

Supplementary material

1. Diagnostic criteria

The diagnosis was made according to standard diagnostic criteria for VS/UWS, MCS, and emergence from MCS.^[1-3]

The bedside diagnosis of VS/UWS was made in the presence of: 1) intermittent wakefulness with sleep/wake cycles (i.e. periodic eye opening); 2) absence of signs of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli; and 3) absence of signs of language comprehension or expression. All three criteria had to be met.

The Aspen Workgroup defined MCS as “a condition of severely altered consciousness in which there is minimal but definite behavioral evidence of conscious awareness”.^[4] The diagnosis of MCS was made according to the presence of at least one of the following criteria upon bedside examination: 1) simple command following; 2) intelligible verbalization; 3) recognizable verbal or gestural “yes/no” responses (without regard to accuracy); and 4) movements or emotional responses triggered by an environmental stimuli and that could not be attributed to reflexive activity. Since MCS is a clinically heterogeneous entity, MCS was subcategorized as MCS+, in which the patients had high-level behavioral responses (e.g. command following or specific responses), and MCS-, in which the patients had low-level but non-reflex responses (e.g. visual pursuit, localization of pain or smiling to emotional stimuli).

Emergence from MCS (EMCS) was diagnosed according to the bedside observation of reliable and consistent demonstration of at least one of the following: 1) functional interactive communication; and/or 2) functional use of two different objects.^[4]

2. Behavioral and outcome scale

CRS-R ^[5] was evaluated at baseline to confirm the diagnosis, to assess prognosis, and to determine the treatment strategy. The CRS-R comprises 23 items in six subscales: auditory, visual, motor, oromotor, communication, and arousal functions. The subscales are scored 0-3 for the oromotor, communication, arousal subscales, 0-4 for the auditory function subscale, 0-5 for the visual function subscale, and 0-6 for the motor function subscale. Low values indicate poor functions. The final score is calculated by adding all the subscale scores together. Based on the CRS-R, the patients can be categorized as: VS/UWS, MCS, and EMCS. In a given patient, the highest CRS-R score observed was used to diagnose VS/UWS or MCS.

Alteration of consciousness was assessed using the GCS (Teasdale and Jennett 1974), based on motor scores (1 to 6), verbal scores (1 to 5), and eye scores (1 to 4). In patients with endotracheal intubation, the verbal score was 1. A GCS score of ≤ 8 defined unconsciousness. In patients with TBI, mild TBI was defined as a GCS score of 13 to 15, moderate as 9 to 12, and severe as ≤ 8 .

The GOS ^[6] was used to evaluate the neurological outcomes: 1) death; 2) vegetative state; 3) severe disability; 4) moderate disability; and 5) good recovery.

3. Data management

Demographic and clinical data were recorded: 1) age at onset of coma; 2) sex; 3) time from injury to coma; 4) etiology of coma (categorized as TBI, HIE, or stroke); 5) neurologic examination and behavioral assessment; 6) laboratory blood tests; 7) presence of focal injuries, cortical atrophy, and/or subcortical atrophy at imaging; 8) possible clinical and surgical complications; and 9) pharmacological therapy. Neurophysiological such as SEP and ERP, and neuroimaging such as functional MRI or PET data were optional because not all patients underwent them based on availability of the tests and on the costs to the patient/family.

References

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- 5 Kalmar K, Giacino JT. The JFK Coma Recovery Scale--Revised. *Neuropsychol Rehabil* 2005;**15**:454-460 [doi: 10.1080/09602010443000425]
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Supplementary Table 1. Information about individual patient demographics

Pat ien t	Cente r	Sex	Age	Etiolog y	Diagnos is	Post injury days	GCS(0)	CRS-R(0)	Outcome	GO S	CT/MRI findings
1	NT	M	64	TBI	VS/UW S	49	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2	Right frontal apical lesions
2	NT	M	61	TBI	VS/UW S	30	7T (4-T-3)	3 (0-0-1-0-0-2)	VS/UWS	2	Bilateral frontal lobe hematoma
3	NT	F	48	TBI	VS/UW S	40	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2	Multiple lesions, hydrocephalus
4	NT	M	70	TBI	VS/UW S	52	5T (2-T-3)	2 (0-0-1-0-0-1)	VS/UWS	2	Diffuse cortical and subcortical atrophy
5	NT	M	61	TBI	VS/UW S	31	4T (2-T-2)	2 (0-0-1-0-0-1)	VS/UWS	2	Multiple lesions
6	NT	M	63	TBI	VS/UW S	36	3T (2-T-1)	1 (0-0-0-0-0-1)	MCS-	3	Multiple lesions, hydrocephalus
7	NT	F	79	TBI	VS/UW	50	4T (2-T-2)	2 (0-0-1-0-0-1)	VS/UWS	2	Left frontal parietal and

					S							corpus callosum softening
8	NT	F	19	TBI	VS/UW S	35	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2		Bilateral frontotemporal lobe lesions
9	NT	M	67	TBI	VS/UW S	54	3T (2-T-1)	1 (0-0-0-0-0-1)	VS/UWS	2		Cerebral hernia
10	NT	M	48	TBI	VS/UW S	99	3T (2-T-1)	1 (0-0-0-0-0-1)	D/MCS-	1		Bilateral frontal lesions
11	NT	M	48	TBI	VS/UW S	60	5T (2-T-3)	3 (1-0-1-0-0-1)	D/MCS-	1		Bilateral frontal hematoma
12	NT	F	29	TBI	VS/UW S	62	6T (3-T-3)	3 (0-0-2-0-0-1)	CS	5		Right craniocerebral operation
13	NT	F	42	TBI	VS/UW S	95	7T (4-T-3)	7 (2-1-2-0-0-2)	CS	4		Right frontal temporal lobe hemorrhage
14	NT	M	13	TBI	VS/UW S	35	3T (1-T-2)	1 (0-0-1-0-0-0)	CS	5		Left frontal parietal lobe hemorrhage
15	NT	M	51	TBI	VS/UW S	29	8T (4-T-4)	7 (2-1-2-0-0-2)	CS	5		Bilateral frontal lobe and right temporal lobe

												hematoma
16	NT	F	52	stroke	VS/UW S	37	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2	Left thalamic hemorrhage	
17	NT	F	49	stroke	VS/UW S	37	3T (1-T-2)	1 (0-0-1-0-0-0)	VS/UWS	2	Occipital hemorrhage	
18	NT	M	74	stroke	VS/UW S	410	5T (4-T-1)	2 (0-0-0-0-0-2)	VS/UWS	2	Cerebellar hematoma	
19	NT	F	45	stroke	VS/UW S	29	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2	Subarachnoid hemorrhage	
20	NT	M	40	stroke	VS/UW S	179	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Left occipital lobe hemorrhage	
21	NT	M	46	stroke	VS/UW S	51	3T (1-T-2)	1 (0-0-1-0-0-0)	VS/UWS	2	Bilateral apical occipital softening foci	
22	NT	F	46	stroke	VS/UW S	33	3T (2-T-1)	1 (0-0-0-0-0-1)	VS/UWS	2	Left hemisphere infarction	
23	NT	F	70	stroke	VS/UW S	35	4T (2-T-2)	2 (0-0-1-0-0-1)	D/VS/U WS	1	Subarachnoid hemorrhage	

24	NT	F	66	stroke	VS/UW S	33	3T (2-T-1)	1 (0-0-0-0-0-1)	D/VS/U WS	1	Left basal ganglia hemorrhage
25	NT	F	62	stroke	VS/UW S	89	5T (4-T-1)	2 (0-0-0-0-0-2)	VS/UWS	2	Left hemisphere infarction
26	NT	M	53	stroke	VS/UW S	43	5T (4-T-1)	2 (0-0-0-0-0-2)	MCS-	3	Bilateral subdural hemorrhage
27	NT	M	71	stroke	VS/UW S	30	8T (4-T-4)	7 (1-1-2-1-0-2)	CS	3	Bilateral multiple infarction with hemorrhage
28	NT	M	32	stroke	VS/UW S	75	8T (4-T-4)	8 (2-1-2-1-0-2)	EMCS	3	Moyamoya disease, thalamic hemorrhage
29	NT	M	19	stroke	VS/UW S	47	6T (4-T-2)	5 (1-1-1-0-0-2)	CS	5	Left frontal lobe hemorrhage
30	NT	M	64	stroke	VS/UW S	30	7T (4-T-3)	6 (1-1-2-0-0-2)	CS	4	Left basal ganglia hemorrhage
31	NT	M	58	stroke	VS/UW S	28	7T (4-T-3)	6 (1-1-2-0-0-2)	CS	4	Left thalamic hemorrhage
32	NT	M	76	stroke	VS/UW	41	5T (2-T-3)	3 (0-0-2-0-0-1)	EMCS	3	Left anterior occipital lobe

					S						hemorrhage
33	NT	M	48	stroke	VS/UW S	30	7T (4-T-3)	6 (1-1-2-0-0-2)	CS	5	Left frontal and basal ganglia hemorrhage
34	NT	M	60	stroke	VS/UW S	76	5T (4-T-1)	4 (1-1-0-0-0-2)	LIS	3	Pons hemorrhage
35	NT	F	46	HIE	VS/UW S	152	3T (2-T-1)	1 (0-0-0-0-0-1)	VS/UWS	2	Bilateral cerebral hemisphere edema
36	NT	M	34	HIE	VS/UW S	52	7T (4-T-3)	3 (0-0-1-0-0-2)	MCS-	3	Diffuse axonal injury
37	NT	M	56	TBI	MCS-	34	9T (4-T-5)	11(2-3-3-1-0-2)	CS	4	Left frontal occipital occipital hemorrhage
38	NT	M	79	stroke	MCS-	69	8T (4-T-4)	10(2-3-2-1-0-2)	CS	4	Left cerebellar hemorrhage
39	NT	M	48	stroke	MCS-	37	8T (4-T-4)	9 (2-2-2-1-0-2)	CS	3	Right thalamic hemorrhage
40	NT	M	63	stroke	MCS-	29	9T (4-T-5)	11(2-3-3-1-0-2)	CS	5	Right temporal and parietal lobe hemorrhage
41	NT	M	58	stroke	MCS-	40	11 (4-2-5)	12(2-3-3-2-0-2)	CS	4	Right hemisphere infarction
42	NT	M	50	stroke	MCS-	36	8T (4-T-4)	8 (2-2-2-0-0-2)	CS	5	Right hemisphere infarction

43	NT	M	65	stroke	MCS-	28	9T (4-T-5)	11(2-3-3-1-0-2)	CS	4	Right basal ganglia hemorrhage
44	NT	M	66	stroke	MCS-	32	9T (4-T-5)	10(2-2-3-1-0-2)	LIS	3	Brain stem infarction
45	NT	M	28	stroke	MCS-	29	5T (4-T-1)	8 (2-3-0-0-0-2)	LIS	3	Brain stem hemorrhage
46	NT	M	46	TBI	MCS+	35	9T (4-T-5)	16(3-4-5-2-0-2)	CS	5	Right frontal temporal lobe contusion with hemorrhage
47	NT	M	31	stroke	MCS+	32	10T(4-T-6)	13(3-3-3-1-0-3)	LIS	3	Brain stem hemorrhage
48	NT	M	43	stroke	MCS+	35	5T (4-T-1)	8 (3-3-0-0-0-2)	LIS	3	Brain stem hemorrhage
49	NT	M	52	stroke	MCS+	28	10T(4-T-6)	16(3-4-5-2-0-2)	LIS	3	Brain stem infarction
50	NT	M	43	stroke	MCS+	634	5T (4-T-1)	12(4-5-0-0-1-2)	LIS	3	Brain stem hemorrhage
51	BJ	M	40	TBI	VS/UW S	68	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Bilateral frontal lobe contusion
52	BJ	F	16	TBI	VS/UW S	38	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Right basal ganglia and lateral ventricle cerebral hemorrhage, hydrocephalus
53	BJ	F	30	TBI	VS/UW S	153	7T (4-T-3)	5 (1-1-1-0-0-2)	MCS-	3	Hydrocephalus

54	BJ	M	34	TBI	VS/UW S	62	7T (4-T-3)	5 (1-1-1-0-0-2)	CS	4	Multiple softening foci after bilateral crest craniotomy
55	BJ	M	67	TBI	VS/UW S	378	8T (4-T-4)	6 (1-1-2-0-0-2)	MCS-	3	Bilateral frontal lesions
56	BJ	M	7	TBI	VS/UW S	138	6T (4-T-2)	5 (1-1-1-0-0-2)	VS/UWS	2	Bilateral frontal and corpus callosum hemorrhage, hydrocephalus
57	BJ	F	73	TBI	VS/UW S	93	6T (3-T-3)	2 (0-0-1-0-0-1)	D/MCS-	1	Left parietal and temporal lesions
58	BJ	M	54	TBI	VS/UW S	71	4T (2-T-2)	2 (0-0-1-0-0-1)	VS/UWS	2	Bilateral multiple hematoma
59	BJ	M	61	TBI	VS/UW S	496	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Bilateral subdural effusion
60	BJ	M	80	TBI	VS/UW S	89	3T (2-T-1)	1 (0-0-0-0-0-1)	CS	4	Bilateral frontal temporal softening
61	BJ	M	56	stroke	VS/UW S	114	2T (1-T-1)	0 (0-0-0-0-0-0)	VS/UWS	2	Left basal ganglia and brain stem hemorrhage

62	BJ	M	49	stroke	VS/UW S	63	5T (4-T-1)	3 (0-0-1-0-0-2)	MCS-	3	Left thalamus, frontal occipital lobe hemorrhage
63	BJ	M	43	stroke	VS/UW S	38	3T (2-T-1)	1 (0-0-0-0-0-1)	VS/UWS	2	Right basal ganglia hemorrhage
64	BJ	M	50	stroke	VS/UW S	91	7T (4-T-3)	5 (1-0-1-1-0-2)	VS/UWS	2	Bilateral parietal and temporal lesions, diffuse cortical atrophy
65	BJ	M	45	stroke	VS/UW S	69	5T (3-T-2)	3 (1-0-1-0-0-1)	VS/UWS	2	Brain stem hemorrhage
66	BJ	M	41	stroke	VS/UW S	38	5T (2-T-3)	3 (1-0-1-0-0-1)	VS/UWS	2	Right parietal lobe hemorrhage into the ventricle
67	BJ	M	53	stroke	VS/UW S	154	7T (4-T-3)	5 (1-0-1-1-0-2)	VS/UWS	2	Brain stem hemorrhage
68	BJ	M	38	stroke	VS/UW S	216	7T (4-T-3)	6 (1-1-1-1-0-2)	VS/UWS	2	Brain stem hemorrhage
69	BJ	F	52	stroke	VS/UW S	154	8T (4-T-4)	6 (1-1-2-0-0-2)	CS	4	Left frontal lobe hemorrhage

70	BJ	M	56	stroke	VS/UW S	97	7T (4-T-3)	6 (1-1-1-1-0-2)	D/LIS	1	Brain stem hemorrhage
71	BJ	F	34	HIE	VS/UW S	58	4T (2-T-2)	2 (0-0-1-0-0-1)	VS/UWS	2	Diffuse cortical and subcortical atrophy
72	BJ	M	54	HIE	VS/UW S	82	8T (4-T-4)	5 (1-0-2-0-0-2)	VS/UWS	2	Ischemia and hypoxia
73	BJ	F	43	HIE	VS/UW S	263	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Ischemia and hypoxia
74	BJ	M	52	HIE	VS/UW S	308	7T (4-T-3)	5 (1-1-1-0-0-2)	VS/UWS	2	Diffuse ischemia and demyelination
75	BJ	M	49	HIE	VS/UW S	87	4T (3-T-1)	1 (0-0-0-0-0-1)	VS/UWS	2	Diffuse cortical and subcortical atrophy
76	BJ	F	27	HIE	VS/UW S	47	5T (3-T-2)	3 (1-0-1-0-0-1)	VS/UWS	2	Diffuse cortical and subcortical atrophy
77	BJ	F	38	TBI	MCS-	236	8T (4-T-4)	8 (2-2-2-0-0-2)	MCS-	3	Postoperative changes of bilateral frontal temporal lobe
78	BJ	F	56	TBI	MCS-	291	9T (4-T-5)	10(2-3-3-0-0-2)	MCS-	3	Diffuse white matter damage

79	BJ	F	13	TBI	MCS-	166	7T (4-T-3)	9 (2-3-2-0-0-2)	CS	5	Diffuse lesions, hydrocephalus
80	BJ	F	72	TBI	MCS-	143	7T (4-T-3)	9 (2-3-2-0-0-2)	CS	3	Bilateral multiple contusion
81	BJ	M	47	TBI	MCS-	290	11 (4-2-5)	12(2-3-3-2-0-2)	CS	4	Multiple ischemic lesions and cerebral edema
82	BJ	M	69	TBI	MCS-	88	9T (4-T-5)	11(2-3-3-1-0-2)	D/MCS-	1	Multiple intracranial hematoma
83	BJ	M	63	stroke	MCS-	61	9T (4-T-5)	11(2-3-3-1-0-2)	CS	4	Right frontal and temporal lesions
84	BJ	M	85	stroke	MCS-	29	9 (4-1-4)	7 (1-2-2-0-0-2)	CS	3	Left frontal and parietal lesions, diffuse atrophy
85	BJ	M	60	stroke	MCS-	28	7 (3-1-3)	6 (1-2-2-0-0-1)	CS	4	Right parietal and occipital lesions
86	BJ	M	53	stroke	MCS-	64	8T (4-T-4)	9 (2-2-2-1-0-2)	CS	4	Right thalamus-capsular lesion
87	BJ	M	70	stroke	MCS-	132	9T (4-T-5)	10(2-3-3-0-0-2)	MCS-	3	Right basal ganglia hemorrhage, hydrocephalus

88	BJ	M	9	HIE	MCS-	102	7T (4-T-3)	9 (2-3-1-1-0-2)	MCS-	3	Diffuse cortical and subcortical atrophy
89	BJ	M	31	HIE	MCS-	80	8T (4-T-4)	13(2-3-5-1-0-2)	CS	5	Brain edema
90	BJ	M	24	TBI	MCS+	91	10T(4-T-6)	13(3-4-3-1-0-2)	CS	5	Left temporal lobe subdural hemorrhage
91	BJ	M	50	TBI	MCS+	126	11 (4-1-6)	17(3-5-5-1-1-2)	CS	4	Right parietal lobe lesions
92	BJ	M	39	stroke	MCS+	29	10T(4-T-6)	17(3-4-4-0-0-2)	CS	4	Left frontal lobe and intraventricular hemorrhage
93	BJ	M	47	stroke	MCS+	85	13 (4-3-6)	17(3-4-5-2-1-2)	CS	4	Bilateral parietal and temporal lesions

CRS-R=coma recovery scale-revised; GCS=Glasgow Coma Scale; GOS=Glasgow Outcome Scale; NT=Nantong; BJ=Beijing; M=male; F=female; TBI=traumatic brain injuries; HIE=hypoxic ischemic encephalopathy; VS/UWS=vegetative state/unresponsive wakefulness syndrome; MCS=minimally conscious state; EMCS=emergence from minimally conscious state; LIS=locked-in syndrome; CS=conscious state; D=death