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

We thank Dr D Sinicropi and Dr R Williams-Chestnut of Genentech, Inc, USA for the NGF antibody.

Triphasic waves in serotonin syndrome

The serotonin syndrome was first described in 1960 in depressed patients with delirium due to monoamine oxidase inhibitors and 5-tryptophan administration. 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. The serotonin syndrome has been noted to occur with several serotonergic agents, particularly when multiple agents are used.

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 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 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 had several strokes, 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 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 static 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 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—though 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 diseases.

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
patients with relapsing–remitting multiple sclerosis, not in the one with chronic-progressive multiple sclerosis. IL-1β was not detectable in serum (n = 118 samples) or CSF (n = 33 samples). IL-1α could be detected in all serum samples but not in CSF. Hence serum IL-1α concentrations were subject to further analysis. The median serum IL-1α concentrations varied individually (range 45–422 pg/ml), but were all within the normal range. In the 19 patients 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-1α concentrations by three to four weeks (one time point, P < 0.05 in sign test, figure). Individually defined extreme IL-1α 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.

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-1β and IL-1α 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, München, 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 –70°C. IL-1β and IL-1α were measured by commercially available enzyme linked immunosorbent assay (ELISA) kits (R and D Systems, Minneapolis, MN; sensitivity 1 pg/ml for IL-1β and 20 pg/ml for IL-1α; 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 score of EDSS points. A relative MRI maximum was defined as a time point with > 1 Gd enhancing lesion if preceded and followed by less MRI activity. Serum IL-1α concentrations were individually defined as extreme (> 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 “Boxplot.” The association between changes in IL-1α concentrations and MRI activity was tested with the sign test (increase or decrease of IL-1α concentration or number of relapse 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-1β was not detectable in serum (n = 118 samples) or CSF (n = 33 samples). IL-1α could be detected in all serum samples but not in CSF. Hence serum IL-1α concentrations were subject to further analysis. The median serum IL-1α concentrations varied individually (range 45–422 pg/ml), but were all within the normal range. In the 19 patients 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-1α concentrations by three to four weeks (one time point, P < 0.05 in sign test, figure). Individually defined extreme IL-1α 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.

We report a patient with the intermediate syndrome with results of repetitive nerve 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 was found to be severely poisoned with pralidoxime (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 respiratory 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 at the 15th day she was neurologically normal. Neurophysiological studies were carried out on the 7th, 14th, and 18th days. She recovered completely after three weeks. Results from motor and sensory examination and studies on the median nerve on the 18th day were normal.

Repetitive nerve stimulation of the ulnar nerve was carried out on the 17th day. On the 15th day she was neurologically normal. Neurophysiological studies were carried out on the 7th, 14th, and 18th days. She recovered completely after three weeks. Results from motor and sensory examination and studies on the median nerve on the 18th day were normal.

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 (MCID) was 59 and 60%.

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 down 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 cell. Regulation of the number of AChRs and...
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J Neurol Neurosurg Psychiatry 1997 62: 200-201
doi: 10.1136/jnnp.62.2.200-b

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