

# MRI evidence for the involvement of basal ganglia in epileptic seizures: an hypothesis

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**ABSTRACT** – Recent clinical and experimental studies have suggested that the basal ganglia are involved in epileptic seizures as a propagation pathway or as a remote inhibitory control circuit. The present case report may provide additional evidence from post-ictal magnetic resonance imaging (MRI) supporting this hypothesis. A healthy 13 year-old boy was admitted for a complex partial status epilepticus. MRI, performed one week later, revealed bilateral T2 hyperintense signals in the striata and a left temporal arachnoid cyst. Left temporal slow waves were noted on EEG recording. No obvious metabolic alterations were identified. During the next six years of follow-up, no seizure occurred and striatal alterations progressively disappeared. The clinical characteristics of the seizures, EEG slow waves, and probably the presence of an arachnoid cyst suggest that seizures originated from the left temporal lobe. The long-lasting MRI changes suggest that bilateral striatal alterations may have been secondary to an inflammatory process, which in turn could have disrupted a striatal inhibitory control over seizures. On the basis of these arguments, we speculate involvement of basal ganglia in epileptic seizures, as a part of a modulatory control system over seizures rather than a propagation pathway. Future reports will support or invalidate our hypothesis.

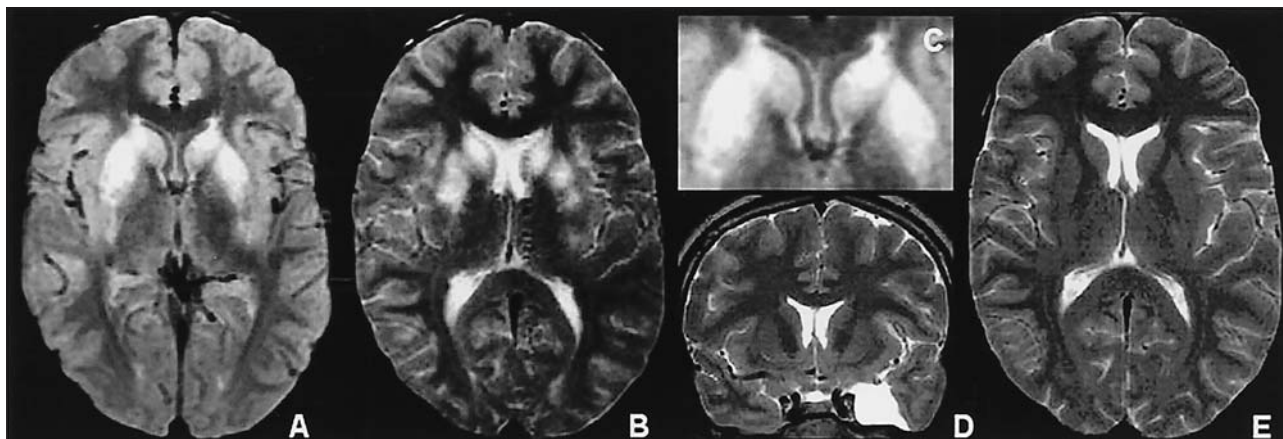
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During the last two decades, converging experimental and clinical lines of evidence for the involvement of the basal ganglia in seizures have accumulated [1]. The basal ganglia may represent a propagation pathway as suggested by functional imaging studies. Increased perfusion of the basal ganglia has been reported during spontaneous [2, 3] or electrically induced seizures [4]. Recently, experimental data have suggested that the basal ganglia may also be a part of a remote inhibitory control system of

epileptic discharges. Pharmacological modulations of some constituents of this circuit allow to be suppressed seizures in various animal models [5-7]. Transient images following seizures have been reported in both computed tomography (CT) and magnetic resonance imaging (MRI) studies [8-10]. Since their localization is often concordant with ictal symptoms and EEG alterations, post-ictal MRI may represent a non-invasive tool to visualize cerebral structures in which epileptic discharges have occurred [10].

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**Figure 1.** Initial and control MRI examinations. A-C: 7-mm axial T2-weighted images performed 1 week after the partial status epilepticus. Note the increased signal intensity bilaterally involving the putamen and the head of the caudate nucleus. **A)** first echo (TR 2000/TE 60). **B)** second echo (TR 2000/TE 120). **C)** magnification of the striata. **D)** left temporal arachnoid cyst. **E)** Control MRI (5 mm, TR 3906/TE 100) performed 6 years later was normal.

We report the case of a healthy boy with transient, bilateral increased T2 signals within the striata on MRI performed after a seizure. Since the child's symptoms consisted exclusively of seizures, and increased T2 signals were strictly localized within the striata, the pathophysiological link between basal ganglia and seizures is discussed.

## Case study

On August 31, 1990, a 13 year-old boy presented with a prolonged seizure characterized by a loss of consciousness with eyes rolling upwards and urinary incontinence, without clonic movements. The patient remained confused, and vomited during the transfer to the first hospital. On admission, the child became comatose and was sent to our hospital. During the second transfer, he exhibited a 5-minute secondarily generalized convulsive seizure beginning with eye and head deviation to the left, and remained confused afterwards. On admission, there was no neurological deficit or fever, and blood pressure was normal. Confusion disappeared after diazepam injection (10 mg IV). Except for slight asthma, a benign cranial trauma and a varicella infection at the age of four, the boy had been in good health until 12 days before the seizures when he briefly complained about a febrile headache. EEG recording showed bilateral, fronto-temporal slow waves predominating on the left side during drowsiness. The day after the seizures, clinical examination was normal. Contrast CT revealed a small hypodensity in the head of the left caudate nucleus, and a left temporal arachnoid cyst. Magnetic resonance imaging (MRI), performed 1 week after the seizures (September 7, 1990), showed bilateral, increased T2 signals within the putamen and the head of the caudate nucleus (*figure 1*). A first diagnostic investigation was normal (plasma electrolytes, glycemia,

blood gases, carboxyhemoglobin and methemoglobin levels, blood and urine aminoacidograms, volatile fatty acids, ketonic bodies, lactate, pyruvate, ammoniemia, urine organic acids, screening for toxics, and hemoculture). Valproate treatment was begun. Seizures did not recur. Control EEGs were normal (1990, 1994) or revealed some left- or bi-temporal theta waves (1991, 1992). T2 hyperintensities were markedly decreased on the first control MRI performed 7 months after the initial episode. Valproate was continued for 4 years, and then stopped without recurrence of seizures. The last EEG and MRI (*figure 1*) performed 6 years after the initial event were normal, as well as neurological examination. At this time, a second diagnostic investigation only revealed low levels of a type III mixed cryoglobulinemia composed of polyclonal IgM (6 mg/L) and IgG (traces), and fibronectine (1 880 µg/L) with no evidence for autoimmune or lymphoproliferative disease. Serological assessments suggested prior infection with cytomegalovirus, varicella-zoster, Epstein-Barr and rubella viruses, and were negative for HIV, syphilis, hepatitis B and C, herpes simplex virus, measles and mumps virus, enterovirus, and *Borrelia burgdorferi*.

## Discussion

We report a case of transient, bilateral T2, increased signals in the striatum observed in a healthy boy after a complex partial status epilepticus followed by a brief episode of secondary generalization. No obvious metabolic alterations were identified.

T2 hyperintensities on MRI are considered to reflect histological alterations such as edema. Thus, transient MRI changes observed in the present study were indicative of striatal alterations, which could have preceded or fol-

lowed seizures. Since symptoms consisted exclusively of seizures, and increased signals were strictly localized within the striatum, a causal relation between striatal MRI changes and seizures is therefore conceivable.

The focal clinical onset of seizures, the left temporal EEG slow waves, and the presence of a left-sided temporal arachnoid cyst suggested that seizures originated from the left temporal lobe. Bilateral, striatal, increased signals could reflect the propagation of epileptic discharges as suggested by the secondary generalization of the seizure. Indeed, previous studies have suggested the involvement of the basal ganglia through epileptic discharges, as assessed by SPECT or PET examinations [2-4]. Post-ictal MRI may be used to visualize the cerebral structures in which seizures occur since both localization of transient post-ictal MRI changes and epileptic discharges are often concordant [8-10]. Seizure-related MRI changes frequently consist of increased T2 signals, which typically involve the cortex [8, 9]. They generally occur after repeated and/or prolonged seizures and disappear when seizures stop or decrease in frequency [8-10]. Their pathophysiology may be related to focal hemodynamic, metabolic and histological alterations, such as edema, secondary to an excessive epileptic activity [9, 10]. Thus, striatal T2 hyperintensities observed in the present report could suggest the involvement of the striata in the propagation of epileptic discharges.

However, since seizures are highly prevalent in the population, such striatal increased signals should be reported more frequently. Moreover, it is somewhat surprising that a short secondarily generalized seizure led to such intense, bilateral, and long-lasting MRI changes, while no MRI changes were found in the cerebral region from which the partial status epilepticus was suspected to have originated (*i.e.* left temporal lobe).

The alternative explanation for these symmetrical increased signals could be that they were due to an inflammatory process, which preceded the seizures. Indeed, compared with cortical images, transient CT or MRI changes involving the striatum are rare and have been mostly reported in association with pathological conditions known for their basal ganglia tropism such as infectious, metabolic or toxic encephalopathy [11, 12]. More frequently, striatal alterations have been reported as bilateral striatal necrosis with severe symptoms, long lasting clinical sequelae, and persisting lesions [13]. When considering the possible causes of striatal inflammation, we noted that our patient suffered from a brief fever a few days prior to the seizures, which is compatible with an infectious process as previously reported with EBV infection [11]. Moreover, control diagnostic investigations revealed a mixed cryoglobulinemia, which is known to induce cerebral lesions through vasculitis [14]. However, the cryoglobulinemia level was low and there was no evi-

dence that it was already present at a significant level when striatal lesions were found (assay not performed).

The fact that the boy only presented with seizures, suggests a possible link between striatal lesions and the occurrence of seizures. Indeed, several experimental studies have shown that the basal ganglia are involved as an endogenous system exerting a remote inhibitory control over seizures. An increase in striatal activity may participate in seizure arrest and/or in the limitation of seizure recurrence by inhibiting neurons of the substantia nigra reticulata [6, 7]. Conversely, bilateral lesions of the caudate-putamen decrease the threshold for experimentally induced seizures [5]. Thus, we speculate that the striatal alterations observed in our patient might have led to a decrease in striatal inhibitory activity resulting in seizures by lowering the epileptogenic threshold. The focal onset of the seizures could have been favored by the presence of the arachnoid cyst.

In conclusion, in spite of the limitations of this case report (no seizure documented on EEG, no definite proofs of a metabolic, inflammatory or infectious process) and considering all the points raised in the discussion, we formulate the hypothesis that this observation may be consistent with the involvement of basal ganglia in epileptic seizures, as a part of a modulatory control system over seizures rather than a propagation pathway. □

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