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Editorial

The Role of Neuroimaging in the Diagnosis, Prognosis and Management of Disorders of Consciousness and Locked-in Syndrome

Abstract: Disorders of consciousness and locked-in syndrome are two completely different neurological conditions which share unresponsiveness or minimal responsiveness at an observable behavioral level. The key element of disorders of consciousness is the loss of self- and environmental awareness, while the main feature of locked-in syndrome is extreme motor entrapment despite preserved awareness. In both cases accurate diagnosis may come late and patients are at risk of being wrongly diagnosed and missing out on appropriate rehabilitative opportunities. Clinical assessment alone often does not suffice in establishing the correct diagnosis and prognosis. The contribution of advanced neuroimaging techniques is essential in order to properly recognize patients' conditions and formulate a tailored rehabilitative approach. Neuroimaging findings are also crucial in identifying the neuropathological substrate of the disorders: they contribute to elucidating the dynamics of cortical-subcortical networks in disorders of consciousness and the neural correlates of recently reported non-motor symptoms in locked-in syndrome.

BEDSIDE ASSESSMENT OF BEHAVIORAL UNRESPONSIVENESS

The growing number of people sustaining traumatic brain injury, stroke and anoxic damage, combined with advances in emergency treatments, have led to an increasing number of patients with disorders of consciousness or locked-in syndrome. Thanks to the widespread diffusion of life support procedures, most of the patients who would have died in the past now survive. However, some of them show persistent *behavioral unresponsiveness or minimal responsiveness*, which may be the result either of an impairment of consciousness or of an extreme limitation of their expressive repertoire. The neuropathological substrate for poor behavioral responsiveness is different in these two cases. In the former, consciousness, the prerequisite for purposeful behavior and interaction with the environment is lacking, while in the latter consciousness is preserved but it lacks viable efferent pathways to express itself [1, 2]. These conditions are known respectively as disorders of consciousness and locked-in syndrome and are extremely different conditions. The bedside assessment of the above patients is very challenging. Misdiagnoses may be avoided by bearing in mind that behavioral unresponsiveness or minimal responsiveness is not synonymous with unconsciousness [3]. Resources such as neuroimaging and neurophysiological tools can be of help in the proper diagnosis of each patient and in prognostic assessment.

DISORDERS OF CONSCIOUSNESS

The times has been that, when the brains were out, the man would die, and there an end. But now they rise again with twenty mortal murders on their crowns, and push us from our stools. This is more strange than such a murder is.

Shakespeare, Macbeth (Act 3, Scene 4, Page 5)

Understanding the complex phenomenon of consciousness is a notoriously challenging task and the links between conscious experience and behavior are not always as straightforward as they seem. Investigating patients with acquired brain injury offers a special opportunity to learn more about consciousness and its behavioural patterns. Disorders of consciousness include coma, unresponsive wakefulness syndrome/vegetative state and minimally conscious state. Coma is characterized by the loss of both wakefulness and awareness while the unresponsive wakefulness syndrome/vegetative state is regarded as a condition of lacking awareness despite recovered wakefulness [4, 5]. Minimally conscious state is characterized by a partial recovery of awareness which is deduced by the regaining of sporadic, fluctuating and non-reproducible purposeful behaviors [6]. The emergence from a minimally conscious state

to a condition of full consciousness is denoted by the recovery of 'core' abilities such as functional object use and the attempt to communicate [7]. New diagnostic categories have recently been introduced. These include minimally conscious state plus/minus, according to the complexity of patients' behaviors, and functional locked-in state, where consciousness is only measurable *via* para-clinical testing [8]. Several assessment difficulties may be encountered in patients with disorders of consciousness when they face additional barriers that hinder their ability to reveal any improvement in consciousness. Such barriers include the presence of aphasia, severe spasticity and concomitant neurological impairments, which all contribute to the rate of misdiagnoses in these patients [9, 10]. Advanced neuroimaging techniques may provide an additional window into the brain of patients, in order to overcome assessment difficulties and to expand our knowledge of consciousness-related networks.

LOCKED-IN SYNDROME

'Sight and hearing were the only senses remaining... It was only, however, by means of one of these senses that he could reveal the thoughts and feelings that still occupied his mind, and the look by which he gave expression to his inner life was like the distant gleam of a candle which a traveller sees by night across some desert place, and knows that a living being dwells beyond the silence and obscurity. In his eyes, shaded by thick black lashes, was concentrated, as it often happens with an organ which is used to the exclusion of the others, all the activity, address, force, and intelligence which were formerly diffused over his whole body; and so although the movement of the arm, the sound of the voice, and the agility of the body, were wanting, the speaking eye sufficed for all' (The Count of Monte Cristo).

Locked-in syndrome is one of the most severe forms of motor disability imaginable. These people are completely entrapped in a non-responsive body and can communicate through an eye-coded system based on eye-blinks and vertical ocular movements which are the only motor outputs preserved [2]. When the syndrome occurs in its total form, ocular and eyelid movements are also compromised: in such cases patients are at increased risk of being misdiagnosed as having a disorder of consciousness, with dramatic detrimental consequences. Thorough training for health professionals in the assessment of such patients is critical. Neuroimaging techniques are essential in order to properly recognize the strategic pontine lesion which is responsible for the interruption of efferent pathways and to investigate any cortical changes which may occur after the initial damage. Patients with locked-in syndrome are traditionally depicted as having fully preserved cognitive functioning, as cortical and sub-cortical structures supporting higher cognitive functions are not involved in the primary damage [2]. However, some cognitive and emotional impairments have recently been reported [11 - 15]. These impairments may be interpreted by thoroughly investigating how cortical-subcortical pathways react to the sudden interruption of efferent corticospinal and corticobulbar tracts.

AIM OF THE SPECIAL ISSUE

The purpose of this special issue is to present updates on the new elements that neuroimaging research may provide in the field of behaviorally unresponsive states. Although behavioral assessment is still the gold standard for the evaluation of these patients, it is sometimes invalidated by the presence of multifaceted cerebral damage which blocks all the communication channels of the patients, leading to unresponsiveness in terms of observable motor behavior. In such cases neuroimaging may be of help in disentangling the wide spectrum of disorders of consciousness (unresponsive wakefulness syndrome/vegetative state and minimally conscious state) and in differentiating these from other minimally responsive states like locked-in syndrome or functional locked-in state. The contribution of neuroimaging research is also valuable in order to recognize the *ghost networks* underlying consciousness. Most importantly, it can help to optimise relationships, treatment, care and rehabilitation. In the case of locked-in syndrome, neuroimaging may, for example, provide a better understanding of cognitive disturbances as a prerequisite to formulate appropriate goal-oriented rehabilitative approaches. This Special Issue serves to share progress made in this challenging area of neuroscience, suggest some possible directions for future research and highlight how increased understanding of these conditions can translate into improved practice in terms of providing people with the best possible care and support. We hope this special issue will be of interest for researchers who handle these challenging patients.

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Francesca Pistoia

Neurological Institute

Department of Biotechnological and Applied Clinical Sciences

University of L'Aquila

67100 L'Aquila - Italy

Email: francesca.pistoia@univaq.it

Antonio Carolei

Neurological Institute

Department of Biotechnological and Applied Clinical Sciences

University of L'Aquila

L'Aquila

Italy