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Review

Moving into the wide clinical spectrum of consciousness disorders: Pearls, perils and pitfalls

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ABSTRACT

The last few years have been characterized by a growing interest of the medical and scientific world for the field of consciousness and its related disorders. Medically speaking, consciousness can be defined as the state of awareness of self and environment and the alertness to external stimulation, besides responsiveness to inner need.

Transient loss of consciousness can be due to alterations in cerebral blood flow leading to fainting or syncope, migraine, metabolic dysfunctions, unexpected intracranial pressure increases, epileptic seizures, and sleep disorders. Chronic disorders of consciousness are a tragic success of high-technology treatment, in an attempt to maintain or reestablish brain function, which is to be considered as the main goal of therapeutics. Management of vegetative or a minimally conscious state individuals involves charily getting the right diagnosis with an evidence-based prognosis, also taking into account the medical, ethical, and legal key factors of the ideal treatment. This paper is aimed at exploring the wide spectrum of consciousness disorders and their clinical differential diagnosis, with particular regards to those with a negative impact on patient and their caregiver quality of life, including epilepsy, sleep disorders, and vegetative/minimally conscious state.

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1. Introduction

The terms consciousness, confusion, stupor, unconsciousness, and coma have been given many different meanings so that it is really difficult to avoid ambiguity in their use. Medically speaking, consciousness can be defined as the state of awareness of self and environment and the alertness to external stimulation, besides responsiveness to inner need [1]. Advances in neurobiology of consciousness lead to believe that the upper brainstem nuclei have a pivotal role in arousal, and that the activity of the thalamus and cortex provides much of the content of consciousness [2,3].

In particular, consciousness has 2 clinical elements:

- (1) *wakefulness*, which is mediated by the ascending reticular activating system (ARAS) of the brainstem and its thalamo-cortical connections, and
- (2) *awareness* of one's self and the environment, which is mediated by the cerebral cortex and its intracortical, thalamo-cortical, and cortico-sub-cortical connections [4].

Alterations one or both of these components may lead to disordered state of consciousness [5]. Disordered states of consciousness define a broad category encompassing a spectrum of cognitive abnormalities, i.e. from mild confusional states, delirium and dementia to coma, vegetative state (VS), minimally conscious state (MCS), and brain death (Figure).

2. Episodic impairment of consciousness

Transient loss of consciousness can be due to alterations in cerebral blood flow leading to fainting or syncope, migraine, metabolic dysfunctions, unexpected intracranial pressure increases, cerebral ischemia or hemorrhage, epileptic seizures, and sleep disorders [6]. Differentiating anxiety attacks, psychogenic non-epileptic seizures (PNES), and malingering from the abovementioned conditions may be really difficult.

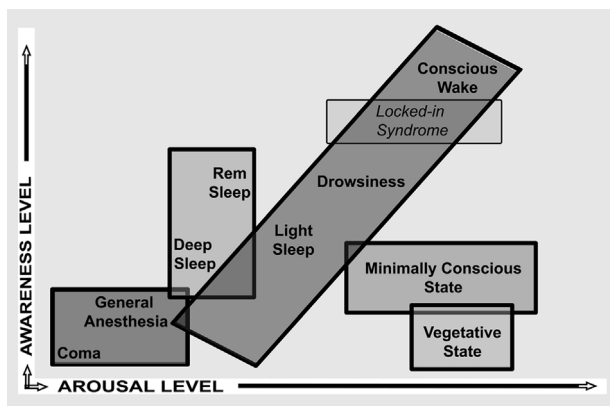


Figure – The key elements of consciousness, i.e. wakefulness and awareness of environmental and self that are positively correlated in the physiological states. A complete dissociation between such elements is clearly seen in vegetative state. Notably, individuals suffering from coma are unconscious and cannot be awakened.

Notably, the right diagnosis may not be reached without accurate laboratory tests and long follow-up periods.

2.1. Syncope

Syncope may be caused by a reduced cardiac output owing to heart arrhythmias, outflow obstacle, orthostatic hypotension, hypovolemia or reduced venous return. Metabolic dysfunction, caused by hypoxia, anemia, hypoglycemia or drugs, may usually lead to presyncope (i.e. a sensation of an imminent faint) or, less commonly, to syncope. Of note, consciousness may be impaired in absence seizures, generalized tonic-clonic seizures (GTCS), and complex partial seizures that, in most cases, can be easily distinguished from syncope.

However, the differential diagnosis may be very difficult when syncope is associated to myoclonic jerks, upward version of the eyes and short automatism [7-11].

2.2. Epileptic seizures

Epileptic seizures (ES) are the manifestation of cortical neuron abnormal hypersynchronization with a consequent hyperexcitable discharges. Physiologically, ES has been defined as an abrupt alteration of brain function, subsequent to a paroxysmal high-frequency and high voltage electrical discharge, mainly arising from an assemblage of excitable neurons in any part of the cerebral cortex [12,13]. It is noteworthy that seizures are frequent, aspecific expressions of neurologic disorders, including brain injury, since the leading function of the brain is the transmission of electrical impulses.

Epilepsy is defined as a brain disease characterized by a durable tendency to produce epileptic seizures with the consequent neurobiological, neuropsychological, and psychosocial complications. The diagnosis of epilepsy usually requires the existence of at least 2 unprovoked seizures 24 h apart [14]. Seizures are divided into two categories: partial seizures and generalized seizures. Partial seizures result from a neural discharge within a specific brain area, with focal symptoms that may progress (with or without consciousness impairment) to secondarily generalized seizure, resulting in tonic-clonic activity [15].

Primary generalized seizures are thought to be generated in the thalamus and other related subcortical areas, although EEG recording usually shows a simultaneous activation of both the cerebral hemispheres. Thus, they present with bilateral symptoms and/or signs, and are constantly associated to loss of consciousness. Tonic seizure is the rigid (usually brief) contracture of muscles, whereas the clonic seizure is the longer rhythmic shaking; the consequent GTCS, also defined “a grand mal”, may be considered one of the most dramatic medical illnesses. Patients affected by GTCS and idiopathic generalized epilepsy usually do not have any evidence of history, general or neurologic, laboratory or neuroimaging examination abnormalities. The awake EEG performed in individuals with GTCS may be normal, although some interictal EEG patterns may be typical of specific generalized epilepsy syndromes [16]. Of note, it is sometimes difficult to distinguish ES from PNES, anxiety attacks, and malingering [17].

Status epilepticus is traditionally defined as a continuous, incessant seizure that lasts more than 30 min, or recurrent

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