first demonstration of NGF in human cerebral blood vessels. The NGF concentrations measured in cerebral blood vessels are similar to those in human skin and nerve. There seems to be a decline of NGF with aging, and we propose to extend the range of study to younger subjects. NGF is produced by vascular smooth muscle cells and fibroblasts, and processes such as atheromatous change may contribute to decreased NGF production in old age. The relevance of the regional differences in NGF concentrations in the circle of Willis is unknown; as there is evidence that the density of the sensory and sympathetic peptidergic innervation is greater in the anterior circle of Willis, there seems to be an inverse correlation with NGF concentrations. One explanation for this may be less uptake and transport of NGF away from the blood vessels by the fewer fibres in the posterior circle of Willis, perhaps analogous to the higher NGF concentrations found in the frontal cortex when cholinergic fibres that take up NGF from this region and transport it to basal regions have degenerated in Alzheimer's disease.

The presence of NGF in blood vessels is consistent with the neurotrophic theory—that is, that NGF regulates the density of vascular sympathetic and peptidergic sensory fibres. There is increasing evidence to support the hypothesis that NGF may regulate nociception in humans,[1] and that NGF in blood vessels may regulate the presentation of migraine and other vascular head pain. The frequency and severity of migraine declines with age, as do NGF dependent substance P, CGRP and NPY concentrations in human cerebral vessels.[3] The target organ (the blood vessel) has been shown to be responsible for the reduced cerebral vessel innervation in aged rats, and NGF infusion can reverse this neuronal atrophy.[4] Biopsies of tender superficial temporal arteries in migraine may show oedema, attributed to local release of substance P, and in cluster headache they may show increased mast cells during headache free intervals.[5] NGF sensitises nociceptor fibres, produces neurogenic inflammation via substance P and CGRP, and is associated with increased numbers of mast cells.[1] Oestrogens upregulate NGF receptor mRNA in sensory neurons: migraine is commoner in women, and may be related to menstruation. Corticosteroids help inflammatory vascular head-

NGF concentrations in human cerebral arteries

Artery	*Number*	*NGF (ng/g) Mean (SEM)*
Anterior cerebral (AC)	7	0·82 (0·19)
Internal carotid (IC)	7	0·78 (0·16)
Posterior cerebral (PC)	7	2·02 (0·53)
Superior cerebellar (SC)	7	2·14 (0·45)
Posterior communicating	6	1·87 (0·58)

P values were determined by student's t test.
AC v SC $P < 0.02$; IC v PC $P < 0.04$; IC v SC $P < 0.015$.
Mean NGF concentration v age of subject $r = -0.8$, $P < 0.034$.

ache, as in temporal arteritis, and also reduce NGF synthesis, which is increased by inflammation.[1] Modulation of NGF activity may thus provide a new approach to prevent and treat vascular headaches.

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P ANAND
A PARRETT
Department of Neurology, St Bartholomew's and Royal London School of Medicine and Dentistry, Whitechapel, London E1 1BB, UK
L CHADWICK
P HAMLYN
Department of Neurosurgery, St Bartholomew's and Royal London Hospitals, London, UK

Correspondence to: Dr P Anand.

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Triphasic waves in serotonin syndrome

The serotonin syndrome was first described in 1960 in depressed patients with delirium due to monoamine oxidase inhibitors and L-tryptophan administration.[1] Symptoms of the serotonin syndrome include mental status changes, behavioural changes, myoclonus, rigidity, hyperreflexia, and autonomic instability with low grade fevers, diarrhoea, headache, tachycardia, and pupillary dilatation.[2] The serotonin syndrome has been noted to occur with several serotomimetic agents, particularly when multiple agents are used.[3]

Psychiatry and pharmacology literature has described the serotonin syndrome for several years. As the use of serotonin reuptake inhibitors has increased, cases have begun to appear in the neurology literature—often associated with combination regimens that include serotonin reuptake inhibitors and dopaminergic agents. These cases have been attributed to the serotomimetic effects of dopamine and its agonists. I describe a patient admitted for acute confusion who met criteria for the serotonin syndrome, responded well to supportive care, and whose EEG showed prominent triphasic wave activity.

A 76 year old man had a history of Parkinson's disease, recurrent depression, chronic constipation, and non-insulin dependent diabetes mellitus. He had right sided tremors, bradykinesia, hypophonia, and significant gait instability with occasional visual hallucinations. Due to his depression and concerns regarding the use of tricyclic antidepressants in a patient already at risk for autonomic dysfunction, he was started on 50 mg sertraline at bedtime. He initially responded well, experiencing no notable side effects. About three days before admission, amantidine was added to his drug regimen which already included sertraline and Sinemet. The patient was brought to the emergency department by his wife due to increasing confusion, diarrhoea, and frequent falls that had begun a day earlier.

On examination, the patient had a low grade fever, extreme rigidity in all limbs, agitation, confusion, and ongoing visual hallucinations. Over the next four hours he developed multifocal and startle myoclonus. He had not received any neuroleptic or antibiotic drugs in more than six months.

Electrolytes, creatine kinase, liver functions, a complete blood count, and ammonia concentration were all normal. Blood cultures and urinalysis were also unremarkable. A 16 channel EEG was obtained and showed pronounced triphasic wave activity and diffuse slowing. Supportive care with intravenous fluids and acetaminophen were initiated and all outpatient medications were stopped. Within 24 hours the patient's myoclonus began to subside and in 48 hours he had returned to baseline without any sequelae. He continues to do well on Sinemet alone for his Parkinson's disease.

Case reports of the serotonin syndrome have noted EEG abnormalities—delta range activity, slow waves, spike and waves, and polyspike and waves—but triphasic waves have not previously been reported.[4 5] The diagnosis of the serotonin syndrome in the Parkinson's disease population is a difficult one as many of the features of the serotonin syndrome are present in Parkinson's disease alone. A high level of suspicion for the serotonin syndrome in patients with Parkinson's disease taking serotonin reuptake inhibitors is necessary to make the diagnosis. Electroencephalography may play an important part in the diagnosis of the serotonin syndrome, particularly in the setting of other concurrent neurological disease.

G L DIKE
Department of Neurology, Johns Hopkins Hospital, Pathology 509 600 N Wolfe Street, Baltimore MD 21287, USA.

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Pseudoseizures or non-epileptic seizures (NES); 15 synonyms

Medical jargon is often confusing, particularly when the condition described falls within the domain of two medical specialties. This confusion reaches its zenith with those seizure disorders that do not have an epileptic aetiology. There are at least 15 synonyms for a condition that occurs in 10%[1] to 26%[2] of adults investigated for refractory seizures. This causes confusion for patients, doctors, and researchers. The adoption of a common term must be the rational way forward, but which one to choose?

The label pseudoseizures is the most commonly used. Its great weakness is that it is not acceptable to patients as the label implies that the seizures are not real. The reality of the "fit" is seldom an issue. The label pseudoepileptic seizures is both less well known and pejorative. Labels that are offensive to patients are counterproductive and best avoided.

The aetiology of this disorder is currently a matter for speculation. Terms that imply a psychological causation are misleading. Psychogenic seizures, hysterical seizures, psychogenic attacks, and hysterical attacks are all inappropriate for this reason.

A good descriptive label is non-epileptic attacks but this is seldom used. Non-epileptic attack disorder (NEAD) is rarely used and is complicated. Functional seizures, hysteroepilepsy, pseudoepilepsy, hysterical epilepsy, pseudoepileptic attacks, and psychoseizures are the least commonly used terms. These labels should all be abandoned.

This leaves the term *non-epileptic seizures (NES)* as the favoured candidate; it is non-judgmental, often used, acceptable to patients, and best describes the problem without implying causation.

DAVID A SCULL
Institute of Neurology, Queen Square, London WC1N 3BG, UK.

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Multiple sclerosis: longitudinal measurement of interleukin-1 receptor antagonist

Inflammatory activity in multiple sclerosis is regulated by a network of proinflammatory and antiinflammatory cytokines. Identifying downregulatory cytokines opens new potential therapeutic options in multiple sclerosis.[1 2] The interleukin-1 receptor antagonist (Il-1ra) is the only known naturally occurring specific antagonistic cytokine; Il-1ra competes with Il-1 for receptor binding and lacks agonist activity. Il-1ra has been implicated in the pathogenesis of stroke and several inflammatory diseases.[3] Human Il-1ra is available as a recombinant protein; the first controlled study using Il-1ra for therapy (in