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Original article

# "The locked-in syndrome": Can it be unlocked?

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ABSTRACT

Locked-in syndrome is one of the most disabling states characterized by the preservation of conscious mind within a quadriplegic and anarthric body. Recently, there has been increased public awareness about this rare condition, and more cases are reported. The commonest causative lesion is bilateral ventral pontine damage secondary to vertebrobasilar artery occlusion. Clinicians need to be familiar with the condition because there is a high chance of erroneous diagnosis, such as coma or vegetative state, after a prolonged unconscious state. It is often the relatives or carers who recognize the conscious state first and report that the patient can communicate through his eyes. Because of complications, such as aspiration and sepsis, about 40–70% of sufferers die in acute phase of illness. However, advancements in medical care, rehabilitation, and communication technology have enabled many chronic locked-in syndrome patients to lead meaningful lives in the society with the help of family and friends.


## 1. Introduction

Locked-in syndrome (LIS) can best be described as a disease process where the brain is fully functional while confined within a nonfunctional body. Often described as the closest thing to being "buried alive," this devastating condition is characterized by the preservation of consciousness within a quadriplegic and anarthric body.

The condition was first described in 1966 by Plum and Posner,[1] and although rare, public awareness of "the Locked-in syndrome," "maladie de l'emmuré vivant," or "cerebromedullospinal disconnection" has increased a great deal over the last 10 years. Much of this can be attributed to high-profile celebrities, such as theoretical physicist, Stephen Hawking, or even references to the syndrome in popular American dramas, *CSI: New York* and *Desperate Housewives*. *Parisien* journalist and editor in chief of the fashion magazine *Elle*, Jean-Dominique Bauby, played the most important role in creating awareness.[2] He suffered from this condition after a brainstem stroke in 1995 and sought to show the world that such impediment of movement and speech need not prevent patients from living a fulfilling life. He has proven it through his book, "*Le Scaphandre et le papillon*" (Ed. Robert Laffont), dictated through communication aides using his left eyelid alone. Before his death, he founded the Association of Locked in Syndrome (ALIS) in France, aimed to help patients and their families. ALIS has got a unique database of patients with LIS, very useful in researching this disease (www.club-internet.fr/alis).

Geriatricians should be familiar with LIS because of high incidence of stroke and increasing post-stroke survival in the elderly. On the other hand, we will come across veteran LIS patients who are surviving for decades because of advancement in medical care and rehabilitation facilities.[3]

## 2. The LIS

The American Congress of Rehabilitation Medicine (1995) defined LIS as the presence of (1) sustained eye opening (bilateral ptosis should be ruled out as a complicating factor); (2) preserved basic cognitive abilities; (3) aphonia or severe hypophonia; (4) quadriplegia or quadriparesis; and (5) a primary mode of communication that uses vertical or lateral eye movement or blinking of the upper eyelid.

LIS can be subdivided on the basis of the extent of motor impairment: (1) classical LIS—total immobility except for vertical eye movements or blinking; (2) incomplete LIS—with remnants of voluntary movements; (3) total LIS—complete immobility, including all eye movements, combined with preserved consciousness.[4]

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The condition differs from the persistent vegetative state. In persistent vegetative state, a patient may be awake without awareness. On the contrary, LIS is a state of wakefulness *with* detectable awareness, where survival does *not* depend on artificial help.[5,6] The *detectable awareness* relies on the fact that vertical gaze and upper eyelid movement are preserved. For this reason, voluntary vertical and upper eyelid movement must be assessed in all unresponsive individuals.[7]

## 3. Etiology (Box 1)

LIS is mostly caused by bilateral ventral pontine lesions.[1] Pons lies superior to the medulla oblongata as the upward curving, "middle section" of the brainstem. It bridges the cerebellar hemispheres and higher brain centers with the spinal cord, acting to control arousal, autonomic function, blood pressure, respiratory function, and movement. The disease processes pathologically affecting the large ventral aspect of the pons or "basis pontis" can cause bilateral interruption to the corticospinal and corticobulbar tracts running through the structure, disrupting voluntary supply to the limbs and medullary motor nuclei. It prevents voluntary movement and speech leading to the LIS.[8] Because consciousness and cognition are controlled by areas of the brain above the pons, they remain preserved. Similarly, the tegmentum of the pons is spared, leading to preserved vertical eye movements and blinking.[7,8]

The most common cause of damage to the ventral pons is through vertebrobasilar artery occlusion, more specifically, basilar artery thrombosis.[8] There can be atheromatous plaques leading to direct ischemia, thrombosis, thromboembolism, aneurysm, or dissection.[9]

## 4. Clinical features

Mostly patients with acute brainstem lesions remain comatosed for days or weeks requiring mechanical ventilation in critical-care settings. They gradually wake up remaining paralyzed and voiceless. Sometimes, patients presenting with herald hemiparesis progress into complete locked-in state in hours.[10] There is loss of voluntary limb movement accompanied by upper motor neuron signs, for example, limb spasticity, exaggerated deep tendon reflexes, and extensor plantar responses bilaterally.

Consciousness is preserved; however, impaired attention, executive function, memory, and perception have been observed.[11] Complete anarthria is secondary to facio-glosso-pharyngo-laryngeal paralysis, also leading to dysphagia and lack of facial expression.[12] Because the supranuclear ocular motor pathways lie more dorsally, there is sparing of the midbrain tectum, leading to communication through eyelid and vertical eye movement. To communicate "yes" can be indicated by one blink or looking up and "no" can be indicated by two blinks or looking down. In contrast, horizontal eye movement palsy leads to blurring and diplopia of vision. Emotional lability has been reported along with an increase in depressive states.[13]

Box 1. Causes of locked-in syndrome

- Cerebrovascular disease;
- Iatrogenic, e.g., muscle relaxants used in anesthesia;
- Traumatic brain injury;
- Neuronal damage (e.g., central pontine myelinolysis, end-stage amyotrophic lateral sclerosis);
- Brain stem tumor;
- Encephalitis;
- Transient—Guillain-Barre syndrome.

In a case series of 50 chronic LIS, nearly all patients complained of spasticity, 75% had difficulty in swallowing oropharyngeal secretions, 66% had sialorrhea, and 61% had respiratory difficulties of various types.[14]

## 5. Diagnosis

By definition, LIS is a clinical diagnosis. It is important to carefully assess vertical eye movement and upper eyelid movement in the otherwise unresponsive individual.[7,15] Reassessments at time intervals are very important as patients may present after a period of unconsciousness or vegetative state where cognitive function has been dismissed.[7] Unless the physician is familiar with LIS, there is a likely chance of erroneous diagnosis of coma, vegetative state, or akinetic mutism. Clear lines of communication with family members and carers play a major role. It is often the relatives who realize first that the patient is conscious and could communicate through eye movements. In an ALIS survey of 44 patients, the consciousness was first realized by family members in 55%, physicians in 23%, nurses in 18%, and others in 4% of cases.[15]

The time elapsed between brain insult and diagnosis was on average 78 days and several patients were diagnosed after 4 years! This further adds to the high chances of misdiagnosis.

## 6. Investigations (Box 2)

No one investigation can definitively establish LIS. There are several tests and neuroimaging techniques that aid in diagnosis. The basic investigations are similar to those of any other stroke.

Computed tomography (CT) is well known to be inferior to magnetic resonance imaging (MRI) in imaging of the posterior aspects of the brain. Lesions in the brainstem are best visualized through MRI and, more specifically, through MRI with diffusion-weight imaging for the detection of acute infarcts. CT of the head has a role to play when intracranial hemorrhage is suspected or when MRI is contraindicated, whereas magnetic resonance angiography is the imaging modality of choice when visualizing the extracranial arteries looking for a cause of ischemia or infarction. It has largely replaced conventional angiogram now.

LIS is defined as a state of wakefulness *with* detectable awareness within a non-functional body. Although the electroencephalogram (EEG) cannot definitively identify such awareness, a normal EEG in an unresponsive patient helps to distinguish LIS from other forms of coma, such as the persistent vegetative state.[5,6]

Positron emission tomography-scanning studies of brain have shown no clinically significant metabolic signs of reduced function in LIS patients when compared with those of age-matched controls. This is in contrast to vegetative states.[16] In future, it can be a very important differentiating tool. High cost and poor availability are the major limitations presently.

## 7. Treatment

There is currently no medical cure for LIS. The treatment revolves around the general management of stroke and critical-care

Box 2. Investigative aides in diagnosis of locked-in syndrome

Magnetic resonance imaging—brain;
Magnetic resonance angiogram;
Transcranial dopplers;
Computed tomography—brain
Positron emission tomography scan
Electroencephalogram