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Does body shadow improve the efficacy of virtual reality-based training with BTS NIRVANA? A pilot study

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Abstract

Background: Aim of the present study was to evaluate whether the presence of body shadows during virtual reality (VR) training with BTS NIRVANA (BTs-N) may lead to a better functional recovery.

Methods: We enrolled 20 poststroke rehabilitation inpatients, who underwent a neurocognitive-rehabilitative training consisting of 24 sessions (3 times a week for 8 weeks) of BTs-N. All the patients were randomized into 2 groups: semi-immersive virtual training with (S-IVT_S group) or without (S-IVT group) body shadows. Each participant was evaluated before (T0) and immediately (T1) after the end of the training (Trial Registration Number: NCT03095560).

Results: The S-IVT_S group showed a greater improvement in visuo-constructive skills and sustained attention, as compared with the S-IVT group. The other measures showed nonsignificant within-group and between-group differences.

Conclusion: Our results showed that body shadow may represent a high-priority class of stimuli that act by "pushing" attention toward the body itself. Further studies are needed to clarify the role of body shadow in promoting the internal representation construction and thus self-recognition.

Abbreviations: AM = attentive matrices, ARE = asymptotic relative efficiency, BTs-N = BTS NIRVANA, FAB = Frontal Assessment Battery, FIM = Functional Independence Measure, MI = Motricity Index, MMSE = Mini-Mental State Examination, MoCA = Montreal Cognitive Assessment Test, MV = movement visualization, MWU = Mann-Whitney *U*, SD = standard deviation, S-IVT = semi-immersive virtual training without body shadows, S-IVT_S = semi-immersive virtual training with body shadows, TCT = Trunk Control Test, TMT = Trail Making Test, VR = virtual reality, WSR = Wilcoxon signed rank.

Keywords: body shadow, cognitive, rehabilitation, stroke, virtual reality

1. Introduction

Stroke is one of the leading causes of death and disability, and this has been described as a worldwide epidemic.^[1] The effects of a stroke may include sensory, motor, and cognitive impairment, as well as a reduced ability to perform self-care and participate in social and community activities.^[2] Although most recovery is thought to occur in the first few weeks after stroke, patients may make improvements on functional tasks many months after

having a stroke,^[3] given that neuroplasticity exists also in the chronic phase.

Cognitive impairment and neuropsychiatric symptoms, including attention and concentration, memory, spatial awareness, perception, praxis, and executive functioning deficits, frequently occur in poststroke patients. Indeed, about two-thirds of stroke survivors may experience cognitive changes.^[4,5] These changes have a significant impact on long-term outcome and appear to be associated with an increased risk of disability, depression, and quality of life.^[6] Early recognition and monitoring of cognitive changes in stroke is necessary to optimize patient care, and this can guide therapy and rehabilitation strategies.^[7]

The use of alternative rehabilitation tools is a growing field, given that the standard rehabilitation for stroke is not always so effective in improving functional outcomes.^[8] Virtual reality (VR) has a prominent role in promoting functional recovery after stroke, as it can integrate multisensory stimulation to provide a realistic environment and to enrich motivational training improving patients' adherence to the rehabilitative program.^[8]

VR has been defined as the "use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events,"^[9] and it is believed to optimize motor learning.^[10] VR offers clinicians the ability to control and grade tasks to challenge the user, as VR programs often incorporate multimodal feedback provided in real time.

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However, there are few studies on the role of VR training in cognitive rehabilitation (CR) of stroke patients, though an improvement in balance and gait has been reported.^[11] Virtual rehabilitation system provides 3 different types of information to the patient: movement visualization (MV), performance feedback, and context information.^[12] Movement observation plays an important role for central sensory stimulation therapies, such as mirror therapy or mental training; indeed, the observation or imagination of body movements facilitates motor recovery^[13-15] and provides new possibilities for cortical reorganization. Thus, it appears that MV is a key element of VR-based rehabilitation intervention.^[11] The presence of body shadow, considered as MV, has recently been a target of an increasing number of studies, mainly showing that information conveyed by shadows can support several tasks performed in everyday life.^[16] When applied to body shadows, the shadow-correspondence problem may thus be central to a perceptual decision that promotes selfidentification and self-recognition.[16]

The aim of the present study was to detect the differences in functional outcomes between the presence or not of body shadow during a VR training with BTS NIRVANA (BTs-N), using an interactive-semi-immersive program.

2. Materials and methods

We enrolled 20 poststroke inpatients (12 males and 8 females, mean age 64 ± 6), who attended our Robotic and Behavioral Neurorehabilitation Center from June 2016 to January 2017. The inclusion criteria were ischemic or hemorrhagic stroke in the chronic phase (at least 6 months after the ischemic/hemorrhagic accident) with a severe upper limb impairment; presence of moderate-to-mild cognitive impairment (Mini-Mental State Examination [MMSE] from 11 to 26) assessed after the stroke; and absence of disabling sensory alterations (ie, audio-visual deficits) and severe psychiatric illness.

The exclusion criteria were age >75 years, presence of severe medical and psychiatric illness, and intake of drugs potentially affecting neurocognitive functions. The study was approved by the Local Ethical Committee, and registered on the www. clinicaltrials.com (NCT03095560). All the patients provided informed consent to enter the study. All the participants were randomized (by using a randomized block design) into 2 groups: semi-immersive virtual training with (S-IVT_S) or without (S-IVT) body shadow, and underwent the same conventional physiotherapy program in addition to a VR neurocognitive-rehabilitative training (24 sessions of BTs-N, 45 minutes daily, 3 times a week, for 8 weeks). Each participant was evaluated by skilled neuropsychologist and neurologist before (T0) and immediately (T1) after the end of the training. Primary outcomes were assessed using the Montreal Cognitive Assessment Test (MoCA) and the Functional Independence Measure (FIM). In addition, we administered the Frontal Assessment Battery (FAB) to assess executive functions, attentive matrices (AM), and Trail Making Test (TMTA, TMTB, and TMTB-A) to measure the attention process, and the Trunk Control Test (TCT) and Motricity Index (MI) for upper and lower limbs to evaluate motor function.

NIRVANA is a device based on optoelectronic infrared sensors, through which the patient can interact with a virtual scenario. The system is connected to a projector or a big screen, reproducing an interactive series of exercises, thanks to an infrared video camera analyzing the patient's movements, it creates interactivity. In the BTs-N device we used, the projector was located behind the patient in the S-IVT_S group, projecting the

shadow of the patient on the screen, whereas the projector was located in front of the patient in the S-IVT group, being thus the shadow not visible. The virtual cognitive rehabilitative program with BTs-N we carried out in both the groups is described in details in Table 1.

A Wilcoxon signed rank (WSR) test was employed to compare within-group changes from baseline (T0) to post-treatment (T1). Baseline between-group differences were tested through the Mann-Whitney U test (MWU). The MWU was also used for between-group comparisons by computing the differences between T1 and T0 for all outcome measures. We set the alpha-level for significance at .05, adjusted for multiple comparisons using a Bonferroni correction. Data are reported as median and interquartile distribution.

To understand how large the differences between S-IVT_S and S-IVT were, we calculated the effect size Cohen *d*. Given the relatively small sample size, we applied Hedge *g* correction to the biased effect size estimate. Effect size is simply a way of quantifying the size of the difference between 2 groups, that is, it is a quantitative measure of the strength of a phenomenon. Indeed, the amount of variation found within- or between-group is quantified in the calculation of the effect size. For these reasons, effect size is an important tool in reporting and interpreting effectiveness of a treatment. Specifically, Cohen *d* is defined as the difference between 2 means divided by a standard deviation (SD) for the data.

According to the available literature on the effects of VR training in patients with stroke, we calculated a minimal sample size based on the asymptotic relative efficiency (ARE) of the MWU relative to the t tests. We estimated that a minimal sample of 20 participants per group would be necessary to confirm the data of our pilot study.

3. Results

Clinical data at T0 and T1 are summarized in Table 2. There was a large effect size for the improvement in MoCA in the S-IVTs group (P < .001, d = 0.9) at T1 as compared with T0, which was more evident than that observed in S-IVT group at the same interval (P = .02, d = 0.6; MWU: P = .03, d = 0.6). In particular, only S-IVTs group showed a large effect size for the amelioration in visuo constructive (P = .002, d = 0.7; MWU: P = .02, d = 0.9), and a moderate effect size for the improvement in attention (P = .001, d = 0.6; MWU: P = .02, d = 0.6). FIM slightly improved in both the groups, without reaching the statistical significance.

Both the groups improved in all secondary outcome measures at T1 as compared with T0, albeit only AM (S-IVT_S: P < .001, d = 0.8; S-IVT: P = .02, d = 0.6) and MI (S-IVT_S: P < .001, d = 0.6; S-IVT: P = .002, d = 0.4) reached the statistical significance with moderate-to-large effect size. Such improvements were more evident in the S-IVT_S than S-IVT group (MWU for AM: P = .02, d = 0.6; MWU for MI: P < .001, d = 0.8).

4. Discussion

Our results suggest that the use of VR training with BTs-N is useful in improving cognitive abilities (specifically, visuoconstructive abilities and attention) in the poststroke rehabilitation, as suggested by the moderate-to-large effect size in nearly all outcome measures (favoring S-IVT_S).

Despite more than 40% of stroke survivors may experience a decline in cognitive function, the majority of the published data have paid attention mainly to motor recovery.^[17] Cognition is

Table 1

Virtual Cognitive Rehabilitative Program used in patients undergoing BTs-N System.

Cognitive domain	BTs-N S-IVT _S	BTs-N S-IVT
Executive and visuo-spatial	 To program some movements finalized to virtual touch, to move or manipulate specific objects, in different directions (ie, balls, flowers, butterfly, and so on); or to realize specific associations (ie, number-color) with a dynamic interaction in virtual environment. When the patient touches virtual objects determine a video and audio feedback (using sprites task, observing his or her shadow reflected on the virtual scenarios). These rehabilitation exercises with audio-visual stimuli involve the visuo-spatial and praxis abilities of patients, resulting in a very motivational training. In particular, the subject realizes ideo-motor sequences (from simple to complex serious of actions), after the verbal consign by therapist. The patient observes his or her shadow during the execution of executive and visuo-spatial virtual tasks. 	To program some movements finalized to virtual touch, to move or manipulate specific objects, in different directions (ie, balls, flowers, butterfly, and so on); or to realize specific associations (ie, number-color) with a dynamic interaction in virtual environment. When the patient touches virtual objects determine a video and audio feedback (using sprites task, interacting directly with some virtual scenarios, without observing his or her shadow). These rehabilitation exercises with audio-visual stimuli involve the visuo-spatial and praxis abilities of patients, resulting in a very motivational training.
	The level of difficulty increases (from first to third level) with the increase of the complexity of virtual ideo-motor difficult to realize.	The level of difficulty increases (from first to third level) with the increase of the complexity of virtual ideo-motor difficult to realize.
Attention process	To select, with an immediate and recall feedback (audio and video), some various elements (colors, musical strings, geometric or shapeless, animals, and so on) are observed in the virtual environment. These elements remain visible to observer for a variable time, established by the interaction among the virtual system, therapist, and patient. The patient touches the virtual target element, in a specific time, and so, this action causes a visual change with a peculiar audio feedback (positive reinforce); otherwise the element disappears (negative reinforce) (<i>Hunt task</i>). The patient observes his or her shadow during the execution of attention virtual tasks. <i>The level of difficulty increases with the increase in the number of distracters and reducing the usable time of execution.</i>	 To select, with an immediate and recall feedback (audio and video), some various elements (colors, musical strings, geometric or shapeless, animals and so on) are observed in the virtual environment. These elements remain visible to observer for a variable time, established by the interaction among the virtual system, therapist, and patient. The patient touches the virtual target element, in a specific time, and so, this action causes a visual change with a peculiar audio feedback (positive reinforce); otherwise the element disappears (negative reinforce) (<i>Hunt task</i>). The level of difficulty increases with the increase in the number of distracters and reducing the usable time of execution. Memory training tasks are conducted on paper and pencil
Memory	immediate and recall time) to remember these (egg, season, colors, balls, numbers, environments, animals, geometric form or not, fruit, job, and so on) with a dynamic interaction in semi-immersive virtual environment (<i>sprites task</i>). The patient remembers where (the position; visuo-spatial memory) and the name (verbal information) of element(s) observed. The patient observes his or her shadow during the execution of memory virtual tasks.	approach in a virtual rehabilitative setting with an interaction between patient and BTs-N System.
		The forms of these virtual tasks include recalling a series of locations of items on a specific rehabilitative table (in a cognitive room), recalling digits or letters in either the order presented or reverse order, or recalling specifically where a particular number or name or digit was in a sequence. The patient interacts directly with these virtual scenarios, without observing her shadow. The patient is immersive in virtual environment, without her shadow, during the execution of memory virtual tasks.
	The level of difficulty increases with the increase in the number of elements to remember and with the reduction of the time to execution.	The memory training is articulate in 3 level of complexity (easy, medium, and high difficulty) in relation to time and number of verbal and not stimuli to remember.

BTs-N = BTS NIRVANA, S-IVT_S = semi-immersive virtual training with body shadows, S-IVT = semi-immersive virtual training without body shadow.

not a unitary concept, but it incorporates multiple domains, including attention, executive functions, problem solving, visual-spatial ability, language, social cognition, and emotions.^[18]

Executive function is the term generally used to describe the brain processes that we employ to organize ourselves and solve problems. Moreover, executive function is strictly related to other important "subfunctions," including inhibition (ie, the ability to suspend prepotent/default responses), mental flexibility (ie, the ability to switch back and forth between rules or response sets), and working memory. These functions are critically important for quality of life, as they are implicated in job performance, social relationships, and both basic and instrumental activities of daily living.^[19]

Attention is the behavioral and cognitive process of selectively concentrating on a discrete aspect of information, whether deemed subjective or objective, while ignoring other perceivable information. Focalization and concentration of consciousness are of its essence.

Table 2

Clinical data of the experimental and control group at T0 and T1.

		S-IVT _s		S-IVT	
		To	T ₁	To	T ₁
MoCA	Total	17±1	21 ± 1	21±1	24±2
	Executive functions	0.2 ± 0.4	0.3 ± 0.5	0.3 ± 0.5	0.2 ± 0.4
	Visuo-constructive skills	1.7 ± 0.5	3.3 ± 0.8	3.3 ± 0.8	3.7±0.5
	Naming	3	3	3	3
	Memory	0	0	0	0
	Selective attention	0.8 ± 0.8	1.7 ± 0.5	1.6 ± 0.5	2
	Sustained attention	0.2 ± 0.4	1	1	1
	Calculation	1.5 ± 1.1	1.8±1	1.8 ± 1	2.3±0.8
	Sentence repetition	1.7 ± 0.5	1.8 ± 0.4	1.8 ± 0.4	1.8 ± 0.4
	Verbal fluency	0.3 ± 0.5	0.3 ± 0.5	0.3 ± 0.5	0.5±0.5
	Abstraction	0.7 ± 0.8	0.8 ± 0.8	0.8 ± 0.8	0.8 ± 0.8
	Delayed recall	1.7±0.8	2.2±0.8	2.2 ± 0.8	3.5±1.2
	Orientation	5.3 ± 1	5±1	5 ± 1	5.1 <u>+</u> 1
FAB		13.8 ± 2.2	14.5 ± 1.9	14 ± 2.4	14 <u>+</u> 1.9
AM		28.9 ± 0.9	41.1±4.5	41.2±4.5	50.7 <u>+</u> 6.6
TMT	A	89.2±19.3	88.3 ± 18.7	88.3±18.7	85.8±18.3
	В	265 ± 77	265 ± 77	265 ± 77	260 <u>+</u> 78
	BA	193 ± 64	193 ± 63	177 ± 74	174 <u>+</u> 73
TCT		64 ± 12	71 ± 15	71±15	76 ± 12
MI		18 ± 10	23 ± 11	20 ± 11	23±11
FIM		62±9	67 <u>±</u> 8	64±8	68 ± 8

AM = attentive matrices, FAB = Frontal Assessment Battery, FIM = Functional Independence Measure, MI = Motricity Index, MoCA = Montreal Cognitive Assessment Test, TCT = Trunk Control Test, TMT = Trail Making Test.

Visuo-spatial ability is the capacity to understand, reason, and remember the spatial relations among objects or space that includes your own body parts.^[20–22]

Besides the aforementioned cognitive alterations, memory deficits can also be considered a relatively common consequence of stroke,^[23] such problems being persistent, debilitating, and often difficult to treat.^[17] Although we used MMSE for the patients' screening, we preferred MoCA for the assessment, given that such test is divided into subitems better investigating those domains we believed may benefit from BTs-N training, also taking into account that several studies have considered MoCA as a valuable tool for cognitive assessment in poststroke patients.^[24-26]

CR therapy encompasses any intervention targeting the restoration, remediation, and adaptation of cognitive functions.

CR techniques may be classified in 2 main categories, that is, conventional/classic (paper/pencil exercises) and computerassisted/not conventional (ie, computerized cognitive rehabilitation [CCR]), both based on the use of cognitive strategies to retrain or alleviate the patient's deficits in attention and concentration, visual processing, language, memory, reasoning and problem solving, and executive functions. Conventional techniques consist of manual exercises with the therapist, whereas computerized exercises train cognitive skills in gamelike programs. Computer use in CR extends to memory training, attention, problem solving, and job simulation. CCR uses multimedia and informatics resources with particular hardware systems and software, that is, ad hoc programs built to reactivate compromised neuropsychological functions.^[27]

VR and interactive technologies have emerged as a valuable tool in stroke rehabilitation by providing the opportunity to practice cognitive and motor activities that cannot be practiced within the clinical environment, such as performing simulations of real-life scenarios and activities in urban virtual environments.^[28]

Despite the growing scientific and engineering activity in VRbased systems, the majority of the studies were designed to address motor impairments.^[28,29] Indeed, according to a recent Cochrane review,^[8] there are only few randomized controlled studies that include CR and/or cognition assessment,^[30] though a positive effect of VR in poststroke balance and gait deficit has been reported.^[31,32]

Timing of CR therapy is also noteworthy, as previous literature has indicated that functional recovery typically occurs in ~95% of stroke patients within the first ~3 months from the acute event.^[33]

In fact, it is thought that most of the neurological recovery that occurs following a stroke is a direct result of brain plasticity and its ability to repair and reorganize,^[34] largely depending on the lesion severity and site.^[35]

On the assumption that reorganization would occur to replace functions of a damaged brain part, a VR rehabilitation training may sustain the improvement in cognitive abilities through complex mechanisms.^[8] Action observation, in association with physical training, can enhance the effects of rehabilitation training after stroke^[36,37] and, more than just playing or training, the implementation of VR training may gear use-dependent neuroplasticity changes.^[8]

In keeping with this argument, growing evidence suggests the role of "mirror neurons" during the execution or observation of actions performed by other individuals, thus enhancing motor and cognitive recovery.^[38]

Thus, the more significant improvement in visuo-constructive abilities, attentive functions, and upper limb motricity in the S-IVT_S patients could be due to the shadow effect (ie, the patient's shadow on the screen while performing VR training) of BTs-N.

Body shadow processing can be reflected at the level of the human mirror neuron system, even when shadows are not relevant for the specific task.^[16] This issue makes body shadow

potentially capable of contributing to the construction of the internal representation of body shape and its extension in space. When applied to body shadows, the shadow-correspondence problem may thus be central to a perceptual decision that promotes self-identification and self-recognition,^[39,40] potentially leading to better functional outcomes.

It is worth noting that not only diagnostic resources and treatments evolve, but also the rehabilitation techniques with therapies and devices, which in the future (and present) can help stroke patients, as demonstrated by our promising tool.

There are some limitations to acknowledge. The sample size is obviously small, as this is a pilot study. Therefore, larger sample trials should be fostered to confirm these interesting data. Baseline data were slightly different between the groups. This might obviously influence S-IVT aftereffects. However, baseline between-group differences were tested through the MWU, which did not disclose significant differences between the 2 groups. This fact may depend on either the relatively high SD or the small sample enrolled (as a pilot study). This aspect needs verification in future larger sample studies.

In conclusion, our results suggest that body shadow may represent a high-priority class of stimuli that act by "pushing" attention toward the body itself, thus contributing to cognitive and motor recovery. Further studies should be developed to clarify the role of body shadow in the self-recognition and the internal representation construction, which, in turn, can be considered future target of neurorehabilitation.

References

- Feigin VL, Mensah GA, Norrving B, et al. GBD 2013 Stroke Panel Experts GroupAtlas of the Global Burden of Stroke (1990–2013): The GBD 2013 Study. Neuroepidemiology 2015;45:230–6.
- [2] Miller EL, Murray L, Richards L, et al. Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: a scientific statement from the American Heart Association. Stroke 2010;41:2402–48.
- [3] Teasell R, Rice D, Richardson M, et al. The next revolution in stroke care. Expert Rev Neurother 2014;1307–14.
- [4] Jacquin A, Binquet C, Rouaud O, et al. Post-stroke cognitive impairment: high prevalence and determining factors in a cohort of mild stroke. J Alzheimers Dis 2014;40:1029–38.
- [5] Douven E, Schievink SH, Verhey FR, et al. The cognition and affect after stroke—a prospective evaluation of risks (CASPER) study: rationale and design. BMC Neurol 2016;16:65.
- [6] Campbell BC, Murray J, Holmes J, et al. Frequency of anxiety after stroke: a systematic review and meta-analysis of observational studies. Int J Stroke 2013;8:545–59.
- [7] Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. Clin Psychol Rev 2012;32:329–42.
- [8] Laver KE, George S, Thomas S, et al. Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev; 2015, no. 9, Article ID CD008349.
- [9] Lam YS, Man DW, Tam SF, et al. Virtual reality training for stroke rehabilitation. NeuroRehabilitation 2006;21:245–53.
- [10] Sveistrup H. Motor rehabilitation using virtual reality. J Neuroeng Rehabil 2004;1:10.
- [11] Ferreira Dos Santos L, Christ O, Mate K, et al. Movement visualization in virtual reality rehabilitation of the lower limb: a systematic review. Biomed Eng Online 2016;15(supple 3):144.
- [12] Schüler T, Ferreira dos Santos L, Hoermann S. Harnessing the experience of presence for virtual motor rehabilitation: towards a guideline for the development of virtual reality environments. In: Proceedings of the Tenth International Conference on Disability, Virtual Reality and Associated Technologies (ICDVRAT), September 2–4, Gothenburg.
- [13] Calayan LSM, Dizon JMR. A systematic review on the effectiveness of mental practice with motor imagery in the neurologic rehabilitation of stroke patients. Internet J Allied Health Sci Pract 2009;7:10.

- [14] Thieme H, Mehrholz J, Pohl M, et al. Mirror therapy for improving motor function after stroke. Cochrane Database Syst Rev 2012;3: CD008449.
- [15] Zimmermann-Schlatter A, Schuster C, Puhan MA, et al. Efficacy of motor imagery in post-stroke rehabilitation: a systematic review. J Neuroeng Rehabil 2008;5:8.
- [16] Pavani F, Galfano G. The multisensory body revealed through its cast shadows. Front Psychol 2015;6:666.
- [17] Das Nair R, Cogger H, Worthington E, et al. Cognitive rehabilitation for memory deficits after stroke: an updated review. Stroke 2017;e28–9.
- [18] Van Zomeren AH, van den Burg W. Residual complaints of patients two years after severe head injury. J Neurol Neurosurg Psychiatry 1985;48:21–8.
- [19] Hammack SE, Cooper MA, Lezak KR. Overlapping neurobiology of learned helplessness and conditioned defeat: implications for PTSD and mood disorders. Neuropharmacology 2012;62:565–75.
- [20] Ali M, Hazelton C, Lyden P, et al. Recovery from poststroke visual impairment: evidence from a clinical trials resource. Neurorehab Neural Rep 2013;27:133–41.
- [21] Barrett KM, Brott TG, Brown RD, et al. Sex differences in stroke severity, symptoms, and deficits after first-ever ischemic stroke. J Stroke Cerebrovasc Dis 2007;16:34–9.
- [22] Rowe F, Wright D, Brand D, et al. A prospective profile of visual field loss following stroke: prevalence, type, rehabilitation and outcome. Biomed Res Int 2013;2013:719096.
- [23] Sun J-H, Tan L, Yu J-T. Post-stroke cognitive impairment: epidemiology, mechanisms and management. Ann Transl Med 2014;2:80.
- [24] Koski L. Validity and applications of the Montreal cognitive assessment for the assessment of vascular cognitive impairment. Cerebrovasc Dis 2013;36:6–18.
- [25] Cumming TB, Bernhardt J, Linden T. The Montreal cognitive assessment: short cognitive evaluation in a large stroke trial. Stroke 2011;42:2642–4.
- [26] Godefroy O, Fickl A, Roussel M, et al. Is the Montreal cognitive assessment superior to the mini-mental state examination to detect poststroke cognitive impairment? A study with neuropsychological evaluation. Stroke 2011;42:1712–6.
- [27] De Luca R, Calabrò RS, Bramanti P. Cognitive rehabilitation after severe acquired brain injury: current evidence and future directions. Neuropsychol Rehabil 2016;25:1–20.
- [28] Klinger E, Kadri A, Sorita E, et al. AGATHE: a tool for personalized rehabilitation of cognitive functions based on simulated activities of daily living. IRBM 2013;34:113–8.
- [29] Navarro MD, Lloréns R, Noé E, et al. Validation of a low-cost virtual reality system for training street-crossing. A comparative study in healthy, neglected and non-neglected stroke individuals. Neuropsychol Rehabil 2013;23:597–618.
- [30] Zhang L, Abreu BC, Masel B, et al. Virtual reality in the assessment of selected cognitive function after brain injury. Am J Phys Med Rehabil 2001;80:597–604.
- [31] McEwen D, Taillon-Hobson A, Bilodeau M, et al. Virtual reality exercise improves mobility after stroke: an inpatient randomized controlled trial. Stroke 2014;45:1853–5.
- [32] Lloréns R, Gil-Gómez JA, Alcañiz M, et al. Improvement in balance using a virtual reality-based stepping exercise: a randomized controlled trial involving individuals with chronic stroke. Clin Rehabil 2015;29: 261–8.
- [33] Jørgensen HS, Nakayama H, Raaschou HO, et al. Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. Arch Phys Med Rehabil 1995;76:406–12.
- [34] Bayona NA, Bitensky J, Teasell R. Plasticity and reorganization of the uninjured brain. Top Stroke Rehab 2005;12:1–0.
- [35] Hasbini MJ, Underhill SM, de Erausquin G, et al. Synapse loss and regeneration: a mechanism for function decline and recovery after cerebral ischemia? Neuroscientist 2000;6:110–9.
- [36] Celnik P, Webster B, Glasser DM, et al. Effects of action observation on physical training after stroke. Stroke 2008;39:1814–20.
- [37] Rizzolatti G, Fabbri-Destro M. The mirror system and its role in social cognition. Curr Opin Neurobiol 2008;18:179–84.
- [38] Buccino G, Solodkin A, Small SL. Functions of the mirror neuron system: implications for neurorehabilitation. Cogn Behav Neurol 2006;19:55–6.
- [39] Ouhnana M, Kingdom FA. Objects versus shadows as influences on perceived object motion. Iperception 2016;7:2041669516677843.
- [40] Ainley V, Tajadura-Jiménez A, Fotopoulou A, et al. Looking into myself: changes in interoceptive sensitivity during mirror self-observation. Psychophysiology 2012;49:1504–8.