Prolonged Disorder of Consciousness — a New Concept in the Evaluation of Chronical Disorders of Consciousness in ICU Patients. A Multi-Disciplinary Concensus

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Abstract

Chronic disorders of consciousness (DOC) develop after severe traumatic and non-traumatic brain damage and are characterized by the restoration of wakefulness in a patient after a coma without the recovery of consciousness. To optimize the diagnosis and treatment of patients with chronic DOC, a Russian working group on the problems of chronic DOC was organized, which included specialists in various areas, primarily anesthesiologists, critical care physicians and neurologists. While discussing the termi-

Продленное нарушение сознания — новое понятие в оценке нарушений сознания у пациентов ОРИТ. Междисциплинарный консенсус

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Реферат

Хронические нарушения сознания (ХНС) представляют собой состояния, развивающиеся после тяжелого повреждения головного мозга травматического и нетравматического генеза и характеризующиеся восстановлением

nology of chronic DOC, the group identified that currently there is no definition for the state that falls into the period from the recovery of wakefulness and until 28 days after the brain damage when vegetative state/unresponsive wakefulness syndrome (VS/UWS) or minimally conscious state (MCS) may be diagnosed. In the intensive care unit (ICU) setting, there is often no consultant to provide critical care physicians with the correct diagnosis of the latter clinical syndromes, and neurophysiological tests are not feasible either. Therefore, there is a need to create a set of simple, understandable and easily reproducible strategies for managing this category of patients in the ICU. Thus, the working group proposed the term "prolonged disorders of consciousness" to be used for the patients with the signs of VS/UWS or MCS syndromes during their stay in the ICU until 28 days after initial brain damage and/or until the correct differential diagnosis of a type of chronic DOC is made. With the introduction of prolonged disorders of consciousness definition, the regular ICU staff will better understand how to provide an optimal set of supportive therapy and early rehabilitation activities in the lack of specific diagnostics techniques and dedicated specialists. Allocation of this category of patients allows us to create an algorithm for their better diagnosis and management and ensures consistent and effective interdisciplinary care at various levels. On the one hand, this approach will help us allow to free up ICU beds that are in high demand, while on the other, it will maximize the opportunity to realize the rehabilitation potential of DOC patients due to timely transfer to specialized centers.

Conclusions. If the term "prolonged disorder of consciousness" is accepted by professional communities of specialists (critical care physicians, neurologists, neurosurgeons, etc.), it will be used in guidelines for the management of DOC patients.

Keywords: rehabilitation triage scale, chronic disorder of consciousness, prolonged disorder of consciousness, vegetative state, coma

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бодрствования у пациента после комы, которое не сопровождается восстановлением сознания. Для решения проблем диагностики и лечения пациентов с ХНС была сформирована Российская рабочая группа по хроническим нарушениям сознания, включающая врачей различных специальностей, в первую очередь — анестезиологов-реаниматологов и неврологов. В процессе обсуждения терминологии ХНС было установлено, что в имеющейся номенклатуре нет подходящего определения для описания периода между выходом пациента на уровень бодрствования и констатируемым через 28 дней с момента повреждения головного мозга диагноза «вегетативное состояние / синдром ареактивного бодрствования» (ВС/САБ) или состояния минимального сознания (СМС). В условиях отделения реанимации и интенсивной терапии (ОРИТ) для этого нет специалиста-консультанта и возможности проведения нейрофизиологических тестов. Имеется потребность в создании комплекса простых и легко воспроизводимых стратегий ведения данной категории пациентов в условиях ОРИТ. В связи с этим рабочая группа предложила для описания статуса пациента с признаками ВС/САБ или СМС в период его пребывания в ОРИТ в первые 28 дней после развития нарушения сознания и/или до проведения дифференциальной диагностики ХНС термин «продленное нарушение сознания» (ПНС) (Prolonged disorders of consciousness). Использование данного термина вооружает персонал ОРИТ пониманием того, как без привлечения специфической диагностики и высококвалифицированных специалистов проводить оптимальный комплекс поддерживающей терапии и ранней реабилитации пациентов. Предложенные подходы к выделению этой категории пациентов позволяют сформировать алгоритм диагностики и ведения и призваны обеспечить максимальный уровень междисциплинарной согласованности и преемственной эффективности на этапах медицинской реабилитации. Это, с одной стороны, позволит освобождать койки высокой потребности в ОРИТ, а с другой — обеспечит максимальную возможность реализации реабилитационного потенциала пациентов с ХНС благодаря своевременному переводу в специализированные центры.

Заключение. При условии принятия термина «продленное нарушение сознания» профессиональными сообществами профильных специалистов (анестезиологов-реаниматологов, неврологов, нейрохирургов) он будет использован в клинических рекомендациях по ведению пациентов с ХНС.

Ключевые слова: шкала реабилитационной маршрутизации, хроническое нарушение сознания, продленное нарушение сознания, вегетативное состояние, кома

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Chronic disorders of consciousness (DOC) develop after severe traumatic and n on-traumatic brain damage and are characterized by the restoration of wakefulness in patients after a coma without the recovery of consciousness [1–3]. At each stage of the disease, chronic DOC patients are brought to the attention of various specialists, primarily critical care physicians and neurologists. Consistent views on the approaches to diagnosis, management and rehabilitation are essential for providing these patients with the best available care [3].

During the XI Russian Congress of Neurologists in St. Petersburg on June 18, 2019, the Russian Working Group on the Problems of Chronic Disorders of Consciousness was organized on the initiative of the Research Center of Neurology (Moscow) to optimize the diagnosis and treatment of patients with chronic DOC. It included representatives of the major Russian clinical and research centers dealing with DOC patients. The w orking group developed a s trategy for a u nified terminology and criteria for the diagnosis of chronic disorders of consciousness [1]. The m ost important achievement by the end of 2020 was the development of the draft c linical g uidelines f or t he m anagement of chronic disorders of consciousness, aimed at the practical implementation of unified approaches to the d iagnosis, treatment and rehabilitation of these patients. During the discussion, the members of the working group were faced with the problem that currently there is no suitable definition for t he s tate within the p eriod between the recovery of wakefulness and the time point when the patients become eligible for the diagnosis of vegetative state/unresponsive wakefulness syndrome (VS/UWS) or minimally conscious state (MCS), i.e. 28 days from the moment of brain damage.[2] Furthermore, establishing the correct diagnosis of VS/UWS or MCS often requires assistance from an attending specialist who has the necessary experience in managing chronic DOC patients. Several neurophysiological tests might also be needed. However, this is hardly available in most intensive care units (ICU) throughout Russia. Therefore, there is a need to create a set of simple, understandable and easily reproducible strategies for managing this category of patients in the ICU. This problem was discussed at the meeting of the working group held during the 3rd Physical and Rehabilitation Medicine Congress in 2019. Eight principles were then proposed.

1. The term "prolonged disorders of consciousness" is recommended to be used for the patients with the signs of VS/UWS or MCS during their stay in the ICU until 28 days after initial brain damage and/or until the correct differential diagnosis of a type of chronic DOC is established [3].

In general, from the clinical point of view, chronic DOC can be described as an absence of any signs of conscious behaviour in patients who regained wakefulness (i.e. opening their eyes) after being in a coma. They do not have a purposeful response to external stimuli, including gaze fixation and visual pursuit. At the same time, reflexive non-purposeful movements of the trunk and limbs, the grasping reflex, as well as reflex movements in response to a pain stimulus might be observed. VS/UWS patients may demonstrate primitive auditory or visual startle reflexes, i.e., a stereotypical reaction (such as flinching, blinking, contraction of facial muscles, etc.) in response to a loud and sharp sound. Orientation reflexes, such as turning the head and eyes in the direction of the sound stimulus, might be also seen. Brainstem reflexes (pupillary, oculocephalic, vestibulo-ocular, corneal reflexes, as well as gag and cough reflexes), sucking and swallowing of saliva usually remain intact. However, more complex coordinated acts like chewing and swallowing food is not possible in VS/UWS patients, which precludes oral feeding due to the high risk of aspiration. Since the functions of the autonomic

nervous system are spared, most patients have intact hemodynamics and present with spontaneous breathing (usually through a tracheostomy tube or cannula); usually, there are no severe abnormalities of thermoregulation and metabolism, and the function of the digestive system is generally preserved.

The key difference between MCS and VS/UWS is the elements of conscious behaviour. These signs may be subtle, sometimes barely noticeable, and inconsistent; however, to diagnose MCS they must be reproducible and sufficiently distinct to distinguish them from reflexive, involuntary activities (see the diagnostic criteria below).

Thus, criteria for VS/UWS include [2]:

- no evidence of awareness of self or environment and an inability to interact with others;
- no evidence of sustained, reproducible, purposeful, or voluntary behavioural responses to visual, auditory, tactile, or noxious stimuli;
- no evidence of language comprehension or expression;
- presence of sleep-wake cycles, that do not necessarily align with the time of the day;
- sufficiently preserved hypothalamic and brainstem autonomic functions to permit survival with appropriate care;
- variably preserved cranial nerve reflexes (pupillary, oculocephalic, corneal, vestibulo-ocular, and gag) and spinal reflexes.

The presence of a higher level of awareness, i.e. MCS, may be suspected if the patient demonstrates [24]:

- purposeful behaviour, including movements or affective behaviours that occur in contingent relation to relevant environmental stimuli and are not due to reflexive activity, e.g.:
  - pursuit eye movement or sustained fixation;
  - appropriate smiling or crying in response to the linguistic or visual content of emotional but not to neutral topics or stimuli;
  - vocalizations or gestures that occur in direct response to the linguistic content of questions;
  - reaching for objects that demonstrates a clear relationship between object location and direction of reach;
  - touching or holding objects in a manner that accommodates the size and shape of the object;
- following simple commands;
- gestural or verbal yes/no responses (regardless of accuracy);
- intelligible verbalization.

The working group proposed the following recommendations for the management of patients with prolonged DOC status:

2. In the ICU setting, the assessment of the level of consciousness is recommended to be performed daily in all patients using validated clinical scales and radiological and neurophysiological approaches.

Assessment of the level of consciousness is a crucial element of initial diagnostics and monitoring in the ICU setting since in most clinical situations consciousness reflects the degree of primary and secondary damage of the nervous system. It is important to check patient status regularly to notice the end of the coma and its transition to the chronic disorder of consciousness. Instruments to assess the level of consciousness include the globally recognised Glasgow Coma Scale, which was recently accompanied by the Full Outline of UnResponsiveness score (FOUR) [4, 5]. The latter provides more detailed characteristics of neurological status in disorders of consciousness resulting from the brain damage[6–8]. The decrease of the level of consciousness is an indication for brain imaging study using computed tomography (CT) or magnetic resonance imaging (MRI), as a part of workup to determine the cause of the lack of arousal.

3. In the context of the primary quantitative and qualitative assessment of the level of consciousness, including the ICU setting, it is recommended to take into account factors that may confound clinical data, namely, results of brain imaging [*9, 10*].

The major problem of behavioural assessment in a DOC patient is the high risk of a false negative result due to the inability of the person to demonstrate a response to the stimulus because of a motor or sensory deficit, or an incorrectly performed examination. To establish the correct diagnosis of the prolonged disorder of consciousness, an impact of any factors that affect the level of consciousness should be excluded or minimized, i.e. the effect of medications (sedatives, muscle relaxants, analgesics, etc.), concurrent conditions, such as hemodynamic instability, hypoglycemia, electrolyte disorders, non-convulsive status epilepticus, and acute primary or secondary brain damage, e.g., lesion leading to the mass effect, such as haematoma, tumour and intratumor haemorrhage, extensive focal ischemia, multi-focal infarctions resulting from cerebral vasospasm in subarachnoid haemorrhage, inflammatory process (meningitis, meningoencephalitis or brain abscess).

In all cases when the level of awareness during the examination is suspected to be lower than it is expected, and there may be a case of "covert consciousness", one should take the necessary measures to exclude the possible reversible causes that may have an impact on conscious behaviour:

- Exclude concurrent conditions, accompanied by electrolyte disturbances or abnormal glucose levels.

- Exclude infectious process with systemic inflammatory response and hyperthermia.
- Perform any available neuroimaging study to exclude conditions that require neurosurgical intervention. e.g. hypertensive hydrocephalus, etc.
- Perform electroencephalography (EEG) to exclude non-convulsive status epilepticus.

4. In patients with prolonged disorders of consciousness, it is recommended to perform a continuous evaluation of pain syndrome. Pain should be prevented and managed according to the current clinical guidelines [11–13].

In patients who survived after severe brain damage, especially in the context of traumatic brain injury (TBI), pain in the acute period can be associated both with the injury and its complications (e.g., fractures, concomitant damage of internal organs), as well as with treatment, including invasive manipulations (tracheostomy, catheters and nasogastric tube placement, etc), and surgical interventions. As the condition of the patient with prolonged disorders of consciousness becomes stable, pain is more often associated with secondary causes, such as increased muscle tone and contractures, subluxation of the shoulder joint, pressure ulcers, and concomitant diseases. Uncomfortable position of the patient, urinary retention, constipation, discomfort due to the gastrostomy, tracheostomy or venous catheter represent the most important sources of pain.

Diagnosis of pain in patients with prolonged disorder of consciousness is a problem since they cannot describe their feelings. One should focus on external signs, such as the appearance of pain grimaces, moans, anxiety, unusual motor reactions, tachycardia or rapid breathing. However, this behaviour may be associated not with a pain stimulus but rather with the abnormal activation of subcortical structures. If a patient with a prolonged disorder of consciousness demonstrates the signs that may reflect pain, every effort should be made to eliminate its cause and provide adequate analgesia, regardless of the level of consciousness. It is also should be noted that it is impossible to reliably assess the level of consciousness of the patient suffering from pain. Before the examination, one needs to make sure that the behavioural assessment is not hindered by pain, uncomfortable position and other similar factors. In the acute period, preventive analgesia is necessary following the severity of the initial damage of the brain and other organs, and the interventions performed. Later in course of the disease, priority should be given to non-pharmacological approaches to pain management, including adequate positioning of the patient with regular changes in body position, physical therapy and other measures to prevent increased muscle tone (for example, the use of splints), control of emptying of the bladder and bowels [14]. When choosing medications for pharmacological treatment, the cause and the expected intensity of pain should be considered, as well as possible side effects, primarily sedative, that may have an impact on the level of consciousness.

5. At the stage of ICU stay the prevention of the consequences of intensive care syndrome is recommended that is stated in the clinical guidelines of the Federation of Anesthesiologists and Clinical Care Specialists of Russia (FAR) and the Union of Rehabilitologists of Russia (SRR). Early motor and cognitive rehabilitation provided by the multidisciplinary rehabilitation team of the department of early rehabilitation should be initiated in the first 48–72 hours in coma patients and continued until transferring to the next stage of rehabilitation [15].

The crucial principle of management is that it should be provided with the interdisciplinary team, including neurologists, intensive care specialists, neurosurgeons, psychologists, neuropsychologists, psychiatrists, rehabilitation specialists, speech therapists, therapists, orthopedists, qualified nursing staff and social workers [16].

Patients with prolonged disorder of consciousness usually spend at least 2–3 weeks in the ICU. Considering the pathogenesis of the consequences of intensive care syndrome, the first 48 hours of ICU stay is associated with an extremely high probability of developing complications of prolonged immobilization and the use of sedatives. The syndrome may manifest as critical illness myopathy and polyneuropathy, insomnia, emotional and cognitive disorders, etc. Prevention and treatment of this syndrome should be included in the management program of patients with chronic disorders of consciousness. In general, the management of this category of patients should be guided by common approaches to the care of patients with severe brain damage, considering several specific problems that often occur in chronic DOC. The main aspects of supportive care for chronic DOC patients include the following [17]:

- protection of airways;
- correction of disorders of functions controlled by the midbrain: respiration, hemodynamics, thermoregulation;
- maintaining fluid and electrolyte balance;
- adequate nutrition support;
- control of bowel and bladder functions;
- oral hygiene;
- prevention and treatment of complications associated with immobilization:
  - pressure ulcers;
  - infectious complications (primarily respiratory infections and urinary tract infections);
  - venous thromboembolism;
  - increased muscle tone with contractures;
- stimulation of patient mobility and correction of postural disorders;

- diagnosing and treatment of pain syndrome;
- detection and treatment of seizures;
- treatment of paroxysmal sympathetic hyperactivity.

Early initiation of rehabilitation

Data from various categories of patients with severe TBI, as well as from patients with prolonged disorders of consciousness of primarily traumatic etiology, indicate the effectiveness of early rehabilitation [18]. The same applies to the intensity of rehabilitation: in TBI patients, intensive rehabilitation programs have been shown to be effective both in terms of outcomes and from an economic point of view. Post-traumatic chronic DOC patients, who received at least 90 minutes of training per day, demonstrated improvement in the level of consciousness and a decrease in the severity of complications (disorders of the respiratory system, pressure ulcers and increased muscle tone).

6. Patients with prolonged disorders of consciousness should undergo daily examinations by a speech therapist, including volume viscosity test with fibrolaryngoscopy to assess the swallowing status and select the nutrition texture for training for feeding [***19–20***].

Dysphagia is diagnosed in all patients with chronic disorders of consciousness. The mechanisms of dysphagia are associated not only with the lack of coordinated activity of various control centers but also with the mechanisms of learned non-use due to prolonged tracheoesophageal dissociation by tracheostomy cannula. Training for feeding using small bolus volumes (beginning from 5 ml) contributes to the restoration of swallowing as an integral process. However, it should be underlined, that VS/UWS patients lack an effective oral phase of the swallowing, and they should not receive oral nutrition due to the risk of aspiration. The restoration of the oral phase of swallowing in a patient with chronic DOC may indicate an increase in the level of consciousness.

7. It is recommended that in patients with prolonged disorders of consciousness during ICU stay the prevention of cognitive and emotional disorders should be performed using psychostimulotherapy and multisensory stimulation [***21***].

As a mandatory therapeutic and preventive measure, it is necessary to consider maintaining a friendly atmosphere towards the patient in the ICU, especially when sedation is implicated. To achieve this, visits of loved ones, as long as audio, video, tactile, taste, and other positive multisensory stimuli might be applied. It is important to eliminate the inevitable discomfort associated with the ICU stay to the maximum extent. This includes the avoidance of the tension of tubes and catheters, providing a comfortable position of the body and its continuous change. It is necessary to exclude or minimize the fixation of the patient

8. Patients with prolonged disorders of consciousness diagnosed in the ICU setting (1st stage of rehabilitation) should be counselled (via in-person or telemedicine consultations) with the specialists in DOC care from the rehabilitation center of 3rd or 4th level no later than 14 days from the brain damage to assess the status of the patient, give advice on the management plan and determine triage pathways. When determining the triage of patients with chronic DOC, Rehabilitation Triage Scale should be used [***22***].

In the absence of regional-level rehabilitation center, one should apply for telemedicine consultation via the website of the Federal State Budgetary Institution "All-Russian Center for Emergency Medicine «Zaschita". When requesting the type of consultation, one should specify "chronic disorder of consciousness. Rehabilitation Triage Scale 6.» According to the results of the telemedicine consultation with the specialists of one of the accredited rehabilitation centers, the patient should be referred to the 2nd stage of rehabilitation or the community center of palliative care.

Indications for hospitalization to the 3rd or 4th level rehabilitation center

1. Prolonged disorder of consciousness that persists for more than 3 weeks.
2. The cause of the medical condition that led to the development of the prolonged disorders of consciousness has been established and managed properly.

Contraindications for hospitalization to the 3rd or 4th level rehabilitation center

1. Persistent infectious and inflammatory syndrome.
2. Multiple organ failure requiring ICU treatment.
3. Comorbidities with an unfavourable course and a poor prognosis, that was confirmed by the relevant specialists.
4. Condition requiring referral to a palliative care center:
   - Severe electrolyte abnormalities and/or nutritional deficiency, accompanied by weight loss above 20 % in the last 3 months, albumin levels less than 20 g/l, creatinine above 200 mmol/l, despite adequate nutrition and infusion therapy for 60 days from the onset of the disease.
   - Infectious and inflammatory conditions that are resistant to treatment within 20 days from

the onset of the disease, relapsing despite adequate antibiotic therapy, including aspiration pneumonia in patients with tracheostomy and gastrostomy; refractory pressure ulcers Stage III or IV.

Criteria for quality assurance of care for patients with prolonged disorders of consciousness in the ICU [23]

1. Neuroimaging was performed to diagnose the initial brain damage and the cause of the prolonged disorder of consciousness; clinical diagnostics of the prolonged disorder of consciousness with the repeated neurological examination of the patient using the Glasgow Coma Scale and the FOUR scale were performed.
2. Conditions that may prevent the correct diagnosis of a violation of consciousness were excluded.
3. In-person or telemedicine consultation with a specialist in DOC care from the rehabilitation center of 3rd or 4th level was performed.
4. Measures were taken to prevent the consequences of intensive care syndrome following the FAR clinical guidelines.
5. Tracheotomy was performed.
6. Gastrostomy was performed.
7. The patient is able to breath spontaneously.
8. There are no contractures and pressure ulcers.
9. Body weight deficit is less than 20 %.

The proposed term "prolonged disorders of consciousness" fits seamlessly into the logic of the evolution of the postcomatous state (fig. 1). The concept of prolonged disorders of consciousness refers to the period from the end of the comatose state to 28 days after brain damage, i.e., the moment when one of the forms of chronic disorders of consciousness should be diagnosed.

With the introduction of prolonged disorders of consciousness definition, the regular ICU staff will better understand how to provide an optimal set of supportive therapy and early rehabilitation activities in the lack of specific diagnostics techniques and dedicated specialists until these patients will be transferred to the next stages of rehabilitation. Allocation of this category of patients allows us to create an algorithm for their better diagnosis and management and ensures consistent and effective interdisciplinary care at various levels of rehabilitation. The use of the Rehabilitation Triage Scale in this category of patients will ensure their inclusion in the emerging system of medical rehabilitation. On the one hand, this approach will help us allow to free up ICU beds that are in high demand, while on the other, it will maximize

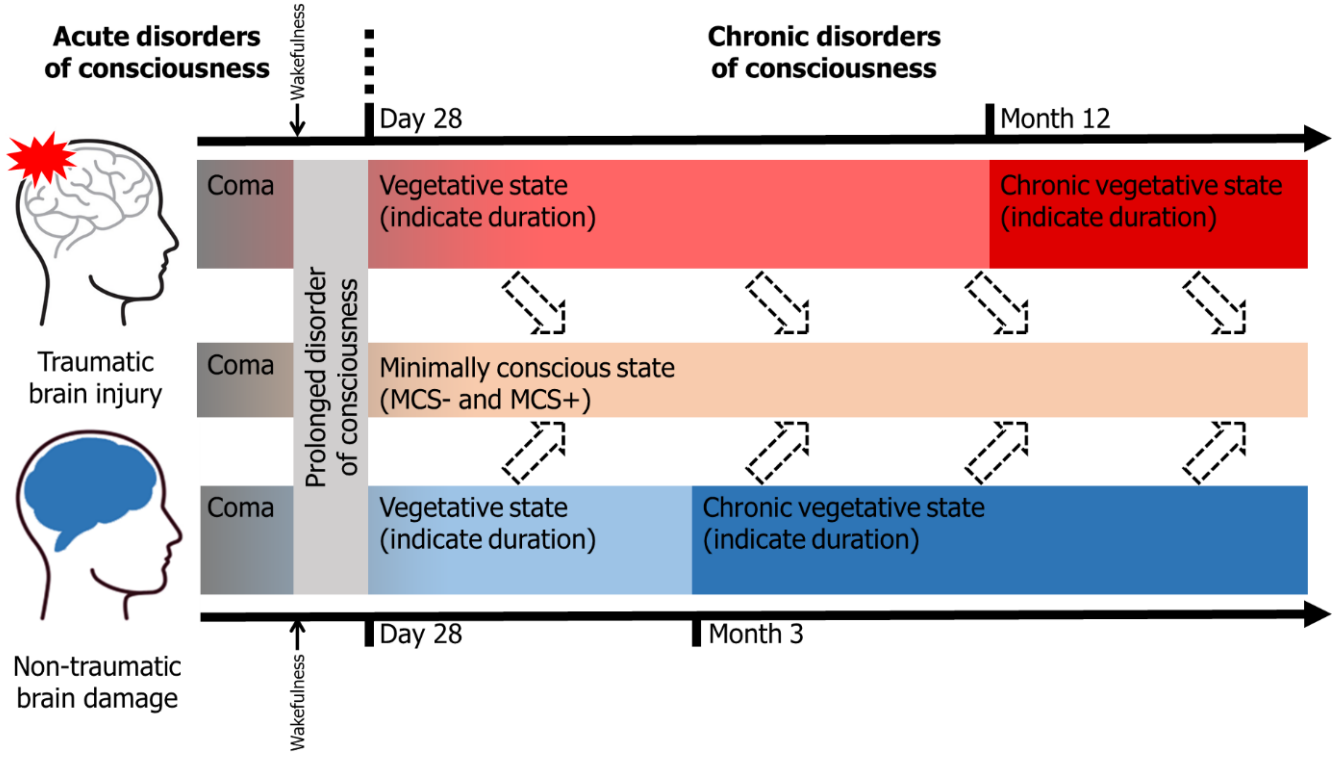

Fig 1. Evolution of the patient's condition from coma to chronic disorders of cosciousness [1]

the opportunity to realize the rehabilitation potential of DOC patients due to timely transfer to specialized centers. If the stated position is supported during a broad discussion with the communities of specialists (critical care physicians, neurologists, neurosurgeons, etc.), it will be included in the clinical guidelines for the management of chronic DOC patients.

Conflict of interest. The authors declare that they have no conflict of interest.

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