# Motor Behavior Unmasks Residual Cognition in Disorders of Consciousness

Alessandro Pincherle, MD,[1,2]
Jane Jöhr, PhD,[1,2]
Camille Chatelle, PhD,[3]
Jean-Michel Pignat, MD,[1,2]
Renaud Du Pasquier, MD,[1,2]
Philippe Ryvlin, MD, PhD,[1,2]
Mauro Oddo, MD, PhD,[4] and
Karin Diserens, MD[1,2]

Disorders of consciousness (DOC) are a common consequence of severe brain injuries, and clinical evaluation is critical to provide a correct diagnosis and prognosis. The revised Motor Behavior Tool (MBT-r) is a clinical complementary tool aiming to identify subtle motor behaviors that might reflect residual cognition in DOC. In this prospective study including 30 DOC patients in the early stage after brain injury, we show that the revised MBT-r has an excellent inter-rater agreement and has the ability to identify a subgroup of patients, underestimated by the Coma Recovery Scale-Revised, showing residual cognition and a subsequent recovery of consciousness.

ANN NEUROL 2019;00:1–5

Disorders of consciousness (DOC) are a common consequence of severe brain injuries. Physicians in intensive care units (ICUs) are challenged with providing diagnoses and prognoses, which, in turn, lead to complex therapeutic and ethical decisions. In addition, bedside clinical examinations may be hampered by several factors, which often lead to misdiagnosing conscious patients as unconscious.[1–4]

Using complementary methods, including functional brain imaging and electroencephalography, residual cognition has been identified in patients who are behaviorally indistinguishable from those with unresponsive wakefulness syndrome (UWS), leading to a new terminology called cognitive-motor dissociation (CMD).[5–7] In this respect, the validated scales used in the clinical evaluation of DOC are mainly based on residual motor output, therefore limiting their ability to unmask a patient's cognitive abilities to interact, in case of impaired motor efference/output. The Motor Behavior Tool (MBT)[8] was developed as a complement to the Coma Recovery Scale-Revised (CRS-R),[9] to identify subtle motor behavior not taken into account in the CRS-R that could be useful to identify residual cognition in DOC patients. A previous preliminary study reported the usefulness of the MBT to predict outcome early after severe brain injury.[8]

A new version of the MBT, with a simplified scoring method not requiring any post-hoc computation, has been conceived to be used as a stand-alone bedside clinical motor observational tool complementing the CRS-R assessment.

In this prospective study, we therefore administered the revised MBT (MBT-r) to a cohort of 30 patients with DOC in the early stage after brain injury to (1) assess interrater agreement and (2) support previous findings suggesting that the MBT-r can unmask a subgroup of patients with DOC, underestimated by the CRS-R, thus providing a reliable early prediction of consciousness/awareness recovery.

## Patients and Methods

The study has been approved by the CHUV Hospital review board and an informed consent obtained from the patient's relatives.

Patients admitted in 2017 to the ICU, following a severe brain injury were consecutively included in the study. Inclusion criteria were (1) age ≥ 16 years, (2) legally authorized surrogate available to provide informed consent, (3) history of severe acquired brain injury within the last 28 days, (4) Glasgow Coma Scale total score between 3 and 8 at the time of enrollment, and (5) continuous therapeutic sedation stopped at least 24 hours before the first assessment. Exclusion criteria included paroxysmal autonomic instability with dystonia and/or intractable/unmanageable hemodynamic instability and/or seizure disorders.

All therapeutic decisions, including withdrawal of life-sustaining therapies, were performed using a multimodal

From the [1]Department of Clinical Neurosciences and [2]Neurology and Acute Neurorehabilitation Unit, University Hospital CHUV, Lausanne, Switzerland; [3]Coma Science Group, GIGA Consciousness, University Hospital of Liege, Liege, Belgium; and [4]Neurointensive Care Unit, University Hospital CHUV, Lausanne, Switzerland

Address correspondence to Dr Karin Diserens, Department of Clinical Neurosciences, Acute Neurorehabilitation Unit, University Hospital CHUV, Bâtiment Champ de l'Air, Rue du Bugnon 21, 1011 Lausanne, Switzerland. E-mail: karin.diserens@chuv.ch

Received Jul 27, 2018, and in revised form Jan 15, 2019. Accepted for publication Jan 15, 2019

View this article online at wileyonlinelibrary.com. DOI: 10.1002/ana.25417.

© 2019 American Neurological Association 

approach[10] by physicians at the ICU who were not involved in the present study and blinded to the MBT-r results.

Three examiners, blinded to the patients' imaging and clinical history, independently assessed (within 24 hours) each patient with the CRS-R,[9] using the MBT-r to score additional motor and behavioral responses observed during the CRS-R. The test administration and examiner's tasks were pseudo-randomized to prevent order effects.

The MBT-r (see Table 1 for details) was designed to detect "positive" motor signs expression of residual cognition (limb, facial, ocular, or oral intentional or nonreflexive movements appearing spontaneously or in response to the environment or signs of verbal or behavioral interaction, not always reproducible).

Residual cognition was considered present when at least one positive item was scored. Negative signs were not considered in the scoring, but only used as red flags to suspect brainstem or pyramidal tract lesions.

Inter-rater agreement of the MBT-r was measured for each clinical item as well as for the MBT-r classification (ie, presence/absence of residual cognition). Cohen's kappa coefficient (κ) was used to measure inter-rater agreement; acceptable inter-rater agreement was set at κ > 0.7.

According to the best CRS-R scores out of the three - assessments,[9] patients were classified as coma, UWS,

**TABLE 1. The Motor Behavior Tool Revised**

| | | Item | Notes/Instructions | Cohen's κ |
|---|---|---|---|---|
| Positive signs | 1 | Spontaneous nonreflexive movements | Observation of the patient without any stimulation. At least one nonreflexive movements defined as intentional motor pattern nonstereotypical, not contextualized, and nonrepetitive | **0.786** |
| | 2 | Response to command | Any scorable response to verbal command | **0.703** |
| | 3 | Visual fixation or visual pursuit | Any clearly discernible visual fixation or visual pursuit in any direction | **0.869** |
| | 4 | Responses in a motivational context | Any increased in the frequency of nonreflexive motor responses in a salient context (eg, mother tongue, patient's own name) | 0.525 |
| | 5 | Defensive nonreflexive response to a noxious stimulation: nipple | Twisting the patient's nipple while keeping the patient's healthier arm between the patient's body and the examiner's arm. Any attempt to push away the examiner's arm that is not a sterotypical posture involving extension and internal rotation of the arms | **0.850** |
| | 6 | Defensive nonreflexive response to a noxious stimulation: nailbed | Deep pressure to nailbeds of four extremities. Any limb movement whose kinematics differs from a motor reflex response in terms of orientation planes and the type of elicited muscles is scored as defensive. | **0.725** |
| | 7 | Response to a noxious stimulation: grimace | Observation of at least one grimace during administration of noxious stimulation | **0.765** |
| Negative Signs | 8 | Abnormal motor or neurovegetative responses to stimulation | Observation of slow, stereotyped flexion or extension of the upper and/or lower extremities after noxious stimulation or neurovegetative responses (ie, tachycardia, hypo-/hyperventilation, hypertension, excessive sweating) to stimulation | 0.585 |
| | 9 | Signs of roving eyes or absence of oculocephalic reflex | Slowly roving eyes movements are typical of metabolic encephalopathy indicating diffuse cerebral dysfonction. Oculocephalic responses imply intact brainstem pathways. | **0.700** |

The revised Motor Behavior Tool (MBT-r) aims to identify "signs of residual cognition" in behaviorally unresponsive or minimally responsive patients according to the CRS-R. This tool consists of a set of seven items that explore different positive motor signs (items 1–7) as well as various reflex responses (items 8 and 9, negative signs). The MBT-r uses a noncumulative binary scoring system, with 1 and 0 indicating the presence or absence of a clinical item, respectively. Patients with at least one "positive" sign are classified as having "signs of residual cognition." "Negative" signs are used to identify patients with abnormal autonomic responses or brainstem dysfunction and are not considered in the final MBT-r scoring. The "positive" item "response in a motivational context" has a κ < 0.7; therefore, it might not be considered as a reliable isolated sign to detect residual cognition.

minimally conscious state (MCS), or emergence from MCS (EMCS) and grouped as unconscious (coma/UWS) or conscious (MCS/EMCS).

The Glasgow Outcome Scale (GOS) score at hospital discharge and 3 and 6 months later was used to determine each patient's outcome. GOS scores were dichotomously categorized as favorable for patients with consciousness recovery (ie, good recovery, moderate disability, or severe disability) or unfavorable for patients without consciousness recovery (ie, vegetative state or death).

Favorable and unfavorable outcomes were compared according to the CRS-R (conscious/unconscious) and MBT-r classification (presence/absence of residual cognition) by means of $2 \times 2$ contingency tables and chi-squared tests. Results were considered significant at $p < 0.05$.

## Results

Table 2 lists the patient's demographics, clinical characteristics, and outcomes. No etiology effect was observed on the outcomes (data not shown; $p = 0.804$, Fisher's exact test).

The CRS-R diagnosed 24 patients as unconscious and 6 patients as conscious, with all three examiners generating identical classifications.

The MBT-r diagnosed 6 patients without signs of residual cognition and 24 patients with signs of cognition.

The MBT-r-based classifications exhibited excellent inter-rater reliability ($\kappa = 1$). Inter-rater agreement for each MBT-r item is listed in Table 2. Only one item showed an inter-rater agreement with a $\kappa < 0.7$ (see Table 2).

Among the 24 patients classified as unconscious with the CRS-R, 18 (75%) showed signs of residual cognition with the MBT-r; all 6 patients (100%) classified as conscious with the CRS-R showed signs of residual cognition with the MBT-r (Fig 1A).

Among the 24 patients identified as unconscious by the CRS-R, 10 (41.7%) had a favorable outcome whereas none of the 6 identified as conscious by the CRS-R had an unfavorable outcome ($p = 0.019$, Fisher's exact test).

Among the 24 patients identified as showing residual cognition by the MBT-r, 16 (66.7%) had a favorable outcome, whereas the 6 remaining patients without residual cognition all had an unfavorable outcome ($p = 0.005$, Fisher's exact test; Fig 1B).

A strong consistency between the outcomes measured at hospital discharge and at 3 and 6 months was observed (see Table 2).

The 8 patients with residual cognition at MBT-r but unfavorable outcome were older ($75.1 \pm 10.9$ versus $59.0 \pm 15.9$; $p = 0.018$, *t* test) and displayed a higher rate of negative signs (25% versus 50%; $p = 0.22$, Fisher's exact test) than patients with favorable outcome, without any difference in etiology ($p = 0.74$, Fisher's exact test).

## Discussion

The present study reports an excellent inter-rater agreement of the MBT-r for classifying patients with or without residual cognition, early after therapeutic sedation withdrawal. In addition, the MBT-r identified signs of residual cognition in 75% of patients who were classified as unconscious (coma/UWS) by the CRS-R. Moreover, presence of residual cognition at an early stage was related to subsequent consciousness recovery, in agreement with previous findings with the first version of the MBT.[8] Our data, prospectively obtained in an ICU setting, support the notion that a wide range of cognitive capacities might be detected early after brain injury, and, more important, that their assessment is critical for determining an accurate prognosis.[11,12] The integration, as early as possible in the ICU setting, of MBT-r–based clinical observation might improve/contribute to outcome prediction based on electrophysiological and functional neuroimaging.[7]

When examining brain-damaged patients with altered states of consciousness, it remains challenging to reliably document the presence or the absence of any motor behavior that reflects conscious/cognitive activity. The MBT-r allows for assessing subtle motor/behavioral signs that may indicate nonreflexive intentional responses rather than reflexive motor reactions. Nonreflexive intentional responses may reflect the expression of residual/preserved interactive capacity, which has been proposed as a marker for consciousness.[13] Furthermore, the MBT-r considers facial grimacing after noxious stimulation as a positive interaction sign, even in the absence of appropriate motor responses. As originally described,[14,15] the absence of motor responses, if accompanied by facial grimacing, suggests that the defect is motor instead of consciousness related.

The MBT-r–based outcome prediction, in terms of consciousness recovery, may indeed highlight the involvement of blocked motor efference/output, rather than a true consciousness disorder, in a subset of patients with DOC who show minimal responsiveness at the bedside. Given the prognostic implications,[11,12] establishing whether a patient has residual cognition is of great significance, and we believe that the MBT-r may serve as a simple and economic tool for distinguishing CMD from other DOC. However, without valid references to confirm the presence of CMD,[5–7] this should be regarded as a working hypothesis and further confirmed by experiments comparing/integrating the MBT-r with functional neuroimaging and/or neurophysiological measurements.[16]

TABLE 2. Patient's Demographics, Clinical Characteristics, and Outcomes

| ID | Sex | Age | Etiology | Time to clinical Appraisal (days) | CRS-R | MBT-r Residual Cognition | Time to Discharge (days) | GOS at Discharge | GOS at 3 Months | GOS at 6 Months |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 56 | Hemorrage | 6 | Coma | N | 4 | 1[a] | — | — |
| 2 | M | 73 | Hemorrage | 5 | MCS | Y | 211 | 4 | 4 | 5 |
| 3 | F | 58 | Hemorrage | 12 | MCS | Y | 47 | 4 | 4 | 5 |
| 4 | M | 68 | Metabolic | 8 | UWS | Y | 21 | 5 | 5 | 5 |
| 5 | F | 72 | Hemorrage | 7 | Coma | Y | 36 | 4 | 4 | 4 |
| 6 | M | 71 | Trauma | 7 | Coma | N | 5 | 1[b] | — | — |
| 7 | F | 58 | Hemorrage | 12 | Coma | Y | 29 | 3 | 4 | 4 |
| 8 | M | 78 | Hemorrage | 8 | UWS | Y | 3 | 1[a] | — | — |
| 9 | M | 27 | Trauma | 17 | MCS | Y | 29 | 5 | 4 | 5 |
| 10 | F | 25 | Trauma | 16 | Coma | Y | 17 | 3 | 3 | 3 |
| 11 | F | 56 | Hemorrage | 6 | Coma | Y | 19 | 3 | 4 | 4 |
| 12 | M | 65 | Hemorrage | 11 | Coma | Y | 9 | 1[a] | — | — |
| 13 | F | 70 | Stroke | 8 | Coma | Y | 13 | 3 | 3 | 4 |
| 14 | M | 69 | Hemorrage | 3 | EMCS | Y | 39 | 3 | 3 | 3 |
| 15 | F | 34 | Anoxia | 12 | Coma | N | 1 | 1[b] | — | — |
| 16 | F | 82 | Anoxia | 15 | UWS | N | 3 | 1[a] | — | — |
| 17 | M | 53 | Hemorrage | 7 | Coma | Y | 35 | 3 | 3 | 3 |
| 18 | M | 73 | Trauma | 23 | MCS | Y | 34 | 3 | 4 | 4 |
| 19 | M | 40 | Trauma | 14 | UWS | Y | 44 | 5 | 5 | 5 |
| 20 | M | 57 | Metabolic | 11 | Coma | N | 15 | 1[b] | — | — |
| 21 | M | 54 | Metabolic | 5 | UWS | Y | 10 | 1[a] | — | — |
| 22 | M | 75 | Hemorrage | 8 | EMCS | Y | 35 | 3 | 3 | 3 |
| 23 | M | 69 | Hemorrage | 8 | UWS | Y | 50 | 3 | 3 | 3 |
| 24 | F | 83 | Hemorrage | 6 | Coma | Y | 2 | 1[a] | — | — |
| 25 | M | 73 | Hemorrage | 11 | UWS | Y | 7 | 1[a] | — | — |
| 26 | F | 72 | Trauma | 5 | Coma | N | 4 | 1[a] | — | — |
| 27 | F | 77 | Hemorrage | 12 | MCS | Y | 7 | 1[a] | — | — |
| 28 | M | 84 | Trauma | 7 | UWS | Y | 22 | 1 | — | — |
| 29 | M | 59 | Anoxia | 20 | UWS | Y | 26 | 3 | 3 | 3 |
| 30 | F | 87 | Hemorrage | 2 | UWS | Y | 7 | 1[a] | — | — |
| Mean ± SD | | 63.9 ± 16.0 | | 9.7 ± 4.9 | | | 16.8 ± 15.0 | | | |

[a]Withdrawal of life support measures because of neurological complications.
[b]Withdrawal of life support measures because of non-neurological complications.
MCS = minimally conscious state; UWS = unresponsive wakefulness syndrome; EMCS = emergence from minimally conscious state; NA = not available (the patient moved to another country); SD = standard deviation; MBT-r = revised Motor Behavior Tool; GOS = Glasgow Outcome Scale.

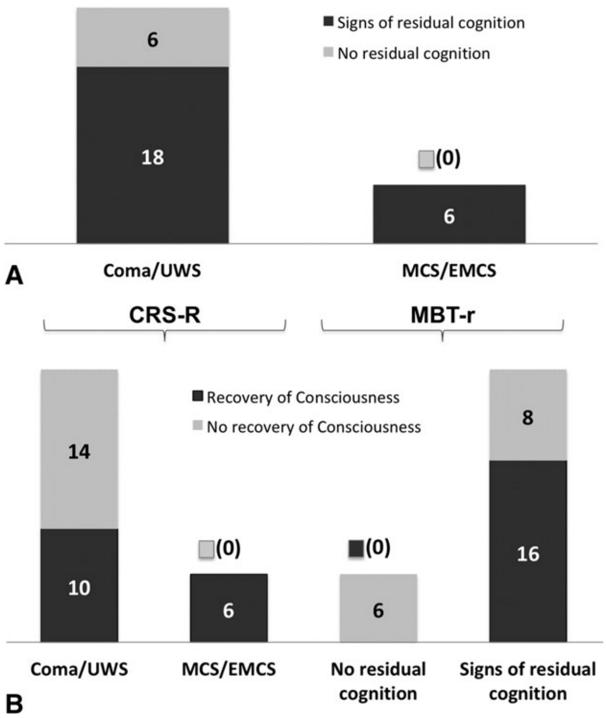


**FIGURE 1: CRS-R classification and residual cognition as detected by MBT-r (A) and prediction of consciousness recovery according to CRS-R and MBT-r (B). CRS-R = Coma Recovery Scale-Revised; ECMS = emergence from minimally conscious state; MBT-r = revised Motor Behavior Tool; MCS = minimally conscious state; UWS = unresponsive wakefulness syndrome.**

The findings from this study should be viewed in the context of several limitations. First, our results may not be generalizable to all patients with DOC attributed to the relatively small and heterogeneous cohort. To avoid selection bias, we consecutively included all ICU cases, including aged patients and severe cases, often having a fatal outcome. It has to be noted that all the therapeutic decisions, including withdrawal or limitation of life-sustaining treatment, were taken by physicians blinded to the study results following a consolidated multimodal approach.[10] We believe therefore that the risk of self-fulfilling prophecy is limited in our study. However, multicenter studies in larger populations involving different countries with different regulations are needed to confirm these results.

In conclusion, our data confirm that the MBT-r, used as a complement to CRS-R, is a useful clinical tool that identifies signs of residual cognition underestimated by the CRS-R and predicts consciousness recovery in acute patients with DOC.

## Acknowledgment

We thank the Foundation Biaggi for supporting this research project.

## Author Contributions

AP, JJ, CC, RdP, PR, and KD contributed to the conception and design of the study; AP, JJ, CC, JMP, and MO contributed to the acquisition and analysis of data; AP, JJ, and CC to drafting the text and preparing the figures.

## Potential Conflicts of Interest

Nothing to report.

## References

1. Bosco A, Lancioni GE, Olivetti Belardinelli M, et al. Vegetative state: efforts to curb misdiagnosis. Cogn Process 2010;11:87–90.
2. Childs NL, Mercer WN. Misdiagnosing the persistent vegetative state. Misdiagnosis certainly occurs. BMJ 1996;313:944.
3. Andrews K, Murphy L, Munday R, Littlewood C. Misdiagnosis of the vegetative state: Retrospective study in a rehabilitation unit. BMJ 1996;313:13–16.
4. 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.
5. Curley WH, Forgacs PB, Voss HU, Conte MM, Schiff ND. Characterization of EEG signals revealing covert cognition in the injured brain. Brain 2018;141:1404–1421.
6. Schiff ND. Cognitive motor dissociation following severe brain injuries. JAMA Neurol 2015;72:1413–1415.
7. Edlow BL, Chatelle C, Spencer CA, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. Brain 2017;140:2399–2414
8. Pignat JM, Mauron E, Johr J, et al. Outcome prediction of consciousness disorders in the acute stage based on a complementary motor behavioural tool. PLoS One 2016;11:e0156882.
9. 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.
10. Ltaief Z, Ben-Hamouda N, Suys T, et al. [Multimodal neuromonitoring for the critical care management of acute coma]. [Article in French]. Rev Med Suisse 2014;10:2350–2355.
11. Luaute J, Maucort-Boulch D, Tell L, et al. Long-term outcomes of chronic minimally conscious and vegetative states. Neurology 2010; 75:246–252.
12. Faugeras F, Rohaut B, Valente M, et al. Survival and consciousness recovery are better in the minimally conscious state than in the vegetative state. Brain Inj 2018;32:72–77.
13. Fischer DB, Truog RD. What is a reflex? A guide for understanding disorders of consciousness. Neurology 2015;85:543–548.
14. Plum F, Posner J. *The Diagnosis of Stupor and Coma*. Philadelphia, PA; Davis; 1980.
15. Posner J, Plum F. Plum and *Posner's Diagnosis of Stupor and Soma*. New York, NY: Oxford University Press; 2007.
16. Casarotto S, Comanducci A, Rosanova M, et al. Stratification of unresponsive patients by an independently validated index of brain complexity. Ann Neurol 2016;80:718–729.