

# Unilateral striatal damage following status epilepticus of ipsilateral frontal lobe origin

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A 35-year-old man with an old contusional haematoma in the right frontal lobe developed status epilepticus (SE) of right frontal origin. On magnetic resonance (MR) images 10 days after SE, the right striatum showed signal enhancement with Gd-DTPA administration. Subsequent MR imaging 1 month later indicated prolonged T1 and T2 relaxation times in the right striatum. Prolonged seizure activity in the frontal lobe may have induced excitatory neurotoxicity in the ipsilateral striatum, with occurrence of delayed neuronal damage as a result.

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*Key words:* status epilepticus; striatum; frontal lobe epilepsy.

## INTRODUCTION

Animal experiments have shown that prolonged seizures in the absence of anoxia are capable of producing cerebral lesions, 'epileptic brain damage'<sup>1,2</sup>. Hippocampal and extrahippocampal changes, including neuronal loss in the amygdala and entorhinal and perirhinal cortices, are typically seen in various animal models of status epilepticus (SE)<sup>3–9</sup>. Furthermore, signs of ongoing neuronal damage have been noted in rats even after cessation of SE<sup>4</sup>.

In humans as well, selective neuronal necrosis is a well-known consequence of SE<sup>10–12</sup>. Most post-mortem histologic analyses in patients dying of SE demonstrate neuronal loss in the medial temporal lobe, particularly the hippocampus, amygdala, and surrounding cortical areas<sup>11–13</sup>. However, structural changes observed in such human pathological studies may be related to the disease underlying the seizures or to systemic complications of the insult<sup>13,14</sup>. We report a case in which unilateral striatal damage became evident in serial magnetic resonance (MR) images following SE originating from the ipsilateral frontal lobe.

## CASE REPORT

A 35-year-old man had undergone surgery on May 24 1993 because of depressed frontal bone fractures and contusional haemorrhage in the right frontal lobe sustained as a result of a motor vehicle accident on April 7 1993. Although mild disturbance of consciousness was noted initially, he made a good recovery. Residual deficits included bilateral anosmia, left temporal hemianopsia, and blindness in the right eye. No clinical seizures occurred, and no antiepileptic drug was prescribed. In mid-December 1998, a subgaleal accumulation of pus was noted in the frontal region. The infected bone flap was removed and both frontal sinuses were surgically occluded on June 3 1999. Causative agents proved to be *Staphylococcus aureus* and *Peptostreptococcus micros*. Pre-operative MRI failed to reveal any abnormal enhancement in the striatum.

The patient had a generalized seizure on May 8 2000. A lesion, representing the only contusional haemorrhage in the right frontal lobe, showed prolonged relaxation times in T1- and T2-weighted MR images (Fig. 1). A small lesion with similar

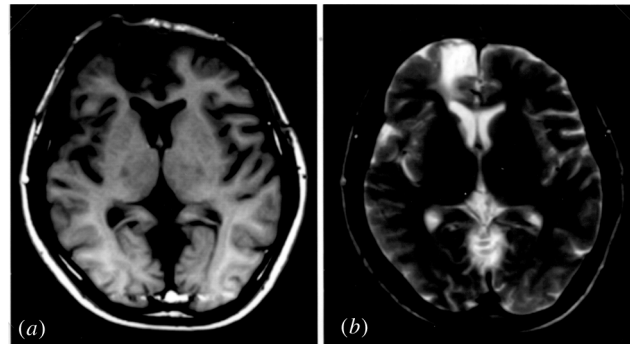


Fig. 1: Axial T1-weighted image (a) and T2-weighted image (b) on May 8 2000, showing prolonged relaxation times in a right frontal lesion representing an old contusional haemorrhage. A small lesion with similar signal characteristics is also noted in the head of the right caudate.

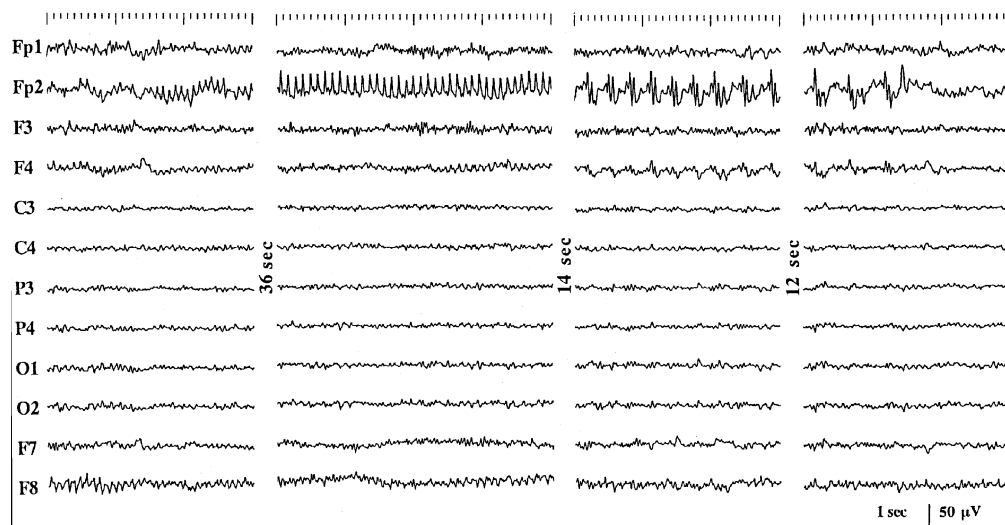


Fig. 2: Electroencephalographic seizure activity is apparent in the right frontal region (Fp2 according to the International 10–20 system).

characteristics was also noted in the head of the right caudate nucleus. Electroencephalography (EEG) on May 10 showed intermittent rhythmic delta activity and frequent electrographic seizure activity in the right frontal region (Fp2 according to the International 10–20 system of electrode placement); (Fig. 2). Administration of valproate (600 mg/day) was initiated.

On May 18, frequent generalized seizures occurred. Seizures were stereotyped, beginning with tonic-clonic activity of the left arm that rapidly spread to involve the entire body and was followed by post-ictal confusion and left hemiparesis. When intravenous administration of phenytoin, diazepam and lidocaine failed to control SE, barbiturate coma was induced under controlled mechanical ventilation between May 20 and 24.

On May 26, the patient regained consciousness and the left hemiparesis improved. In T1-weighted MR images on May 29, the right putamen showed signal

enhancement with Gd-DTPA administration (Fig. 3). Seizures were controlled by 250 mg of phenytoin per day, and no additional neurological abnormality was noted. In MR images on June 20, the signal in the right striatum was hypo- to iso-intense in T1-weighted images and hyper-intense in T2-weighted images (Fig. 4). EEG on June 21 demonstrated slow wave activity localized to the right frontal region, but no paroxysmal activity was noted. During a year of follow-up, the right striatal lesion persisted on repeated MR imagings, however the patient did not develop a delayed neurological deficit such as unilateral dystonia.

## DISCUSSION

Serial MR imaging represents a practical non-invasive method for monitoring long-term progression of cerebral damage following SE<sup>14,15</sup>. In several case

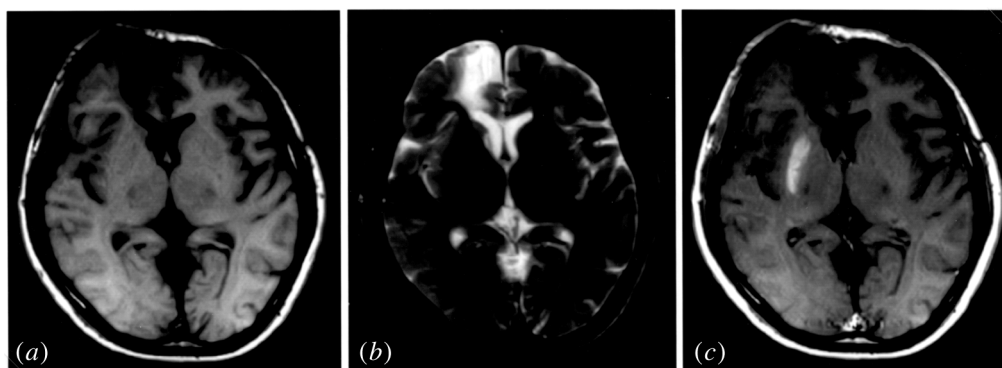


Fig. 3: Axial T1-weighted image (a), T2-weighted image (b), and Gd-DTPA enhanced T1-weighted image (c) on May 29. Signal in the right striatum is enhanced by Gd-DTPA (c).

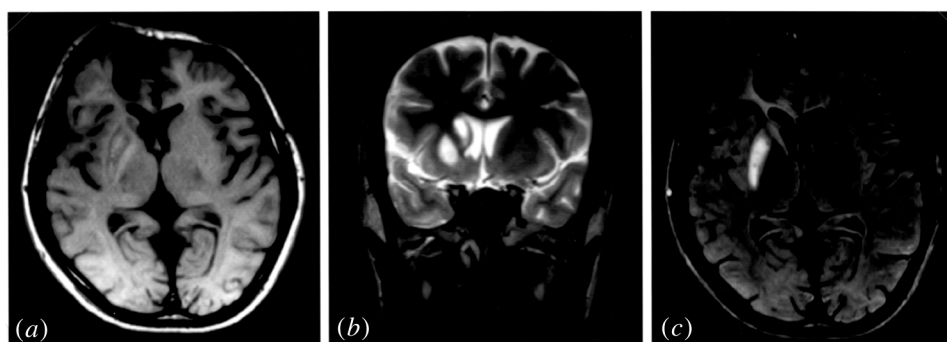


Fig. 4: Axial T1-weighted image (a), coronal T2-weighted image (b), and axial fluid-attenuated-inversion-recovery (FLAIR) image (c). The right striatum shows hypo- to iso-intense in (a) and hyper-intense in (b) and (c).

reports, short-term increases of T2 signal intensity after SE were followed by progressive hippocampal atrophy<sup>15,16</sup>. Wiesmann *et al.*<sup>17</sup> described one patient in whom progression of hippocampal atrophy continued for up to 58 months after generalized SE. Some authors maintain that T2 changes associated with SE are transient, and therefore represent oedema following SE<sup>18–25</sup>. However, VanLadingham *et al.*<sup>26</sup> recently reported quantitative MR imaging evidence suggesting that prolonged complex febrile seizures produce hippocampal damage. In particular, two of these four patients who demonstrated short-term increases in the hippocampal volume and signal intensity had follow-up MR imaging that showed hippocampal atrophy within 8–10 months. Since these reported MR changes were progressive and apparently irreversible, these findings are likely to represent selective neuronal damage. In our case, MR imaging 10 days after SE demonstrated enhancement of the right striatum with Gd-DTPA administration. MR images obtained 1 month later showed prolonged signal intensity in the right striatum in T1- and T2-weighted images. Since these findings persisted during 6 months of follow-up, irreversible delayed neuronal damage appears to have developed in the right striatum.

Cerebral damage following SE has recently been evaluated in terms of signal change on diffusion-weighted MR imaging and decreases in apparent diffusion coefficient (ADC) measurements<sup>14,27–29</sup>. Although the regions with decreased ADC corresponded to the epileptogenic region, the pathophysiologic significance was not clear<sup>14,29</sup>.

The most important factor linking seizure activity to selective neuronal death appears to be entry of calcium into neurons. When the mechanisms mediating intracellular sequestration and outward transport of calcium are overwhelmed, marked increases in intracellular calcium concentration occur. This activates a wide range of enzymes causing diverse secondary effects. In SE, glutamate, aspartate, and acetylcholine are thought to play major roles as excitatory neurotransmitters, while gamma-aminobutyric acid may be the dominant inhibitory transmitter. The excitotoxic mechanisms are mediated by the N-methyl-D-aspartate (NMDA) glutamate receptor; activation of these receptors during the course of epileptic discharges results in excessive calcium entry and subsequent cell death<sup>10,12</sup>.

The parts of the human brain most vulnerable to damage from SE include: the CA1 and CA3 segments and the hilus of the hippocampus; the amygdala; the

pyriform cortex; the cerebellar cortex; the thalamus; and layers 3 and 4 of the cerebral cortex<sup>11,12,15</sup>. In a reported patient with frontal focal SE, progressive changes on MR imaging were confined to the epileptogenic region of the superior frontal gyrus, which appeared normal in images obtained prior to SE<sup>30</sup>. Striatal necrosis following SE of ipsilateral frontal lobe origin, such as in our case, has not been described previously. Delayed striatal necrosis is a well-known consequence of global ischaemia of the brain<sup>31</sup>; its pathophysiological mechanism is thought to be similar to that of epileptic brain damage<sup>32</sup>. In this ischaemic insult, the striatal lesion is usually bilateral and symmetric<sup>31</sup>. Extensive glutamatergic afferents from the cortex project to the striatum, terminating mainly at NMDA receptors<sup>33</sup>. Seizure semiology, EEG features, and MR images in our case were all consistent with a diagnosis of frontal lobe epilepsy. The side of the damaged striatum was identical to that of the epileptogenic focus. These findings suggest that prolonged seizure activity propagated along anatomic pathways from the frontal lobe to the ipsilateral striatum, causing excitotoxic secondary damage. A possible predisposing factor in this case was an abnormal blood supply to the right striatum such as medial striate arteries, the recurrent artery of Heubner and lenticulostriate arteries secondary to the distant head injury and meningitis.

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