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 examination.

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 discontinuation after one month. A further contact six months later, after the winter, disclosed that his temperature perception had remained normal without further treatment. He claimed to have discontinued 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 two months of the agent parallels what was reported in earlier studies of Syntropin in memory disorders, as well as our experience of those whose cognitive states improved in our own study.

Concluding, 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 reported the symptom in three with very poor cognitive ability, and 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; two from the neurological out-patient clinic to which five among 502 seen medicolegally (1%), and five from 167 treated in a residential rehabilitation unit (3%). The symptom thus seems to be more frequent. The relative frequencies, given the different kinds of populations, raise the possibility of an association with some severe injury, although they might simply reflect the greater opportunities for observation and comment with inpatients.

Nine patients were male, the female/male 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 of 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 or of residual disorders. Seven of the 13 was 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 or of residual disorders. 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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). Evidence in rats and humans supports the view that sympathetic fibres and sensory neuropeptides are dependent on nerve growth factor (NGF); we have isolated NGF concentrations in human cerebral vessels.

The circle of Willis was collected post-mortem from subjects with no known neurological disorder (mean age 72 years, range 61-95; 36 men, 34 years old, 26 years, range 18 to 28 hours), and dissected before storage at ~70°C. A specific enzyme linked immunoassay was used to measure NGF-like immunoreactivity, with recombinant human NGF as standard. 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 other neural tissues. The presence 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 attherosomous 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 ganglionic 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 that the uptake and transport of NGF away from the blood vessels by the few fibres in the posterior circle of Willis, perhaps analogous to the higher NGF concentrations found in the frontal cortex of mice when compared to the frontal cortex of NGF from this region and transport it to basic 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, and that NGF in blood vessels may regulate the presentation of migraine and other vascular head pain. The frequency and severity of migraine decline with age, as do NGF dependent substance P, CGRP and NPY concentrations in human cerebral vessels. The organ (the blood vessel) has been shown to be vulnerable to the effects of cerebral vasel innervation in aged rats, and NGF infusion can reverse this neuronal atrophy. Biopsies of tender superficial temporal arteriae in migraine patients may show oedema, attributed to local release of NGF. As a potent vasodilator and dependent headache they may show increased mast cells during headache free intervals. NGF sensitizes nociceptor fibres, produces neurotoxicity in cultures of dorsal root ganglion cells, and is associated with increased numbers of mast cells. Oestrogens upregulate NGF receptor mRNA in sensory neurones; migraine is commoner in women, and may be related to the immunomodulatory and anti-inflammatory effects of oestrogens.
We have inflammation.'

"waves"

Triphasic serotonin administration.'

omic changes, to take inhibitors often-often associated with combination regimens that include serotonin reuptake inhibitors and dopaminergic agents. These cases have been attributed to the serotonimic 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 transmural 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, amantadine 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 confussion, diarrhea, and frequent falls that had begun on his "pill" 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 staring movements. He had not received any neuroleptic or antibiotic drugs in more than six months. Electrolytes, creatine kinase, liver function test results, and serotonin 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 his 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. 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.

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. 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. IL-1ra is available as a recombinant protein; the first controlled study using IL-1ra for therapy (in