Advancing Our Knowledge of Cognition in Disorders of Consciousness: A Critical Revisit

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Abstract

This narrative review aims to elucidate an emerging state of consciousness termed "cognitive-motor dissociation", characterized by brain activity patterns closely resembling those observed in healthy individuals. This distinctive phenomenon is notably evident in patients diagnosed with comatose states, unresponsive wakefulness states, or minimally conscious states. Employing functional magnetic resonance imaging or electroencephalography holds promise for identifying cognitive-motor dissociation. The emergence of cognitive-motor dissociation not only introduces a fresh conceptual framework but also provides valuable predictive insights into outcomes and prognoses for individuals with disorders of consciousness. However, the recognition of cognitive-motor dissociation raises ethical considerations, particularly in evaluating the decision-making capacity regarding life-or-death choices for individuals in this state. Therefore, it is crucial to advocate for further scientific and comprehensive research to enhance our understanding of cognitive-motor dissociation and navigate its nuanced complexities.

Keywords: **cognitive-motor dissociation, coma, unresponsive wakefulness syndrome, minimally conscious state, functional MRI, EEG**

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INTRODUCTION

Consciousness can be defined as a state marked by both arousal and an awareness of oneself and one's surroundings [(1)]. Much research has been conducted to uncover the neuronal foundations of consciousness. This exploration has led to the proposition of the existence of an ascending reticular activating system (ARAS) situated in the upper brainstem tegmentum (reticular formation) and the central thalamus, which plays a pivotal role in facilitating widespread cortical activation[(2)]. Thus, disorders of consciousness encompass a spectrum of conditions that disrupt this pathway and are broadly categorized into three main groups. These categories consist of coma, unresponsive wakefulness state (UWS) (formerly referred to as vegetative state), and minimally conscious state (MCS), each defined by distinct levels of awareness and alertness[(3)]. Coma is characterized by the complete failure of the arousal system, marked by the absence of spontaneous eye opening and an inability

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to be roused even with vigorous sensory stimulation[4]. UWS is distinguished by the total absence of any observable behavioral signs indicating self-awareness or environmental awareness, while the capacity for spontaneous or stimulus-induced arousal remains intact[5]. To diagnose a MCS and differentiate it from UWS, one relies on the observation of cognitively-mediated behaviors[3]. These behaviors must be reproducible or sustained for a sufficient duration to distinguish them from reflexive actions[3]. Advancements in the field of imaging and electrophysiological tools have led to the emergence of a novel concept within the realm of disorders of consciousness. It is now possible to demonstrate brain activity patterns of UWS, MCS or comatose patients resembling those of individuals considered to have normal cognitive function[6]. This intriguing state of consciousness has been designated with a new term, "cognitive-motor dissociation (CMD)", also referred to covert consciousness[7]. This groundbreaking concept challenges our understanding of consciousness and raises important questions about the nature of awareness in individuals who outwardly appear to be unconscious. In this review, we aimed to introduce and elucidate CMD.

THE CONCEPT OF CMD

The concept of CMD is originated in a report of a 26-year-old female patient diagnosed with acute disseminated encephalomyelitis[8]. At the time of her diagnosis, she presented with a clinical profile consistent with a persistent vegetative state, characterized by apparent unresponsiveness. However, what added a layer of intrigue to this case was the surprising outcome of a face-recognition test administered to her[8]. Unexpectedly, positron emission tomography (PET) scans revealed that her brain's activation patterns closely resembled those observed in previous studies involving healthy individuals[8]. This observation challenged the established assumptions regarding her cognitive function and sparked a reevaluation of our understanding of consciousness in disorders of consciousness.

THE PREVALENCE OF CMD

Dr. Adrian Owen has dedicated many years to advancing this field[9]. In 2006, he and his colleagues introduced two verbal instructions to elicit mental imagery tasks in a 23-year-old female patient who was diagnosed in a UWS state. The functional magnetic resonance imaging (fMRI) findings showed that activated cortical areas in this patient closely resembled those observed in healthy volunteers, despite her condition[6]. A study involving 54 patients (23 UWS and 31 MCS) with disorders of consciousness demonstrated 5 (9.3%) patients were able to willfully modulate their brain activity through fMRI using the above-mentioned two mental imagery tasks[10]. Of them, one patient was able to use this technique to express yes or no to questions during fMRI[10]. Another study showed 3 of 16 (19%) patients with UWS were able to generate electroencephalography (EEG) responses to two distinct commands of mental imagery tasks, i.e., squeeze your right hand and squeeze your toes[11]. Overall, the prospect of utilizing task-based fMRI and EEG are two potential tools for detecting CMD in patients with disorders of consciousness for their adoption and implementation[12,13], and EEG may be easier than fMRI in the intensive care unit settings. A systematic review and meta-analysis demonstrated that CMD ratio in disorders of consciousness was 25.0% and 21.3% by using task-based fMRI and EEG tests respectively[13]. However, the incidence of CMD in various case series or cohort studies can exhibit substantial variability, with reported rates ranging from as low as 9.3% to as high as 43.6%[10,13,14]. This variability appears to be influenced by the diversity of mental imagery tasks, and techniques employed in these studies and unmeasurable false negative results.

THE PROGNOSIS OF CMD

A long-term follow-up of severe disorders of consciousness in 102 patients (59 UWS and 43 MCS) showed 30 (29.4%) patients regained consciousness and developed some communicative capacities[14]. Among them, 6 (5.9%) patients regained consciousness 3 years more after the acute brain injury[15]. Much research has been dedicated to investigate the relationship between the CMD and the prognosis of these severe disorders of consciousness. A study included 78 patients (45 UWS and 33 MCS) in an experiment utilizing an EEG-based brain-computer interface[14]. Among these participants, statistically significant brain-computer interface accuracies were identified as indicators of CMD[14]. For the UWS patients, 15 of 18 patients diagnosed with CMD (83.3%) regained consciousness, while only 5 of the remaining 27 patients without CMD (18.5%) experienced such a positive outcome[14]. Among the MCS patients, 14 of 16 patients diagnosed with CMD (87.5%) demonstrated improvements in their Coma Recovery Scale-Revised scores, while only 4 of the other 17 patients without CMD (23.5%) exhibited gain of the scores[14]. In another prospective study, 104 patients with acute brain injuries admitted to the intensive care unit were enrolled[16]. Utilizing machine learning techniques, EEG recordings were analyzed to detect brain activation in response to commands instructing patients to move their hands[16]. Brain activation in response to commands, indicative of CMD, was present in 16 patients. Among them, 8 (50%) demonstrated an improvement, resulting capabilities to follow commands before their discharge[16]. In contrast, among the 88 patients who did not display this brain activation, indicative of non-CMD, only 23 of them (26%) experienced improvements[16]. When assessing the long-term outcomes at 12 months, 7 out of the 16 patients with CMD (44%) achieved a Glasgow Outcome Scale-Extended (GOS-E) level of 4 or higher[16]. In contrast, only 12 of the 84 patients without CMD (14%) reached a GOS-E level of 4 or higher[16]. These results indicated that patients diagnosed with CMD have notably good prognoses compared to those without CMD. Besides, the recovery trajectories of clinically unresponsive patients diagnosed with CMD after brain injury exhibit clear distinctions from those without CMD[17].

THE ETHICAL ISSUE FOR CMD

A noteworthy survey conducted in France explored the self-assessed well-being of a cohort of chronic locked-in syndrome patients[18]. These individuals are aware but unable to move or communicate verbally due to complete paralysis of nearly all voluntary muscles in the body except for vertical eye movements and blinking[19]. This study revealed that 47 of 65 (72.3%) patients reported feeling happiness in their current condition[18]. Intriguingly, the study also identified a positive correlation between the duration of time spent in a locked-in state and reported happiness, with an odds ratio of 1.5[18]. Compared to locked-in syndrome, the issue of cares in CMD may be even more complex and challenging than in locked-in syndrome because it relies on diagnostic techniques rather than direct expression by the individuals themselves. The diagnosis of CMD plays a pivotal role in providing essential information for family counseling, informed decision-making, and the development of tailored rehabilitation programs[20]. However, it raises significant ethical concerns, particularly regarding the autonomy of individuals in such an unconscious state, i.e., CMD, to make life-or-death decisions. Addressing this issue calls for in-depth deliberations that involve both legal and

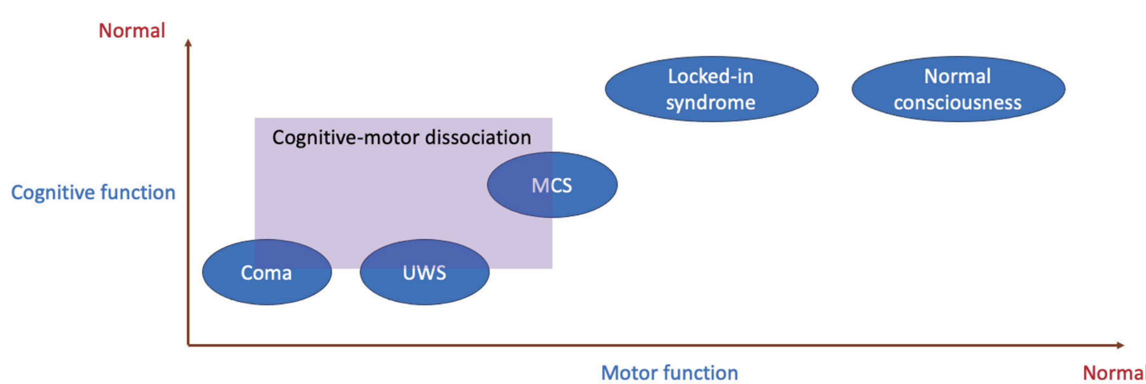

Figure. The distinctions among clinical disorders of consciousness are best revealed on a 2-dimensional axis by comparing the degree of impaired cognitive function against the degree of motor function.
Abbreviations: UWS = unresponsive wakefulness syndrome; MCS= minimally conscious state.

medical experts. Crafting suitable legislation to navigate these complex ethical concerns represents a significant and formidable challenge. In addition, knowledge gaps exist and reducing the educational gaps for health care personnel about the incidence and potential prognostic relevance of CMD might improve the care of patients with disorder of consciousness[21].

CONCLUSION

With the continuous advancement of diagnostic techniques, the potential for acquiring novel insights into disorders of consciousness becomes increasingly promising. CMD, which is characterized by the detection of volitional brain activity through task-based fMRI or EEG in patients whose bedside behavioral diagnosis suggests a state of coma, UWS, or MCS, represents an emerging concept that could offer valuable predictive insights into both outcomes and prognosis. The classification of these clinical disorders of consciousness is most effectively achieved by assessing the degree of impaired cognitive function and motor function (Figure). Nonetheless, this emerging field also presents a complex web of ethical considerations. Consequently, it is paramount that further scientific and comprehensive research be undertaken to gain a deeper and more nuanced understanding of these intricate issues.

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The authors declare no competing interests.

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