pressure. It should be recognised that in the setting of a cerebellar or brainstem infarction, unilateral proposis may herald increasing intracranial pressure mandating immediate treatment.

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Normal frontal cortex histology and immunohistochemistry in patients with motor neuron disease

In the light of the association between frontotemporal dementia and motor neuron disease, two recent studies have examined neuropathological function, and distribution of cerebral blood flow3 or metabolism,1 in patients with motor neuron disease without overt clinical evidence of dementia. These authors showed subclinical evidence of the characteristic changes of frontotemporo-occipital dementia, with failure on tasks of frontal lobe function, and hypometabolism, or reduced cerebral blood flow, particularly in the orbitofrontal area.

Brains from patients with motor neuron disease with clinically evident frontotemporal dementia show both microvacuolation of the outer cortical laminae and ubiquitinated inclusions1 in neurons of the superficial layers of the frontal and temporal cortices. Inclusions are also seen in hippocampal granule cells.1 We have therefore examined the brains of 17 unselected patients referred for routine necropsy to a general pathology department with the clinical diagnosis of motor neuron disease, without dementia. Formal neuropathological testing had not been carried out. Brains were stained with haematoxylin and eosin for routine histological examination, and immunohistochemistry for ubiquitin, using standard techniques, for detection of inclusions. Ubiquitinated inclusions typical of motor neuron disease were present in the anterior horn cells of the spinal cord in all cases; frontal cortex was normal, with no evidence of either microvacuolation or inclusions.

In patients with motor neuron disease and frontotemporal dementia usually present with dementia, subsequently developing signs of amytrophy. It is therefore possible that the neuropathological hallmarks of microvacuolation and inclusions are a relatively late feature. It will be important to examine pathologically brains from patients with motor neuron disease who have been prospectively tested in life; nevertheless others have failed to demonstrate frontal cortical atrophy in motor neuron disease without dementia, and it is possible that patients with motor neuron disease can seemingly have significant neuropsychological and functional deficits without overt evidence of structural or pathological change.

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Very severe amnesia with acute onset after isolated hippocampal damage due to systemic lupus erythematosus

Neuropsychiatric lupus designates the whole spectrum of behavioural and cognitive impairments occurring in systemic lupus erythematosus. Up to 75% of patients with systemic lupus erythematosus may be affected. Typical manifestations are strokes, seizures, dementia, psychosis, and confusional states. We describe a patient with acute onset of isolated hippocampal damage, and persistent severe, and persistent global amnesia due to systemic lupus erythematosus.

This 55 year old previously healthy farmer was confused after a nap in the afternoon. He had no known vascular risk factor. At admission, he was alert but confused for time and place and repeatedly asked the same questions about where he was and what had happened to him. Physical examination was normal. He could not repeat three words after a two minute delay. Routine blood tests were normal except for schistocytes. His CSF had a normal cell count, protein, and glucose content.

His behaviour was remarkable only for a most pervasive amnesia: the patient never recalled visitors, specifics from test sessions, or daily events. He always recognised his family and long time friends but never the examiners or other people on the ward. He easily oriented himself in his own home but did not find his way around on the ward, where he spent three months. Whereas very remote memory seemed preserved, he was unaware of events of the past 10 to 15 years. He easily recognised the photographs of cattle he had owned more than 15 years ago, but not those he had owned more recently. He referred confabulations repeatedly that he did not know the answers to questions. He was initially placid and unconcerned but became depressed after a month; he often cried and complained about his bad memory.

Neuropsychological evaluations established normal oral and written language, arithmetic skills, praxis, finger gnosia, and right-left discrimination but failed to confirm verbal or visual memory.

The patient was treated with prednisone (75 mg daily for 12 weeks), cyclophosphamide (150 mg daily for 10 weeks), and
intravenous immunoglobulin (0-4 g/kg body weight per day for five days) with no improvement of the amnesia or the thombocytopenia, although the antinuclear, anti-ds-DNA, and anti-ss-DNA antibodies disappeared. After six months, a single generalized tonic-clonic seizure occurred. At a follow up examination after 11 months, the amnesia was still extremely severe (table). At 20 months, both the amnesia and the thombocytopenia were unchanged. No new seizure or additional cognitive or other sequelae of systemic lupus erythematosus had occurred.

Anterograde amnesia of comparable severity, often with temporally graded retrograde amnesia, has previously been reported after bilateral medial temporal lobe damage involving the hippocampus and adjacent cortex due to resection for epilepsy treatment, stroke, herpes encephalitis, or trauma.\textsuperscript{2} In our patient, the MRI indicated isolated bilateral medial temporal lobe damage with initially swollen, then atrophied, hippocampi. To our knowledge, this is the first account of systemic lupus erythematosus presenting with acute, extremely severe, and persistent global amnesia with radiological evidence of circumscribed medial temporal lobe damage.

Neuropsychiatric manifestations in systemic lupus erythematosus have been attributed to brain infarction due to cardiac embolism or to vascular occlusion associated with antiphospholipid antibodies, thrombotic thrombocytopenic purpura, infections, medication, or autoimmune processes.\textsuperscript{1,2} Vasculitis is rare. There was no evidence for thrombocytopenic purpura or infection in our patient. Cardiac embolism may simultaneously damage both medial temporal lobes. This mechanism was initially suspected in our patient because of the acute onset but is highly unlikely in view of the MRI, which did not disclose any vascular lesion. An autoimmune mechanism is more likely. Antibodies against neurons, neurofilament protein, ribosomal protein, and phospholipid have been implicated in the pathogenesis of neuropsychiatric lupus erythematosus.\textsuperscript{1} Autoimmune processes may selectively affect the medial temporal lobe: limbic encephalitis, a paraneoplastic syndrome with complex-partial seizures and progressive cognitive decline, has been associated with an antibody against neuronal nuclei (anti-Hu).\textsuperscript{4} Limbic encephalitis usually develops insidiously but acute onset similar to viral encephalitis has been reported.\textsuperscript{4} These findings support the contention that our patient’s bilateral hippocampal damage was based on an autoimmune process. The lack of improvement after immunosuppressive treatment may indicate irreversible damage to the medial temporal lobe or persistence of the presumed antibody, as suggested by the persistence of thombocytopenia despite normal haematopoiesis.

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Lamotrigine control of idiopathic trigeminal neuralgia

Carbamazepine is the drug of choice for idiopathic trigeminal neuralgia, being effective initially in 75% of patients; no other available drug is as effective, although pilocarpine and oxcarbazepine may be superior. Unfortunately, up to one third of patients cannot tolerate the drug in the doses required to alleviate the pain, and carbamazepine may cause aplastic anaemia, agranulocytosis, and hypersensitivity reactions. Carbamazepine may control idiopathic trigeminal neuralgia by suppressing Na+ currents either in the trigeminal causal nucleus directly, or in the gasserian ganglion. Recently, a novel antiepileptic drug lamotrigine has become available, and this is at least as potent as carbamazepine in inactivating Na+ currents, with fewer side effects. A search of the medical literature did not disclose previous studies of lamotrigine effects on idiopathic trigeminal neuralgia. Thus we obtained authorisation to prescribe lamotrigine in four patients with idiopathic trigeminal neuralgia, from whom informed consent was obtained.

Patient 1, a 55 year old man, developed typical idiopathic trigeminal neuralgia parainfernally on the right trigeminal branch. Oral carbamazepine (200 mg twice daily) almost completely controlled the paroxysms. In view of possible complicating side effects, the patient accepted the switch to lamotrigine. Carbamazepine was then stopped and replaced with lamotrigine on the following day (at which time the paroxysms had recurred) at 50 mg once a day by mouth, increased by 50 mg aliquots each day to a maximum of 200 mg twice daily, and then brought to a maintenance dose of 200-400 mg in divided daily doses. A similar regimen may be applied for idiopathic trigeminal neuralgia, although an initially fast dose increase is recommended. Doses of lamotrigine can be as high as 1300 mg daily. Carbamazepine and phenytoin speed up the elimination of the drug, whereas valproate slows it.

Lamotrigine is a potent antiglutamatergic agent. Depression of excitatory transmission in the trigeminal causal nucleus is believed to be part of the range of action of antiepileptic trigeminal neuralgia drugs, and thus lamotrigine release of idiopathic trigeminal neuralgia may not necessarily be due to Na+ current inactivation.

Our preliminary data require confirmation with a placebo controlled study.

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Clinical evaluation of vasospasm in subarachnoid haemorrhage by in vivo microdialysis

Patients in whom subarachnoid haemorrhage is complicated by vasospasm are at risk of developing cerebral infarction. Failing such a complication may, unfortunately, be difficult. Animal experiments have shown that cerebral ischaemia is associated with raised extracellular glutamate concentrations, which can be measured by in vivo microdialysis. We therefore assessed the role of subarachnoid haemorrhage in whom extracellular glutamate was monitored, by in vivo microdialysis, for four hours every day for four days after operation.

A 38 year old farmer reported to the hospital with a five day history of severe frontal headaches, nausea, and vomiting. Before admission he had an episode of right sided mild focal vasospasm for 24 hours. He also complained of photophobia and mild neck stiffness. Except for the neck stiffness no focal neurological findings were evident on examination. Lumbar puncture showed a bloody CSF. Intracerebral microdialysis was performed as previously described1 after stabilisation of the patient in the intensive care unit. The microdialysis catheter was placed at 12-18 mm below the baseline normal in humans (20-25 μmol/l) as previously reported. A angiogram one day later showed severe focal vasospasm at the bifurcation of the right anterior cerebral artery. Subsequent CT showed bilateral frontal hypodensities suggesting ischaemic changes (fig 1). The early severe focal vasospasm may have led to a rupture of the aneurysm clip. At the time of the initial study, the patient was very drowsy. The samples on day 2 disclosed a significant decrease in the glutamate concentration to 17 (9-36) μmol/l, showing an improvement in the level of consciousness in the patient. On day 3 there was some increase in drowsiness, possibly related to generalised vasopression and impending bifrontal ischaemia. The microdialysis fluid collections on this day also showed a significant increase in extracellular glutamate concentrations, to 24-53 (19-71) μmol/l. On day 4 clinical state improved with the patient being fully awake. The microdialysis recordings during this time showed a progressive decline in the glutamate concentrations to 42-13 (37-77) μmol/l (see fig 2). The patient was asymptomatic by a neurological committee on human experimentation at the University of Saskatchewan and informed consent was obtained before the study.

The increase in extracellular glutamate in cerebral ischaemia has been well documented in small animals with the use of in vivo microdialysis and in vitro studies. The microdialysed induced glutamate response has also been seen in the human brain.1 This increase in glutamate may be important in the developement of selective neuronal damage and cere-