Visual-spatial training in patients with sub-acute stroke without neglect: a randomized, single-blind controlled trial

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Summary

Many people who have suffered a stroke will experience sensorimotor impairments that disrupt their performance of motor skills, including balance and gait. Furthermore, stroke-induced brain damage can result in visual disorders that may significantly impact performance of normal daily activities.
The primary aim of this study was to investigate the effects, on balance, of visual-spatial training as an add-on intervention to conventional neurorehabilitation in patients with subacute stroke without neglect; secondarily, it aimed to assess the effects of this training on activities of daily living. Thirty inpatients (17 M, age: 57.3±12.9 years) with a diagnosis of subacute stroke (< 180 days) were enrolled in this study and randomized into two groups: the visual-spatial training group and a control group. All patients were evaluated, using the Tinetti Balance and Gait Scale (TBG), the Berg Balance Scale, computerized posturography, and the Barthel Index (BI), both before (T0) and after (T1) four weeks of training sessions. In addition to conventional neurorehabilitation, each group performed a total of twelve 20-minute rehabilitation sessions (3 times/week for 4 weeks). Significant TIME x GROUP interactions were recorded in the experimental group with respect to the control group for the TBG score [F (1,18) =15.59; p = 0.0004] and BI score [F (1,28) =6.35; p = 0.01]. Both groups recorded non-significant improvements on the instrumental postural assessment. These data suggest that visual-spatial training as an add-on intervention to conventional neurorehabilitation could be an effective complementary strategy to improve balance and activities of daily living.

KEY WORDS: postural balance, stroke rehabilitation, vision disorders.

Introduction

Post-stroke rehabilitation is a major healthcare problem that places considerable pressure on healthcare budgets (Paolucci et al., 1998; Lloyd-Jones et al., 2010). Stroke rehabilitation is highly resource intensive and it has been reported that the "economic burden of neurorehabilitation may vary greatly depending on disease severity" (Iosa et al., 2019). The onus for providing stroke care lies largely with rehabilitation services.
Balance is a complex multi-factorial system in which motor, sensory and cognitive components interact with one another and with the environment under varying task demands and situational contexts. A deficiency in any individual element can lead to a balance impairment (Gervais et al., 2014; Zou et al., 2018). Postural control is achieved through the integration of somatosensory, visual and vestibular inputs, which can sometimes be functionally redundant (as generally happens) or in conflict with each other. Afferent and efferent information is combined by a central integration mechanism (Horak, 2006). After a stroke, many people experience sensorimotor impairments that disrupt balance and gait motor performance (Duncan et al., 1992; Morone et al., 2014). For example, visual field defects occur in approximately 30% of stroke patients (Feigenson et al., 1977; Rossi et al., 1990), and many additional stroke patients have impaired visual perception but intact visual fields. Stroke-induced damage to the human cerebral cortex can result in a number of distinct visual perceptual impairments that may have significant implications for the rehabilitation of nonvisual functions and performance of normal daily activities (Anderson et al., 1995). Most of the movements executed in a given day are voluntary and goal-directed, requiring the capacity to plan movements according to those goals. It is therefore vital to enhance attention and movement planning in community-dwelling adults post-stroke, as they are known to have difficulty performing another task while walking (Tramontano et al., 2017). Post-stroke patients show many changes in the motor strategies used to achieve postural control; most of these changes are due to central nervous system impairment, but some might be considered adaptive behaviours (Tasseel-Ponche et al., 2015). For these reasons, a useful role could be played by a multidisciplinary rehabilitation interventions that provide early, customized, intensive, task-specific and multisensory stimulation (Belda-Lois et al., 2011; Wolpert et al., 2011; Masiero et al., 2014). Several studies have already shown a positive effect of integrative multisensory stimulation, in the form of proprioceptive training (Aman et al., 2014) or vestibular training (Tra-

montano et al., 2018) for example, in improving balance and gait in patients with sub-acute stroke. Also, visuospatial training can improve motor control functions in patients with hemineglect (Wang et al., 2015). Recent evidence suggests that such improvements are a result of the combination of visual and balance training, which appears to facilitate changes at a multimodal level: individuals with balance impairments and binocular visual dysfunction after stroke achieved a significant improvement in balance and gait through the combination of balance and visual therapy (Schow et al., 2016). Numerous studies have investigated the effects of visual training in stroke patients with hemispatial neglect, and recorded improvements in visual functioning and activities of daily living (ADL) (Kerkhoff et al., 1992; Kasten et al., 1999; van Wyk et al., 2014). Recently, a single study demonstrated that visual computer interface training in chronic non-neglect stroke patients can improve visual functioning and ADL (Elshout et al., 2018). These studies support the idea that the visual influence becomes predominant when inputs from other sources are reduced (Smania et al., 2008), and that reliance on visual input could be a compensatory strategy used by patients with stroke in order to bypass their balance impairment (Bonan et al., 2004). Under these premises, the main objective of this study was to investigate whether visual-spatial training (VST) as an add-on intervention to conventional neurorehabilitation can lead to an improvement in balance skills.

The secondary aim was to assess the effects of VST on ADL in patients with sub-acute stroke without neglect. The rationale behind the study is that specific visual training could enhance the processing (and/or central integration) of specific sensory afferents (i.e., somatosensory, visual and vestibular), leading to improved balance performance in patients with sub-acute stroke without neglect.

Materials and methods

Trial design

We used a two-arm, four-week, single-blind, parallel randomized controlled trial design. The participants were recruited and enrolled from the Neurorehabilitation Unit of the Fondazione Santa Lucia (FSL), a scientific research and healthcare institute, using a consecutive sampling approach.

A clinician carried out the enrollment and a researcher who was not involved in the study conducted the random group assignments. He was the sole person responsible for this process and securely stored the randomization list. Simple randomization with a 1:1 allocation ratio was performed.

Participants

Thirty hospitalized patients (17 M, age: 57.3±12.9 years) with a diagnosis of subacute stroke (< 180 days) were enrolled in this study. Inclusion criteria: hemorrhagic or ischemic stroke with unilateral mild hemiplegia; ability to walk without any device or need of continuous physical assistance to support body weight or maintain balance (Functional Ambulation Classification ≥ 3).

Exclusion criteria: cognitive deficits affecting the capacity of patients to understand the task instructions (Mini-Mental State Examination score > 24); severe unilateral spatial neglect (positive results on the: Letter Cancellation Test, Barrage Test, Sentence Reading Test and Wundt-Jastrow Area Illusion Test), severe aphasia, and presence of neurological, orthopedic or cardiac comorbidities (all of them clinically evaluated), significant visual acuity impairment caused by cataracts, diabetes, retinopathy and/or glaucoma. In order to evaluate visual defects all patients performed an ophthalmological examination that included assessment of visual acuity with Snellen tables at 5 meters and 40 cm, while campimetric defects due to hemianopia or quadrantopia were assessed with the Octopus 101 perimeter (Haag-Streit, Mason, OH) using a 30° screening program. Ocular fundus examination was also performed.

As mentioned the participants were recruited and enrolled, using a consecutive sampling approach, through the Neurorehabilitation Unit of the FSL. This phase lasted from April 2016 to February 2018.

The patients were randomized into two groups: the visual-spatial training group (VSTG) (15 patients; 6 F; age: 52.8±9.2 years) and a control group (CTRL) (15 inpatients; 7 F, age: 61.7±15.2 years) (the demographic and clinical characteristics of the two groups are reported in Table I). The sample size estimation was performed through power analysis for non-parametric between-groups comparisons (α = 0.05; β = 0.8; ES = 0.5) (Cohen,

Table I - Demographic and clinical characteristics.

	TOTAL Sample (30)	VSTG (15)	CTRL (15)
Sex (female)	13	6	7
Age (mean yrs±SD)	57.3±12.9	52.8±9.2	61.7±15.2
Stature (mean cm±SD)	169.2±8.4	170.6±10.7	167.7±5.5
Body weight (mean kg±SD)	75±21.3	75±24.7	75.9±18.8
Side of lesion (right)	12	8	4
Type of lesion (ischemic)	20	10	10
Campimetric deficits	16	8	8

Demographic and clinical characteristics of the total sample of patients and after their randomization into the experimental group and control group. Non-significant differences in demographic and clinical data were recorded between the two groups at baseline.

Abbreviations: VSTG, experimental group; CTRL, control group; yrs, years; SD, standard deviation.

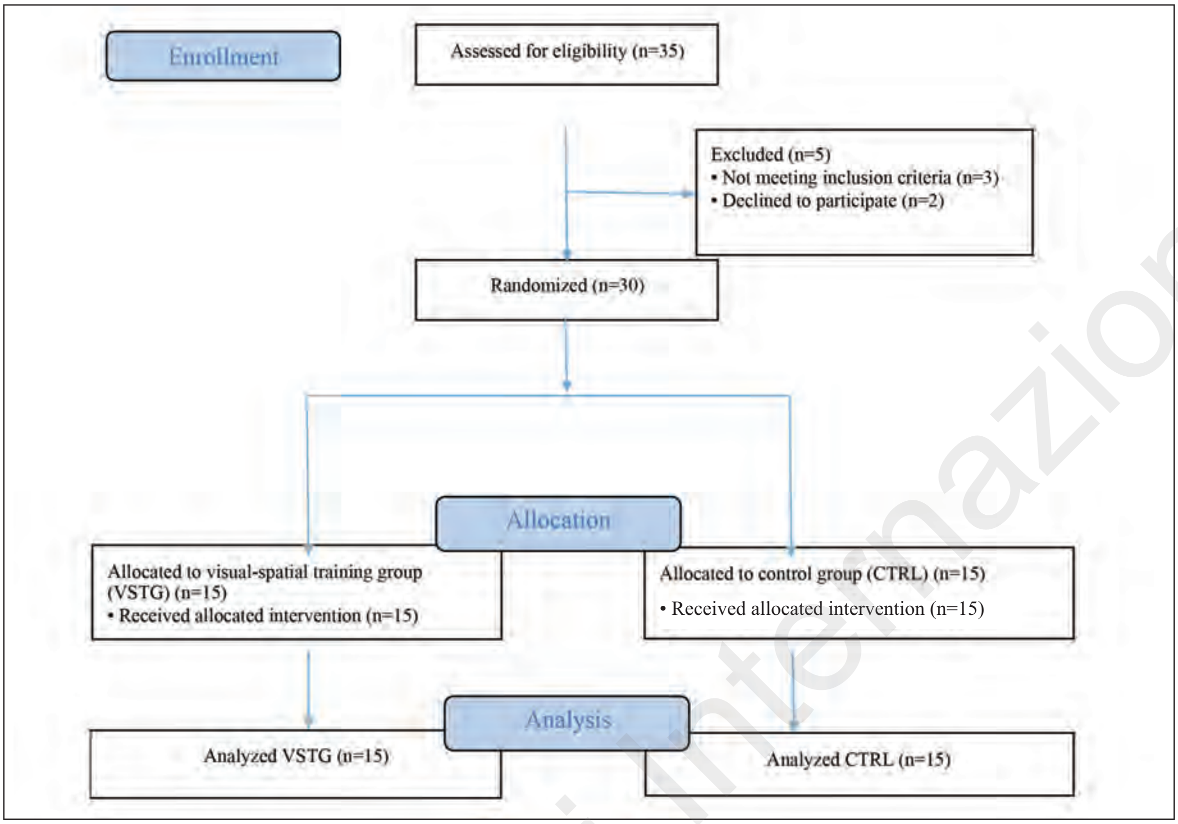

Figure 1 - Flow diagram of the study.
Abbreviations: VSTG, experimental group; CTRL, control group.

1977) using the Tinetti Balance and Gait scale score as outcome measure (Park et al., 2018). According to this sample size estimation, the inclusion of at least 15 patients per group was needed.
The study was approved by the local independent ethics committee and conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All the participants gave their written informed consent to participate in the study (Fig. 1).

Outcomes
Primary and secondary outcomes were evaluated before (T0) and after treatment (T1). A clinician, who was blinded to the patients' group allocation, performed all the evaluations. Patients were examined in the morning to reduce the effect of fatigue, frequently reported later in the day. Any assistive devices as well as orthoses needed by patients were permitted during assessments. Each patient was always assessed using the same devices, orthoses and shoes. The Tinetti Balance and Gait Scale (TBG), used for assessing balance and risk of falls (Tinetti, 1986), and the Barthel Index (BI), used for assessing ADL (Mahoney and Barthel, 1965), were taken as the primary outcome measures, while the Berg Balance Scale (BBS) for static and dynamic balance (Berg et al., 1989) and computerized posturography for assessing postural control (Tamburella et al., 2014) were the secondary outcome measures.

Postural assessment
A FreeMed® BASE model baropodometric platform (Sensor Medica®, Rome, Italy) was used for the stabilometric measurements.
The reliability of this platform has been shown in previous studies (Romero-Franco et al., 2013). Calculations of center of pressure (CoP) movements were performed using the FreeStep® Standard 3.0 software (Sensor Medica®, Rome, Italy). The assessment was performed in a sound-isolated room. Data from the platform were converted in accordance with instructions provided by the manufacturer and transformed into coordinates of the CoP. Stabilometric parameters measured in order to express deviation of the CoP were: total excursion of the CoP (TE), defined as the length or the total distance of the CoP over the course of the trial duration and area of the 95% confidence ellipse (CEA), i.e. the smallest ellipse that will cover 95% of the points of the CoP diagram. Participants performed the static standing measures with eyes open (OE) during the first analysis and with closed eyes (CE) during the second analysis. The analysis was repeated three times for each condition. The following parameters of the statokinesigram were considered for both the OE and CE conditions: CoP sway length, and ellipse surface area; these derive from the coordinates of the CoP along the frontal (X; right-left; X-mean) and sagittal (Y; forward-backward; Y-mean) planes (Barbero et al., 2012).

Interventions

For four weeks (5 days/week), both groups performed two daily 40-minute sessions of conventional post-stroke neurorehabilitation therapy. In addition, both groups underwent twelve 20-minute rehabilitation sessions (3 times/week for 4 weeks): in the VSTG these consisted of visual-spatial exercises aimed at enhancing peri-personal and extra-personal perception, while the CTRL group's sessions focused on trunk stabilization and weight transfer to the paretic leg.

Visual-spatial training

The VSTG participants performed three different visuospatial training exercises (VSTex) 3 times/week for 4 weeks as add-on to conventional neurorehabilitation (Fig. 2). For VSTex (i) and VSTex (ii), the patients were asked to sit with their back straight, without resting on the back of the chair, not to cross their legs or arms, and to keep their head still, moving only their eyes. Each 20-minute session consisted of cycles of three minutes of exercise followed by two minutes of rest. For the VSTex (iii), the patients were asked to walk between parallel bars four times per session, with two minutes of rest between each of the four times.

VSTex (i) - Specular vision training

For this exercise, the patient sits on a chair in front of a table on which two vertical plexiglass panels are positioned parallel to each other and totally included in his/her visual field.

On the panels, eight rectangles of two different colors have been placed. The operator sits opposite the patient, on the other side of the two plexiglass panels, in the same visual field conditions. The operator fixates one of the rectangles, the patient must fixate the same rectangle targeted by the operator, and then remain still for a few seconds, so as to allow the operator to verify the correctness of his gaze. If this is correct, the operator switches gaze to another reference point. In the event of error, however, the operator invites the patient to look better and correct his/her gaze. In this exercise, the same process of increasing difficulty was adopted for all the subjects (Piquè Batalla, 2014).

VSTex (ii) - Mirror training

The patient is positioned in front of two mirrors arranged orthogonally to each other, sitting on a chair set at a 45 degree angle to the intersection of the two mirrors. On the mirrors there are 12 markers, 6 per mirror (numbered from 1 to 12). Because of the way the mirrors are positioned, in addition to the real numbers, 12 reflecting images are created. The patients performed a training exercise to identify, using their gaze, real or reflected numbers, as requested by the operator. The subjects were asked to fixate the numbers for at least one second, to allow the therapist to verify the accuracy of the test (Duñabeitia et al., 2011).

VSTex (iii) - Target identification during walking

This activity consists of making the participants walk, just once, back and forth between the parallel bars, and asking them to identify certain characteristics of objects that have been placed in a range of action determined by the patient's visual field. The boundaries of this space did not exceed a distance of 5 m from the patient. The same objects were used for all the patients, and consisted of 5 green sticks, each 10 cm long. The operator blindfolded each patient before each trial, and then hid the sticks, after which the patient, opening his eyes, had to look for them during the walking task. After finishing walking, the patient, with his/her eyes closed, had to tell the operator which was the nearest and which the farthest stick, and how many he/she had seen.

CTRL - Balance training

The balance exercises were focused on trunk stabilization and weight transfer to the paretic leg and consisted of three exercises. First, patients were seated, blindfolded, on a fit ball for 5 minutes with the supervision of an expert physiotherapist who helped them to maintain the correct position. Second, patients were asked to maintain balance in a standing position on a Freeman board for 5 minutes. The third exercise consisted of transferring body weight to the paretic leg using parallel bars for 10 minutes (Tramontano et al., 2018).

Statistical analysis

All results were analyzed by means of two-way ANOVA for repeated measures with the variables TIME (T0 *vs* T1) and GROUP (VSTG *vs* CTRL), and considering as significant TIME X GROUP interactions with $p < 0.05$ after Bonferroni post-hoc analysis correction. All data were analyzed with STATISTICA 8.0 Software (StatSoft Inc., Tulsa, OK, USA).

Results

Thirty-five participants were screened for eligibility. In accordance with the inclusion/exclusion criteria, 30 participants were enrolled in the period from April 2016 to February 2018 and randomized into the VSTG and the CTRL group. No subject dropped out of the treatment and/or missed evaluations.

A significant TIME x GROUP interaction was recorded for the TBG [$F_{(1,18)}=15.59$; $p = 0.0004$], Bonferroni *post-hoc* analysis showed a significant increase in balance function in the VSTG ($p < 0.0001$). A significant TIME x GROUP interaction was recorded for the BI [$F_{(1,28)}=6.35$; $p = 0.01$], with Bonferroni post-hoc analysis showing a significant score increase in ADL abilities in the VSTG vs CTRL group (VSTG: $p < 0.0001$). A non-significant TIME x

Figure 2 - Visual-spatial training exercises.

Table II - Results.

	VSTG		CTRL		p-value			
	T0	T1	T0	T1	T x G	TIME	GROUP	Post-hoc
TBG	18.4 ±5.02	25.9±2.91	19.1±6.38	22±4.73	0.0004	< 0.0001	0.33	< 0.0001
BBS	39.9±9.89	49.2±6.62	38.9±12.39	44.8±10.83	0.09	< 0.0001	0.45	
BI	70.9±18.71	92.4±11.12	69.1±24.42	70.1±21.36	0.01	< 0.0001	0.27	< 0.0001
CEA OE	524.7±542	296.7±256.88	633.1±875.74	624.4±918.17	0.46	0.42	0.30	
CEA CE	624.5±636.43	483.2±526.82	568.3±599.85	422.8±404.06	0.98	0.12	0.74	
TE OE	1347.4±498.14	1086.9±294	1268.3±206.76	1092.6±368.71	0.55	0.004	0.74	
TE CE	1543.7±542.54	1256.6±379.7	1409.6±243.11	1219.9±416.7	0.55	0.006	0.50	

Mean ± standard deviation of clinical scale and stabilometric assessment scores and, respectively, p-value of TIME x GROUP interaction pre (T0) and post treatment (T1). Significant results are underlined. Post-hoc p-value refers to T0 vs T1 comparison in the VSTG.
Abbreviations: VSTG, experimental group; CTRL, control group; T x G, TIME x GROUP interaction; Post-hoc, Bonferroni test result T0 vs T1; TBG, Tinetti Balance and Gate scale; BBS, Berg Balance scale; BI, Barthel Index; CEA, area of the 95% confidence ellipse with open eyes (OE) and closed eyes (OE); TE, total excursion of the center of pressure with open eyes (OE) and closed eyes (CE).

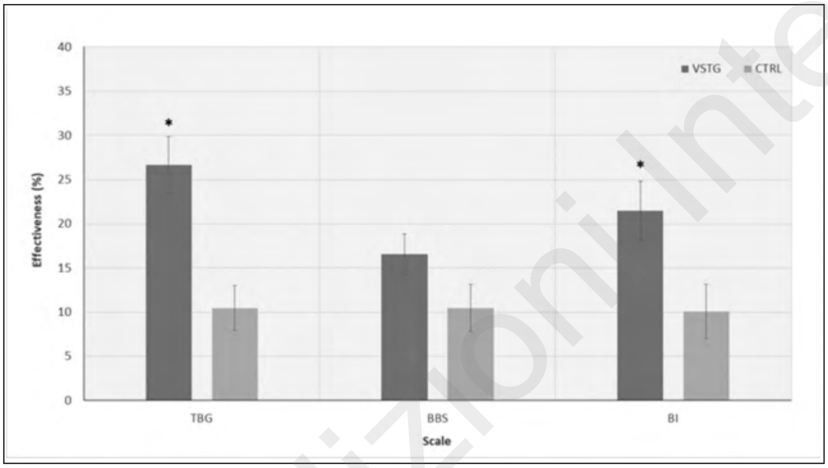

Figure 3 - Mean score increase (%) in clinical scale scores between baseline (T0) and post-treatment (T1) assessments in the two groups.
Effectiveness formula ((T1-T0))/(Max Score)*100. * = p-value < 0.05 (TIME x GROUP interaction). Error bars indicate standard error.
Abbreviations: VSTG, experimental group; CTRL, control group; TBG, Tinetti Balance and Gait scale; BBS, Berg Balance Scale; BI, Barthel Index.

GROUP interaction was recorded for BBS [$F_{(1,28)}=2.95$; $p = 0.09$] (Fig. 3). As for the stabilometric measurements, a significant TIME effect was recorded for total excursion of the CoP (TE OE and TE CE), but we recorded no effect of TIME for the area of the ellipse (CEA OE and CEA CE), and no TIME x GROUP interaction was recorded (Table II). In both groups, a significant TIME effect was recorded for all the clinical scales.

Discussion

Our data suggest that an add-on visuospatial training in stroke patients led to improved personal ADL and balance skills compared with the results in the control group. Accurate control of posture, balance and gait, through the environment, involves a series of sensorimotor processes that continually encode and compare information from visual, vestibular, proprioceptive and sensorimotor feedback.

The extent to which visual information dominates this process is best demonstrated when people stand with their eyes closed: postural sway increases by between 20 and 70% (Lord et al., 2010). The high prevalence of visual impairment associated with ageing creates a public health concern because of its potentially negative effect on the risk of falls and injury (Reed-Jones et al., 2013).

Studies on the rehabilitation of sensorimotor integration deficits in stroke patients show that patients become dependent on the visual system when inputs from other sources are reduced.

For example, Bonan et al. (2004) showed that static and dynamic balance improved more after rehabilitation under visual deprivation than under free vision. Bayouk et al. (2006) included exercises executed while the proprioception of the feet and ankles and/or vision was manipulated, and then Smania et al. (2008), through a specific training program including different conditions of manipulation of sensory inputs, achieved a significant improvement in balance control and in gait ability that is not transient but persistent for several days. The aim of our study, too, was to investigate the importance of correct integration between somatosensory inputs, by training the visual afferents in post-stroke patients. The visual system should be trained to correctly support integration of the information that subtends the maintenance of balance, such as vestibular information, in order to avoid mismatches. The difference compared with the other studies is that our purpose was to observe the effect of

the training on balance not in chronic patients, but in patients with subacute stroke without neglect.
Moreover, we did not evaluate possible improvements in gait parameters, because we decided to consider only the effect on balance and changes at postural level.
The exercises used in the VSTG permitted these patients, through specific training of visual and spatial functions, to improve their perception of the space around their body. It is demonstrated that poor functional vision is related to weaker balance and mobility performance in community-dwelling older adults (Aartolahti et al., 2013). It is possible that the VST generated improvement in the perception of space and distances and managed to improve balance and gait; this improvement can be reflected in everyday life in a reduction of accidental falls. There are already some studies that have shown the positive effects of visual training for the improvement of ADL in stroke patients with hemispatial neglect and in chronic non-neglect (Kerkhoff et al., 1992; Kasten et al., 1999; van Wyk et al., 2014; Elshout et al., 2018). Equally, our study confirms an improvement in ADL after VST in patients with subacute stroke without hemispatial neglect. Improved visual perceptual processing could translate into a greater ability to perform ADL following stroke: in fact, VST in our patients improved the ability to perform many activities like feeding, toilet use, transfer, dressing and bathing.
These results show the potential clinical importance of visual integration and its concrete impact on personal ADL. In short, VST improves balance skills and ADL in sub-acute stroke patients.
A number of reasons may explain the absence of drop outs in our study. First, the duration of the trial was congruous with duration of inpatient stays at the FSL. Moreover, the safety of this non-invasive treatment meant that there were no adverse events. In addition, the content of the exercises was varied, stimulating and interactive, thus keeping patients willing to participate in the study through to the end. This study is not to be considered a post-treatment visual assessment, as the aim was not to investigate the effects of VST on visual deficits, but rather its effects on global motor outcomes through stimulation of the perceptual components of visual function (detection, localization, identification of visual stimulus).
The non-significant results of the postural assessment, show that the CEA OE improved more in the VSTG than in the CTRL group, indicating an effect of the VST on postural stability assessed with stabilometric measurements. Another limitation to consider is a lack of a multisensory instrumental assessment (Bergamini et al., 2017) of dynamic balance and gait parameters, which should have been carried out to better clarify the effects of VST, and the absence of a follow-up evaluation.
Our results show that a neurorehabilitation program focusing on balance rehabilitation in patients with sub-acute stroke should include multisensory stimulation. Future studies could investigate the effects, on balance skills, of multisensory training of somatosensory, vestibular and visual cues.
In conclusion, visuospatial training as an add-on intervention to conventional neurorehabilitation could be useful for improving outcome, in terms of balance and autonomy in ADL, in patients with sub-acute stroke without neglect.

Acknowledgements

The Authors wish to thank Prof. Carlo Caltagirone, Dr. Maria Grazia Grasso and Dr. Marco Traballesi for their support in patients' recruitment.

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