

mainly on clinical features.<sup>2-5</sup> Factors predisposing to AIE include age, acute or chronic renal failure, and other neurotoxic drugs.<sup>5</sup> The diagnosis is facilitated by analysis of aciclovir and CMMG in serum and CSF. In cases with renal failure, the half life of aciclovir extends from 3 to 20 hours and as a result aciclovir is metabolised to CMMG by alcohol and aldehyde dehydrogenases.<sup>4</sup> At present, reliable dose recommendations are not available for patients with renal failure.

In a case study of 93 patients, mainly with renal failure,<sup>4</sup> we found mean (SD) serum aciclovir concentrations of 21.0 (30.7)  $\mu\text{mol/l}$  (in 49 patients with neurotoxicity) and 7.2 (6.7)  $\mu\text{mol/l}$  (in 44 asymptomatic patients receiving aciclovir), while CMMG concentrations were 34.1 (39.4)  $\mu\text{mol/l}$  in patients with neurotoxicity and 4.7 (4.7)  $\mu\text{mol/l}$  in asymptomatic patients. CMMG levels of  $>10$   $\mu\text{mol/l}$  seemed to be associated with neurotoxicity. A high CMMG level is a strong predictor of AIE in patients with renal failure.<sup>4</sup> Haemodialysis is effective in clearing aciclovir and CMMG, and to a lesser extent so is peritoneal dialysis.<sup>4</sup>

This case highlights the difficulties in diagnosing AIE and the value of measuring aciclovir and CMMG levels in making the diagnosis.<sup>4</sup> In cases with renal failure and herpes simplex or varicella-zoster encephalitis, aciclovir should not be discontinued prematurely, but a total daily dose exceeding 400 mg is not generally recommended in patients with renal impairment. Pharmacokinetic studies of aciclovir and CMMG are being undertaken at Karolinska University Hospital, Sweden, with the aim of achieving dose recommendations for patient with renal failure.

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### Normal memory and no confabulation after extensive damage to the orbitofrontal cortex

Subarachnoid haemorrhage caused by the rupture of an anterior communicating artery (ACoA) aneurysm is often followed by amnesia, confabulation, and personality change including social decision making.<sup>1-3</sup> However, the regions responsible for each symptom have not been determined conclusively. We describe a patient who showed personality change, but neither memory impairment nor confabulation, after extensive damage to the bilateral orbitofrontal cortex demonstrated by magnetic resonance imaging, providing evidence that the destruction of the medial orbitofrontal cortex alone cannot cause amnesia and confabulation.

### Case report

The patient was a 45 year old, right handed man with a 16th grade education. He was not an apathetic person and worked hard as a manager before the onset. His past medical history was unremarkable and he had no medication. He had sudden onset of headache, became unconscious, and was admitted to an emergency hospital. Brain computed tomography showed a subarachnoid haemorrhage in the cisterns around the brainstem, longitudinal cerebral fissure, and bilateral Sylvian fissure caused by a ruptured aneurysm of the ACoA. On the same day, he underwent an operation to repair the ruptured aneurysm. There were slight brain oedema and vasospasm (four to 10 days). He did not become delirious, agitated, or suspicious. He had 200 mg of phenitoin each day to prevent secondary seizures. His family noted that he showed mild anterograde amnesia, which improved over two months, but no retrograde amnesia.

The patient was discharged home after three months. He began working again as a manager at his company, but could not do his job as well as before the onset. Twenty months after the onset, he was admitted to our hospital for assessment of his problems.

On admission, the patient was fully alert and oriented. General physical and neurological examinations were unremarkable. During his stay in hospital, he had no problems communicating with others, kept his appointments and could find his way around the hospital. His family and his superior at his company reported that his personality had changed since the onset of his illness (in terms of lack of concern for others including his family, his appearance, and his future; the loss of spontaneity, initiative, and self motivation; disinhibition; and rigidity of thought).

General neuropsychological assessments were performed between the second and 12th hospital days. He was attentive, cooperative, and showed no confabulatory response. His intelligence level was normal on the Wechsler Adult Intelligence Scale-Revised (full IQ, 113; verbal IQ, 114; performance IQ, 109), Mini Mental State

Examination (30 of 30), and Raven Progressive Colored Matrices (35 of 36). He showed no linguistic deficit on the Western Aphasia Battery. The results of the Wisconsin Card Sorting Test (six categories achieved) and Verbal Fluency Test (animals, initial syllables "A", "Fu", and "Ni": 15, 10, 10, and 15/minute, respectively) were normal. His immediate memory spans were normal (forward: verbal, 7; spatial, 6; and backward: verbal, 6; spatial, 6). The indices on the Wechsler Memory Scale-Revised were above average, except for a somewhat low score for delayed index (general, 112; verbal, 110; visual, 108; attention/concentration, 112; delayed, 85). He showed no retrograde amnesia in a structured interview, on the Autobiographical Memory Interview (incidents 9, 9, 8 and personal semantic 21, 20, 21 for childhood, early adult life, and recent, respectively), and on the Public Events test (14, 15, 14, and 16/16 for 60th, 70th, 80th, and 90<sup>th</sup>, respectively).

Brain magnetic resonance imaging performed 20 months after the onset (fig 1) showed bilateral lesions in the ventromedial prefrontal lobe extending to the frontal pole and subcortical regions under the middle and superior frontal gyri. Additional lesions were seen in the left insula and the right ventral anterior nucleus of the thalamus.

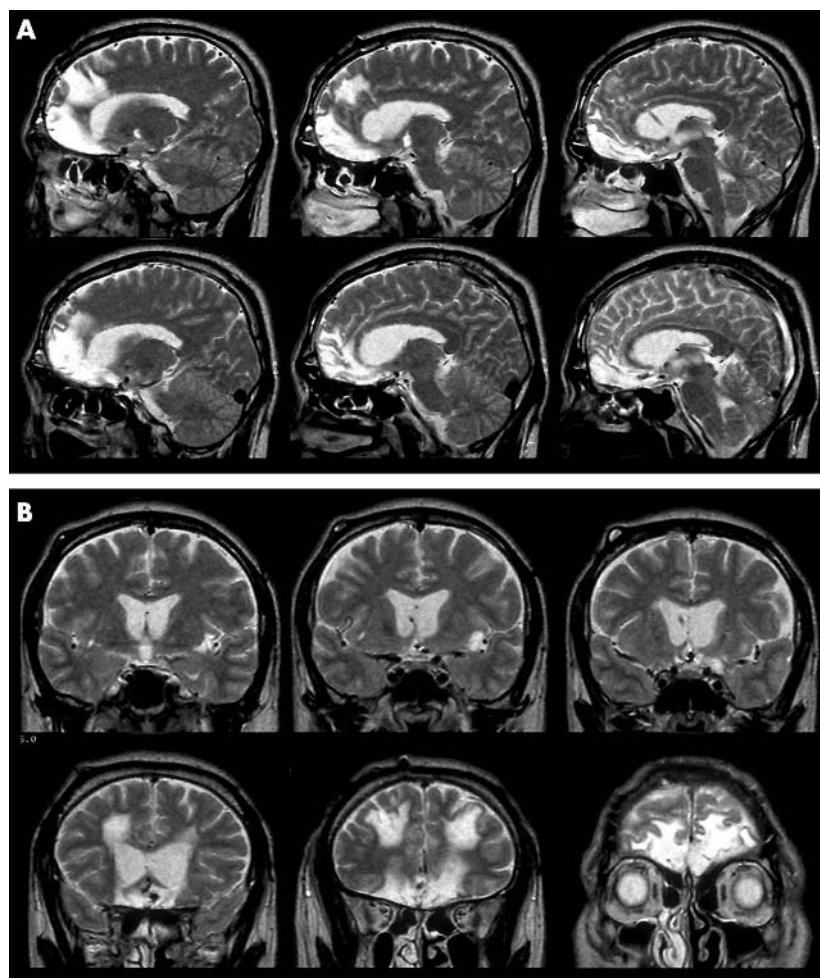
### Discussion

After extensive damage to the bilateral orbitofrontal cortex, with no concomitant lesion in the basal forebrain, the patient showed personality change as a result of a subarachnoid haemorrhage, but neither memory deficits on comprehensive neuropsychological assessment nor confabulation. His personality change could be classified as a combined type (apathetic and disinhibited) and was consistent with those (lack of concern, loss of spontaneity, disinhibition, impaired decision making, and rigidity of thought) generally agreed in the literature to be the result of dysfunction of the frontal lobe, particularly the orbitofrontal cortex.<sup>1-3</sup>

Importantly, the patient showed no memory deficit. Damage to the basal forebrain without damage to the frontal lobe causes amnesia.<sup>4</sup> With regard to the orbitofrontal cortex, it has been argued that destruction of this region is not necessary for the development of amnesia or basic cognitive function.<sup>1,3</sup> However, there has so far been no conclusive evidence as to whether or not damage to the orbitofrontal cortex alone (especially the medial caudal part of it) gives rise to amnesia.<sup>1</sup> Our present study provides evidence that damage to the orbitofrontal cortex alone does not result in amnesia and therefore strengthens the notion that the basal forebrain is one of the crucial sites for human memory.

It should be noted that the assessment of memory in our present study is based on standardised tests. This means that memory that is not measurable using these standardised tests (for example, temporal context memory) may be related to the function of the orbitofrontal cortex. In addition, we cannot draw a strong conclusion regarding frontal lobe function, because we did not use tests sensitive to damage to the ventromedial prefrontal cortex (for example, the Iowa Gambling Task<sup>5</sup>).

The patient showed no confabulation. Damage to the orbitofrontal lobe alone might not be sufficient for confabulation to be



**Figure 1** (A) Sagittal and (B) coronal T2 weighted magnetic resonance images showing extensive lesions in the bilateral orbitofrontal cortex. The core structures of the basal forebrain (medial septal nucleus, vertical and horizontal limb nuclei of Broca's diagonal band, and nucleus basalis of Meynert) were not damaged. In the sagittal sections, the images in the upper row show the right hemisphere and those in the lower row show the left hemisphere. In each row, the first, second, and third images are 15 mm, 10 mm, and 5 mm away from the longitudinal cerebral fissure, respectively. In the coronal sections, the left side of the image corresponds to the right side of the brain. In the upper row, the first, second, and third images are 0 mm, 5 mm, and 10 mm rostral from the anterior commissure. In the lower row, the first, second, and third images are 20 mm, 30 mm, and 50 mm rostral from the anterior commissure.

manifest. In one study, confabulation was seen in amnesic but not in non-amnesic patients with rupture of the ACoA and frontal lobe lesions,<sup>1</sup> and in another study of amnesic patients with rupture of the ACoA, only those with frontal lobe lesions showed confabulation,<sup>3</sup> suggesting that both frontal lobe lesions and amnesia are necessary for the development of confabulation. In contrast, a patient with confabulation and amnesia after damage to the basal forebrain but without frontal lobe damage has been reported.<sup>4</sup> Further studies involving comprehensive neuropsychological and magnetic resonance imaging examination are needed to determine whether both frontal and basal forebrain involvement or basal forebrain involvement alone is required for the manifestation of confabulation.

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## Adult onset SSPE: experiences in West Yorkshire over a 12 month period

Subacute sclerosing panencephalitis (SSPE) is a rare delayed complication of measles virus infection in infancy. It is characterised by behavioural changes, myoclonus, cognitive impairment, visual disturbance, pyramidal and extrapyramidal signs, and ultimately coma leading to death.<sup>1</sup> Typically, SSPE presents in childhood or early adolescence, but adult onset cases are recognised. Widespread measles immunisation in the UK has led to a dramatic fall in the incidence of SSPE in children, leading to the disease almost becoming extinct.<sup>2</sup> However, a latent disease pool remains and cases may still come to the attention of adult neurologists, as borne out by our recent experience in West Yorkshire.

## Case histories

An 18 year old man gave a three week history of blinking episodes lasting approximately one second, associated with a brief head jerk. These were not present in sleep. Examination revealed myoclonic jerks involving the neck associated with blinking. Initial electroencephalograms (EEGs), blood tests, and a magnetic resonance imaging scan were normal. Several anticonvulsant medications failed to suppress the jerks, which by four weeks had spread to the legs, causing unsteadiness. The mini mental test examination score at this stage was 26 of 30. He began to deteriorate rapidly, with disorientation, blunted affect, dystonic posturing of the left arm, bradykinesia, and rigidity. Cerebrospinal fluid (CSF) was sent for analysis of 14-3-3 and S-100 proteins, which were negative. A further EEG, nine weeks after onset, demonstrated high voltage periodic complexes occurring every 10 seconds, consistent with SSPE. CSF and serum measles titres were raised at 35110 mIU/ml and 152930 mIU/ml, respectively. The CSF to serum albumen ratio was 1:300, consistent with intrathecal antibody synthesis. There was no past history of measles, although he had received MMR (measles mumps rubella) immunisation at age 9. Oral inosiplex (isoprinosine) and subcutaneous interferon  $\alpha 2b$  were started and an Ommaya reservoir was inserted to administer intraventricular interferon  $\alpha 2b$ . By this stage, the myoclonus had subsided but he had gaze paresis, mutism, widespread spasticity, and required gastrostomy feeding. He received intraventricular treatment for six weeks before reservoir infection necessitated its removal. His condition plateaued and he was maintained on inosiplex alone. Eventually, he was discharged home in a dependent state.