J Neurol (2008) 255:217–223
DOI 10.1007/s00415-008-0658-4

ORIGINAL COMMUNICATION

A combined clinical and MRI approach for outcome assessment of traumatic head injured comatose patients

Nicolas Weiss
Damien Galanaud
Alexandre Carpentier
Sophie Tezenas de Montcel
Lionel Naccache
Pierre Coriat
Louis Puybasset

Received: 3 December 2006
Received in revised form: 10 May 2007
Accepted: 14 May 2007
Published online: 19 February 2008

N. Weiss · P. Coriat · Pr. L. Puybasset (✉)
Unité de NeuroAnesthésie-Réanimation
Département d'Anesthésie-Réanimation
Hôpital de la Pitié-Salpêtrière
47–83, Bd de l'hôpital
75013 Paris, France
Tel.: +33-142173371
E-Mail: louis.puybasset@psl.aphp.fr

D. Galanaud
Neuroradiology department
La Pitié-Salpêtrière Hospital
Assistance Publique – Hopitaux de Paris
and Université Pierre et Marie Curie-Paris 6
Paris, France

A. Carpentier
Neurosurgery
La Pitié-Salpêtrière Hospital
Assistance Publique – Hopitaux de Paris
and Université Pierre et Marie Curie-Paris 6
Paris, France

S. Tezenas de Montcel
Biostatistics and medical information department
La Pitié-Salpêtrière Hospital
Assistance Publique – Hopitaux de Paris
and Université Pierre et Marie Curie-Paris 6
Paris, France

L. Naccache
Neurophysiology department
La Pitié-Salpêtrière Hospital
Assistance Publique – Hopitaux de Paris
and Université Pierre et Marie Curie-Paris 6
Paris, France

Abstract Traumatic brain injury (TBI) is associated with substantial consumption of health care resources. No clinical or paraclinical examination can reliably predict neurological evolution. In this study, we evaluated the ability of a combined clinical and MRI approach to predict outcome. *Methods* This prospective study took place between June 2001 and March 2005 in a Neurosurgical Intensive Care Unit in Paris, France. Inclusion criteria were TBI patients still mechanically ventilated and without clinical signs of awareness after 2 weeks. Four clinical signs were assessed after cessation of sedation: grasping, yawning, chewing and paroxysmal sympathetic storm. FLAIR and T2* acquisitions on MRI were used in order to localize brain lesions. Statistically linked regions (clusters) were defined. Outcome was assessed at one year by Glasgow Outcome Scale (GOS). *Findings* 73 patients were included: 41 had poor outcome (GOS 1–3) and 32 had good outcome (GOS 4–5). Lesions in the clusters "right upper pons and right lower midbrain", "hypothalamus and basal forebrain", "left parietal, left temporal, left occipital lobes and left insula" and the presence of grasping or chewing were associated with poor outcome in multivariate analysis. This combined clinical and MRI approach gives a much better prediction than MRI approach only ($P < 0.009$), with an area under the ROC curve of 0.94 (95 % CI, 0.89–1.00). *Interpretation* These data suggest that MRI associated with clinical assessment improves outcome prediction in severe TBI patients.

Key words coma · MRI · TBI · brainstem · outcome

Introduction

Traumatic brain injury (TBI) is associated with substantial neurological impairment and consumption of health care resources [2]. Despite difficulties in predicting neurological evolution, recognizing which patients will permanently stay severely impaired remains a key issue for neuro-intensive care.

Development of conventional MRI has led to a better exploration of TBI and provides a more precise exploration of brainstem, central gray and hemispherical structures [8, 22]. Some data suggested a poor prognosis in TBI patients with brainstem lesions on MRI [8, 13].

JON 2658

Furthermore, it has been shown that the addition of information on brainstem reflexes improves the prognostic precision [4]. Assessment of brainstem reflexes could however represent a risk in case of combined spinal trauma or sprain in severe TBI patients. In neurointensivist clinical experience, some clinical symptoms appearing at sedation cessation are thought to be associated with poor outcome. To our knowledge, these have never been prospectively evaluated. Some of these settings are easily identifiable as paroxysmal sympathetic storm [3] or chewing.

We postulated that adding clinical data to MRI findings improves neurological outcome prognosis. So we conducted a prospective study in severe comatose head-injured patients in order to evaluate the ability of clinical data combined to MRI to improve recovery prediction.

Material and methods

The study was approved by our local ethical committee (Comité de Protection des Personnes, Pitié-Salpêtrière, Paris, France). In accordance with the Helsinki Declaration, patient's next of kin gave their informed consent and were made aware of the MRI results.

Patients

Severe head injured patients admitted to our Neurosurgical Intensive Care Unit from June 2001 to March 2005 were prospectively assessed for possible enrollment. Inclusion criteria were TBI patients still mechanically ventilated and without clinical signs of awareness after 2 weeks despite a sedation cessation for more than 48 hours. The exclusion criteria were an age lower than 16 years, a contraindication to MRI (including hemodynamic instability or acute respiratory distress syndrome) and previous neurological impairment.

All patients were treated according to a systematic algorithm previously described [17]. No clinical decision of care withdrawal or withholding was taken according to the MRI results.

At admission, the following data were assessed: age, sex, presence of mydriasis at the scene, Glasgow Coma Scale, presence of subdural or epidural hematomas and mechanism of the accident. Therapeutic intensity was determined by the use of osmotherapy (hypertonic saline), norepinephrine, thiopental, neuromuscular blockers, therapeutic hypothermia, the duration of mechanical ventilation, and length of stay. ICU medical complications (seizures, acute respiratory distress syndrome) were assessed. Occurrence of grasping, yawning, chewing and paroxysmal sympathetic storm was noted after cessation of sedation. Paroxysmal sympathetic storm was defined as [3]: (1) temperature of at least 38.5 °C, (2) pulse of at least 130 beats/min, (3) tachypnea, (4) agitation, and (5) dystonia (rigidity or decerebrate posturing) with at least 1 cycle per day for a minimum of 3 days.

Outcome assessments

Neurological impairment was assessed at one year by a single neurosurgeon physician (AC) using the Glasgow Outcome Scale (GOS): 1, dead; 2, vegetative state; 3, severe neurological impairment; 4, moderate impairment; 5, no impairment. The Vegetative State diagnosis was made according to Multi-Society Task Force on Persistent Vegetative State (PVS) [1]. For statistical purposes, outcome was dichotomized in poor (GOS 1 to 3) and good outcomes (GOS 4 and 5).

MRI

Cerebral MRI was performed if clinical status allowed it without danger for the patient. All patients were mechanically ventilated at the time of MRI. MRI acquisitions were performed on a 1.5 T clinical MRI scanner (GE Medical Systems, WI). A sagittal T1 weighted acquisition, an axial T2* acquisition, and an axial FLAIR acquisition were programmed. Slice thickness was 5 mm. Electrocardiogram, oxygen saturation, end-tidal fraction of CO_2 and non-invasive arterial pressure were monitored during the procedure. MRI were performed under sedation and after neuromuscular blockers administration.

Two neurologists (NW, LN) and one neuroradiologist (DG), blind to the clinical status, analyzed the MRI images according to the following methodology and give a unique consensual interpretation. In the vertical axis, brainstem was divided in 6 levels: upper medulla, lower pons, middle pons, upper pons, lower midbrain and upper midbrain. Each level was analyzed separately for the right and the left side. A similar analysis was performed for the thalamus, hypothalamus and basal forebrain. Hemispheres were divided into frontal, parietal, temporal and occipital lobes on each side. Lesions of the left insula, genu and splenium of corpus callosum were also noted.

Lesions were defined as presence of areas of increased signal on FLAIR and/or decreased signal on T2*. Regarding brainstem, thalami, hypothalami, basal forebrain, left insula, splenium and genu of corpus callosum, lesions were classified for absence (0) or presence (1). Regarding hemispherical lobes, lesions were classified for absence (0), moderate lesion (1, one or two punctiform areas of increased signal) and severe lesion (2, more than two punctiform areas of increased signal).

Influence of bilateral lesions for each anatomical structure previously described, the influence of bilateral and symmetrical lesions on the outcome was studied.

Statistical analysis

Continuous variables are expressed as the mean ± SD and categorical variables as percentage of the group from which they were derived. Continuous variables were compared by using Student t-tests. Chi-square test (Fisher's exact test when appropriate) was used to compare categorical variables.

Univariate analysis was used to compare the variables between the GOS 1–3 and the GOS 4–5 groups. A principal component analysis was performed using varimax rotation in order to determine groups of lesions in brainstem and hemispherical regions separately (clusters). For each cluster, the sum of the lesions was computed. A multivariate analysis was performed using forward stepwise logistic regression with GOS 1–3 versus GOS 4–5 as the outcome variable of interest. Variables with $P < 0.1$ on univariate analysis were included in the multivariate model. A second multivariate model included all clinical variables with $P < 0.1$ on univariate analysis in addition to the MRI variables. Results of regression analysis are reported as adjusted odds-ratio (OD) and 95 % confidence intervals (CI). The receiver operating characteristic (ROC) curves were used to determine the best threshold for cluster or index approaches, either alone or combined to clinical data models. Calibration and discrimination of the logistic models were assessed using Hosmer-Lemeshow statistics and the area under the ROC curves, respectively. All statistical tests were two-tailed. P values that were less than 0.05 were considered to indicate statistical significance. Statistical analyses were performed with the use of the SAS statistical package, version 8.2 (SAS Institute Inc., Cary, NC).

Results

Patients

During the 45 months inclusion period, 395 patients were hospitalized in the ICU for TBI. Among these, 85 patients had enrollment criteria and 78 finally underwent MRI. Four MRI were not analyzed because of artifacts due to movements. In another case, clinical assessment was not available at one year. The final analysis was thus based on a sample of 73 patients.

All patients were admitted in comatose condition and were mechanically ventilated within the first 24 hours after trauma. Mechanism of injury was a motor vehicle accident in 55 (75 %), a fall in 12 (16 %), and an assault in 6 (8 %) cases. At one year, 22 % of patients were dead (GOS = 1), 34 % were in permanent vegetative state or had major sequels (GOS 2–3), and 44 % had minimal or none neurological impairment (GOS 4–5). Baseline characteristics of the patients are shown in Table 1. These were comparable for the two GOS 1–3 and GOS 4–5 groups except for age, GCS at admission and subdural hematoma.

Distributions of neurological symptoms at cessation of sedation are shown in Table 2. All patients with grasping had cortical frontal lesions and the two were correlated ($P < 0.05$). Chewing was correlated to brainstem lesions ($P < 0.05$) but not yawning. On multivariate analysis, three clinical factors were independently associated with poor outcome: age (OR = 1.8 per decade increase (95 % CI, 1.1–3.0), $P < 0.03$), chewing (OR = 27.9 (95 % CI, 3.2–258.46), $P < 0.004$), and grasping (OR = 13.9 (95 % CI, 1.4–139.9), $P < 0.03$). Calibration and discrimination of the model were appropriate as shown by the Hosmer-Lemeshow statistic (7.82; $P > 0.25$) and the area under the ROC curve 0.81 (95 % CI, 0.72–0.90) (Fig. 1). The area under the ROC curve of the motor score of the GCS was 0.68 (95 % CI, 0.54–0.82].

Table 2 Neurological symptoms at sedation cessation according to GOS at 1 year

	All patients n = 73	GOS 1–3 n = 41	GOS 4–5 n = 32	P
Grasping	13 (18 %)	12 (29 %)	1 (3 %)	< 0.003
Yawning	14 (19 %)	12 (29 %)	2 (6 %)	< 0.01
Chewing	23 (32 %)	21 (51 %)	2 (6 %)	< 0.0001
Paroxysmal sympathetic storm	20 (27 %)	15 (37 %)	5 (16 %)	< 0.02
TBI to sedation cessation delay (days)	15 ± 1	16 ± 1	14 ± 2	NS

GOS Glasgow outcome scale

Table 1 Baseline characteristics of the patients

	All patients n = 73	GOS 1–3 n = 41	GOS 4–5 n = 32	P
Age (years)	36 ± 14	40 ± 15	31 ± 13	< 0.02
Sex (M/F)	58/15	37/4	21/11	NS
Mydriasis at scene	31 (42 %)	22 (54 %)	9 (28 %)	NS
GCS at admission	6 ± 3	5 ± 3	7 ± 3	< 0.01
Eyes	1 ± 1	1 ± 1	1 ± 1	NS
Verbal	1 ± 1	1 ± 1	2 ± 1	NS
Motor	3 ± 2	2 ± 2	4 ± 2	< 0.01
Subdural hematoma	20 (27 %)	17 (41 %)	3 (9 %)	< 0.003
Epidural hematoma	12 (16 %)	8 (20 %)	4 (13 %)	NS
Hypertonic saline use	36 (49 %)	21 (51 %)	15 (47 %)	NS
Norepinephrine use	65 (89 %)	37 (90 %)	28 (88 %)	NS
Thiopental use	24 (33 %)	13 (32 %)	11 (34 %)	NS
Neuromuscular blockers use	30 (41 %)	17 (41 %)	13 (41 %)	NS
Therapeutic hypothermia	14 (19 %)	11 (27 %)	7 (22 %)	NS
Seizures in ICU	7 (10 %)	4 (10 %)	3 (9 %)	NS
ARDS	20 (27 %)	12 (29 %)	8 (25 %)	NS
TBI to MRI delay (days)	26 ± 21	25 ± 6	23 ± 7	NS
Mechanical ventilation (days)	29 ± 16	31 ± 17	25 ± 13	NS
Length of stay (days)	46 ± 27	51 ± 30	40 ± 21	NS

M male; *F* female; *NS* not significant; *GCS* Glasgow coma scale; *GOS* Glasgow outcome scale; *ICU* intensive care unit; *ARDS* acute respiratory distress syndrome; *TBI* traumatic brain injury. Intubated patients were scored at 1 for GCS verbal response. Subdural hematoma, epidural hematoma, hypertonic saline use, norepinephrine use, thiopental use, neuromuscular blockers use, therapeutic hypothermia, seizures in ICU and ARDS are given as the number of patients presenting these features

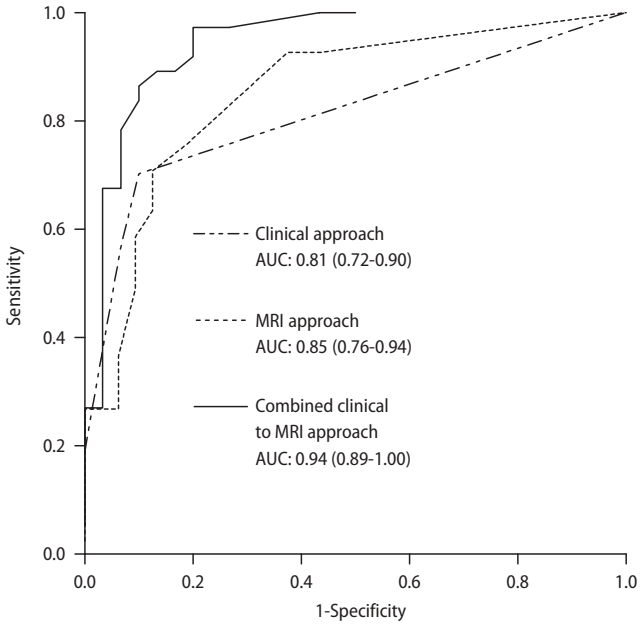

Fig. 1 Receiving operating characteristic curves of clinical approach (half-dotted line), MRI approach (dotted line) and combined clinical to MRI approach (solid line) and poor outcome at 1 year (Glasgow outcome scale score of 1–3). *AUC* area under the curve

MRI

Only 3 patients (4 %) had no lesion on MRI. Forty-one patients (56 %) had brainstem lesions. Twenty-seven (37 %) patients had lesions in thalami or hypothalami or basal forebrain. Only 5 (7 %) patients had no cortical lesions. Forty-one patients (56 %) had more than 2 cortical lesions.

Lesions distribution according to GOS is shown on Table 3. In univariate analysis, four clusters were observed in the brainstem: "upper medulla", "lower and middle pons", "right upper pons and right lower midbrain", "left upper pons, lower midbrain and upper midbrain"; three in the diencephalon and the basal forebrain: "hypothalamus and basal forebrain", "right thalamus", "left thalamus" and five in the hemispheres: "right and left frontal lobes", "right parietal and right temporal lobes", "left parietal, left temporal, left occipital lobes and left insula", "splenium of corpus callosum and right occipital lobe" and "genu of corpus callosum". In the multivariate model including MRI data only, 3 independent clusters were associated to GOS 1–3 (Table 4): "right upper pons and right lower midbrain", "hypothalamus and basal forebrain" and "left parietal, left temporal, left occipital lobes and left insula". These factors remained independently associated with poor outcome when clinical data were taken in account. Calibration and discrimination of the model including MRI data only and of the model including clinical and MRI data were appropriate as shown by the Hosmer-

Table 3 MRI findings, lesions distribution according to GOS at 1 year

	GOS 1–3 n = 41		GOS 4–5 n = 32	
	Right	Left	Right	Left
Upper Medulla	2 (5 %)	2 (5 %)	0	0
Lower pons	3 (7 %)	1 (2 %)	0	0
Middle pons	7 (17 %)	2 (5 %)	1 (3 %)	0
Upper pons	13 (32 %)*	7 (17 %)	2 (6 %)	4 (12 %)
Lower midbrain	13 (32 %)*	10 (24 %)*	2 (6 %)	1 (3 %)
Upper midbrain	6 (14 %)	6 (14 %)*	3 (9 %)	0
Thalamus	4 (10 %)	6 (14 %)	1 (3 %)	2 (6 %)
Hypothalamus	8 (20 %)*	8 (20 %)	0	1 (3 %)
Basal forebrain	13 (32 %)	15 (37 %)*	4 (12 %)	2 (6 %)
Left insula	7 (17 %)	NA	1 (3 %)	NA
Corpus Callosum				
Splenium	10 (24 %)	NA	4 (12 %)	NA
Genu	3 (7 %)	NA	0	NA
Frontal	31 (75 %)*	24 (59 %)*	15 (47 %)	11 (34 %)
moderate lesion	19 (46 %)	9 (22 %)	9 (28 %)	7 (22 %)
severe lesion	12 (29 %)	15 (37 %)	6 (19 %)	4 (12 %)
Parietal	6 (14 %)	9 (22 %)	4 (12 %)	1 (3 %)
moderate lesion	3 (7 %)	4 (10 %)	3 (9 %)	1 (3 %)
severe lesion	3 (7 %)	5 (12 %)	1 (3 %)	0
Temporal	19 (46 %)	19 (46 %)*	9 (28 %)	6 (18 %)
moderate lesion	10 (24 %)	9 (22 %)	6 (19 %)	4 (12 %)
severe lesion	9 (22 %)	10 (24 %)	3 (9 %)	2 (6 %)
Occipital	6 (15 %)	4 (10 %)	2 (6 %)	3 (9 %)
moderate lesion	4 (10 %)	4 (10 %)	2 (6 %)	2 (6 %)
severe lesion	2 (5 %)	0	0	1 (3 %)

NS not significant; *NA* not applicable; *GOS* Glasgow outcome scale; * $P < 0.05$ between GOS 1–3 and GOS 4–5 for homolateral regions

Table 4 Independent risk factor for poor outcome – logistic regression analysis

	Odds Ratio (95 % CI)	P
MRI approach		
Right upper pons and right lower midbrain	5.1 (1.8–14.5)	< 0.003
Hypothalamus and basal forebrain	2.3 (1.2–4.3)	< 0.02
Left parietal, left temporal, left occipital lobes and left insula	3.3 (1.4–7.9)	< 0.009
Combined clinical to MRI approach		
Right upper pons and right lower midbrain	4.7 (1.2–18.1)	< 0.03
Hypothalamus and basal forebrain	2.6 (1.2–5.7)	< 0.03
Left parietal, left temporal, left occipital lobes and left insula	4.0 (1.3–11.8)	< 0.02
Grasping	21.2 (1.7–271.2)	< 0.02
Chewing	26.9 (3.7–197.5)	< 0.002

OR are given per one lesion increase for the different clusters

Lemeshow statistic, respectively 8.26 ($P > 0.21$) and 6.44 ($P > 0.37$) and the area under the ROC curve 0.85 (95 % CI, 0.76–0.94) and 0.94 (95 % CI, 0.89–1.00) (Fig. 1). The area under the ROC curve was significantly higher in the model including clinical and MRI data ($P < 0.009$).

Influence of bilateral lesions as shown in Table 5, every patient with a bilateral lesion of the brainstem at any of the levels studied from lower pons up to upper midbrain had a poor outcome. Conversely, none of the patients with a good outcome had a bilateral lesion of the brainstem. At the supratentorial level, this was also true for thalamus and hypothalamus, but not for the different hemispheric lobes (data not shown).

Discussion

Our approach combines clinical assessment and MRI to predict outcome after severe TBI. The MRI assessment was based on statistically linked regions (clusters) defined by principal component analysis. The clusters "right upper pons and right lower midbrain", "hypothalamus and basal forebrain" and "left parietal, left temporal, left occipital lobes and left insula" were the three that were independent predictors of poor outcome on the multivariate analysis. When considering the clinical symptoms at cessation of sedation, "grasping" and "chewing" had the two highest OR in the combined clinical and MRI approach. This model had an area under the ROC curve higher than clinical approach only and MRI approach only and thus improves outcome prediction. Finally, all patients with bilateral and symmetrical lesions of brainstem and/or diencephalon had a poor outcome.

Table 5 Influence of bilateral lesions of the brainstem, the diencephalon and the basal forebrain according to GOS at 1 year

Location of lesions	Extent of lesion	n	GOS 1–3 n = 41	GOS 4–5 n = 32
Medulla	No lesion	71	39	32
	Unilateral	2	2	0
	Bilateral	0	0	0
Lower pons	No lesion	70	38	32
	Unilateral	2	2	0
	Bilateral	1	1	0
Middle pons	No lesion	65	34	31
	Unilateral	6	5	1
	Bilateral	2	2	0
Upper pons	No lesion	51	25	26
	Unilateral	18	12	6
	Bilateral	4	4	0
Lower midbrain	No lesion	54	25	29
	Unilateral	12	9	3
	Bilateral	7	7	0
Upper midbrain	No lesion	61	32	29
	Unilateral	9	6	3
	Bilateral	3	3	0
Thalamus	No lesion	61	32	29
	Unilateral	11	8	3
	Bilateral	1	1	0
Hypothalamus	No lesion	62	31	31
	Unilateral	5	4	1
	Bilateral	6	6	0
Basal forebrain	No lesion	52	24	28
	Unilateral	8	6	2
	Bilateral	13	11	2

GOS Glasgow outcome scale
The total number of lesions is greater than the number of patients since one given patient could have more than one level affected

Fifty-six percent of the patients had brainstem lesions. This percentage is similar to the one described by Firsching et al. [8] who found brainstem lesions on MRI in 64 % of their patients. Our findings are also consistent with Jellinger and Seitelberger results who noted 49 % of brainstem injury at autopsy [10]. Firsching et al. [8] reported a higher mortality rate in patients having brainstem lesions and Kampfl et al. [12] described that 36 of 42 patients in PVS had brainstem lesions. These authors [13] hypothesized that the dorsolateral upper brainstem was of great importance for outcome prognosis, showing lesions in this area in 74 % of PVS patients compared to 26 % in aware patients. Furthermore, Parvizi and Damasio [22] showed that, in patients with brainstem strokes who were in a coma, lesions were located either in the pons alone or in the upper pons and the midbrain. This corroborated our multivariate analysis, which found "right upper pons and right lower midbrain" lesions to be independently associated with poor outcome. The reasons why only right brainstem lesions are prognostic factors in our multivariate analysis are unclear. More left hemispherical lesions could be associated to more right brainstem lesions due to herniation or contre-coup lesions. Lesions in the left hemisphere probably shift patients to poor outcome by impairing their responsiveness.

"Hypothalamus and basal forebrain" cluster had intermediate OR for poor outcome in the MRI and in the combined clinical and MRI approach. Murdoch et al. [20] reported histological evidences of neuronal damage in the nucleus basalis of Meynert, the major nucleus of basal forebrain, in the majority of TBI patients who died after head injury. Indeed, cortical activity is modulated by widespread projections from basal forebrain to cerebral cortex [23].

We observed that the cluster "left parietal, left temporal, left occipital lobes and left insula" was independently associated with poor outcome. This was neither found by Kampfl et al. [13], nor by Levin et al. [18]. Nevertheless, PET studies, comparing vegetative patients with resting healthy controls, showed metabolic dysfunction in a wide fronto-parieto-cingulate network

[15]. Laureys et al. also found a significant difference in effective connectivity in the left hemisphere in this network with evidence that left-side anterior regions differently modulate the posterior cingulate cortex in vegetative patients compared to controls. So lesions in this network could explain the influence of this cluster on prognosis. We chose to focus on left insula since it has been shown that lesions in this region could be associated to adverse cardiac outcome in stroke patients [14].

"Right upper pons and right lower midbrain" had the highest OR in multivariate analysis. This finding supports Ommaya and Genarelli's model. These authors observed in primates that the depth of the deepest parenchyma lesion was correlated to awareness impairment [21]. Depth of lesion seems also predictive of outcome in human TBI [18].

Chewing was an important predictive factor of poor outcome in the combined clinical and MRI multivariate analysis. Several studies in primates and rats [11] have localized the central pattern generator for chewing in the brainstem. This brainstem involvement is confirmed by clinical studies in sleep bruxism [16] or Meigge's syndrome [19].

Unilateral grasping has been associated with controlateral frontal lobe lesions and results from a failure of the frontal cortex to inhibit the parietal lobe function [7]. Recently, it has been proposed that lesions in the supplementary motor cortex and cingulate gyrus could be implicated [6]. The importance of grasping in our analysis could be related to lesions in the fronto-parieto-cingulate network, either in frontal or in cingulate cortices. The limits of morphological MRI to show some lesions or fibers disruption might explain why chewing and grasping seem more sensitive in identifying brainstem and hemispherical lesions than MRI in our study. This was confirmed by the ROC curves showing a greater area under the curve when clinical data were taken in account.

Every patient with a bilateral lesion of the brainstem, the hypothalamus or the thalamus, at any of the levels studied, had a poor outcome. Conversely, none of the patients with a good outcome had a bilateral lesion of these regions. This is consistent with Firsching's findings on poor outcome of bilateral lesions [8]. Parvizi and Damasio [22] also observed that patients who were in coma after a brainstem stroke had mostly bilateral lesions of the tegmentum.

This study has several limitations: the limited number of patients included, the semi-quantitative approach used to measure brain injury, the lack of precision of morphological MRI to visualize brain lesions and the absence of electrophysiological assessment since previous articles demonstrated a predictive role of EEG or Evoked Potentials in TBI [24]. It remains to be shown what MRI combined with the clinical markers adds to EEG markers, somatory evoked potentials or mismatch negativity on auditory oddball. It has recently been proven that MR spectroscopy was able to show lesion invisible on morphological MRI in TBI patients [5, 9]. Diffusion tensor could also demonstrate early fiber destruction in alertness regions and might also be helpful in predicting outcome. Finally, whether these results could be used in neurological diseases different than TBI remains unknown.

Acknowledgements The authors thank the nurses of the Neuro-Surgical Intensive Care Unit and the technicians of the Department of Neuro-Radiology for their active participation.

References

1. (1995) Practice parameters: assessment and management of patients in the persistent vegetative state (summary statement). The Quality Standards Subcommittee of the American Academy of Neurology. Neurology 45:1015–1018
2. Anderson CV, Wood DM, Bigler ED, Blatter DD (1996) Lesion volume, injury severity, and thalamic integrity following head injury. J Neurotrauma 13:35–40
3. Blackman JA, Patrick PD, Buck ML, Rust RS Jr (2004) Paroxysmal autonomic instability with dystonia after brain injury. Arch Neurol 61:321–328
4. Born JD, Albert A, Hans P, Bonnal J (1985) Relative prognostic value of best motor response and brain stem reflexes in patients with severe head injury. Neurosurgery 16:595–601
5. Carpentier A, Galanaud D, Puybasset L, Muller J-C, Lescot T, Riedl V, Dormont D, van Effenterre R (2006) Combined magnetic resonance imaging and spectroscopy to predict long-term neurological outcome in severe traumatic brain injury. J Neurotrauma 23: 674–685
6. De Renzi E, Barbieri C (1992) The incidence of the grasp reflex following hemispheric lesion and its relation to frontal damage. Brain 115 Pt 1:293–313
7. Denny-Brown D (1958) The nature of apraxia. J Nerv Ment Dis 126:9–32
8. Firsching R, Woischneck D, Diedrich M, Klein S, Ruckert A, Wittig H, Dohring W (1998) Early magnetic resonance imaging of brainstem lesions after severe head injury. J Neurosurg 89:707–712
9. Garnett MR, Blamire AM, Corkill RG, Cadoux-Hudson TA, Rajagopalan B, Styles P (2000) Early proton magnetic resonance spectroscopy in normal-appearing brain correlates with outcome in patients following traumatic brain injury. Brain 123 (Pt 10): 2046–2054
10. Jellinger K, Seitelberger F (1970) Protracted post-traumatic encephalopathy. Pathology, pathogenesis and clinical implications. J Neurol Sci 10:51–94
11. Jordan LM, Brownstone RM, Noga BR (1992) Control of functional systems in the brainstem and spinal cord. Curr Opin Neurobiol 2:794–801

12. Kampfl A, Franz G, Aichner F, Pfausler B, Haring HP, Felber S, Luz G, Schocke M, Schmutzhard E (1998) The persistent vegetative state after closed head injury: clinical and magnetic resonance imaging findings in 42 patients. J Neurosurg 88:809–816
13. Kampfl A, Schmutzhard E, Franz G, Pfausler B, Haring HP, Ulmer H, Felber S, Golaszewski S, Aichner F (1998) Prediction of recovery from post-traumatic vegetative state with cerebral magnetic-resonance imaging. Lancet 351:1763–1767
14. Laowattana S, Zeger SL, Lima JAC, Goodman SN, Wittstein IS, Oppenheimer SM (2006) Left insular stroke is associated with adverse cardiac outcome. Neurology 66:477–483
15. Laureys S, Goldman S, Phillips C, Van Bogaert P, Aerts J, Luxen A, Franck G, Maquet P (1999) Impaired effective cortical connectivity in vegetative state: preliminary investigation using PET. Neuroimage 9:377–382
16. Lavigne GJ, Kato T, Kolta A, Sessle BJ (2003) Neurobiological mechanisms involved in sleep bruxism. Crit Rev Oral Biol Med 14:30–46
17. Lescot T, Bonnet MP, Zouaoui A, Muller JC, Fetita C, Coriat P, Puybasset L (2005) A quantitative computed tomography assessment of brain weight, volume, and specific gravity in severe head trauma. Intensive Care Med 31: 1042–1050
18. Levin HS, Mendelsohn D, Lilly MA, Yeakley J, Song J, Scheibel RS, Harward H, Fletcher JM, Kufera JA, Davidson KC, Bruce D (1997) Magnetic resonance imaging in relation to functional outcome of pediatric closed head injury: a test of the Ommaya-Gennarelli model. Neurosurgery 40:432–440; discussion 440–431
19. Mascia MM, Valls-Sole J, Marti MJ, Sanz S (2005) Chewing pattern in patients with Meige's syndrome. Mov Disord 20:26–33
20. Murdoch I, Nicoll JA, Graham DI, Dewar D (2002) Nucleus basalis of Meynert pathology in the human brain after fatal head injury. J Neurotrauma 19:279–284
21. Ommaya AK, Gennarelli TA (1974) Cerebral concussion and traumatic unconsciousness. Correlation of experimental and clinical observations of blunt head injuries. Brain 97:633–654
22. Parvizi J, Damasio AR (2003) Neuroanatomical correlates of brainstem coma. Brain 126:1524–1536
23. Selden NR, Gitelman DR, Salamon-Murayama N, Parrish TB, Mesulam MM (1998) Trajectories of cholinergic pathways within the cerebral hemispheres of the human brain. Brain 121 (Pt 12):2249–2257
24. Carter BG, Butt W (2005) Are somatosensory evoked potentials the best predictor of outcome after severe brain injury? A systematic review. Intensive Care Med 31:765–775