ache, as in temporal arteritis, and also reduce NGF synthesis, which is increased by inflammatory cytokines. Overproduction of NGF activity may thus provide a new approach to prevent and treat vascular headaches.

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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 serotonergic 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.4 These cases have been attributed to the serotonergic 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 waves.

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, hyperreflexia, 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 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 staring myoclonus. He had not received any neuroleptic or antibiotic drugs in more than six months.

Electrolytes, creatinine kinase, liver functions, a complete blood count, and serum 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 was initiated and all outpatient medications were stopped. Within 24 hours the patient's myoclonus began to subside and in 48 hours he had returned home without a 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.14 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.1214 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 conditions.15 Hematologic IL-1ra is available as a recombinant protein; the first controlled study using IL-1ra for therapy (in

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

Medical jargon is often confusing, particularly when the condition described falls within the domain of two or more specialties. This confusion reaches its zenith with those seizure disorders that do not have an epileptic etiology. There are at least 15 synonyms for a condition that occurs in 10% to 20% 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 pseudoepileptic seizures 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 absolute. 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 cause 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, hyperventilation, pseudoseizures, hysterical epilepsy, pseudoseizure 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.
Pathophysiology of the intermediate syndrome of organophosphorus poisoning

We report a patient with the intermediate syndrome resulting from organophosphorus poisoning who was treated with different experimental stimulation studies and single fibre EMG. A hypothesis for the pathophysiology of the intermediate syndrome is proposed.

A 28 year old previously healthy Asian woman drank a bottle of parathion (probably about 60 ml). She was admitted swiftly to hospital and treated with gastric lavage and intravenous atropine and a single dose of pralidoxime. After three to four days she developed motor and sensory weakness and was unable to lift her head. On the fifth day her vital capacity fell. Her facial muscles were weak, as was shoulder abduction and hip flexion. The distal muscles were normal. She had normal reflexes and no sensory deficit. She was intubated, respirated, and atropine was continued.

Her muscle strength slowly improved and she was weaned from the respirator. On the 15th day she was neurologically normal. Neuropathological studies were carried out on the 7th, 14th, and 18th days. She recovered completely after three weeks. Results from motor and sensory function and EMG studies on the median nerve on the 18th day were normal.

Repetitive nerve stimulation of the ulnar nerve was carried out by a long-term recording from the adductor digiti minimi. On day 7 a single stimulus produced a repetitive discharge but the second and subsequent stimuli did not figure. The repetitive discharge was present at every stimulus with rates at 1/2s but not at 3/4s. It was present when the trial stimulus followed a few seconds after tetanus at 20s for five seconds.

No decremental responses were seen at rates up to 50%; nor was a decrement present after one minute of exercise or after 10 seconds of repetitive stimulation at 20s or 50%. Incremental responses were not seen. Single fibre EMG from the clinically normal extensor digitorum communis showed two single fibre pairs with borderline jitter values; the mean consecutive difference (MCD) was 59 and 66 (range 40-80). Frontalis muscle was examined on day 7 and showed increased jitter with blocking. Of 17 fibre pairs, 12 had increased jitter and seven of these had greater than 10% blocking (figure). As expected, blocking was only seen in pairs with a considerably raised MCD.

The intermediate syndrome follows the acute cholinergic crisis of organophosphorus poisoning and is seen in up to 20%-50% of cases depending on the severity of poisoning and duration, and on the type of organophosphorus compound. It differs from myasthenia gravis in that it is a constant rather than progressive weakness, responds adversely to neostigmine, and recovers within 18 days. There are no associated autoimmune phenomena. Decremental responses to repetitive nerve stimulation have been seen sometimes but usually it has been the clinically unaffected peripheral muscles that were studied.

We propose that loss of regulation of acetylcholine receptors (AChRs) could explain the syndrome and neurophysiological findings. These receptors have a half life of 10 days before undergoing endocytosis and proteolysis within the muscle fibre. Regulation of the number of AChRs and

The letter to the editor was published recently. Its agonist, IL-1ß—the predominant IL-1 isoform in humans—is consistently expressed in acute multiple sclerosis plaques. It is conceivable, but so far neither confirmed nor disproved, that the natural specific antagonist IL-1ra is involved in the counterregulation of inflammatory activity in multiple sclerosis. If this were the case, IL-1ra would be a novel candidate for immunomodulatory therapy in multiple sclerosis.

We conducted a pilot study of nine patients with definite multiple sclerosis. The patients were followed up for one year by clinical examination (EDSS) and MRI every three to four weeks (resulting in 14 time points with code numbers 1 to 14), in parallel to measuring IL-1ß and IL-1ra concentrations in serum and CSF. Five patients with a relapsing-remitting multiple sclerosis (two men, three women; ages 27-34; duration of disease one to three years), and four patients with chronic progressive multiple sclerosis (one man, three women; ages 40-59; duration of disease five to 28 years) were studied. Cranial MRI (Siemens Magnetom 1.0 Tesla, Munich, Germany) images were obtained according to standard guidelines. They were T2 and T1 weighted, with and without 0.1 mmol/kg Gd-DTPA enhancement. Serum (n = 118) and CSF samples (n = 33) were frozen within two hours of collection and stored at -80°C. IL-1ß and IL-1ra were measured by commercially available enzyme linked immunosorbent assay (ELISA) kits (R and D Systems, Minneapolis, MN, sensitivity 1 pg/ml for IL-1ß and 20 pg/ml for IL-1ra; intra-assay precision < 8.5%). The assays were performed in a blinded fashion, one assay for each patient. A clinical relapse was defined as an increase by >1.0 EDSS point. A relapse MRI maximum was defined as a time point with >1 Gd enhancing lesion if preceded and followed by less MRI activity. Serum IL-1ra concentrations were individually defined as extremes (>3 box lengths from upper boundary) using individual box plots for each patient (box length between 25th and 75th percentile) according to the SPSS procedure "Box plot". The association between changes in IL-1ra concentrations and MRI activity was tested with the sign test (increase or decrease of IL-1ra concentration or number of active MRI lesions between two time points).

Relative MRI maxima and clinical relapses were only seen in the group of patients with relapsing-remitting multiple sclerosis, not in the one with chronic-progressive multiple sclerosis. IL-1ß was not detectable in serum (n = 118 samples) or CSF (n = 33 samples). IL-1ß could be detected in all serum samples but not in CSF. Hence serum IL-1ra concentrations were subject to further analysis. The median serum IL-1ra concentrations varied interindividually (range 45-422 pg/ml), but were all within the normal published range. In the patient with the highest total number (64) of Gd enhancing lesions (patient 1), an increase or decrease of MRI activity was followed by an increase or decrease of IL-1ra concentrations by three to four weeks (one time point, P < 0.05 in sign test, figure). Individually defined extreme IL-1ra concentrations were only seen in patients with relapsing-remitting multiple sclerosis. There were four such extreme concentrations in four different patients. Two of those coincided with relative maxima of MRI activity, and one with a clinical (spinal) relapse.

Smaller increases in serum concentrations of IL-1ra were not specific for multiple sclerosis activity, as they were also found in the group of patients with chronic-progressive multiple sclerosis during the observation period. This is probably due to the fact that IL-1ß and IL-1ra are involved in a wide range of inflammatory activities. The longitudinal design including monthly visits proved to be a better type of follow-up for individual extreme IL-1ra peaks. Because of the few patients, a significant association could be shown in only one patient. In her, very high disease load (demonstrated by MRI activity) probably allowed us to detect this association. We could not detect IL-1ra in CSF, or IL-1ß in CSF or serum, probably because the concentrations were below the detection limit of our ELISA assays. Because the biologically active concentration of IL-1ra is at least one magnitude higher than that of IL-1ß, IL-1ra may be more easily detectable than IL-1ß.

In conclusion, we found that fluctuations of IL-1ra may be associated with multiple sclerosis activity. The role of IL-1ra in multiple sclerosis therefore warrants further study.

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