



Spasticity in disorders of consciousness: a behavioral study

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Background. Spasticity is a frequent complication after severe brain injury, which may impede the rehabilitation process and diminish the patients' quality of life.

Aim. We here investigate the presence of spasticity in a population of non-communicative patients with disorders of consciousness. We also evaluate the correlation between spasticity and potential factors of comorbidity, frequency of physical therapy, time since insult, presence of pain, presence of tendon retraction, etiology and diagnosis.

Design. Cross-sectional study.

Setting. University Hospital of Liège, Belgium.

Population. Sixty-five patients with chronic (>3 months post insult) disorders of consciousness were included (22 women; mean age: 44±14 y; 40 with traumatic etiology; 40 in a minimally conscious state; time since insult: 39±37 months).

Methods. Spasticity was measured with the Modified Ashworth Scale (MAS) and pain was assessed using the Nociception Coma Scale-Revised (NCS-R).

Results. Out of 65 patients, 58 demonstrated signs of spasticity (89%; MAS≥1), including 40 who showed severe spasticity (61.5%; MAS≥3). Patients with spasticity receiving anti-spastic medication were more spastic than unmedicated patients. A negative correlation was observed between the severity of spasticity and the frequency of physical therapy. MAS scores correlated positively with time since injury and NCS-R scores. We did not observe a difference of spasticity between the diagnoses.

Conclusion. A large proportion of patients with disorders of consciousness develop severe spasticity, possibly affecting their functional recovery and their quality of life. The observed correlation between degrees of

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spasticity and pain scores highlights the importance of pain management in these patients with altered states of consciousness. Finally, the relationship between spasticity and treatment (*i.e.*, pharmacological and physical therapy) should be further investigated in order to improve clinical care.

Clinical Rehabilitation Impact. Managing spasticity at first signs could improve rehabilitation of patients with disorders of consciousness and maximize their chances of recovery. In addition, decreasing this trouble could allow a better quality of life for these non-communicative patients.

KEY WORDS: Muscle spasticity - Pain - Therapeutics - Persistent vegetative state - Brain injuries - Nociception.

Spasticity is defined as a velocity-dependent increase in muscle tone.¹ This is a serious complication to brain injury, often accompanied by dyski-

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nesia, spasms or muscle flaccidity.² Spasticity results from impaired reflex functions and pathological changes in rheologic muscle properties such as atrophy, stiffness and fibrosis.³ In addition to hyperexcitability of the stretch reflex, patients may suffer from spastic dystonia (*i.e.*, muscle constriction in the absence of voluntary movement), and/or spastic co-contraction (*i.e.*, contraction of both agonist and antagonist muscles).^{4,6} These modifications can induce pain and reduce functional autonomy.⁷ Spasticity has also been reported to be associated with muscle contracture, tendon retraction, fixed equinovarus feet and pain in patients suffering from multiple sclerosis⁸ or stroke.^{9, 10} All these complications increase the clinical impact of spasticity on recovery by impeding the patient's ability to perform activities of daily living and by increasing the cost of treatment.^{11, 12} Spasticity occurs in approximately 25% to 42% of patients with acquired brain injury.¹³⁻¹⁵ Although the onset is usually within the first few days or weeks post-insult, spasticity may appear in the short-, medium-, or long-term period post-insult.²

The occurrence of spasticity in severe brain damaged patients with disorders of consciousness (DOC) has been poorly explored. DOC includes patients in coma,¹⁶ in vegetative/unresponsive wakefulness syndrome (VS/UWS)^{16, 17} and in minimally conscious state (MCS).¹⁸ Patients in VS/UWS are characterized by the presence of reflexive responses to external stimuli and are considered unconscious.¹⁹ Patients in MCS show reproducible but minimal and fluctuating signs of consciousness.¹⁸ By definition, these patients are unable to express their feelings and cannot communicate about potential discomfort or pain.^{20, 21} To our knowledge, only a few studies of small sample size have described motor patterns in patients with DOC. These studies reported the presence of abnormal primitive reflexes, altered tonus, considerable posturing and varied degrees of reduced range of joint motion^{22, 23} as well as abnormal cortical excitability of the motor cortex.²⁴ In addition, other studies show that some patients fail to show clinical signs of consciousness due to severe motor impairments including spasticity, thus leaving them vulnerable to misdiagnosis.²⁵⁻²⁸ The need to understand and prevent spasticity in this population is therefore urgent.

The aim of our study was to measure the occurrence and clinical impact of spasticity in patients with DOC. We assessed the presence of spasticity in

a cohort of chronic patients in VS/UWS or MCS. We also evaluated the correlation between spasticity and potential factors of co-morbidity, frequency of physical therapy, time since insult presence of pain, presence of tendon retraction, etiology and diagnosis.

Materials and methods

Population

We enrolled medically stable patients with DOC admitted to the University Hospital of Liège in Belgium for one week of diagnostic assessments. This week includes repeated behavioral examinations with an array of neuroimaging-based examinations such as magnetic resonance imaging, positron emission tomography, and electroencephalography. The aim is the detection of consciousness and possible means of communication. All patients came from their homes, nursing homes or rehabilitation centers. Inclusion criteria were: 1) a diagnosis of VS/UWS or MCS; 2) time since onset of condition more than 3 months; and 3) age 16 years and over. Exclusion criteria were: 1) documented neurological disorders previous to the acquired brain damage; and 2) presence of skin or musculoskeletal lesions (*e.g.*, bedsores, fractures, wounds). The study was approved by the ethical committee of the University Hospital of Liège and written informed consents were obtained from the legal representatives.

In total, we included 65 patients in this cross sectional study (22 women; mean age: 44±14 years). Forty patients were of traumatic etiology, 14 suffered from anoxia, 6 had a subarachnoid hemorrhage, 4 presented mixed etiology (trauma and anoxia) and 1 patient had an encephalomyelitis. The time since insult varied from 3 months to 12 years with a mean±SD of 39±37 months. Patients were diagnosed as being in VS/UWS (N.=25) or in MCS (N.=40) based on repetitive assessments using the Coma Recovery Scale-Revised (CRS-R).^{29, 30} Clinical data are reported in Table I. We took the highest diagnosis observed during the week of assessments. Anti-spastic medication was classified as oral treatments (baclofen, clonazepam, tizanidine) or intrathecal baclofen therapy. The amount of physical therapy received as part of the usual patient's cares program varied between 0 and 6 sessions per week, including stretching of all limbs for at least 20 minutes.

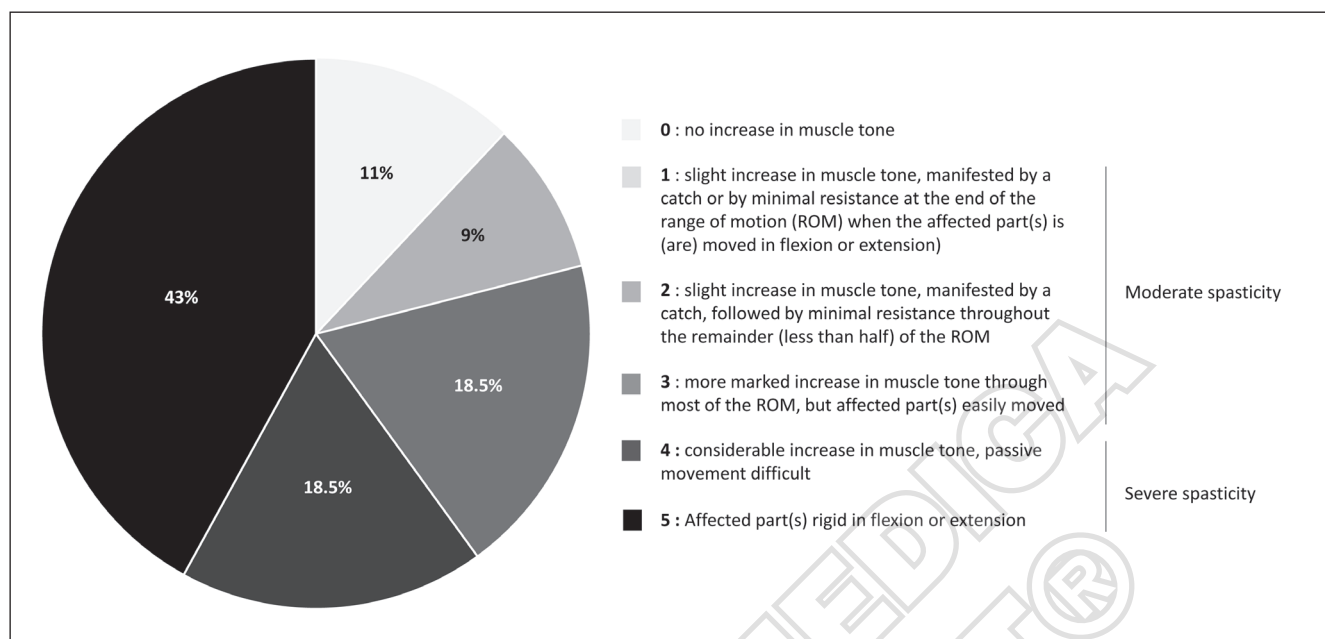


Figure 1.—Proportion of patients with different level of spasticity according to the MAS scores.

Material

Spasticity was assessed once for each patient with the Modified Ashworth Scale (MAS); a 6-level ordinal scale with documented reliability.³¹ Higher scores indicate increasing severity of the spasticity (see Figure 1 for the description of the scale). All patients were examined by the same physiotherapist to minimize inter-rater variability. Assessment of spasticity followed the guidelines of the scale (*i.e.*, patients assessed in a resting position) and included passive flexion and extension of upper and lower extremity joints (shoulder, elbow, wrist, fingers, hip, knee, and ankle). The mean MAS score of assessable (*i.e.*, without joint total fixation that makes the evaluation impossible) joints of the upper limbs (left and right shoulder, elbow, wrist, fingers) and lower limbs (left and right hip, knee and ankle) were used for our correlation analyses.

Among the 65 studied patients, 48 were also assessed with the Nociception Coma Scale-Revised (NCS-R), a validated and reliable scale assessing behavioral signs of pain in patients with DOC.³² The scale measures motor, verbal and facial responses to potential pain. Its total score ranges from 0 to 9, with a score of 4 or higher indicating the presence

of pain. The assessment was conducted during patient's daily care, on the same day as the spasticity assessment.

Patients were diagnosed using the CRS-R, which consists of 23 hierarchically arranged items and includes 6 subscales assessing auditory, visual, motor, verbal, communication and arousal functions.^{29, 30} This scale is currently considered the most accurate tool for the detection of consciousness in postcomatose patients.³³

Statistical analysis

MAS data were evaluated on a scale ranging from 0 to 5, assigning the 1+ a value of 2, the 2 a value of 3, and so on. We used the Mann-Whitney U tests to investigate the difference of MAS scores according to the level of consciousness (*i.e.*, VS/UWS vs. MCS), joint deformities (*i.e.*, presence vs. absence of upper limb tendon retraction and equinovarus feet), and medication (*i.e.*, presence *vs.* absence of pharmacological treatment).³⁴ We used the Wilcoxon test to assess differences in MAS scores between upper and lower extremities. Correlations between MAS scores and NCS-R total scores, time since insult, and frequency of physical therapy were assessed with

TABLE I.—Clinical data for patients in UWS and MCS.

Diagnosis	Etiology	Gender	Age (years)	Time since injury (months)	UL– MAS mean±SD	LL – MAS mean±SD
25 UWS/UWS	12 TBI	8 w	39±14	40±41	2.9±1.5	2.3±1.9
40 MCS	28 TBI	14 w	38±14	35±28	2.8±1.3	2.5±1.4

VS/UWS: vegetative state/unresponsive wakefulness syndrome; MCS: minimally conscious state; TBI: traumatic brain injury, w: women; UL: upper limb; LL: lower limb; MAS: Modified Ashworth Scale.

Kendall's Tau tests.^{35, 36} Differences in MAS scores according to the etiology (*i.e.*, anoxic, hemorrhagic, traumatic and mixt) were assessed by Kruskal-Wallis ANOVA.

Results

Out of 65 patients, 58 showed signs of spasticity (89%; MAS≥1). Out of these 65 patients, 40 suffered from severe spasticity (61.5%; MAS≥4) (Figure 1, Table II). Seven patients (11%) showed no signs of spasticity (MAS=0) including five patients (8%) who were flaccid. Six patients (9%) had a maximal score of 2, 12 (18.5%) had a maximal score of 3, 12 (18.5%) had a maximal score of 4 and 28 (43%) had a maximal score of 5.

We found a significant difference in spasticity between the upper and lower limbs (T=446.5; Z=2.55; P=0.01).

A negative correlation was found between MAS scores and the frequency of physical therapy for both the upper limbs (tau=-0.20, Z=-2.37; P=0.018; Figure 2A) and the lower limbs (tau=-0.20; Z=-2.41; P=0.016).

A positive correlation was found between MAS scores and time since insult for both upper limbs (tau=0.23; Z=2.71; P=0.007; Figure 2B) and lower limbs (tau=0.21; Z=2.46; P=0.014), and between MAS scores and NCS-R total scores for the upper limbs only (upper limbs, tau=0.31, Z=3.11; P=0.001; Figure 2C; lower limbs: tau=0.18; Z=1.80; P=0.072).

Twenty-seven patients (42%) had tendon retraction in the upper limbs (*i.e.*, metacarpophalangean joint, wrist and elbow) and 37 (57%) fixed equinovarus feet (Table II). The presence of retraction was associated with higher MAS score for the upper limbs (U=155; Z=4.71; P<0.001) and equinovarus feet were associated with higher MAS scores of the lower limbs (U=139.5; Z=4.89; P<0.001).

Thirty-nine out of 58 patients who showed sign of spasticity (67%) received oral anti-spastic treatment

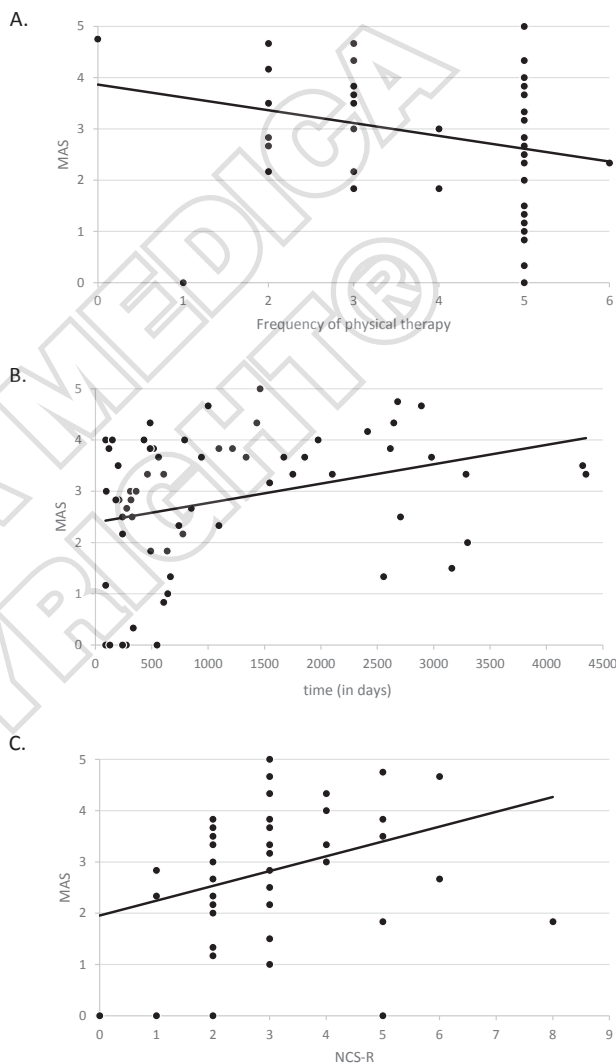


Figure 2.—A) Correlation between Modified Ashworth Scale (MAS) mean scores and the frequency of physical therapy per week (tau=-0.20; P=0.018). B) Correlation between MAS mean scores and the time since insult (tau=0.23; P=0.006). C) Correlation between MAS mean scores and the scores at the Nociception Coma Scale-Revised during cares (tau=0.31; P=0.001).

TABLE II.—*Percentage of motor disabilities and medication.*

Presence of	% of patients – CI 95% (N.=65)
Spasticity	88±12%
Severe spasticity (MAS >3)	61.5±11.8%
Upper extremity tendon retraction	42±10.8%
Fixed equinovarus feet	57±11.7%
Medication of spastic patients (N.=58)	74±12%

(34 baclofen, 3 tizanidine, 2 clonazepam), 4 patients (7%) received intrathecal baclofen therapy and 15 patients (26%) did not receive any pharmacological treatment (Table II). Patients on antispastic medication (N.=43, 74%) showed more spasticity than patients without antispastic treatment for the lower limbs (U=209.5; Z=2.52; P=0.01) but not for the upper limbs (U=260; Z=1.67; P=0.09) (Table III).

Upper and lower limbs MAS scores did not differ according to the etiology (Chi square 2.05; P=0.56 and Chi square 0.71; P=0.87, respectively) (Table III).

No difference was found between MAS score and the level of consciousness (upper limbs: U=459; Z=0.55; P=0.59; lower limbs: U=477.5; Z=-0.30; P=0.76) (Table III).

Discussion

Current literature reports the presence of spasticity in 25 to 42% of patients after stroke or traumatic brain injury.¹³⁻¹⁵ In our cohort of 65 chronic patients with DOC, 89% showed spasticity, of whom 61.5% to severe degrees. This result suggests that spasticity is even more frequent in patients with DOC than in patients with milder brain injuries. This high rate of spasticity supports previous results from a pilot study conducted by Pilon et al. in 1996, reporting important motor and posturing impairments in 12 patients with DOC.²² Extensive brain lesions, prolonged immobility, as well as weakness, disuse, and absence of movement of muscles in contracted positions are likely to be causative factors, as they are known to increase spasticity and contracture.³⁷

Our analyses demonstrated a negative correlation between the degree of spasticity and the frequency of physical therapy. This result suggests that frequent physiotherapy may have a positive effect on patient's spasticity. One could, however, argue that patients showing less spasticity might receive more

physical therapy as our result is based on a correlation. But in our view, this is less likely to be the case because the amount of physical therapy is not determined by the severity of spasticity, but rather depends on the health system of the country and assurance reimbursement (*i.e.* in Belgium patients with DOC should receive 30 minutes of physical therapy 5 days a week). On the other hand, it is possible that patients showing more spasticity receive less physical therapy, especially at the chronic stage. Some patients may show signs of pain (*e.g.*, grimace or other facial expressions) during stretching, which may lead the physical therapist to stop or reduce the time of stretching. Another explanation could be that due to high level of tendon retraction or joint fixation, stretching is very limited and the effects of physical therapy being reduced, patients receive less therapy. Overall, we cannot strongly claim from our results that less spasticity is the result of more physical therapy.

Additionally, our findings on physical therapy contradict a recent study reporting no improvement of spasticity after 6 to 36 weeks of physiotherapy (*i.e.*, manual stretching, casting, and pharmacological treatment) in 10 patients in VS/UWS and MCS.³⁸ The small sample size and the absence of a control group in the study likely contribute to this result. Moreover, a recent study showed that a soft splint placed for 30 minutes in the hand of spastic patients with DOC could decrease the severity of spasticity of the flexor hand muscles and increase the patient's hand opening, although the effect was short lasting.³⁹ It is thought that stretching has an immediate positive effect on spasticity and contractures.^{40, 41} The duration of these effects, however, appears to fluctuate among studies.⁴² Further investigation focusing on the effect of physical therapy and the type of rehabilitation (*e.g.*, stretching, tilt-table, massage or passive bike movement trainer) should be performed.

In our study, spasticity appeared to increase over

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time. This result highlights problems of patient management (*e.g.*, mobilizations, stretching) associated with immobility. Spasticity and immobilization induce adaptive anatomical muscles changes and reflexes modifications (*e.g.*, muscle atrophy, loss of sarcomeres and accumulation of connective tissue and fat)³⁷ constituting a self-reinforcing negative effect.

A positive correlation was observed between MAS of the upper limbs and NCS-R scores during daily cares. Nursing and mobilization, especially for the upper limbs as they are more spastic, thus appear associated with pain in spastic patients, as previously observed in patients with other neurological diseases (*e.g.*, multiple sclerosis).⁴³ This is critical as patients with DOC are, by definition, unable to communicate potential discomfort.²¹ Interventions to alleviate potential pain are therefore mandated in this patient group.

Concerning side-effects, about half of our sample suffered from tendon retraction (upper extremity: 42% and equinovarus feet: 57%), the presence of which was associated with higher level of spasticity. This supports the notion that spasticity increases the risk of tendon retraction.^{9, 10} Immobilization of joints could also be a driving factor in this regard.³⁷ The high proportion of patients with tendon retractions and joint fixations indicates that muscle hyperactiv-

ity should be treated at an early stage to minimize the risk of fixation.

Surprisingly, patients without antispastic medication showed lower MAS scores, specifically for the lower limbs, than medicated patients. This probably reflects that patients who do not show signs of spasticity do not need anti-spastic medication, while patients who suffer from spasticity certainly need anti-spastic medication to decrease the severity of spasticity but this treatment may not be sufficient enough to completely abolish it. The reason why only the lower limbs showed a significant difference could be due to weaker spasticity intensity in the lower limbs as compare to the upper limbs. This difference could be even more important without the influence of an anti-spastic medication. Therefore, the spasticity of the lower limbs for the unmedicated patients is the less pronounced (Table III). So far, available treatments can reduce spasticity by inhibiting excitatory pathways (*e.g.*, baclofen), by stimulating inhibitory pathways (*e.g.*, diazepam) or by inducing local muscle paralysis (*e.g.*, botulinum toxin). Until now, no standard treatment is known to totally suppress spasticity.⁴⁴ Continuous development of pharmacological options for spastic conditions is clearly warranted.

The absence of correlation between MAS scores and etiology or level of consciousness suggests that

TABLE III.—Results of group comparisons with mean, standard deviation (SD) of the MAS and P value.

Test	Limbs		Mean±SD	P value
UL and LL	Upper limb (UL)		2.9±1.4	P=0.001*
	Lower limb (LL)		2.4±1.5	
Medication	UL	Medicated	3.29±0.95	P=0.09
		Unmedicated	2.77±1.19	
	LL	Medicated	2.93±1.38	P=0.01*
		Unmedicated	1.99±1.21	
Etiology	UL	Trauma	3.15±56	P=0.56
		Anoxia	3±2.07	
		Subarachnoid hemorr.	3.83±0.75	
	LL	Mixed	3.25±1.71	P=0.87
		Trauma	3.22±1.87	
		Anoxia	2.79±2.12	
Diagnosis	UL	Subarachnoid hemorr.	2±1.09	
		Mixed	4±1.41	
		VS/UWS	2.9±1.5	
	LL	MCS	2.8±1.3	P=0.59
		VS/UWS	2.3±1.9	
		MCS	2.5±1.4	

MAS: Modified Ashworth Scale; UL: upper limbs; LL: lower limbs; VS/UWS: vegetative state/unresponsive wakefulness syndrome; MCS: Minimally Conscious State.

*significant result.

the onset of spasticity is not directly associated with specific lesions patterns but may appear across a broad range of brain injuries. The high presence of spasticity could be explained by the severity and the extent of cerebral damages in this population, which may induce motor pathway impairments and paralysis, with flaccidity or spasticity.⁴⁵ Moreover, motor deficits are associated with immobility, which increases spasticity and accompanying complications.⁴⁶ In addition to severe brain damage encompassing the pyramidal tracts, other extrapyramidal disorders, such as parkinsonian syndrome,⁴⁷ could be involved in motor disabilities. Parkinsonian symptoms during recovery from DOC are very common although rarely reported.^{48, 49} This possibility could be explored with future neuroimaging studies.

In line with recommendations for stroke patients,⁵⁰ our findings indicate that muscle hyperactivity should be treated early to minimize risk of spasticity and joint fixation, thus improving the prospect of functional recovery. In clinical practice, even at the acute stage, it is therefore highly recommended to apply comprehensive stretching in a daily routine in all patients. Initial treatment of severely brain-injured patients tend to focus on cerebral and cardiopulmonary functions while muscular and motor functions are down-prioritized, as they are not important for the vital prognosis. Antispastic therapy is usually implemented at the sub-acute stage, even if we know that spasticity can occur earlier. Intensivists and medical doctors should therefore give anti spastic drugs as soon as muscle hypertonicity is detected, and physiotherapy sessions should be increased to allow management of respiratory deficiency and movement disorders at the earliest.

At the chronic stage, when patients leave the rehabilitation unit, they should continue to benefit from an adapted care management, including daily mobilizations, several hours on a chair, raising and braces, as well as appropriate pharmacological treatment to minimize the adverse effects of spasticity and immobility.

This study has important limitations. The first one is the single assessment of spasticity. Future longitudinal studies should assess spasticity several times in the same patients, as spasticity may fluctuate over time. Moreover, prospective studies should be done to provide more easily interpretable results, regarding for example the correlation between physiotherapy and spasticity. Second, our population was

heterogeneous with various etiologies and different time since insults, as we enrolled all the patients who were admitted for a week of assessment at the CHU of Liège. We are currently acquiring more data on spasticity in patients with DOC to be able to classify patients according to their specific etiology, brain lesion, rehabilitation and time since insult.

Conclusions

Our study shows an alarmingly high occurrence of spasticity in patients with DOC. As those patients are already limited in their range of movements, spasticity represents one of the most important disabling factors to be treated. Managing spasticity could help this population to initiate and execute movements and may facilitate voluntary gestures, enabling for example a response to command. Complications such as pain or pathological tendon retraction impair these patients' quality of life and functional recovery. Further research should use neurophysiology testing and neuroimaging methods to examine the association between locations of brain lesion and the presence of spasticity, and investigate the possible contribution of an extrapyramidal parkinsonian syndrome. This could give valuable information regarding the physiopathology of spasticity and its onset in both traumatic and non-traumatic etiologies. Additionally, further studies should assess the impact of specific and combined treatments on spasticity or tendon retraction, as well as behavioral signs of pain. The correlation between spasticity and pain highlights the negative effect of spasticity on quality of life and the importance of rapid action to address this complication. Moreover, as motor impairments have been shown to prevent the expression of signs of consciousness at bedside,^{25, 26} it is of critical importance to improve the quality of care and rehabilitation for this population. Clear guidelines of therapy are needed and should be established.

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