
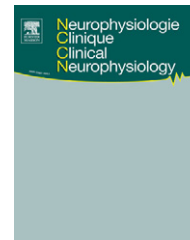




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# Transient post-traumatic locked-in syndrome: A case report and a literature review

## À propos d'un cas de syndrome de dé-efférentation post-traumatique réversible. Revue de la littérature

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### KEYWORDS

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Head trauma;  
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Event related  
potentials;  
P300

### Summary

**Introduction.** — Post-traumatic locked-in syndrome may be particularly difficult to recognize, especially when it follows a state of coma and presents the clinical feature of a “total” locked-in syndrome.

**Patient and methods.** — A 56-year-old male with a closed head injury was admitted in intensive care unit (ICU) with GCS=4 (V1, M2, E1). Computed tomography (CT) scan disclosed a limited subarachnoid haemorrhage in the sylvian region without any brain oedema or ventricular shift. The GCS did not change until day 6. At the same time EEG showed a reactivity to acoustic stimuli consisting in the paradoxical appearance of a posterior rhythm in alpha range (10–12 c/s), blocked by passive eye opening. Early cortical components (N20–P25) of somatosensory evoked potentials were normal on both hemispheres; middle components were also clearly evident. Magnetic resonance imaging of the brain showed both diffuse and midbrain axonal injuries, particularly in a strategic lesion involving both cerebral peduncles. Event related potentials showed N2 and P3 components to stimulation by rare tones.

**Conclusions.** — A comprehensive multimodal neurophysiological approach, using the more informative tests and the proper time of recording, should be included in protocols for patients with severe head trauma, in order to establish the actual patient's clinical state and to avoid

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## MOTS CLÉS

Traumatisme crânien ;  
Syndrome de verrouillage ;  
Syndrome de dé-efférentation ;  
EEG ;  
Potentiels évoqués somesthésiques ;  
Potentiels évoqués cognitifs ;  
P300

that a locked-in syndrome state be mistaken for prolonged coma, vegetative state, minimally conscious state or akinetic mutism. Neurophysiological evaluation before discharge from ICU can be a baseline evaluation useful for the follow-up of low-responsive patients in the neuro-rehabilitation unit.

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## Résumé

**Introduction.** — La reconnaissance d'un syndrome de dé-efférentation (*locked-in*) dans le décours d'un traumatisme crânien peut s'avérer difficile, d'autant plus qu'il succède directement à une période comateuse et qu'il se présente sous une forme complète.

**Patient et méthodes.** — Un homme de 56 ans était admis dans une unité de soins intensifs avec un score de Glasgow de 4 (V1, M2, E1) des suites d'un traumatisme crânien fermé. L'examen tomodensitométrique cérébral objectivait une hémorragie sous-arachnoïdienne limitée dans la région sylvienne droite, sans œdème cérébral ni déviation du système ventriculaire. Le score de Glasgow était inchangé au sixième jour. L'électroencéphalogramme (EEG) montrait une réactivité du tracé aux stimulations auditives, de même que l'apparition paradoxale d'un rythme dans la bande alpha (10–12 c/s) dans les régions postérieures, supprimé par l'ouverture des yeux. Les composantes corticales précoces (N20–P25) des potentiels évoqués somesthésiques étaient normales sur les deux hémisphères ; les composantes moyennes étaient également clairement identifiées. La résonance magnétique cérébrale montrait une atteinte axonale diffuse dans le mésencéphale, et particulièrement une lésion stratégique touchant les deux pédoncules cérébraux. Les potentiels évoqués « cognitifs » montraient la présence des composantes N2 et P3 en réponse aux stimulations rares.

**Conclusion.** — Une évaluation neurophysiologique multimodale exhaustive, utilisant les tests les plus informatifs et la période d'enregistrement appropriée, devrait faire partie de l'évaluation des traumatisés crâniens, afin d'apprécier correctement la situation clinique du patient et de ne pas confondre un syndrome de dé-efférentation (*locked-in*) avec un coma prolongé, un état végétatif, un état de conscience minimal ou un mutisme akinétique. Une évaluation neurophysiologique avant le départ des soins intensifs peut constituer un bilan de départ pour l'évaluation ultérieure des patients peu réactifs dans un centre de réadaptation fonctionnelle.

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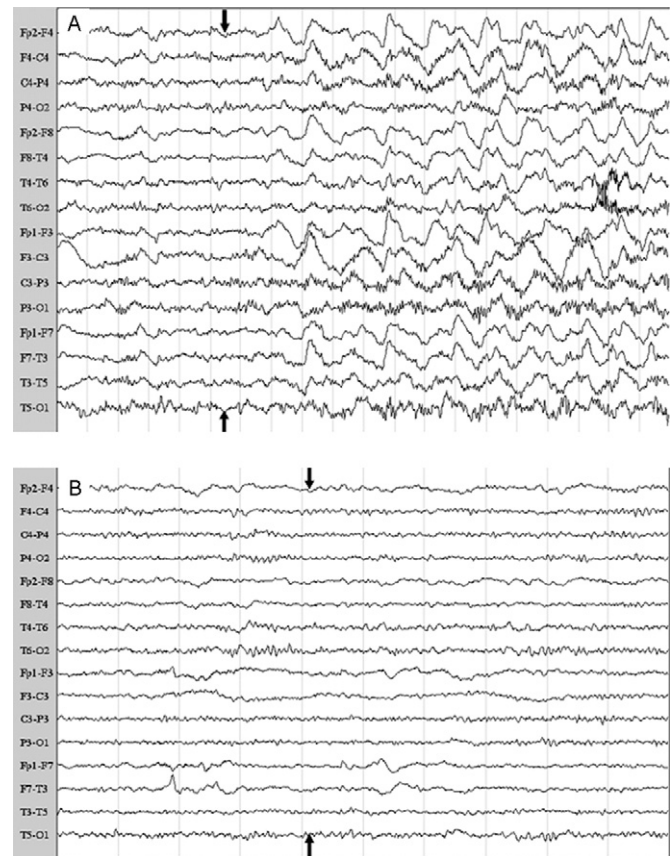
## Introduction

The locked-in syndrome (LIS) was first described in 1844 by Dumas in his novel "Le Comte de Monte-Cristo" [7] as "a dead body with living eyes". It is a state in which selective supranuclear motor de-efferentation produces paralysis of all 4 limbs and the last cranial nerves without interfering with consciousness [28], even if vigilance is often fluctuating, especially in the acute state [12]. Although stroke is the most frequent cause of LIS [18], other aetiologies are known, including traumatic brain injury (TBI) [3], tumor [5], multiple sclerosis [9], pontine abscess [21], brainstem encephalitis, and central pontine myelinolysis [26]. Head trauma is the second most frequent cause of LIS [18]. Post-traumatic LIS is particularly difficult to recognize because it follows a state of coma and may show the clinical feature of "total" LIS, in which even eyes and lids movements are lost [18]. The main diagnostic challenge is recognition of the syndrome itself from other clinical states that can mimic LIS, as coma, vegetative state, akinetic mutism, and minimally conscious state. Keeping these pitfalls in mind, we report the case of a man with severe head trauma, in whom the multimodal neurophysiological approach, as an extension of clinical examination, allowed us early identification of a "total" LIS.

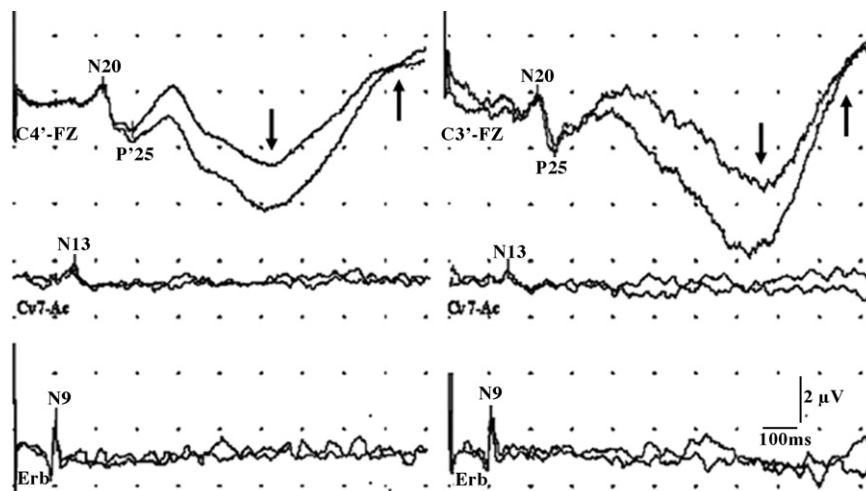
## Case report

A 56-year old male was admitted to our hospital because of closed head injury in a car accident. His medical history did not show any significant disease except for high blood arterial pressure. When he arrived at emergency department, he was comatose (Glasgow Coma Scale [GCS] = 4), with the right pupil larger than the left, both scarcely reactive to light. The first computed tomography (CT) scan showed a limited subarachnoid haemorrhage in sylvian region without any brain oedema or ventricular shift. He was intubated, transferred to the intensive care unit (ICU) and put under mechanical ventilation. Neurosedation (midazolam 0.02 mg/kg per hour) was maintained for the first 2 days. Basing on CT scan, no intracranial pressure (ICP) monitoring was performed. Over the next 6 days GCS did not change (GCS = 4; V1, M2, E1), photomotor response was present, no facial and limb movements were evident spontaneously or in response to pain. A new CT scan did not show any new parenchymal alterations. Electroencephalogram (EEG) recorded on day 7 showed a reactivity to acoustic stimuli with the appearance of an anterior high-voltage rhythmic delta activity and a paradoxical appearance of a posterior rhythm in the alpha range (10–12 c/s), blocked by passive

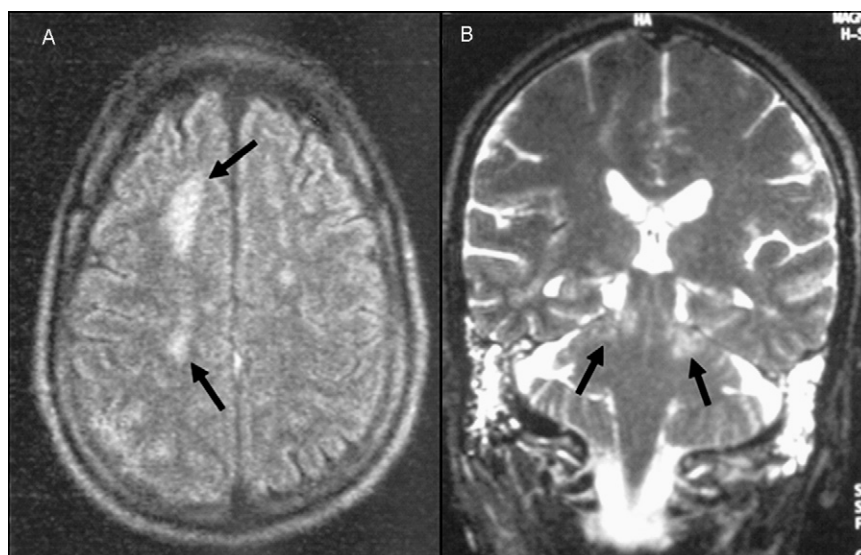
eye opening (Fig. 1). This EEG pattern was suggestive of a mild consciousness disorder rather than of a coma state, as it could have been suspected on the basis of the GCS score. Given the discrepancy between a slight consciousness disorder, as suggested by the EEG, the low score of motor responses ( $M=2$ ), and the absence of facial movements, we suspected a “total” LIS. Median-nerve somatosensory evoked potentials (SEPs) were obtained 8 days after admission in ICU: these showed early cortical component (N20–P25) on both hemispheres with normal amplitude and morphology, and central conduction time (CCT) at upper limits of normal (7.5–7.6 msec) (Fig. 2). Middle SEP components were also clearly evident. Since neurophysiological findings (posterior reactive alpha activity and clear-cut SEP middle components) were not consistent with a state of coma, we suspected a milder consciousness disorder. A magnetic resonance imaging (MRI) of the brain was performed on day 10 and showed both diffuse and midbrain axonal injuries, particularly in a strategic lesion involving both cerebral peduncles (Fig. 3). Considering that a state of complete midbrain de-efferentation might have prevented recognition of an initial consciousness recovery, we recorded Event Related Potentials (ERP) on day 12. Indeed, this test is more appropriate to ascertain the presence of cognitive activity. ERPs were recorded by a passive odd-ball paradigm using auditory stimulation. ERPs consisted of the N1 and P2 components to both frequent and rare tones; N2, P3a and a wide positivity at Pz (in the 500–900 ms range), which is more likely to correspond to a P3b component, were also elicited by target stimuli (rare tones) (Fig. 4). On day 13, the patient underwent tracheotomy and, 2 days later, he was moved to the neurological ward. On day 17, he showed initial expression of communication, moving left toes in response to verbal commands. During the following 4 weeks the patient showed further recovery in his motor function (slight leg flexion, left-hand and mouth closure) in response to verbal commands. A surgical feeding tube was required and the patient was discharged and followed an intensive rehabilitation program, with improvement of tetraparesis. After 12 months, the patient was able to walk without aid; however, his gate was spastic. Cognitive



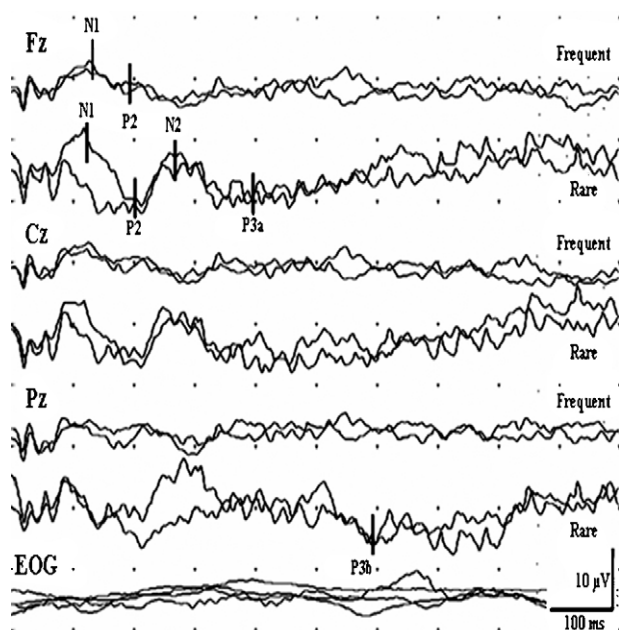
**Figure 1** EEG recorded on day 7. A. Acoustic stimulation (black arrows) determines appearance of rhythmic delta activity on frontal derivations. B. Passive eye opening (black arrows) produced a sudden desynchronisation of posterior rhythmic activity in alpha range (about 10 Hz). Sweep time: 10 sec/pg; Sensibility: 7,0  $\mu$ V/mm.



**Figure 2** Somatosensory Evoked Potentials recorded on day 8. Early cortical components (N20–P25) and middle components (indicated by arrows) with normal latencies and amplitudes are present on both hemispheres.



**Figure 3** MRI performed on day 10. A. T1-weighted axial image. Note the diffuse axonal injury (DAI) in white matter of left hemisphere (arrows). B. T2-weighted coronal image. Note the DAI at level of cerebral peduncles in midbrain (arrows).



**Figure 4** Event Related Potentials in response to frequent and rare tones obtained on day 12. ERP components N1 and P2 are present in response to both 'frequent' and 'rare' tones, and N2 and P3a components are present only in response to 'rare' tones. A wide positivity (in the 500–900 ms range) was also recorded at Pz in response to rare tones, it is very likely to correspond to a P3b component.

functions recovered better than motor ones, the patient was mildly dysarthric but able to verbally communicate.

## Discussion

We described a patient with traumatic brain injury in whom a comprehensive multimodal neurophysiological approach helped us suspect and early recognize a transient LIS.

León Carrión et al. [18] reported that diagnosis of LIS is usually made around the middle of the second month after onset. A delayed diagnosis occurs more frequently in case of TBI because transition from coma to LIS may be very difficult to detect [4]. Many factors contribute to diagnostic misinterpretation. Firstly, a vascular LIS, once suspected, is easily diagnosed by CT and MRI; by contrast there is less knowledge of the post-traumatic LIS, as it is less frequent than the vascular one (13.6% of cases [18]) and CT scan lesions may be non specific and not always localized in ventral pons. Secondly, the clinical feature of "total" LIS, in which also eye and lid movements are lost, precludes all type of communication [18,31], which makes this condition hardly discernible from coma. Thirdly, the classical LIS may not be recognized because of the vigilance fluctuations occurring in the acute state [4,12]. Due to the above-mentioned pitfalls, great care must be taken at time of diagnosis of post-traumatic LIS and all available diagnostic tools should be used. CT scan together with conventional MRI is essential to define pathogenesis and topography of traumatic damage. Functional MRI (fMRI) may offer a complementary approach to the assessment of consciousness in low responsive brain-injured patients [24,25]. However, lacking large-scale multicentre studies [17] the real contribution of functional neuroimaging is currently investigational, not yet clinical [8]. Moreover, these techniques are complex, time consuming, and are not available at the bedside. Neurophysiological techniques overcome many of these limitations. Preserved EEG reactivity of a posterior alpha rhythm [2] is a cardinal feature of LIS. Bassetti et al. [2] considered alpha reactivity appropriate to ascertain preserved consciousness. Some authors reported cases of LIS with non-reactive alpha [12,15] and concluded that the absence of EEG reactivity cannot exclude LIS diagnosis. Nevertheless, reactive alpha rhythm remains the most useful bedside method to suspect a LIS. SEPs have limited diagnostic value in LIS, ranging from fully normal findings to unilateral or bilateral abnormalities [12].

In our patient the EEG reactivity with paradoxical appearance of posterior alpha rhythm, demonstrated an arousable



patient with fluctuating vigilance. Early cortical SEP components were normal and we also recorded middle components of high amplitude. These components are immediately lost at induction of anaesthesia, together with loss of consciousness [27,30], so their presence in our patient was conflicting with the clinical suspicion of deep coma (GCS=4). In patients with severe head injury, lesions are common in both supratentorial and infratentorial compartments, but it is also possible to find a predominant brainstem lesion (8.8% reported by Hashimoto et al. [13]) usually considered to be a diffuse axonal injury caused by vigorous shear force extending to brainstem [19]. The midbrain sensitivity to head deceleration is a well-known phenomenon [14]. This can give rise both to a LIS (in case of a predominantly anterior midbrain lesion), in which case the patient is likely to be conscious, or to another state (in case of a predominantly posterior midbrain lesion involving the midbrain reticular formation), in which case the patient is less-likely to be conscious. The EEG could be useful tool to differentiate both states (normal in anterior lesions, slowed in posterior lesions). In our patient a reactive EEG and normal SEP were indicators of preserved neural conduction across dorso-lateral portion of midbrain. In our patient, MRI showed a strategic topography of diffuse axonal injury involving both cerebral motor peduncles. Then, we attributed the persistent low GCS motor score to a tetraplegia caused by axonal damage involving cerebral peduncles. In fact, the pathogenetic role of this lesional site in determining LIS is in keeping with the recently described exceptional case of vascular "total" LIS due to bilateral infarctions of the cerebral peduncles [32].

Our hypothesis of a transition from coma to LIS based on EEG and SEP findings was then confirmed by MRI findings. Assuming that the complete motor deficits masked the behavioural indicators of consciousness and that there were no other clinical methods available for assessing consciousness, we decided to record ERPs to detect the presence of cognitive activities. The P3b component of ERPs is usually elicited by active discrimination between frequent and infrequent targets, but it can be evoked also by passive discrimination [29] using the same paradigm. The P3b can be studied in non-cooperative patients also. While several authors recorded ERPs in low-responsive patients to determine the prognosis of "awakening" [6], few LIS patients underwent ERPs recording [22]. As these patients presented vascular LIS, neurophysiological data were not adding further information for diagnosis. In our patient, N2–P3b complex elicited by rare stimuli pointed out the presence of cognitive activities and it could provide more convincing arguments favouring some preservation of consciousness [10,11]. The association of ERP data with those obtained by EEG and SEP gave us strong indications that some patients could have some sort of consciousness beyond clinical evidence. We obtained clinical confirmation when the patient showed response to verbal command with movement limited to his left foot.

A high rate of misdiagnosed vegetative states has been reported [1], especially in patients with traumatic brain injuries. We believe that post-traumatic LIS incidence is underestimated, or at least identified with delay of weeks or months, thereby explaining most of the cases of delayed "awakening" [21]. In fact, although trauma is reported as

the second most frequent cause of LIS [18], only 14 post-traumatic LIS have been described [3,4,16,20,23,33]. The moment of LIS diagnosis, type of lesion, and results of neurophysiological examinations were not always reported in these papers. Furthermore, except for the report of Zampella et al. [33], these studies were published before MRI was available and it was difficult to understand the true aetiology (post-traumatic versus vascular) and pathogenesis of LIS. It is difficult to compare our case with the previous literature.

We believe that in clinical practice a comprehensive multimodal neurophysiological approach, using the more informative tests (EEG, EP, ERP), should be included in protocols for evaluation of poorly-responsive patients with severe head trauma in order to establish the actual patient clinical state and to avoid that a LIS state be mistaken for prolonged coma, vegetative state, minimally conscious state or akinetic mutism.

Early recognition of LIS state is important for several reasons. First, the ICU team must realize that the patient is not comatose but "conscious" and they have to reassure the patient that his real state is understood. It is necessary to explain to the relatives the true condition of patient (he can understand but he cannot move). An intensive rehabilitation training specific for LIS (breathing, swallowing, speech) should be started early. It is expert's opinion that the main cause of misdiagnosis of disorders of consciousness is discontinuity evaluation from the acute care to long-term care setting [8]. Neurophysiological evaluation of low responsive patients before discharge from ICU can be useful for the following assessment in neuro-rehabilitation unit.

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