Neurological worsening after seizures in post-stroke epilepsy: a persistent Todd’s paralysis?

Abstract
Transient neurological deficit after a seizure, known as a Todd’s paralysis, has been widely discussed in the literature. However, there is little data about the clinical worsening after a seizure in epilepsy post-stroke such as the case described below. If this worsening is a persistent Todd’s paralysis remains unknown. Aberrant neurogenesis and other mechanisms such as hypoxic or metabolic disturbances may be implicated in the absence of recovery after a seizure in previously infarcted tissue. The possibility of this worsening should be taken in account in order to establish an adequate antiepileptic treatment as early as seizure is suspected.

Keywords: Epilepsy- Paralysis- Todd- Stroke- Treatment.

Neurological deficit after a seizure: Todd’s paralysis
The first report about neurological deficit after a seizure was reported by Brauvais [8] and later confirmed by Todd [9] in his lectures about Epileptical Hemiplegia: “A patient has a fit, distinctly of the epileptic kind; he comes out of it paralyzed in one half of the body; generally that side is paralyzed which had been more convulsed than the other, or which had been alone convulsed; but the paralysis may occur where both sides had been convulsed equally. The paralytic state remains for a longer or shorter time, varying perhaps from a few minutes or a few hours to three or four days, or even much longer”; coined as a Todd’s paralysis [9].

Controversy about the Todd’s paralysis etiology has been reflected by several authors [9-13]. The exhaustion [9-11] or inhibition theories [12, 13] could explain the deficit. The former could be in part related to local anoxia explained by insufficient oxygen supply in a very active neuronal region [12, 13] or substrate depletion [13] during postictal neuronal depression [11]. A region already damaged by an ischemic lesion might predispose to insufficient metabolism [13]. The direct involvement of neuronal structures distally to the damage might be important. Thus the thalamus is involved in cortical injury induced-epilepsy such as a stroke, leading to the idea that a structure remote from but connected to primary damaged tissue can be considerably involved in seizures [4].

Recent experimental studies have shown the implication of neural stem cells in the remodelling after a stroke [5]. This extension of remodelling increased with the size of ischemic damage [6]. Aberrant neurogenesis may be produced after a stroke [6], also in the aged brain of elderly people [7]. These aberrant neurons could be stably integrated play a role in the pathogenesis of epilepsy seen in these patients [6].

Résumé
Le déficit neurologique transitoire après une crise, connu sous le nom de paralysie de Todd, a été largement discuté dans la littérature. Cependant, il existe peu de données sur l’aggravation clinique après une crise d’épilepsie post-AVC comme dans le cas décrit ci-dessous. Si cette aggravation est une paralysie de Todd persistante reste inconnue, la neurogène aberrante et d’autres mécanismes tels que des troubles hypoxiques ou métabolique peuvent être impliqués dans l’absence de reprise après une crise dans le tissu infarci précédemment. La possibilité de cette dégradation doit être pris en compte afin d’établir un traitement adéquat antépileptique dès que l’origine épileptique de la crise est suspectée.

Mots-clés : Épilepsie- Paralysie- Todd- Ischémie cérébrale- Traitement.

Post-stroke Epilepsy
Seizures after stroke are considered as one of the major causes of epilepsy in adults, above all in the elderly [1], and account for up to one-third of newly diagnosed seizures [2]. The early report in the literature recognising the importance of cerebrovascular disease on the seizure production was described by Fine [3]. This author held the idea that when one considered the brain damage resulting from cerebral thrombosis it was surprising that recurrent epilepsy did not occur more often in these patients [3].

The mechanism of the seizures after an ischemic stroke could be explained by regional metabolic dysfunction and the release of excitotoxic neurotransmitters secondary to hypoxia [1]. In the case of hemorrhagic stroke, the combination of space-occupying lesions, ischemia and blood products might provoke early seizures [1].

In either case, meningoencephalitis might produce an epileptogenic effect with delayed seizures [1]. The implication of neuronal structures distally to the damage might be important. Thus the thalamus is involved in cortical injury induced-epilepsy such as a stroke, leading to the idea that a structure remote from but connected to primary damaged tissue can be considerably involved in seizures [4]. Recent experimental studies have shown the implication of neural stem cells in the remodelling after a stroke [5]. This extension of remodelling increased with the size of ischemic damage [6]. Aberrant neurogenesis may be produced after a stroke [6], also in the aged brain of elderly people [7]. These aberrant neurons could be stably integrated play a role in the pathogenesis of epilepsy seen in these patients [6].

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phenomenon. However, there are stroke patients where clinical worsening remains persistent:

A 54-year-old male was admitted on the 23th of November 2011 due to a right hemiparesis and global aphasia (NIHSS 17). A cranial CT showed an extensive ischemic lesion in the left middle cerebral artery (MCA) territory. Clinical evolution showed a NIHSS of 9 one week after admission. Follow-up showed a neurological progressive improvement with a slight motor aphasia and a sensitive-motor right hemiparesis (5-/5) five months later. On May 2012, the patient reported brief myoclonus on the right side with a posterior transient worsening of the previous hemiparesis. A cranial MRI showed a chronic left MCA ischemic stroke without new lesions. A control EEG showed no changes. At the time of writing the patient presented a slight improvement in comprehension but neurological status is persistently worse than previous neurologic deficit. This case illustrates a stroke patient with previous slight neurological sequelae who worsened after the first generalized seizure. While several reports about Todd’s paralysis have been described in the literature, data about clinical worsening of the previous neurological deficit in these stroke patients has been scarcely reported [3, 17]. In 1967 Fine described in one patient a greater deficit of the previous poststroke hemiplegia after a seizure, which was sufficient to clinically appear to be a new acute ischemic or hemorrhagic stroke [3]. Later, Bogousslavsky et al. reported that one fifth of patients with delayed seizures after a stroke may have permanent worsening of their neurologic deficit as a consequence of seizures [17].

Whether persistent worsening of the previous neurologic deficit in stroke patients is a persistent Todd’s paralysis remains unknown. Previous ischemic cerebral lesion may suppose a substrate where both theories, the inhibition and exhaustion theories previously mentioned, may produce longer effects. The hypothesis supported by Bogousslavsky et al. about the clinical worsening in stroke patients, was due to a potential direct harmful effect of the seizures over the previous infarcted area [17]. The absence of new lesions on neuroimaging studies and similarities between anatomo-pathological changes resulting from ischemic injuries and those from seizures may support this hypothesis [17]. On the other hand, evidence from neuropathology, neuroimaging, neuropsychology and laboratory studies has demonstrated neuron injury in recurrent epilepsy [18]. It is well known that status epilepticus can have devastating consequences, but even an isolated seizure may be sufficient to cause injury and prolonged consequences [19]. The damage might be produced as either a direct or indirect mechanism. As a direct mechanism, experimental seizures have shown morphological and anatomical changes such as synaptic reorganization, neuronal loss and gliosis [19]. Moreover, progressive pathological changes may be seen to be associated with epilepsy in relation to neuronal plasticity [6, 7, 19]. Seizure-associated hypoxemia, ischemia or substrate insufficiency might be considered as an indirect mechanism [19]. An increase of the mismatch between supply and demand under ischaemic conditions may allow ionic and mitochondrial disturbances, and an irreversible state of injury [20].

Thus the exhaustion theory might partially account for the worsening of the symptoms in the case of previously damaged ischemic tissue where a seizure may provoke a persistent metabolic and parenchymal lesion. Difficulties in complete recovery by aberrant neurons described in the remodelling after a stroke might play an important role in maintaining the neurological worsening.

### Clinical implications

Taking into account individual variability, it is not possible to determine which stroke patients will develop this clinical worsening. However while the antiepileptic prophylactic treatment is not recommended in ischemic lesions, the clinical implications of the persistence of neurological deficit after a seizure may indicate the initiation of antiepileptic treatment as soon as a seizure is suspected in each individual. In our case, treatment was not initiated at the time of partial seizures due to the preference of the patient himself. The presence of a posterior generalized seizure with a worsening of neurological status pointed towards the need to begin early antiepileptic treatment.

### Conclusions

Whether neurological worsening after a seizure in epilepsy post-stroke is simply a persistent Todd’s paralysis remains unknown. Aberrant neurogenesis and other mechanisms such as hypoxic or metabolic disturbances may be implicated in the absence of recovery after a seizure in previously infarcted tissue. The possibility of this worsening should be taken in account in order to establish an adequate antiepileptic treatment as early as seizure is suspected.

### References