hemiparesis. There was subsequently some progression in the weakness and he was admitted to hospital for investigation. There was a history of previous stroke in June 1989 presenting with expressive dysphasia and hemiplegia which recovered completely over two months. The patient was a regular smoker and had previously had an operation for excision of an arterial embolus. Clinical examination disclosed severe expressive dysphasia although his eyes opened appropriately to speech and the patient flexed his limbs. There was a spastic right hemiparesis with bilateral extensor planter responses. Brain CT showed irregular low density in the right cerebellum and low density in the left frontoparietal region. After admission, the patient developed frequent partial seizures and myoclonus and in view of the diagnostic doubt, an open brain biopsy was carried out on 29 April 1992. Pathological examination of this tissue (1 cm³) revealed infarcted and ischaemic cortical and subcortical tissues with no evidence of vasculopathy or vasculitis. No spongiform change was present in the biopsy and no amyloid plaques were present. Immunocytochemistry for prion protein was negative.³ The patient continued to deteriorate postoperatively and died eight weeks later at another hospital. Necropsy was performed and histological examination of the brain led to the diagnosis of Creutzfeldt-Jakob disease. There were spongiform changes evident in a wide distribution throughout the cerebral cortex and prion protein deposition shown by immunocytochemistry in a compositive synaptic and perivascular pattern. In addition, numerous infarcts were noted throughout the brain, particularly in the right occipital lobe, the right temporal lobe, and the thalamus. The brain biopsy tray which had been repacked and resterilised had deliberately not been used on another patient and the instruments were subsequently destroyed.

This case highlights three major points. Firstly, some cases of Creutzfeldt-Jakob disease will present in an atypical fashion. In these patients, because Creutzfeldt-Jakob disease is not high on the differential diagnosis, brain biopsy may be required to exclude treatable causes of progressive dementia. Secondly, brain biopsy in Creutzfeldt-Jakob disease may fail to confirm the diagnosis because the pathological lesions of Creutzfeldt-Jakob disease may be unevenly distributed within the brain and not detectable in small biopsy specimens using standardised neuropathological diagnostic criteria.⁴ Thirdly, for all patients undergoing brain biopsy, we think that a dedicated set of instruments is appropriate as there may be a delay between performing the operation and obtaining a definitive diagnosis as occurred in this case. Such a precaution minimises the risk of inadvertent iatrogenic transmission. Hopefully, in the not too distant future, advances in "premortem", non-surgical diagnosis of Creutzfeldt-Jakob disease,⁵ will render brain biopsy redundant.

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Transient semantic amnesia: a new syndrome?

The term transient global amnesia was first coined by Fisher and Adams in 1964 to describe a clinical syndrome characterised by the abrupt onset of severe amnesia usually accompanied by repetitive questioning, occurring in middle aged or elderly people, and lasting several hours.¹ The aetiology of transient global amnesia has been a topic of debate, but in the past few years the situation has become considerably clearer with the emergence of the following diagnostic criteria: (1) attacks must be witnessed and information available from an observer who was present for most of the attack, (2) there must be clear cut anterograde amnesia during the attack, (3) clouding of consciousness and loss of personal identity must be absent and the cognitive impairment limited to amnesia, (4) there should be no accompanying focal neurological symptoms and functionally relevant focal signs, (5) epileptic features must be absent, (6) attacks must resolve within 24 hours, and (7) patients with recent head injury or known active epilepsy are excluded.^{2,3} Epidemiological studies which have applied these criteria have established that thromboembolic cerebrovascular disease plays no part in the causation of transient global amnesia, but the incidence of migraine in patients with transient global amnesia is greater than would be expected in the general population. A small minority of cases with unusually brief, and recurrent, attacks eventually manifest temporal lobe epilepsy.³

Turning to the neuropsychological aspects, much has been learned about the organisation and neural basis of human memory since the initial description of transient global amnesia. It is clear that memory is not a unitary function but consists of interactive systems.^{4,5} One broad distinction, which derives from experimental studies of patients with amnesia, is that between explicit and implicit memory; explicit memory refers to memory available to conscious access; implicit memory, by contrast, refers to various types of learned responses such as conditioning, priming, and motor skills which are not available to conscious reflection. Explicit memory can be subdivided into short term (working) and long term memory; episodic and semantic memory are components of long term memory. The first refers to memory for personally experienced and highly temporally specific events or episodes. Semantic memory refers to the permanent store of representational knowledge which includes facts, concepts word, and object meaning. It can be considered as the "database" which we draw on to give meaning to our sensory experiences.

Transient global amnesia provides a model of severe, yet transient, amnesia.⁶⁻⁸ Findings during transient global amnesia have confirmed that there is a profound loss of anterograde episodic memory for both verbal and non-verbal material, together with a variable extent of temporally graded remote memory deficit. By contrast, working and semantic memory seem normal.⁹ These findings are of interest from a theoretical perspective: they confirm the independence of memory subsystems, and also imply that the pathological process in transient global amnesia is confined to those structures known to be critical for the establishment of new episodic memories (the medial temporal complex, the diencephalon, and the basal forebrain). In support of this hypothesis, functional brain imaging studies have shown hypoperfusion of components of the episodic memory system, particularly the medial temporal lobe.¹⁰

If transient global amnesia represents a temporary disruption of episodic memory then it should, in principle, be possible to identify a syndrome of transient impairment of semantic memory. There have in recent years been scattered reports of various atypical forms of transient amnesia including transient verbal amnesia¹¹ and transient topographical amnesia,¹² but only one with any resemblance to the hypothesised syndrome of transient semantic memory loss; Kapur *et al.*¹³ described a patient with temporary loss of memory for people which they suggested might be an analogue of the permanent form of memory loss of people associated with right temporal lobe pathology.¹⁴ This could be regarded, therefore, as a selective loss of a specific subcomponent of semantic knowledge. The present report details, for the first time, a patient with transient loss of general (non-person specific) semantic memory.

The patient, a 50 year old printer's assistant, was admitted to Addenbrooke's Hospital in October 1995 with an acute loss of memory for word and object meaning. He was in excellent general health without risk factors for cerebrovascular disease, but had lifelong migraine; typical attacks consisted of hemicranial headache and nausea followed by unilateral facial numbness. There was no history of psychiatric illness and there had been no recent stressful life events.

On the evening of his admission, he had been working on his stock car in the garage when he developed a typical migraine. At the crescendo of the headache, his father in law entered the garage and asked him if he wanted a marrow from his garden for supper. The patient recalls being puzzled by this question and said "what's a marrow?" The family understandably thought that he was joking with them, but he then seemed to be having difficulty understanding other common terms. They searched the house and found a cucumber which they presented to the patient to show him what a marrow was like: he was unable to name or identify the cucumber. They repeated the process with other fruit and vegetables all of which he was unable to name. In conversation he had difficulty understanding terms such as "stock car" and "engine", but his speech was fluent and grammatically correct. He was aware that he had two children but could not think of their names. Because of the family's increasing concern, their general practitioner arranged for admission to hospital.

When seen by the admitting general medical team he was alert and oriented in time and place. He could recount his name and

performed rapid serial subtraction. Registration of a name and address was normal, but he was unable to name the prime minister or monarch, and said to the examiner "what's a monarch?" There was no evidence of repetitive questioning and the patient gave an accurate history of the events over the past few hours. Physical examination was normal.

The next day, he was reviewed in the Neurology Department. Again orientation and verbal anterograde memory were normal. Digit span was recorded as six forwards and four backwards. His spontaneous language was normal and he was able to name 12 everyday common objects. Category fluency for animal names was, however, reduced in that he produced only eight such exemplars. Brain CT and EEG were normal and he was discharged from hospital.

When I reviewed the patient one month later he was able to give a lucid account of the events surrounding his admission to hospital and remembered being unable to name and identify vegetables and other things shown to him by his family. He also recalled accurately the sequence of events relating to his hospital admission. Cognitive assessment showed him to now be normal. His verbal fluency for animal names had risen from the previously impaired level to 18. More formal neuropsychological assessment disclosed a level of verbal intellectual and memory performance commensurate with his predicted background education and IQ assessed by reading age.

The features of the attack suggest a transient loss of semantic memory with preservation of anterograde episodic and working memory, a syndrome which has hitherto been unrecognised.

The syndrome of progressive, yet selective, loss of semantic memory was first recognised by Warrington.¹⁵ More recently, the term semantic dementia has been applied to this syndrome, the core features of which are as follows: (1) selective loss of semantic memory causing severe anomia, decreased word comprehension, impaired production of exemplars on tests of word fluency, and a loss of general knowledge, (2) sparing of other aspects of language, notably syntax and phonology, (3) unimpaired perceptual and non-verbal problem solving abilities, and (4) preserved anterograde episodic memory.¹⁶⁻¹⁸ Neuroimaging studies in semantic dementia have consistently shown atrophy of the temporal lobe involving particularly the left inferolateral neocortex with sparing of the hippocampal formation.^{17,18} Parallel functional activation studies, using PET, have also pointed to a key role for the inferolateral left temporal lobe in semantic memory.¹⁹

It can be seen from this brief description of semantic dementia that the syndrome described in the present paper seems to be a transient analogue of selective semantic memory loss. In the same way that transient global amnesia is a temporary form of the classic amnesic syndrome resulting from reversible dysfunction of structures critical for episodic memory, transient semantic amnesia is likely to result from a temporary dysfunction of the inferolateral temporal lobes. Of course, this remains a speculative hypothesis as functional imaging studies (SPECT or PET) were not obtained during, or after, the present patients' attack.

It is of interest that our patient was a lifelong migraineur and that the attack occurred in the context of a particularly severe episode of migraine. As mentioned in

the introduction, there is now an established association between transient global amnesia and migraine. A wide range of physical and emotional stressors have been linked to transient global amnesia and a unifying hypothesis was proposed by Olesen and Jorgensen.²⁰ They suggested that the phenomenon of spreading depression could be precipitated by intense volleys of sensory inputs to the hippocampus, releasing the neurotransmitter glutamate; glutamate is a potent cause of spreading depression in animals. It was subsequently suggested that this may, therefore, provide a link between the diverse precipitating factors reported to provoke transient global amnesia. These stressful stimuli may act by causing a surge of excitotoxic neurotransmitter which then temporarily shuts down normal memory function in the hippocampus.³ A similar mechanism could be evoked as the cause of transient semantic amnesia, although the neurotransmitter systems involved in the lateral temporal neocortex are less clearly established.

It is possible that transient semantic amnesia may be more common than has been recognised. In transient global amnesia, the profound loss of anterograde episodic memory results in repetitive questioning and a loss of all new information after a few seconds. Such an attack will not escape the notice of observers and will lead to medical attention. Impairment of semantic memory results in more subtle cognitive dysfunction without the dense lacuna seen in transient global amnesia, as illustrated here.

In conclusion, the present report describes a patient with what seems to be temporary reversible impairment of semantic memory with preservation of anterograde memory function.

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Alopecia with carbamazepine in two patients with focal seizures

In the treatment of patients with epilepsy with antiepileptic drugs, alopecia was reported in association with valproic acid (VPA),¹ and on rare occasions with carbamazepine (CBZ).^{2,3} We recently encountered two young women with partial seizures who developed alopecia after starting CBZ.

Patient 1 was a 32 year old woman with a diagnosis of left frontal lobe epilepsy since the age of 27. Her habitual seizures were simple partial seizures consisting of tonic contraction of her right hand and bilateral orbicularis oculi muscles, followed by eye deviation to the right and clonic convulsion of the right side of her face, which were not usually associated with disturbance of consciousness. A cranial MRI was normal and routine EEG showed normal background activity and intermittent irregular 2-3 Hz slow activity at the left frontotemporal area seen every 50 to 100 seconds. As the seizures had started occurring often, the patient had been started on VPA (1200 mg/day) and diazepam (6 mg/day). Because alopecia developed over a period of several months, these two drugs were discontinued, and then the hair loss stopped. As her seizures became less frequent despite discontinuing VPA and diazepam, no medication had been taken in the next year until she visited our hospital, at which time the seizures had started occurring once every month or every other month. The patient was then given CBZ, increased the dose gradually up to 300 mg/day in two months, and the steady state trough blood concentration was 5.0 mg/l. Three months after starting CBZ, the patient developed appreciable hair loss, as seen previously with VPA. After CBZ was switched to phenobarbital, hair shedding stopped. The patient had no pregnancy, other dermatological problems, endocrine disorders, or autoimmune disturbance such as systemic lupus erythematosus throughout the clinical course.

Patient 2 was a 25 year old woman with a diagnosis of tuberous sclerosis associated with complex partial seizures since the age of 17. She had several small Pringle adenomas on her face and a depigmented macule on her trunk, but otherwise no skin lesions, includ-