The Repetition of Behavioral Assessments in Diagnosis of Disorders of Consciousness

Sarah Wannez, MSc,1 Lizette Heine, PhD,1,2 Marie Thonnard, MSc,1 Olivia Gossseries, PhD,1,3* and Steven Laureys, MD, PhD,1*
Coma Science Group collaborators

Objective: To determine whether repeated examinations using the Coma Recovery Scale-Revised (CRS-R) have an impact on diagnostic accuracy of patients with disorders of consciousness and to provide guidelines regarding the number of assessments required for obtaining a reliable diagnosis.

Methods: One hundred twenty-three adult patients with chronic disorders of consciousness were referred to our tertiary center. They were assessed at least six times with the CRS-R within a 10-day period. Clinical diagnoses based on one, two, three, four, and five Coma Recovery Scale-Revised assessments were compared with a reference diagnosis (ie, the highest behavioral diagnosis obtained after six evaluations) using nonparametric statistics. Results were considered significant at $p < 0.05$ corrected for multiple comparisons.

Results: The number of assessments had a significant effect on the clinical diagnosis. Up to the fourth examination, the diagnosis was still statistically different from the reference diagnosis based on six CRS-R assessments. Compared to this reference diagnosis, the first evaluation led to 36% of misdiagnoses.

Interpretation: The number of CRS-R assessments has an impact on the clinical diagnosis of patients with chronic disorders of consciousness. Up to the fourth examinations, behavioral fluctuations may still impact the diagnostic accuracy. We here suggest performing at least five assessments in each patient with disorders of consciousness within a short time interval (eg, 2 weeks) to reduce misdiagnosis.

Errors of diagnosis are reported to be frequent (up to 40%) in patients with disorders of consciousness (DOC).1–5 Patients in unresponsive wakefulness syndrome/vegetative state (UWS/VS)6 are characterized by the presence of arousal without awareness (ie, only reflexive behaviors), whereas patients in minimally conscious state (MCS7) show inconsistent, but reproducible, purposeful behaviors. Patients in MCS are subcategorized into MCS− and MCS+, based on signs of language processing.8 Patients in MCS+ are able to show response to commands, whereas patients in MCS− only show lower level of conscious behaviors such as visual pursuit or object localization. When patients recover functional communication and/or functional object use, they have emerged from the MCS (EMCS7).

In this context, behavioral misdiagnosis can be attributed to a large number of factors, including motor or language impairments and vigilance fluctuations.9 Bedside evaluation is still considered the “gold standard” in clinical practice.10 Indeed, behavioral scales are often
the only available tools in clinical centers to assess patients’ level of consciousness. To date, the most sensitive and validated scale is the Coma Recovery Scale-Revised (CRS-R).9

Recent guidelines emphasize the importance of repeated or extended assessments to minimize misdiagnosis attributed to fluctuating levels of consciousness.9 However, to our knowledge, no study has investigated the number of examinations needed to increase diagnosis accuracy in patients with DOC.

The aims of our study were twofold: (1) to determine whether the diagnosis is influenced by the number of CRS-R assessments and (2) to evaluate the number of CRS-R examinations required to obtain a reliable and accurate diagnosis.

Patients and Methods

We assessed patients with chronic DOC (ie, time since onset longer than 12 months after a TBI (traumatic brain injury), and longer than 3 months after a non-TBI, as determined by the guidelines) admitted to the university hospital of Liège (Belgium) for multimodal assessment of consciousness. Patients underwent at least six standardized behavioral assessments using CRS-R over a period of maximum 10 days. Note that patients did not have a standardized prescreening assessment before inclusion. All assessments were performed during their stay in our hospital.

Inclusion criteria in the study were to have sustained a severe acquired brain injury leading to a chronic DOC, to be at least 18 years old, and to be medically stable. An exclusion criterion was any modification of pharmacological or rehabilitation treatment during the study period. Patients who were diagnosed as EMCS after the first two assessments were excluded, because, by definition, this state is not a DOC. However, patients detected in EMCS later on were kept in the sample because they represent misdiagnosis (ie, they were initially considered as MCS while they were, in fact, EMCS). The EMCS diagnosis was given as soon as the patient showed functional communication or functional object use in two consecutive evaluations, as stated in the guidelines.7

Patients were, most of the time, assessed in their bed, with the chest raised up to increase arousal and avoid sleepiness. Assessments in a wheelchair were rare. At the beginning of each examination, spontaneous movements were observed for at least 1 minute and the arousal protocol was applied if the patient was drowsy, as recommended by the CRS-R manual. The CRS-R is composed of 23 items distributed in six subscales assessing different functions (ie, auditory, visual, motor and oromotor/verbal functions, communication, and arousal). Each subscale contains multiple items arranged in a hierarchical way, the highest item representing the most complex behavior. While some combinations of these items are impossible according to the scale guidelines, some improbable combinations might indicate specific impairments.13 The clinical diagnosis is thus based on the presence or absence of operationally defined behavioral responses to specific sensory stimuli (eg, if a response to command like “move your feet” is observed at least three times out of four trials, the patient is considered to be in MCS). We here did not use the total score made up from the addition of the different subscales, because even though a recent study proposed a cut-off score of 8 to distinguish between patients in UWS/VS and MCS, it still misclassified 7% of patients.14 A modified score was then proposed, permitting to distinguish UWS/VS and MCS patients, based on the presence of signs of consciousness during the assessment.15 However, it does not allow identifying MCS and MCS patients, nor EMCS. In this study, we thus diagnosed the patients based on the behavioral responses they showed. The complete CRS-R examination lasted between 25 and 50 minutes, depending on the patient’s responsiveness. Patients were assessed at different moments of the day (morning and afternoon), and some CRS-R assessments were performed on the same day. All assessors were well trained and experienced in the use of the CRS-R.

As a dependent variable, we used the clinical diagnosis (UWS/VS, MCS, MCS, or EMCS) based on one, two, three, four, five, and six CRS-R assessments taken together (respecting the chronological order of administration). For each time point, the diagnosis was the highest out of the past and current CRS-R evaluations. In other words, if the patient was diagnosed as UWS/VS at the first CRS-R assessment, MCS at the second and UWS/VS at the third, the concluding diagnosis after three CRS-R examinations was MCS. The highest diagnosis obtained using six CRS-R evaluations was here considered the reference diagnosis.

For the first aim of the study, which was to evaluate the effect of the number of assessments on clinical diagnosis accuracy, we used Friedman’s analysis of variance ANOVA as a non-parametric test for repeated measurements because our data were not normally distributed. To test for any influence of the etiology, we assessed separately TBI and non-TBI patients. We also tested a subgroup of patients whose best diagnosis has been observed at least twice, to eliminate the possibility of false positives biasing the results. To verify that the changes in CRS-R diagnosis were not attributed to a spontaneous recovery or a habituation of the patient to the CSR-R, we performed Friedman ANOVA with CRS-R mixed in a nonchronological order. We first tested the reverse of the chronological order (6-5-4-3-2-1) and then two random orders (2-5-6-4-3-1 and 3-6-4-2-1-5). To test for an effect of time since injury or age, we used another analysis, because these variables are continuous. We first created a new variable representing the number of assessments that indicated the final diagnosis. For example, a patient who was diagnosed: MCS, UWS/VS, MCS, MCS, UWS/VS, UWS/VS was given a value of 3, because three assessments indicated the final diagnosis. This variable ranged from 1 to 6 and indicated whether the patient fluctuated a lot (low value) or was stable (high value). We then correlated this variable with age and time since onset, to assess whether the variability, thus the risk of misdiagnosis, was linked to age or time since injury. For the second aim of the study, which was to define the
We included 123 patients in the study (47 women; mean age, 40 ± 14 years; range, 18–72; 47 TBI; mean time since injury, 4 ± 4 years; range, 95 days–27 years). CRS-R assessments were completed within 3 to 9 days (mean and standard deviation, 6 ± 2).

Using the whole sample of patients, the number of performed CRS-R assessments significantly affected the diagnosis \( (\chi^2_{123,5} = 141.17; p < 0.001) \). This effect was found within TBI \( (\chi^2_{47,5} = 85.28; p < 0.001) \) and non-TBI \( (\chi^2_{76,5} = 58.91; p < 0.001) \) samples. This effect was also identified among the 100 patients whose best diagnosis was observed at least twice \( (\chi^2_{100,5} = 90.30; p < 0.001) \), excluding the possibility of false positives explaining the changes in CRS-R diagnosis. The same result was obtained when CRS-R assessments were considered in the reverse chronological order \( (\chi^2_{123,5} = 162.17; p < 0.001) \), or in random orders \( (\chi^2_{123,5} = 146.29; p < 0.001) \) for the order “2-5-6-4-3-1”; \( \chi^2_{123,5} = 132.09; p < 0.001 \) for the order “3-6-4-2-1-5”). We did not observe any significant correlation between the number of assessments indicating the final diagnosis and the age of the patient (Spearman’s \( r = -0.08; p = 0.374 \)) or the time since onset (Spearman’s \( r = 0.07; p = 0.467 \)).

In the whole group, the diagnoses after one, two, three, and four CRS-R assessments were significantly different from the reference diagnosis (based on six assessments). The Table 1 reports misdiagnosis rates and Wilcoxon signed-rank test results. In the subgroup of patients who had seven CRS-R evaluations (58 of the 123 patients), a significant difference was also observed until the fourth diagnosis, as compared to the reference diagnosis of seven CRS-R \( (\chi^2_{58,6} = 104.11; p < 0.001; \text{see Table } 1) \).

The diagnosis observed during the first assessment was used to determine the rate of misdiagnoses after a single CRS-R, as compared to repeated evaluations. Of the 62 patients initially diagnosed as UWS/VS, 22 (35.5%) were finally diagnosed as MCS. Six of these patients (9.5%) were diagnosed as MCS\(^{−}\) and 16 (26%) as MCS\(^{+}\). Whereas the missed patients in MCS\(^{−}\)
showed a response to command afterward, the missed patients in MCS− subsequently showed one or more of the following behaviors indicative of consciousness: visual pursuit (n = 2); visual fixation (n = 1); automatic motor reactions (n = 2); pain localization (n = 1); and/or object localization (n = 1). Note that the patient showing visual fixation was of traumatic etiology. Among the 28 patients initially considered as MCS−, 16 (57%) were finally diagnosed as MCS+1, all showing consistent or reproducible response to command. Thirty-three patients were initially diagnosed as MCS+, but 6 of them (18%) got a final diagnosis of EMCS, showing functional communication in 4 patients, and functional use of objects in 2. When combining patients in MCS+ and MCS− at the first assessment, 6 patients (10%) were diagnosed as EMCS after six evaluations. The confirmation of EMCS happened at various moments (1 patient at the third, 2 patients at the fourth, 1 patient at the fifth, and 2 patients at the sixth examination). On the other hand, 6 patients (10% of patients with MCS) have shown EMCS signs at one point, but failed to show the same behavior during the following testing. Misdiagnosis rates across the different assessments and according to the diagnosis are displayed in the Figure 1.

FIGURE 1: Misdiagnosis rates (%) of patients after n CRS-R assessments according to the diagnosis. CRS-R = Coma Recovery Scale-Revised.

Discussion

It has been consistently reported that fluctuations in responsiveness are inherent to patients with DOC and could lead to misdiagnosis.1,7,9,10,16 The first aim of the study was to bring empirical evidence that those fluctuations have an impact on the clinical diagnosis, and that repeating behavioral assessments can decrease the rate of misdiagnosis. Here, we found that the diagnosis was significantly influenced by the number of evaluations. Hence, a lack of repeated examinations in patients with DOC can lead to an underestimation of patients’ level of consciousness. We did not observe any effect of age, etiology, or time since onset. Moreover, when the order of the CRS-R assessments was shuffled, the changes in CRS-R diagnosis were still observed. Altogether, these results indicate that the observed fluctuations do not reflect spontaneous recovery. The second aim of the present study was to determine how many CRS-R assessments are needed for a reliable diagnostic workup. We here observed significant differences between diagnosis based on six CRS-R and those based on one, two, three, and four CRS-R evaluations. These results imply that up to the fourth evaluation, fluctuations in responsiveness still impact diagnosis accuracy. No significant difference was observed between the reference diagnosis (based on six CRS-R) and the diagnosis based on five CRS-R, suggesting that a minimum of five CRS-R assessments is required for a reliable clinical diagnosis in DOC. Moreover, to confirm our results, we found similar outcome in a subgroup of patients that benefited from seven CRS-R within the 10-day period, validating the need of five CRS-R to reach a reliable diagnosis.

Reducing the risk of erroneous clinical diagnosis is of medico-ethical importance, given that prognostic and therapeutic decisions might be influenced by the diagnosis of the patient.17 Patients’ prognosis differ according to the diagnosis made a few weeks or months postinjury, as shown by different studies.17–19 Rehabilitation decisions might also depend on the diagnosis. It is therefore essential to correctly identify patients evolving to MCS. Furthermore, indication of treatment also depends on the diagnosis. For example, it is known that half of patients in MCS are responsive to transcranial direct current stimulation, whereas patients in UWS do not seem to be.22 Using a scale that has been standardized and validated is crucial when assessing patients with DOC1 (the CRS-R is considered the most sensitive9). To our knowledge, there is, however, no clear recommendations about the repetition of examinations, except for another scale, the Sensory Modality Assessment and Rehabilitation Technique (SMART), which recommends 10 examinations within 3 weeks (SMART23,24). A preliminary study on a small sample of patients indicated that extended assessment (ie, 10 × 60 minutes with the SMART) might avoid 40% of misdiagnosis as compared to two
Our findings show that a “UWS/VS” diagnosis made after the first assessment might be erroneous in 35% of the cases (as compared to the reference diagnosis after six examinations). The diagnosis of any single evaluation, irrespectively of the chronology, is different from the reference diagnosis (ranging here from 31 to 37%; mean, 35%). Those results are similar to previous studies, reporting 35% to 41% of patients misdiagnosed in UWS/VS1–3,5 by clinical consensus (compared to CRS-R). Moreover, in our study, 26% of the patients initially diagnosed UWS/VS were actually able to answer simple commands (ie, MCS+). Detection of patients in MCS+ is important because command following is the first step toward communication. According to our data, when a clinician did not detect a response to command in a patient at the first testing (UWS/VS or MCS), the diagnosis was erroneous in 36% of the cases (16/62 UWS/ VS and 16/28 MCS+). Previous studies reported that patients in MCS show more frequent visual and motor responses than auditory responses related to consciousness, and it can be influenced by many confounding elements such as examiners’, patients’, or environmental factors.1 One should also keep in mind that despite the statistically significant results indicating that five CRS-R assessments are reliable, a small percentage of patients are still misdiagnosed after five assessments (5%). Ideally, in order to decrease the level of false negatives, behavioral evaluations should be combined with neuroimaging evaluations. For example, a recent study showed the ability of 18-fluorodeoxyglucose positron emission tomography to detect covert consciousness.5 Indeed, almost 30% of patients clinically considered as UWS/VS showed brain metabolism more comparable to patients in MCS (nonbehavioral MCS, MCS*5,31). Some studies also pointed out the usefulness of functional magnetic resonance imaging22,33 and/or psychophysiological techniques34,35 to detect nonbehavioral command following cognitive motor dissociation36 or brain resting activity compatible with MCS. It implies that even with the most sensitive scale, we might still underestimate the level of consciousness of some patients.

Several limitations of the study should be taken into account. First, we have a bias toward positive evolution, because we kept the best diagnosis reached by each patient. Clinical regression could also appear and not be detected because of the way data were analyzed. Indeed, the highest diagnosis was considered as the reference diagnosis, even if subsequent examinations indicated a lower diagnosis. However, given the shortness of the study period, clinical regression is unlikely. By the way, no patient was initially considered MCS without being diagnosed once again as MCS later. Moreover, additional analyses shuffling the order of the CRS-R allow to exclude any effect of spontaneous recovery, given that the changes in CRS-R diagnosis were observed if the assessments were considered backward or in a random order. Second, we did not study the effect of time of assessments because data were not always available, but according to previous studies, morning evaluations might be preferable if one wants to increase the probability to observe signs of consciousness.29,37 However, this might also depend on individual differences. Finally, one could argue that variability can be attributed

---

June 2017 887

---

Wannez et al: Repeated CRS-R Assessments for Diagnosis in DOC
to the clinician’s subjectivity. In our study, a single testing could modify the reference diagnosis, and bias the results if it was only attributed to the rater.38 However, besides the known high inter-rater reliability of the CRS-R,9,11 patients were assessed by skilled and experienced neuropsychologists trained and used to administrate the scale. Moreover, we confirmed the observed variability in a subgroup of patients whose best diagnosis was observed at least twice, reducing the probability of false positives.

In conclusion, the present study confirms that patients with DOC suffer from fluctuations in responsiveness and shows that these fluctuations significantly impact the clinical diagnosis. For both clinical and research purposes, we suggest that patients with chronic DOC are repeatedly assessed (at least five times) in a short time span (eg, 10 days) in order to reduce the influence of behavioral fluctuations.

Acknowledgment
The study was supported by the University and University Hospital of Liège, the French Speaking Community Concerted Research Action (ARC-12/17-01), the Belgian National Funds for Scientific Research (FRS-FNRS), Human Brain Project (EU-H2020-fetflagship-hbp-sga17GA720270), Luminous project (EU-H2020-fetopen-ga686764), the Wallonie-Bruxelles International, the James McDonnell Foundation, Mind Science Foundation, IAP research network P7/06 of the Belgian Government (Belgian Science Policy), the European Commission, the Public Utility Foundation ‘Université Européenne du Travail’, “Fondazione Europea di Ricerca Biomedica”, and the Bial Foundation. L.H., O.B., and C.M. are research fellows, V.C.V., A.T., A.D., and O.G. are postdoctoral fellows, and S.L. is a research director at FRS-FNRS.

We thank Pr Pierre Maquet and Pr Gustave Moonen, from the Neurology department, University Hospital of Liège, as well as the whole Neurology staff, patients, and their families. We thank the Coma Science Group collaborators from the University of Liège (Liège): O. Bodart, J. Annen, V. Charland-Verville, G. Martens, C. Aubinet, C. Martial, and A. Vanhauenhyuse; from the Harvard Medical School (Boston): C. Chatelle and A. Thibaut; from UCLA (Los Angeles) and Casa Colina Hospital and Centers for Healthcare (Pomona, CA, USA): C. Schnakers; from Hôpital Pitié-Salpêtrière (Paris): A. Demertzi.

Author Contributions
S.W., M.T., O.G., and S.L. contributed to conception and design of the study. S.W. and M.T. analyzed the data. S.W. and M.T. drafted the manuscript. L.H., O.G., and S.L. brought major revisions in significant proportions of the manuscript. O.G. and S.L. contributed equally.

Potential Conflicts of Interest
Nothing to report.

References
1. Schnakers C, Vanhaudenhuyse A, Giacino J, et al. Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. BMC Neurol 2009;9:35.
2. Andrews K, Murphy L, Munday R, Littlewood C. Misdiagnosis of the vegetative state: retrospective study in a rehabilitation unit. BMJ 1996;313:13–16.
3. Childs N, Mercer W, Childs H. Accuracy of diagnosis of persistent vegetative state. Neurology 1993;43:1465–1467.
4. van Erp WS, Lavrijsen JC, Vos PE, et al. The vegetative state: prevalence, misdiagnosis, and treatment limitations. J Am Med Dir Assoc 2015;16:85.e9–e85.e14.
5. Stender J, Gosseries O, Bruno MA, et al. Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study. Lancet 2014;384:514–522.
6. Laureys S, Celesia G, Cohadon F, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med 2010;8:68.
7. Giacino JT, Ashwal S, Childs N, et al. The minimally conscious state. Neurology 2002;58:349–353.
8. Bruno MA, Majerus S, Boly M, et al. Functional neuroanatomy underlying the clinical subcategorization of minimally conscious state patients. J Neurol 2012;259:1087–1098.
9. Seel RT, Sherer M, Whyte J, et al. Assessment scales for disorders of consciousness: evidence-based recommendations for clinical practice and research. Arch Phys Med Rehabil 2010;91:1795–1813.
10. Giacino JT, Schnakers C, Rodriguez-Moreno D, et al. Behavioral assessment in patients with disorders of consciousness: gold standard or fool’s gold? In: Progress in Brain Research, Vol. 177. Oxford, UK: Elsevier; 2009:33–48.
11. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004;85:2020–2029.
12. The Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state—part 1. N Engl J Med 1994;330:842–845.
13. Chatelle C, Bodien YG, Carlowicz C, et al. Detection and interpretation of impossible and improbable Coma Recovery Scale-Revised scores. Arch Phys Med Rehabil 2016;97:1295–1300.
14. Bodien YG, Carlowicz CA, Chatelle C, Giacino JT. Sensitivity and specificity of the coma recovery scale-revised total score in detection of conscious awareness. Arch Phys Med Rehabil 2016;97:490–492.
15. Sattin D, Minati L, Rossi D, et al. The Coma Recovery Scale Modified Score: a new scoring system for the Coma Recovery Scale-Revised for assessment of patients with disorders of consciousness. Int J Rehabil Res 2015;38:350–356.
16. Majerus S, Gill-Thwaites H, Andrews K, Laureys S. Behavioral evaluation of consciousness in severe brain damage. Prog Brain Res 2005;150:397–413.
17. Demertzi A, Ledoux D, Bruno MA, et al. Attitudes towards end-of-life issues in disorders of consciousness: a European survey. J Neurol 2011;258:1058–1065.
18. Hirschberg R, Giacino JT. The vegetative and minimally conscious states: diagnosis, prognosis and treatment. Neurol Clin 2011;29:773–786.

19. Bruno M-A, Ledoux D, Vanhaudenhuyse A, et al. Pronostic des patients récupérant du coma (Prognosis of patients recovering from coma). In: Schnakers C, Laureys S, editors. Coma and états de conscience altérée (Coma and disorders of consciousness). Paris: Springer; 2011:17–30.

20. Tamashiro M, Cozzo D, Mattei M, et al. Early motor predictors of recovery in patients with severe traumatic brain injury. Brain Inj 2012;26:921–926.

21. Giacino JT, Fins JJ, Laureys S, Schiff ND. Disorders of consciousness after acquired brain injury: the state of the science. Nat Publ Gr 2014;10(2):99–114.

22. Thibaut A, Bruno MA, Ledoux D, et al. tDCS in patients with disorders of consciousness. Neurology 2014;82:1112–1118.

23. Chatelle C, Schnakers C, Bruno MA, et al. La Sensory Modality Assessment and Rehabilitation Technique (SMART): une échelle comportementale d’évaluation et de revalidation pour les états altérés de conscience. (The Sensory Modality Assessment and Rehabilitation Technique (SMART): A behavioral assessment scale for disorders of consciousness) Rev. Neurol. (Paris). 2010;166:675–682.

24. 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;11:723–734.

25. Chatelle C, Schnakers C, Bruno MA, et al. La Sensory Modality Assessment Rehabilitation Technique—a tool for assessment and treatment of patients with severe brain injury in a vegetative state. Brain Inj 1997;11:723–734.

26. Estraneo A, Moretta P, Cardinale V, et al. A multicentre study of intentional behavioural responses measured using the Coma Recovery Scale-Revised in patients with minimally conscious state. Clin Rehabil 2014;28:803–808.

27. Bagnato S, Boccagni C, Sant’Angelo A, et al. Longitudinal assessment of clinical signs of recovery in patients with unresponsive wakefulness syndrome after traumatic or nontraumatic brain injury. J Neurotrauma 2016;33:1–5.

28. Wannez S, Gosselies O, Azzolini D, et al. Prevalence of Coma Recovery Scale-Revised signs of consciousness in patients in minimally conscious state. Neuropsychol Rehabil 2017 Apr 11. doi: 10.1080/09602011.2017.1310656.

29. Riganello F, Arcuri F, Pugliese ME, et al. Coma Recovery Scale-R: variability in the disorder of consciousness. BMC Neurol. 2015;15:186.

30. Nakase-Richardson R, Yablon SA, Sherer M, et al. Serial yes/no reliability after traumatic brain injury: implications regarding the operational criteria for emergence from the minimally conscious state. J Neurol Neurosurg Psychiatry 2008;79:216–218.

31. Gosselies O, Zasler ND, Laureys S. Recent advances in disorders of consciousness: focus on the diagnosis. Brain Inj 2014;9052:1141–1150.

32. Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med 2010;362:579–589.

33. Vanhaudenhuyse A, Noirhomme Q, Tshibanda LJ, et al. Default network connectivity reflects the level of consciousness in non-communicative brain-damaged patients. Brain 2010;133:161–171.

34. Lulé D, Noirhomme Q, Kleih SC, et al. Probing command following in patients with disorders of consciousness using a brain-computer interface. Clin Neurophysiol 2013;124:101–106.

35. Lehembre R, Bruno MA, Vanhaudenhuyse A, et al. Resting-state EEG study of comatose patients: a connectivity and frequency analysis to find differences between vegetative and minimally conscious states. Funct Neurol 2012;27:41–47.

36. Schiff ND. Cognitive motor dissociation following severe brain injuries. JAMA Neurol 2015;72:1413–1415.

37. Candelieri A, Cortese MD, Dolce G, et al. Visual pursuit: within-day variability in the severe disorder of consciousness. J Neurotrauma 2011;28:2013–2017.

38. Lovstad M, Froslie KF, Giacino JT, et al. Reliability and diagnostic characteristics of the JFK coma recovery scale-revised: exploring the influence of rater’s level of experience. J Head Trauma Rehabil 2010;25:349–356.