pressure.⁵ It should be recognised that in the setting of a cerebellar or brainstem infarction, unilateral proptosis 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,^{1,2} two recent studies have examined neuropsychological function, and distribution of cerebral blood flow³ or metabolism,⁴ in patients with motor neuron disease without overt clinical evidence of dementia. These authors showed subclinical evidence of the characteristic changes of frontotemporal dementia, with failure on tasks sensitive to 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 laminae⁵ and ubiquitinated inclusions⁶ in neurons of the superficial layers of the frontal and temporal cortices; inclusions are also seen in hippocampal granule cells.⁶ 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 neuropsychological testing had not been carried out. Brains were stained with haematoxylin and eosin for routine histological evaluation, and immunostained 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.

Patients with motor neuron disease and frontotemporal dementia usually present with dementia, subsequently developing signs of amyotrophy. 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,⁷ and it is interesting that patients with motor neuron disease can seemingly have significant neuropsychological and functional deficits without overt evidence of structural or pathological changes.

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

Neuropsychiatric lupus designates the whole range 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.¹ We describe a patient with acute onset of isolated, extremely 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 thrombocytopenia ($26 \times 10^9/l$). 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 never confabulated but always indicated 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 gnosis, and right-left discrimination as well as constructive abilities, space exploration, and visual recognition of complex material. Intelligence was low average (Wechsler adult intelligence scale, IQ = 91; VIQ = 89; PIQ = 96). Attention and cognitive speed were normal. Executive functions were initially deficient (in particular high rate of perseverations in fluency tasks) but reached the normal range in the course. The main finding was a profound amnesia (table). Although the immediate memory span was normal, he was unable to recall any previously acquired explicit information, independent of the modality of presentation. Both in recall and recognition tasks, he denied any familiarity with the items and had a high rate of false positives in forced choice recognition tasks. An autobiographical interview and a test probing knowledge about Swiss politicians disclosed a temporally graded retrograde amnesia extending 10 to 15 years backwards. Semantic memory was normal, as evidenced by normal naming and verbal fluency. Motor learning in a mirror drawing task was normal.

Brain MRI was performed three times. In the initial MRI 10 days after onset, both hippocampi seemed discretely swollen with blurring of the cortical structure. In the MRIs after three and 10 months, both hippocampi appeared considerably smaller than in the initial scan (figure). No additional lesions were found; in particular, there was no indication of small hemispheric or thalamic vascular lesions.

Transcranial and carotid Doppler ultrasound examination and echocardiography were normal. Thrombocytopenia persisted (15 to $31 \times 10^9/l$). Haemoglobin and leucocyte count, renal function, and liver enzymes were normal. A bone marrow biopsy showed normal haematopoiesis. Antinuclear (1:400), anti-dsDNA, and anti-ssDNA antibodies were raised. No antibodies were detected against ENA-Sm, phospholipid, thrombocytes (anti-GPIIb/IIIa and anti-GPIb/IX), or neurotrophic viruses. No anti-neuronal antibodies were found (sought after five months when antinuclear antibodies were no longer detectable). Complement factor C4 was slightly decreased (135 mg/l), C3 was normal. A skin biopsy contained deposits of IgG, IgM, and C3 along the basal membrane. These findings were consistent with a diagnosis of systemic lupus erythematosus according to the 1982 American Rheumatism Association criteria.

The patient was treated with prednisone (75 mg daily for 12 weeks), cyclophosphamide (150 mg daily for 10 weeks), and

Summary of the most important memory tests

Test	Time after onset	
	1 month	11 months
Digit span forward	6	8
Corsi block tapping	5	5
Wechsler memory scale:		
Logical memory, immediate	1.5	4
Logical memory, delayed	0	0
Word association learning, immediate	6.5	8
Word association learning, delayed	0	0
California verbal learning test:		
Trail 5	6	6
Interference list	3	2
Short delay free recall	0	3
Short delay, cued recall	7	2
Long delay free recall	0	1
Long delay, cued recall	4	3
Recognition, hits	15	12
Recognition, false positives	18	16
Rey-Osterrieth complex figure:		
Delayed recall	0	0
Rey visual designs learning test:		
Trial 5		3
Long delay free recall		0
Recognition, hits		9
Recognition, false positives		5
Autobiographical memory interview:		
Personal semantic memory		
Childhood	21	
Early adulthood	12	
Recent facts	1	
Autobiographical		
Childhood	9	
Early adulthood	1	
Recent facts	0	

The full list of tests and references can be obtained from the authors.

intravenous immunoglobulin (0.4 g/kg body weight per day for five days) with no improvement of the amnesia or the thrombocytopenia, although the antinuclear, anti-

ds-DNA, and anti-ss-DNA antibodies disappeared. After six months, a single generalised 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 thrombocytopenia were unchanged. No new seizures 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.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.^{1,3} 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 systemic lupus erythematosus.³ 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).⁴ Limbic encephalitis usually develops insidiously but acute onset similar to viral encephalitis has been reported.⁵ 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 thrombocytopenia despite normal haematopoiesis.

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MRI (TR/TE: 2900/80; coronal slices) of the medial temporal lobes. Ten days after onset (A) the MRI shows discrete enlargement of both hippocampi with blurring of the cortical structure. Ten months after onset (B) both hippocampi show considerable atrophy.

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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,¹ although pimozone and oxcarbazepine may be superior.² Unfortunately, up to one third of patients cannot tolerate the drug in the doses required to alleviate the pain,¹ and carbamazepine may cause aplastic anaemia, agranulocytosis, and hypersensitivity reactions.³ Carbamazepine may control idiopathic trigeminal neuralgia by suppressing Na⁺ currents either in the trigeminal caudal nucleus or, alternatively, in the gasserian ganglion.² Recently, a novel antiepileptic drug lamotrigine has become available, and this is at least as potent as carbamazepine in inactivating Na⁺ currents,⁴ 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 paroxysms in the second 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. At 100 mg, paroxysms were controlled to a large degree, and relief grew to complete control at 100 mg three times a day. No adverse effects have been seen over six months.

Patient 2 was a 31 year old woman who developed typical idiopathic trigeminal neuralgia attacks involving the first three right branches. Carbamazepine at 200 mg twice a day almost completely controlled the paroxysms, with some attendant somnolence. At 600 mg daily, control was complete, but the patient was severely ataxic and could not drive. Discontinuation of treatment resulted in relapse. Lamotrigine produced complete relief at 400 mg in divided doses, without side effects, over six months.

Patient 3, a 75 year old woman, developed typical idiopathic trigeminal neuralgia in 1973 in the first and second left branches. Carbamazepine was effective only at 2000 mg (complete relief), with considerable side effects. Alcohol injection of the gasserian ganglion gave complete remission for three years. Subsequent recurrences were again treated with alcohol injection, but relief was always shorter. Glycerol injection was effective for four months. Idiopathic trigeminal neuralgia recurred. There were no sensory deficits or dysaesthesiae. Lamotrigine, begun as for patient 1, gave 90% relief at 150 mg three times a day by mouth. After

two months, however, the economic burden on the patient led to Fogarty percutaneous compression of the gasserian ganglion, with analgesia at short term follow up.

Patient 4 was a 72 year old man who had frequent attacks of idiopathic trigeminal neuralgia in the left second and third branches for a few months. A sense of burning in the gums was reported lately. Notably, 50% of the attacks presented at night. Speaking and chewing triggered intolerable pain. Carbamazepine at 200 mg twice a day initially controlled the attacks, but very soon produced cardiovascular intolerance. Carbamazepine was replaced with lamotrigine and attacks were completely controlled at 400 mg in divided doses over four months.

Lamotrigine may cause initial ataxia, diplopia, nausea, vomiting, and blurring of sight in 15-35% of the patients treated for epilepsy, but these disappear or are much reduced after dose adjustments.⁵ An allergic skin rash is seen in 3-17% of the patients. This can be reduced to no more than 10% if the drug is started at 50 mg once a day for two weeks, increased to 50 mg twice daily for another two weeks, and then brought to a maintenance dose of 200-400 mg in divided daily doses.⁵ A similar regimen may be applied for idiopathic trigeminal neuralgia, although we selected a much faster dose increase schedule for rapid control. 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.⁵

Lamotrigine is a potent antiepileptic agent.⁴ Depression of excitatory transmission in the trigeminal caudal nucleus is believed to be part of the range of action of anti-idiopathic trigeminal neuralgia drugs,⁶ and thus lamotrigine relief of idiopathic trigeminal neuralgia may not necessarily be due to Na⁺ current inactivation.²

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. Predicting 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 report on a patient with 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 had an episode of right sided mild weakness lasting for 24 to 48 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 and a subarachnoid haemorrhage was confirmed on cranial CT. A four vessel angiogram disclosed two large separate wide necked aneurysms on the right anterior communicating artery projecting superiorly and inferiorly. Surgery was complicated by intraoperative rupture of the superior projecting aneurysm during the application of the aneurysmal clips. An intracranial Codman bolt was inserted over the right frontal lobe for microdialysis. Intracerebral microdialysis was performed as previously described¹ after stabilisation of the patient in the intensive care unit. The extracellular glutamate reading for day 1 was 298.09 (19.9) $\mu\text{mol/l}$. This was "high" in comparison with the baseline normal in humans (20-25 $\mu\text{mol/l}$) as previously reported.² An angiogram one day later showed severe focal vasospasm (no filling) of the right anterior cerebral artery. Subsequent CT showed bilateral frontal hypodensities suggesting ischaemic changes (fig 1). The early severe focal vasospasm suggested possible vascular injury related to 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 117.43 (5.86) $\mu\text{mol/l}$. This correlated with an improvement in the level of consciousness in the patient. On day 3 there was some increase in drowsiness, possibly related to generalised vasospasm and impending bifrontal ischaemia. The microdialysis fluid collections on this day also showed a significant increase in extracellular glutamate concentrations, to 242.53 (19.71) $\mu\text{mol/l}$. 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 (3.77) $\mu\text{mol/l}$ (see fig 2). The study was approved by the medical ethics committee on human experimentation at the University of Saskatchewan and informed consent was obtained before the study.

Glutamate is an important neurotransmitter. The increase in extracellular glutamate in cerebral ischaemia has been well documented in small animals with the use of in vivo microdialysis³ and a similar ischaemia induced glutamate response has also been seen in the human brain.^{2,4} This increase in glutamate may be important in the development of selective neuronal damage and cere-