Robotic tilt table reduces the occurrence of orthostatic hypotension over time in vegetative states

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The aim of this study is to evaluate the effects of verticalization with or without combined movement of the lower limbs in patients in a vegetative state or a minimally conscious state. In particular, we aimed to study whether, in the group with combined movement, there was better tolerance to verticalization. This was a randomized trial conducted in a neurorehabilitation hospital. Twelve patients with vegetative state and minimally conscious state 3–18 months after acute acquired brain injuries were included. Patients were randomized into A and B treatment groups. Study group A underwent verticalization with a tilt table at 65° and movimentation of the lower limbs with a robotic system for 30 min three times a week for 24 sessions. Control group B underwent the same rehabilitation treatment, with a robotic verticalization system, but an inactive lower-limb movement system. Systolic and diastolic blood pressure and heart rate were determined. Robotic movement of the lower limbs can reduce the occurrence of orthostatic hypotension in hemodynamically unstable patients. Despite the small number of patients involved (only eight patients completed the trial), our results indicate that blood pressures and heart rate can be stabilized better (with) by treatment with passive leg movements in hemodynamically unstable patients. *International Journal of Rehabilitation Research* **38:162–166**

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Introduction

The vegetative state (VS) is a clinical condition of complete unawareness of the self and the environment, accompanied by sleep–wake cycles, with either complete or partial preservation of hypothalamic and brainstem autonomic function (von Wild *et al.*, 2012). The minimally conscious state (MCS) is a condition of severely altered consciousness in which minimal but definite behavioral evidence of self or environmental awareness is shown (Giacino *et al.*, 2002; Liberati *et al.*, 2014). MCS is distinguished from VS by the presence of behaviors associated with conscious awareness.

Prevalence rates are difficult to evaluate because of the lack of systematic surveillance procedures. In the USA, VS ranges from 25 000 to 420 000 and MCS ranges from 112 000 to 280 0003 for MCS (Hirschberg and Giacino, 2011; Kang *et al.*, 2014; Leonardi *et al.*, 2014). The precise incidence and prevalence rates of severe disorders of consciousness are unavailable in Italy. Values of prevalence in the other industrialized countries range between five and 40 per million population.

Different rehabilitation methodologies were used both to improve the levels of responsiveness and pulmonary ventilation and to prevent multiple complications arising from immobility (muscle, tendon and soft tissue contractures, decubitus ulcers, osteoporosis, thromboembolic disease) (Hirschberg and Giacino, 2011; Kang *et al.*, 2014; Leonardi *et al.*, 2014).

Verticalization with a static table is normally used in positioning and mobilization programs for these patients. In fact, vertical position and gravity stimulation on bone, joint, muscle, and vestibule structures creates an easier way for the patient to be aware of the environment and helps prevent complications (Cooper *et al.*, 2008; Taveggia *et al.*, 2014).

The orthostatic hypotension (OH) and the subsequent possible syncope represent a limitation to the standing position. OH may be because of impairment of the central sympathetic system and the absence of vein blood pump related to the paralysis of the lower limbs. The use of a static table with an integrated system for lower limb movements may be a new rehabilitation solution that may allow combining the positive effect of gravity stimulation with movement of the lower limbs (Smit *et al.*, 1999; Treger *et al.*, 2006; Berger and Kimpinski, 2014). However, in the literature, only a few studies have

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been carried out analyzing these advanced mobilization systems (Luther *et al.*, 2008; Greco *et al.*, 2013).

The aim of this study was to evaluate whether the treatment with an integrated system of movement of lower limbs is more effective than a system with only a static table in vegetative and MCS. Particularly, we aimed to examine whether the group undergoing verticalization with combined movement of the lower limbs showed better blood pressure(BP) and heart rate control that led to improved tolerance to verticalization avoiding OH.

Materials and methods

Patients in VS of MCS according to the Coma Recovery Scale Revised (CRS-R) (7) were enrolled.

Selection criteria

(1) Vegetative and MCS after acute brain injury:
   (a) Levels of Cognitive Functioning (LCF) scale: $2 \leq \text{LCF} \leq 3$.
(2) Interval between experiment period and acute event: 3–18 months.
(3) Patients:
   (a) Independent breathing.
   (b) Mobilization out of bed not yet performed for more than 30 min.
   (c) No significant joint ankyloses, contractions, and/or muscle spasticity with complete loss of joint movement.
   (d) No bone instability (nonconsolidated fractures, vertebral instability, significant osteoporosis).
   (e) No clinical–pathological conditions for which rehabilitation treatments are not suggested (breathing and cardiocirculatory failure).

The study was approved by the competent bioethics committee. The legal proxies of the patients were informed about the aims and methodologies of the study and authorized it by signing the agreement.

Structure of the study

Enrolled patients were randomized into two groups. Patients were allocated to a group by a computer-generated random sequence provided by a researcher not involved in enrollment.

Each group underwent verticalization with a tilt table at 30°. After 10 min, the patients were tilted head-upright at a 65°.

In group A, when the tilt table was at 65°, a robotic system induced hip and knee flexion/extension movements. This cycle of flexion and extension of lower limb was repeated for 30 min at 18 steps/min.

In the control group (B) when the tilt table was at 65°, the patients remained in the vertical position for 30 min without robotic movements.

Every treatment was performed in the morning in a physical therapy room. It was repeated three times a week for 24 sessions.

All patients wore elastic stockings.

The treatment was performed in all patients between 9:00 and 11:00 a.m. in the same rehabilitation room so that the sounds, smells, etc. were the same.

Before baseline measurement, the patients had received no therapy for at least 1 h and had rested supine in bed for at least 20 min.

All patients were fed through a gastrostomy tube with a break 2 h before treatment to minimize the risk of vomiting.

All patients underwent an initial evaluation of cognitive state using the LCF and CRS-R scale (Bekinschtein *et al.*, 2005; Lombardi *et al.*, 2007; Doig and Lane-Brown, 2012; Sattin *et al.*, 2013). Moreover, we studied heart rate and BP for 20 min in the patient's room (bed) immediately before treatment. If during this monitoring BP did not change more than 5 mmHg, the mean value was used as the baseline. This was possible in all patients.

Afterwards, the patients were transferred to a tilt table.

According to the consensus statement of the American Autonomic Society, OH was defined as a decrease in systolic BP more than 20 mmHg or of diastolic BP more than 10 mmHg during verticalization (Kaufmann, 1996).

Tachycardia was considered as an increase of 30 beats/min (bpm) above the baseline (Diehl and Linden, 1999; Medow *et al.*, 2008).

Heart rate and BP were measured continuously and non-invasively. The heart rate and BP measurement were performed using the SOMNOscreen plus, a polygraphy device (SOMNOmedics GmbH, Randersacker, Germany).

Tilting to 30° was performed 10 min after the initial systolic blood pressure measurement. A further tilt to 65° was performed after 10 min. The patient was maintained at 65° for 30 min.

We monitored heart rate and BP for every position (tilted table at 0°, at 30°, at 65° at 0°), especially analyzing the first 4 min, because many studies show that OH occurs in the first four minutes after verticalization (Freeman *et al.*, 2011).

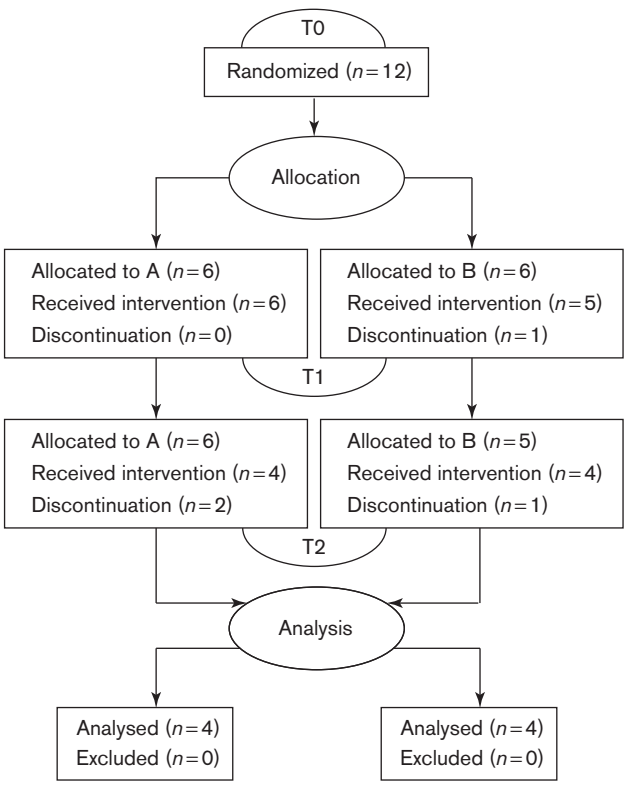
The occurrence of OH was monitored during every treatment. For each patient, we considered the occurrence and length (s) of the OH at the beginning of the treatment (T0), after the 12th session (T1), and after the 24th session (T2) (Fig. 1). According to the study of

Celotto *et al.* (2003), we defined these patients as hemodynamically unstable (Celotto *et al.*, 2003; Digiglio *et al.*, 2014).

Robotic tilt table (Erigo)

The device used for robotic rehabilitation (Erigo Hocoma, Volketswil, Switzerland) consists of a tilt table combined with an integrated leg drive that allows a passive movement of the lower extremities (Hirschberg and Giacino, 2011). As the feet of the patient are fixed to footplates, it induces a hip flexion and extension movement; the knee is flexed or extended too. Applying this cycle of flexion and extension in an alternating manner, Erigo leads to physiological step (Colombo *et al.*, 2005; Borboni and Faglia, 2013; Yakub *et al.*, 2014). The tilt table may be adequately adjusted in terms of height, tilt, and hip angle with an open loop controller. The speed of the alternating stepping movements and the range of motion of hip/knee joints can be adjusted by a control panel. Depending on the blood circulation condition of the patient, the device can be tilted to different angles up to a vertical position. This makes it possible for the patient to become accustomed, step by step, to the upright position (Phillips *et al.*, 1989; Aggogeri *et al.*, 2013; Fazekas, 2013; Krebs and Volpe, 2013; Yoshida *et al.*, 2013). To secure patients on the tilt table during treatments, patients were fixed with special harness.

Fig. 1



Scheme of the study.

Statistical analysis

In our study, we aimed to keep the sample size as small as possible because the primary outcome measure was OH. Therefore, the sample size was determined by sequential testing. Sequential testing analyses of the data will be carried out as they accumulate; the intention is to stop recruitment as soon as the results become statistically significant. To prepare the sequential plan, we considered the following criterion: a result would be considered clinically relevant if at least 3/4 of the patients who had had a presyncope in one of the two groups improved after 24 sessions. (P1¼0.75). Accordingly, P0 was set to 0.25, signifying that an improvement in only one-quarter of the patients was not enough to prove the superiority of the tilt table with an integrated stepping device. CRS-R was compared descriptively before versus after intervention for each treatment group. Nonparametric Mann–Whitney *U*-tests were used to calculate differences between the two treatments (Bonferroni adjustment, P50.025).

The statistician received the results as group A and group B, but was in fact blinded to the real treatment of the patients.

Results

We enrolled 12 patients in a vegetative or a MCS.

Six patients were randomized to group A and six patients to group B.

Among these 12 patients, four (two in each group) were excluded during the study because they developed acute events: one patient developed intracranial hypertension because of hydrocephalus, two patients developed acute respiratory failure, and one patient developed rash of blisters because of herpes zoster virus. One third of the patients dropped out, two of them because of respiratory failure. We may exclude the possibility that respiratory failure was an adverse event of this rehabilitation programme because they also had recurrent respiratory infections before treatment. The demographic and clinical characteristics of each group are shown in Table 1.

In our experiment, no patient developed syncope at any time.

Table 1 Population

	Experimental (*n* = 4)	Control (*n* = 4)	*P*-value
Age (years)	65 ± 8	63 ± 16	1.00
Female sex [*n* (%)]	2 (50%)	2 (50%)	
Time event (days)	188 ± 93	184 ± 143	1.00
LCF	2.5 ± 0.6	2.5 ± 0.6	1.00

LCF, Levels of Cognitive Functioning.

Sympathetic hyperactivity is present in patients with NMS at rest and before syncope. During active standing or passive tilting, excessive tachycardia may be followed by bradycardia and profound hypotension. Recovery of systolic BP is delayed or incomplete.

The average blood pressure before treatment is summarized in Table 2.

No OH was observed in any case after changing the position from supine to 30°.

Otherwise, differences were observed from 30 to 65°.

At the beginning of the treatment (T0), six patients (four in group A and two in group B) showed OH after a change in position from supine to upright. In group A, patients showed a progressive reduction in OH during treatment; three patients (3/4) showed a complete absence of OH at the end of rehabilitation therapy. In group B, hemodynamically unstable patients showed more serious OH after 24 sessions of treatment (Table 3).

Two patients in group B were defined as hemodynamically stable (Czell *et al.*, 2004; Wieser *et al.*, 2014) because they did not show OH at baseline (T0). They showed a different behavior: one did not show any change and one showed more serious OH after treatment. Table 3 shows the duration of OH at the beginning (time T0) and at the end of the study (time T2).

No patient was receiving drugs that could cause OH. No change in pharmacological therapy was made during the rehabilitation treatment.

A comparison of CRS and LCF before and after treatment showed no change in both groups.

Discussion

The OH and the subsequent possible syncope represent a limitation to rehabilitation. We observed an unexpectedly large number of presyncopes, which identified OH as a major problem in rehabilitation.

According to other studies (Czell *et al.*, 2004; Chi *et al.*, 2008; Yoshida *et al.*, 2013; Wieser *et al.*, 2014), we find that adding an integrated stepping device to a tilt table could reduce cardiovascular distress in MCS and VS patients. According to the study of Celotto *et al.* (2003) (Digiglio *et al.*, 2014), we divided patients into two clinical categories: hemodynamically unstable (if they developed OH in the upright position at the beginning of the study) and hemodynamically stable (if they did not develop OH in the upright position at the beginning of the study). We observed that hemodynamically unstable patients showed a reduction in OH after robotic movements of the lower limbs during treatment. OH increased in these subjects. It cannot be determined, if they were treated only with verticalization. Nevertheless, in our study, passive leg movements during head-up tilt showed a stabilizing effect on the blood circulation and it prevented neurally mediated syncope in hemodynamically unstable patients.

Some authors (Williamson *et al.*, 1997; Luther *et al.*, 2008; Greco *et al.*, 2013; Jaeger *et al.*, 2014) have reported that verticalization with the tilt table increased sympathetic activity. This increased sympathetic activity stimulates mechanoreceptors in the ventricle, which leads to an activation of the vagus nerve and a reflexive decrease of sympathetic activity. The vagus activity leads to bradycardia and vasodilatation. We suggest that the sympathetic activity can be reduced by robotic movements of the lower limb, preventing this vicious cycle, which leads to an OH and vasovagal syncope. In addition, we suggest that active movement of the lower limbs produces higher venous return than passive movement. The increased volume of blood circulating maintains cardiac output and helps to reduce OH and inhibits syncope.

Table 2 Blood pressure at baseline

		Time 0	
	Patient	Systolic	Diastolic
Group A	1	127	83
	2	153	90
	3	141	82
	4	128	86
Group B	1	111	74
	2	119	77
	3	127	88
	4	112	72

Data are expressed in mmHg.

Table 3 Seconds of orthostatic hypotension during verticalization

		T0	T1	T2
	Patient	30–65°	30–65°	30–65°
Group A	1	119	48	4
	2	120	1	0
	3	58	8	0
	4	6	0	0
Group B	1	119	120	187
	2	0	84	83
	3	0	0	0
	4	15	120	120

Data are expressed in seconds over a period of 120 s of observation after the verticalization.

Conclusion

In our study, the therapy with a robotic tilt table (Erigo; Hocoma) reduced cardiovascular distress in MCS and VS patients with hemodynamic instability. However, these patients showed increased OH when they were treated only with verticalization. Thus, we suggest analyzing BP of patients before rehabilitative treatment: MCS and VS patients with hemodynamic instability should be treated only with robotic movements of the lower limbs.

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Conflicts of interest

There are no conflicts of interest.

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