LATE RECOVERY OF AWARENESS IN PROLONGED DISORDERS OF CONSCIOUSNESS- A cross-sectional cohort study

Running Head: RECOVERY IN DISORDERS OF CONSCIOUSNESS

Abstract

Purpose: To detect any improvement of awareness in prolonged disorders of consciousness in the long term.

Methods: 34 patients with Prolonged Disorders of Consciousness (27 vegetative state and 7 minimally conscious state; 16 male; aged 21 to 73) were included in the study.

All patients were initially diagnosed with vegetative/ minimally conscious state on admission to our specialist neurological rehabilitation unit. Re-assessment was performed 2 to 16 years later using Coma Recovery Scale-Revised.

Results: Although remaining severely disabled, 32% of the patients showed late improvement of awareness evidenced with development of non-reflexive responses such as reproducible command following and localization behaviours. Most of the late recoveries occurred in patients with subarachnoid haemorrhage (5/11, 45.5%). The ages of patients within the late recovery group (Mean=45, SD=11.4) and non-recovery group (Mean=43, SD=15.5) were not statistically different (p=0.76).

Conclusions: This study shows that late improvements in awareness are not exceptional in non-traumatic Prolonged Disorders of Consciousness cases. It highlights the importance of long term follow up of patients with Prolonged Disorders of Consciousness, regardless of the aetiology, age and time passed since the brain injury. Long term follow up will help clinicians to identify patients who may benefit from further assessment and rehabilitation. Although only one patient achieved recovery of function, recovery of awareness may have important ethical implications especially where withdrawal of artificial nutrition and hydration is considered.

Keywords: Disorders of Consciousness, Vegetative State, Minimally Conscious State, Recovery, Consciousness, Unresponsive Wakefulness Syndrome

INTRODUCTION

Severe disorders of consciousness (DOC) which include vegetative state (VS) and minimally conscious state (MCS) are known to have a very poor clinical outcome and despite extensive research are still poorly understood.[1-4] VS is characterized by complete lack of awareness of the self and the environment, accompanied by sleep-wake cycles with either complete or partial preservation of hypothalamic and brain stem autonomic functions[5]. The diagnosis of MCS is based on the presence of minimal but definite behavioural evidence of self or environmental awareness on clinical assessment[6]. In MCS behavioural responses are characteristically inconsistent and often subtle; hence patients require repeated assessments by experienced clinicians to differentiate MCS from VS. When DOC lasts more than one month it is defined as Prolonged Disorders of Consciousness (PDOC).

Several research studies have shown that it is possible to detect the presence of covert awareness/ consciousness in such patients, by utilizing advanced electrophysiological methods and/or advanced functional neuroimaging techniques in cases where clinical assessments are unable to detect any behavioural sign of awareness. [7-11] Despite these promising developments within severe DOC brain research, currently the diagnosis of VS and MCS is made on clinical grounds.

Although limited and inconsistent, patients with MCS may demonstrate agency and, on rare occasions, may be able to communicate their choices and opinions with respect to their basic treatment and care. Therefore, the distinction between VS and MCS has important ethical implications for the patient, their family and carers, medical, nursing and therapy staff and for wider society especially where withdrawal of clinically assisted nutrition and hydration is considered.

National Clinical Guidelines on Prolonged Disorders of Consciousness[2] state that vegetative state may be classified as a 'permanent VS' if it has persisted for more than six months following non-traumatic brain injury and more than one year following traumatic brain injury as after these time points recovery is deemed 'highly improbable'.

Our current knowledge of long-term outcome in severe DOC is incomplete largely because once a diagnosis is made, patients are discharged to diverse care settings and their follow up rarely extends beyond 12 months after brain injury.[1,12,13] A recent study examined the long-term prognosis (for a mean of 25.7 months from onset of brain injury) in 50 patients with VS. This study reported that late recovery was detected in 25% of the patients; suggesting that late recovery of responsiveness may occur more frequently than previously appreciated.[14] The study also demonstrated a higher chance of recovery in the post-anoxic brain injury sub-group (21.4%) than in earlier published studies which were in the form of case reports.[15-21] Luauté et al.

showed that a third of patients in MCS with mixed aetiologies improved more than 1 year post ictus.[22] In this study however, Glasgow Outcome Scale was used as main outcome measure with no specific attention to improvement of awareness/ responses to given stimuli . We wished to add to the small but growing body of knowledge on the long-term prognosis of PDOC. We specifically wanted to focus on detecting changes in in awareness which can be detected only with structured and detailed assessments and otherwise may be unnoticed. The clinical setting of our unit gave us the unique opportunity to investigate outcomes in PDOC patients many years and even decades after the original ictus.

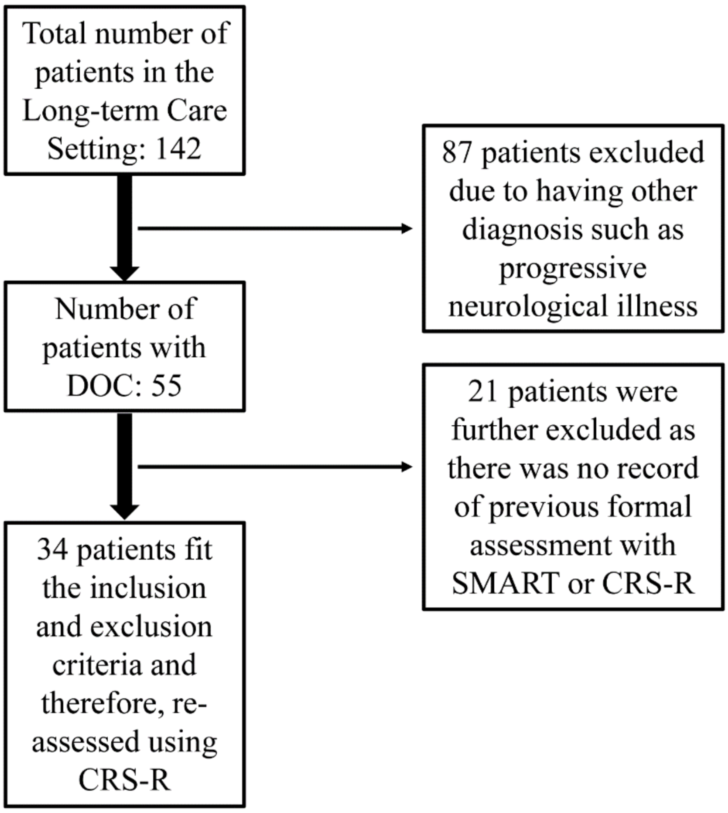
METHODS

The study was conducted in a long term care setting specializing in management and care of patients with profound brain injuries. The patients were given regular sensory stimulation provided in sensory rooms and were exposed to art and music therapy sessions as well as to regular social events. The number of residents in the long term care setting is around 140 and 55 of these had diagnosis of DOC and 34 of these patients received their initial assessments and rehabilitation at our rehabilitation unit where Sensory Modality Assessment Rehabilitation Technique (SMART) assessment is most commonly used to diagnose DOC. SMART [23] is a valid and robust tool used in the assessment of DOC. It is recognised by the Royal College of Physicians guidelines and in the English high courts as the tool of choice to detect awareness and identify potential in patients with DOC.

Although recommended as a good practice, regular and formal re-assessment of PDOC patients is not routinely and widely carried out in the United Kingdom. Following discharge to long term care setting, our patients were monitored closely by clinicians who are experienced in care of people with disorders of consciousness and no apparent recovery of awareness was reported. Nevertheless, due to lack of regular and formal re-assessments subtle changes or improvements masked by aphasia and/or severe motor weakness may have gone unnoticed.

The patients were in a stable medical condition. Case notes of all the patients with a disorder of consciousness were screened and the following features were considered as exclusion criteria: disorders of consciousness secondary to neurodegenerative illnesses; patients who did not have an initial formal assessment of consciousness using validated assessment techniques (SMART± Coma Recovery Scale-Revised (CRS-R) or Wessex Head Injury Matrix) and, patients with severe pathologies independent from the brain injury such as advanced cancer.

The eligibility criteria for this cohort study were that patients: had a diagnosis of VS or MCS established by using SMART assessment, as it was the validated assessment tool most often used in our cohort ± another validated assessment tool; had a brain injury secondary to acquired and non-progressive neurological illness; and, were medically stable at the time of re-assessment. The flow chart in Figure 1 shows the selection criteria for the follow up study.



We documented a range of demographic variables (age and sex), cause of brain injury (e.g. traumatic, anoxic, subarachnoid haemorrhage, ischaemic stroke), time from brain injury to initial SMART assessment, the initial SMART assessment outcome, time from brain injury to follow up assessment, time between first SMART assessment and the follow up assessment and the outcome of the follow up assessment.

All the patients were re-assessed 2 to 16 years after the initial DOC diagnosis by two clinicians who were experienced in clinical assessments of patients with disorders of consciousness. The assessments were undertaken in a quiet, well lit room while patients were in the sitting position. The main outcome measure was recovery of awareness/ responsiveness according to the clinical criteria for MCS and for emergence from MCS, assessed with CRS-R.[24] The SMART and CRS-R apply similar stimuli and specify the method of application, to exclude extraneous variables. CRS-R was chosen as the method of re-assessment as it is a quick and reliable assessment tool for screening purposes.[25] CRS-R includes all the modalities of the SMART assessment with the exclusion of the gustatory and olfactory sensory stimulation techniques. Another difference between SMART and CRS-R is that, CRS-R uses a mirror to assess visual tracking, whereas SMART uses a moving person and a picture of a baby. On the other hand, both tools assess visual tracking in both horizontal and vertical planes. As it was shown that assessment of visual pursuit with mirror is superior to with moving person or object[26,27]; SMART assessment proformas were examined in detail and all additional behaviours which suggested MCS were recorded.

Two clinicians were present during CRS-R assessments. One of the investigators (SD or AK) was not involved in the initial review of case notes and was blinded to the initial diagnosis of the patients. Due to resource constraints, we were not able to have two blinded examiners at the same time however, CRS-R scoring sheets were only completed upon consensus of both clinicians on patients' responses during the assessment. In a few occasions where there was disagreement between the assessors on the responses elicited, the CRS-R scores were recorded for the lower assessment. For example, if one of the clinicians did not agree on the presence of a consistent movement to command, this was scored as "not present".

Data were analysed with SPSS 21 (IBM SPSS, Chicago, IL, USA). Permission for the study was obtained from the Royal Hospital for Neuro-disability audit committee.

RESULTS

34 patients (16 male) met the inclusion and exclusion criterion. The mean age at the time of brain injury was 43 (Range 17-70 years, SD 13 years). The mean age of the study population at the time of re-assessment was 49 (Range 21-73 years, SD 12 years).

The causes of brain injury were: anoxic brain injury in 15 patients; cerebrovascular accident in 13 patients (subarachnoid haemorrhage in 11 patients and massive ischaemic stroke in two patients); traumatic brain injury (TBI) in six patients. 27 (79%) of the patients had a diagnosis of VS on the initial SMART assessment, with seven (21%) diagnosed as being in the MCS. Time from brain injury to initial formal DOC diagnosis with SMART assessment varied between five and 38 months (Mean=10.9, SD=7.1 months). The diagnosis remained same at the time from completion of SMART assessment and admission to long term care facility as patients were under constant review and continued to receive monitoring assessments during period of rehabilitation.

The time from brain injury to re-assessment was between 2 and 16 years. Mean duration of follow-up from brain injury was 6 years. (SD 3 years). Mean time from the initial SMART assessment to re-assessment was 5 years (SD 3.17 years). The time interval between the brain injury and re-assessment was 5.9 (SD 3.4 years, range 2-11 years). (See table 1)

Table 1: Clinical features of patients

		TBI (*n*=6)	Anoxic (*n*=15)	Subarachnoid haemorrhage (*n*=11)	Ischaemic Stroke (*n*=2)	Total Sample (*n*=34)
Mean Age(SD)		38.5(10.9)	49.2(12.5)	53.6(9.2)	58(21.2)	49.2(12.4)
Mean Months BI to SMART (SD)		10.2(2.8)	12.9(10.1)	9.19(3.3)	8.5(2.1)	10.9(7.2)
Mean Years BI to CRS-R (SD)		4.9(2.1)	6.9(3.9)	4.9(3.0)	7.0(1.4)	5.9(3.4)
SMART Outcome	VS	4	15	8	0	27
	MCS	2	0	3	2	7
	Exit MCS	0	0	0	0	0
CRS-R Outcome	VS	2	12	2	1	17
	MCS	4	3	8	1	16
	Exit MCS	0	0	1	0	1
Improvement		33% (2/6)	20% (3/15)	46% (6/13)		32% (11/34)

TBI= Traumatic Brain Injury, VS= Vegetative State, MCS, Minimally Conscious State, CRS-R= Coma Recovery Scale-Revised, SMART= Sensory Modality Assessment Rehabilitation Technique, SD= Standard Deviation

The results of the re-assessment using CRS-R showed that all patients remained severely disabled. However, 32% of the patients showed improvement of awareness with development of more complex responses than they had during initial assessment. The CRS-R scores and responses of the patients who showed improvement in their awareness state are shown in table 2 where we show the patient outcome data categorized by aetiology and on a scale of VS, MCS and exit MCS. Most of the late recoveries occurred in patients with cerebrovascular accidents (6/13, 46%). The ages of patients within the late recovery group (Mean=45, SD=11.4) and non-recovery group (Mean+43.5, SD=15.5) were not statistically different (*p*=0.76).

Only one patient, who suffered from severe subarachnoid haemorrhage and was previously in minimally conscious state, progressed to the level of functional verbal communication and object use which is the criteria for exit MCS/ emergence from DOC. Eight patients had changes of diagnosis (VS to MCS) between initial assessment and re-assessment (table 2).

Table 2: CRS-R Scores of patients with improvement of awareness

Patient ID Sex/Age/Aetiology	Time BI to SMART (months)	Time SMART to CRS-R (years)	SMART Findings	SMART Diagnosis	CRS-R Findings						
					Auditory function	Visual function	Motor function	Oromotor/ Verbal function	Communication	Arousal	CRS-R Total Score (Diagnosis)
Patient 1 M/ 65/SAH	7	9	Visual startle only Motor withdrawal No vocalization	VS	Reproducible movement to command	Visual startle	Object manipulation	Vocalization/ Oral movement	Non-functional: intentional	Eye opening without stimulation	13 (MCS)
Patient 2 F/ 44/ SAH	8	2	Reflexive responses in tactile, visual (pupil constriction only) and auditory	VS	Consistent movement to command	Visual pursuit	Flexion withdrawal	Oral reflexive movement	None	Eye opening without stimulation	12 (MCS)
Patient 3 F/ 21/ TBI	15	3	Visual tracking No command following	MCS	Reproducible movement to command	Visual pursuit	Flexion withdrawal	Oral reflexive movement	None	Attention	12(MCS)
Patient 4 F/ 39/ TBI	12	2	No visual fixation/ tracking Auditory startle only	VS	Localization to sound	Visual pursuit	Abnormal posturing	Vocalization/oral movement	None	Attention	11 (MCS)
Patient 5 M/ 38/ Anoxia	12	2	Inconsistent focusing on a familiar face, eye opening to auditory stimulus	VS	Reproducible movement to command	Object localization/ reaching	Object manipulation	Oral reflexive movement	None	Attention	15 (MCS)
Patient 6 F/ 45/ SAH	9	10	Startle and withdrawal responses to visual and auditory stimuli, no localization	VS	Localization to sound	Visual pursuit	Localization to noxious stimulation	Vocalization/oral movement	None	Attention	13 (MCS)
Patient 7 F/ 65/ Anoxia	38	4	No visual responses, localization of sound	VS	Reproducible movement to command	None	Flexion withdrawal	Vocalization/ oral movement	None	Attention	10 (MCS)
Patient 8 M/ 43/ Infarct	7	5	Localizing responses at visual, auditory and motor domains.	MCS	Consistent movement to command	Object recognition	Functional object use	Intelligible verbalization	Functional: accurate	Attention	23 (exit-MCS)
Patient 9 M/ 57/ Anoxia	10	2	Visual startle but no visual fixation	VS	Auditory startle	Fixation	Flexion withdrawal	Oral reflexive movement	None	Eye opening w/o stimulation	8 (VS/ MCS minus)
Patient 10 F/ 70/ SAH	12	2	No localization of sound, no visual tracking	VS	Reproducible movement to command	Fixation	Object manipulation	Intelligible verbalization (lip read)	Non-functional: intentional	Attention	16 (MCS)
Patient 11 F/ 43/ SAH	10	2	Flexion withdrawal only, visual startle	VS	Reproducible movement to command	Object recognition	Object manipulation	Vocalization/ oral movement	None	Attention	17 (MCS)

TBI= Traumatic Brain Injury, VS= Vegetative State, MCS, Minimally Conscious State, SAH=Subarachnoid Haemorrhage, CRS-R= Coma Recovery Scale- Revised, SMART= Sensory Modality Assessment Rehabilitation Technique, F=Female, M=Male

DISCUSSION

This study shows that late improvements in awareness are not exceptional in non-traumatic VS and MCS patients, regardless of age. Previous studies have reported better outcomes in traumatic VS patients than in our study. However, our study included only four traumatic VS patients and two traumatic MCS patients. The improvement rate was 33% within this subgroup but it is not possible to comment further on how aetiology differentially affects outcome due to the small subgroup sample size. The most significant finding of the present study is that approximately a third of patients in late phase of recovery from severe brain injury showed measurable improvements in their level of awareness. These changes were found in both VS and MCS patients including patients who suffered from non-traumatic brain injuries.

The main methodological difference between this study and previously published work is that all patients included in our study were initially diagnosed at the attached specialist brain injury rehabilitation unit by highly experienced clinical staff using at least two different validated assessment techniques (SMART, WHIM [28]). In our study, the timeline between the brain injury and re-assessment using CRS-R varied between 2 and 16 years. In comparison to previous studies this is an unusually long time window between validated assessments. During this time, very slow processes of neural recovery may have taken place including re-establishment of disrupted brain networks essential for consciousness. The care pathway within the Royal Hospital for Neuro-disability is that patients are initially assessed and treated within a specialist brain injury rehabilitation unit; typically for a period of 4 months. If the patient is stable yet showing no consistent improvement in their DOC they are then transferred to a specialist nursing home environment where they continue to have maintenance level therapy input along with interventions to prevent complications such as pressure sores and contractures. They also are involved with group activities including music therapy. The current study did not aim to investigate the influence of access to specialist rehabilitation or the specialist nursing home settings; however, the rehabilitation and the care received by this cohort of patients may have some bearing on unexpectedly high percentages of improvement of awareness.

In our study only one patient emerged from disorders of consciousness and 8 out of 11 patients with improvement of awareness had a diagnosis change of VS to MCS. This may have significant ethical and legal implications. For example, in the United Kingdom, for the purposes of the law and withdrawal of treatment decisions, the distinction between VS and MCS is important. For people in VS, when considering applications for declaratory relief for withdrawal of clinically assisted nutrition and hydration, the English Courts work on the principal assumption of life-sustaining treatment is not in their best interests and favour withdrawal of life-sustaining treatment. Whereas, for the people in MCS, the decisions are made using a balance sheet approach where perceived benefits from continuation of treatment will be weighed against countervailing disadvantages.[29] As the differentiation between VS and MCS is the cornerstone of decision-making in English courts; regular assessments with validated assessment tools such as SMART, Wessex Head Injury Matrix, CRS-R is necessary and will inform clinicians and families of the patients when considering best interests of the patients with disorders of consciousness.

Our study has some limitations._Firstly, this is a cross-sectional cohort study with 34 patients in one particular long term care setting; hence the results may not be generalizable to the whole PDOC patient population. Second, this was not designed as a prospective follow up study, therefore, fails to provide evidence for possible influential factors for recovery of consciousness as well as how fast and when recovery occur. Another methodological limitation of this study was use of different assessment tools at the time of initial diagnosis and re-assessment (SMART and CRS-R retrospectively). However, both assessment tools are validated diagnostic tools for DOC and both use clear and stringent techniques to assess same modalities. Finally, this study has not captured data on the patients who died while resident in the long term care setting.

Conclusions

This study highlights the importance of long term follow up of patients with disorders of consciousness, regardless of the aetiology, age of the patient and time passed since the brain injury. Recovery of awareness in a third of patients over a long period of time, albeit with a poor functional outcome, supports the findings of recent studies showing that late recovery is possible[14] and it provides behavioural support for the concept that there may be long term axonal regrowth and neural plasticity in disorders of consciousness. [30,31] Our results further increase the ethical dilemmas faced by staff involved in making treatment decisions in this vulnerable patient group. The phenomenon of very late recovery of awareness has an important bearing on questions of withdrawal of artificial nutrition and hydration. Our study raises the question as to whether the word 'permanent' is being used appropriately in the diagnostic term "Permanent Vegetative State" as reported in the recent Royal College of Physicians Guidelines. Prospective multi-centre studies that involve a variety of rehabilitation and long term care settings are now needed in order to comprehend long term prognostic outcomes and mechanisms of recovery in severe PDOC states.

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Disclosure Statement

The authors report no declarations of interest.

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REFERENCES

1. Steppacher I, Kaps M, Kissler J. Will time heal? A long-term follow-up of severe disorders of consciousness. Ann Clin Transl Neurol 2014;1(6):401-8.
2. Royal College of Physicians of London a. Prolonged disorders of consciousness : national clinical guidelines.
3. Bernat JL. Chronic disorders of consciousness. Lancet 2006;367(9517):1181-92.
4. Giacino JT, Fins JJ, Laureys S, Schiff ND. Disorders of consciousness after acquired brain injury: the state of the science. Nat Rev Neurol 2014;10(2):99-114.
5. Laureys S, Owen AM, Schiff ND. Brain function in coma, vegetative state, and related disorders. Lancet Neurol 2004;3(9):537-46.
6. Giacino JT, Ashwal S, Childs N, Cranford R, Jennett B, Katz DI, Kelly JP, Rosenberg JH, Whyte J, Zafonte RD and others. The minimally conscious state: definition and diagnostic criteria. Neurology 2002;58(3):349-53.
7. Cruse D, Chennu S, Chatelle C, Bekinschtein TA, Fernandez-Espejo D, Pickard JD, Laureys S, Owen AM. Bedside detection of awareness in the vegetative state: a cohort study. Lancet 2011;378(9809):2088-94.
8. Bekinschtein TA, Manes FF, Villarreal M, Owen AM, Della-Maggiore V. Functional imaging reveals movement preparatory activity in the vegetative state. Front Hum Neurosci 2011;5:5.
9. Bruno MA, Gosseries O, Ledoux D, Hustinx R, Laureys S. Assessment of consciousness with electrophysiological and neurological imaging techniques. Curr Opin Crit Care 2011;17(2):146-51.
10. Monti MM, Vanhaudenhuyse A, Coleman MR, Boly M, Pickard JD, Tshibanda L, Owen AM, Laureys S. Willful modulation of brain activity in disorders of consciousness. N Engl J Med 2010;362(7):579-89.

11. Kondziella D, Friberg CK, Frokjaer VG, Fabricius M, Møller K. Preserved consciousness in vegetative and minimal conscious states: systematic review and meta-analysis. J Neurol Neurosurg Psychiatry 2016;87(5):485-92.
12. Mohonk Report: A report to congress improving outcomes for individuals with disorders of consciousness, assessment, treatment, and research needs. . 2006.
13. Yelden K, Sargent S, Samanta J. Understanding the decision-making environment for people in minimally conscious state. Neuropsychol Rehabil 2017:1-12.
14. Estraneo A, Moretta P, Loreto V, Lanzillo B, Santoro L, Trojano L. Late recovery after traumatic, anoxic, or hemorrhagic long-lasting vegetative state. Neurology 2010;75(3):239-45.
15. Arts W, van Dongen HR, van Hof-van Duin J, Lammens E. Unexpected improvement after prolonged posttraumatic vegetative state. J Neurol Neurosurg Psychiatry 1985;48(12):1300-3.
16. Sancisi E, Battistini A, Di Stefano C, Simoncini L, Simoncini L, Montagna P, Piperno R. Late recovery from post-traumatic vegetative state. Brain Inj 2009;23(2):163-6.
17. Childs NL, Mercer WN. Brief report: late improvement in consciousness after post-traumatic vegetative state. N Engl J Med 1996;334(1):24-5.
18. McMillan TM, Herbert CM. Further recovery in a potential treatment withdrawal case 10 years after brain injury. Brain Inj 2004;18(9):935-40.
19. Avesani R, Gambini MG, Albertini G. The vegetative state: a report of two cases with a long-term follow-up. Brain Inj 2006;20(3):333-8.
20. Sara M, Sacco S, Cipolla F, Onorati P, Scoppetta C, Albertini G, Carolei A. An unexpected recovery from permanent vegetative state. Brain Inj 2007;21(1):101-3.
21. Estraneo A, Moretta P, Loreto V, Santoro L, Trojano L. Clinical and neuropsychological long-term outcomes after late recovery of responsiveness: a case series. Arch Phys Med Rehabil 2014;95(4):711-6.
22. Luauté J, Maucort-Boulch D, Tell L, Quelard F, Sarraf T, Iwaz J, Boisson D, Fischer C. Long-term outcomes of chronic minimally conscious and vegetative states. Neurology 2010;75(3):246-52.
23. Gill-Thwaites H. The Sensory Modality Assessment Rehabilitation Technique--a tool for assessment and treatment of patients with severe brain injury in a vegetative state. Brain Inj 1997;11(10):723-34.
24. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004;85(12):2020-9.
25. Seel RT, Sherer M, Whyte J, Katz DI, Giacino JT, Rosenbaum AM, Hammond FM, Kalmar K, Pape TL, Zafonte R and others. Assessment scales for disorders of consciousness: evidence-based recommendations for clinical practice and research. Arch Phys Med Rehabil 2010;91(12):1795-813.

26. Thonnard M, Wannez S, Keen S, Brédart S, Bruno MA, Gosseries O, Demertzi A, Thibaut A, Chatelle C, Charland-Verville V and others. Detection of visual pursuit in patients in minimally conscious state: a matter of stimuli and visual plane? Brain Inj 2014;28(9):1164-70.
27. Vanhaudenhuyse A, Schnakers C, Brédart S, Laureys S. Assessment of visual pursuit in post-comatose states: use a mirror. J Neurol Neurosurg Psychiatry 2008;79(2):223.
28. Shiel A, Horn SA, Wilson BA, Watson MJ, Campbell MJ, McLellan DL. The Wessex Head Injury Matrix (WHIM) main scale: a preliminary report on a scale to assess and monitor patient recovery after severe head injury. Clin Rehabil 2000;14(4):408-16.
29. Samanta J., Yelden K., Sargent S. Should people in the minimally conscious state have a (recognised) right to reassessment? Contemporary Issues in Law 2016;14(1):63-83.
30. Demertzi A, Schnakers C, Soddu A, Bruno MA, Gosseries O, Vanhaudenhuyse A, Laureys S. Neural plasticity lessons from disorders of consciousness. Front Psychol 2010;1:245.
31. Voss HU, Uluc AM, Dyke JP, Watts R, Kobylarz EJ, McCandliss BD, Heier LA, Beattie BJ, Hamacher KA, Vallabhajosula S and others. Possible axonal regrowth in late recovery from the minimally conscious state. J Clin Invest 2006;116(7):2005-11.