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Use of virtual reality in improving poststroke neglect: Promising neuropsychological and neurophysiological findings from a case study

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ABSTRACT

After experiencing a stroke in the right hemisphere, almost 50% of patients show unilateral spatial neglect (USN). Virtual Reality technologies offer impressive opportunities for both the rehabilitation and assessment of different cognitive deficits, including USN. A 57-year-old woman, affected by subarachnoid hemorrhage presented a severe left hemiparesis with severe cognitive and behavioral alterations, including temporal and spatial disorientation, reduction of attention and memory process, slowing ideation, USN, and depression of mood. She underwent two different rehabilitation trainings, including standard cognitive training (SCT) in addition to semi-immersive virtual training with her shadow (S-IVT_s) and SCT in addition to a Semi-immersive virtual training, without her shadow (S-IVT). The patient was assessed before and after each of the two different trainings, by using a specific psychometric battery and the event related potential, P300. Only at the end of the use of the S-IVT, we observed a significant improvement in the motor and cognitive function, with regard to USN. SCT in addition to S-IVT with Bts-Nirvana System may be a promising approach in improving attention process, spatial cognition, and mood in patients with post stroke USN, as also demonstrated by the electrophysiological parameters.

KEYWORDS

BTS-Nirvana; cognitive rehabilitation; motor recovery; virtual reality

Introduction

Unilateral spatial neglect (USN) is a syndrome caused by unilateral brain injury, mainly involving the right hemisphere. There are several pathological processes that may cause USN, such as neoplasia, trauma and neurodegenerative disorders; however, stroke is the most frequent cause of USN. As a matter of fact, in the acute stage after right hemisphere stroke, USN may emerge in up to 80% of the patients, but most studies describe rates closer to 50% (Li & Malhotra, 2015). Unilateral neglect is a complex syndrome that is commonly defined as a disorder of perception, attention and action in contralateral side of damage (Azouvi, Jacquin-Courtois, & Luauté, 2017), with loss of spatial awareness of the contralesional side (Rode, Pagliari, Huchon, Rossetti, & Pisella, 2017). Stroke patients with USN do not explore contralateral space effectively and omit to detect stimuli located in that side of space, even if they can move their head and eyes. It has been shown that increasing the attentional demands of the cancellation task aggravates neglect contralesionally (Bowen, Lincoln, & Dewey, 2002). This bias has been interpreted as a consequence of the disruption of

the selective spatial attentional processes (Ricci et al., 2016). USN is characterized by different anatomical-clinical subtypes (auditory, visual, somatosensory, motor, allocentric, egocentric, and representational neglect) that may be associated or dissociated (Rode et al., 2017). These clinical subtypes may occur in association with primary sensory or motor deficits (Li & Malhotra, 2015). Different treatment and rehabilitative approaches for USN has been described. There is not a definite answer to whether there are USN treatments generally applicable to improve the functional behavior, and only a few studies have employed functional-based outcomes (Bowen et al., 2002). Although various rehabilitation interventions have been used in treating USN, evidence of their benefit is lacking (Ricci et al., 2016). In recent years, rehabilitation approaches of neglect can be sorted into two types: top-down and bottom-up methods. (Rode et al., 2017) Top-down methods are based on stimulation of the contralesional side through a voluntary effort by the patient following therapist's instructions. Specifically, these consist in training the direction of the patient's gaze using a prompt to the left. (Rode et al., 2017). On the contrary,

bottom-up methods do not require the patient's awareness regarding his bias. These consist in the manipulation of patient's sensory environment, using sensory stimulation, hemiblinding (or eyeblinding), or prism adaptation (Rode et al., 2017). Rehabilitation after stroke is imperative for patients with USN because it may improve their behavioral, social, and cognitive outcomes, and therefore it can reduce the financial burden on public health services (Bowen, Hazelton, Pollock, & Lincoln, 2013). There is good evidence supporting the use of pursuit intervention over traditional training that is based on saccadic eye movements (Ogourtsova, Souza Silva, Archambault, & Lamontagne, 2015). Recently, there is limited evidence that virtual reality (VR) is more effective than conventional therapy in improving USN in patients with stroke, given that VR may provide enhanced methods for USN assessment and treatment (Fordell, Bodin, Eklund, & Malm, 2016; Laver, George, Thomas, Deutsch, & Crotty, 2011; Pedroli, Serino, Cipresso, Pallavicini, & Riva, 2015). In particular, it has been shown that training with VR can improve spatial attention and the use of such ability in activities of daily living, even in chronic neglect (Saevarsson, Kristjánsson, Bach, & Heinrich, 2012).

The aim of this study is to evaluate the neuropsychological and neurophysiological outcomes in a poststroke individual after an intensive rehabilitative cycle with a combined therapeutic approach, that is, standard cognitive training (SCT) in addition to Semi-immersive Virtual Training (S-IVT) with Bts-Nirvana System.

Material and methods

A 57-year-old woman, affected by subarachnoid hemorrhage involving the right fronto-temporal-parietal region, presented a left hemiparesis; she was total dependent in the activity of daily life. She had severe cognitive and behavioral abnormalities, including temporal and spatial disorientation, reduction of attention and memory process, slowing ideation, USN in the left extracorporeal space and severe mood depression. She underwent two different rehabilitation trainings, including either standard cognitive training (SCT) in addition to Semi-immersive virtual training with her shadow (S-IVT_s) or SCT in addition to a Semi-immersive virtual training, without her shadow (S-IVT). Each rehabilitative session with BTS-Nirvana lasted about 45 minutes. The initial intensive virtual rehabilitative training (the patient performed the cognitive tasks in a virtual scenario with her shadow) included 20 rehabilitation sessions, five times a week for one month. After three weeks of no-treatment in the virtual environment, the patient was submitted to

the Semi-immersive virtual training, without her shadow (S-IVT) for other 20 rehabilitative sessions. The use of the BTS NIRVANA System is different: in the first combined treatment, there is the avatar of the patient (i.e., her shadow), whereas in the second treatment the patient does not see her shadow, providing a better sensorial video-audio immersion (See Table 1). Her cognitive and neurophysiological profile were evaluated in two separate sessions, before and after each of the two different trainings, by using a proper psychometric battery: Mini Mental State Examination (MMSE), Repeatable Battery for Neuropsychological Status (RBANS), Hamilton Rating Scale for Depression (HRS-D), and Behavioral Inattention Test (BIT) to assess visual neglect. The allocation of attention in the patient was obtained by studying the P300 component of the event-related potential (Sawaki & Katayama, 2008). Furthermore, the patient's control of trunk was evaluated by using the Trunk Control Test to better assess the motor recovery.

BTS NIRVANA is the first therapeutic system aiding the rehabilitation process of the patients affected by neuro-motor and cognitive diseases by multisensory stimulation. BTS NIRVANA is particularly recommended in the rehabilitation therapy of patients with movement and attentive dysfunctions caused by stroke. Standard BTS NIRVANA equipment is composed by 1 or 2 markerless infrared sensors, workstation touch screen, camera supports (different models available), BTS NIRVANA software, and Webcam. The system is connected to a projector or a big screen; it reproduces an interactive series of exercises and, thanks to an infrared video camera analyzing the patient's movements, it creates interactivity. BTS NIRVANA is a movement-based system providing patients VR scenarios to interact with: that is, audio-video stimuli (musical sphere) presented in the left, in the right, or in both the sides of interactive virtual scenarios; or specific nature environment, where the patient can change different visuo-spatial elements (see Figure 2).

Results

Our findings showed an improvement in motor (Control of Trunk) and cognitive performances after the VR rehabilitative training. In particular, after S-IVT treatment (comparison T0-T3), in addition to the standard cognitive approach, a nearly complete resolution of the USN was observed, with a significant increase in the attention, visual search, scanning, and spatial cognition scores (Table 2), as shown by the significant reliable change index (RCI) values. RCI is a statistic tool that is used to determine whether a change

Table 1. Virtual cognitive rehabilitative program with BTS-Nirvana system.

Cognitive domain	Nirvana BTS		Nirvana BTS	
	Semi-immersive virtual training with shadow S-IVT_s		Semi-immersive virtual training without shadow S-IVT	
spatial cognition and ideo-motor praxis	To program some movements finalized to virtual touch, to move or manipulate specific objects, in different directions (i.e., balls; flowers; butterfly); or to realize specific associations (i.e., number-color) with a dynamic interaction in virtual environment. When the patient touches virtual objects determinate a video and audio feedback (using sprites task, observing her shadow reflected on the virtual scenarios). These rehabilitation exercises with audiovisual stimuli involve the visuo-spatial and praxis abilities of patients, resulting in a very motivational training.		To program some movements finalized to virtual touch, to move or manipulate specific objects, in different directions (i.e., balls; flowers; butterfly); or to realize specific associations (i.e., number-color) with a dynamic interaction in virtual environment. When the patient touch virtual objects determinate a video and audio feedback (using sprites task, interacting directly with some virtual scenarios, without to observe her shadow). These rehabilitation exercises with audiovisual stimuli involve the visuo-spatial and praxis abilities of patients, resulting in a very motivational training.	
Attention process	In particular, the subject perform ideo-motor sequences (from simple to complex serious of actions), after the verbal consign by therapist. The patient observes her shadow during the execution of virtual tasks.		In particular, the subject perform ideo-motor sequences (from simple to complex serious of actions), after the verbal consign by therapist. The patient is immerse in virtual environment, without seeing her shadow, during the execution of virtual tasks.	
	<i>The level of difficulty increases (from first to third level) with the increase of the complexity of virtual ideo-motor serious to realize.</i>		<i>The level of difficulty increases (from first to third level) with the increase of the complexity of virtual ideo-motor serious to realize.</i>	
	To select, with an immediate and recall feedback (audio and video), some various elements (colors; musical strings; geometric or not form; animals ...) observed in the virtual environment. These elements remain visible to the observer for a variable time, established by the interaction between 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 disappear (negative reinforce) (<i>Hunt task</i>). The patients observes her shadow during the execution of virtual tasks.		To select, with an immediate and recall feedback (audio and video), some various elements (colors; musical strings; geometric or not form; animals ...) observed in the virtual environment. These elements remain visible to observer for a variable time, established by the interaction between the virtual system, therapist and patient. The patient touch the virtual target element, in a specific time, and so, this action cause a visual change with a peculiar audio feedback (positive reinforce); otherwise the element disappear (negative reinforce) (<i>Hunt task</i>). The patient interacts directly with these virtual scenarios, without to observe her shadow. The patients is immersive in virtual environment, without her shadow, during the execution of virtual tasks.	
	<i>The level of difficulty increases with the increase of the numbers of distracters and reducing the usable time of execution.</i>		<i>The level of difficulty increases with the increase of the numbers of distracters and reducing the usable time of execution.</i>	

in an individual's score (e.g., before and after some intervention) is statistically significant or not (based on how reliable the measure is). If the RCI is >1.96 , then the difference is statistically significant (1.96 equates to the 95% confidence interval). The patient also showed an improvement in mood alteration (Table 2). P300 amplitude in the 300–800 ms time window at the Pz electrode was lower for frequent (nontargets) than for infrequent (target) stimuli when stimulating the left hemifield (Figure 1), as confirmed by RCI values

(with α of 0.05, Bonferroni corrected) (nontarget vs. left target, RCI = 1.2; nontarget vs. right target RCI = 3.1; left target vs. right target, RCI = 3.3). Peak times did not show clear effects. Following the first training (S-IVT_s), a mild improvement in P300 amplitude was observed when stimulating the left hemifield (RCI = 2.8), whereas a greater improvement was found after the S-IVT training (RCI = 3.52).

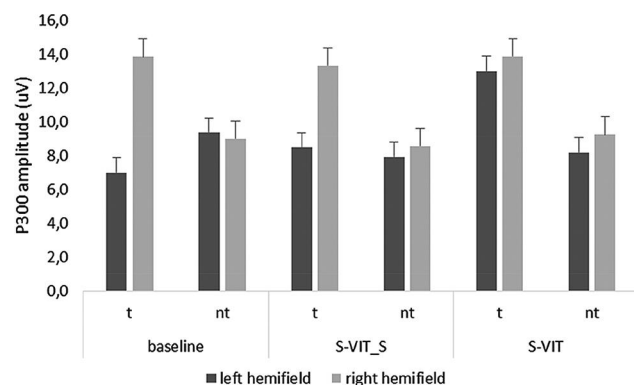


Figure 1. Illustrates the P300 amplitudes to target (t) and nontarget (nt) stimuli provided to the left and right hemifield at baseline and after Semi-immersive Virtual Training with (S-IVT_S) and without shadow (S-IVT). Vertical bars refer to SD.

Discussion

USN is a complex disorder of spatial representation, spatio-motor programming, and spatial attention. The rehabilitative approach could be difficult and, to date, there is not a gold standard method for the rehabilitation of neglect (Pierce & Buxbaum, 2002). It is strictly recommended to use a combination of multiple approaches to develop a personalized rehabilitation process (Kerkhoff & Schenk, 2012), given that a combination of different treatments seem to be more effective than a traditional cognitive rehabilitation program (Arai, Ohi, Sasaki, Nobuto, & Tanaka, 1997). Paper-and-pencil methods are used in traditional rehabilitative training. A typical session consists in repetitive exercises with static, two-dimensional, and geometrical targets that generally require a simple visual



Figure 2. Semi-immersive virtual training with (2a) and without (2b) shadow (S-IVT_s) in BTS NIRVANA system.

search in the near space, repeated several times a week (Newport & Schenk, 2012). Contrarily, for USN rehabilitation, the use of moving stimuli seem to be crucial to modulate visual attention and drive attention to the left side of the space, thereby improving target detection in a specific area (Cipresso, Serino, Pedrol, Gaggioli, & Riva, 2014; Kerkhoff, 2003).

VR for USN rehabilitation provides an advanced human-computer interface that allows the patients to interact with, and become immersed in, a computer-generated environment similar to the real-life experience (Tsirlin, Dupierrix, Chokron, Coquillart, & Ohlmann, 2009). VR rehabilitation of USN seem to be more engaging and consequently more effective than traditional methods. Using advanced technology, patients are trained through simulations that are relevant for everyday life. BTS NIRVANA is a VR platform that uses immersive reality and multisensory stimulation to improve cognitive performances. It uses a movement-based system providing patients virtual reality scenarios to interact with. This study describes the use of a combined rehabilitative program based on a traditional approach and VR, in order to better improve the neurocognitive functioning, with regard to USN. Few studies explored the benefits of VR and computer training in treating neglect. In a single blinded RCT by Kim, Chun, Yun, Song, and Young (2011), VR training led to significantly fewer errors on a cancellation test, with notable improvement also in daily life. Similarly, in a single case study, Mainetti, Sedda, Ronchetti, Bottini, and Borghese (2013) found significant improvement in two neglect tests when the patient played a video game consisting of reaching for different targets within the virtual space. Fordell et al. (2016) developed a new training method, RehAtt, consisting of a computer with monitor, 3D glasses, and a force feedback interface (Robotic pen), to stimulate the motor activation to the contralesional arm. This

software, by combining visual scanning training with multi-sensory stimulation in a 3D VR environment, led to a significant improvement in chronic USN (Saevarsson et al., 2012).

This study is in agreement with such previous studies supporting the hypothesis that VR might be useful in treating USN

In this study, we used event-related potentials (ERPs) to more objectively explore brain function in patients with poststroke neglect. The P300 is a positive ERP component that is most commonly recorded in an oddball stimulus paradigm, where a series of trials with frequent stimuli is interspersed trials with rare stimuli of a

Table 2. Unilateral spatial neglect improvement after neurorehabilitation in the virtual environment.

Conventional subtest	T0		T1		T2		T3	
	S-IVT_s	S-IVT_s	RCI	S-IVT	RCI	S-IVT	RCI	
Line crossing	25	29	5,3	29	5,3	32	7	
Letter cancellation	6	17	2,9	17	2,9	29	4,2	
Star cancellation	14	17		17		25	2	
Figure and shape copying	0	0		0		1		
Line bisection	0	0		0		6		
Representational drawing	1	1		1		1		
Behavioral subtest	T0	T1		T2		T3		
Prescanning	0	0		2	3,8	5	5,9	
Phone dialing	4	6		6		8		
Menu reading	0	0		1		6		
Article reading	0	0		1		5		
Telling and setting the time	7	7		7		9		
Coin sorting	2	3		3		5		
Address and sentence copying	0	2		2		4		
Map navigation	0	1		1		6		
Card sorting	1	2		2		6		
MMSE	13	15		15		20		
HRS-D	20	18		16		9		
TCT	37	62		62		74		

Note. MMSE = mini mental state examination; HRS-D = Hamilton rating scale for depression; BIT = behavioral inattention test; TCT = Trunk control test.

RCI is >1.96 is significant.

different type (Saevarsson et al., 2012; Sutton, Braren, Zubin, & John, 1965). The P300 is known to be modulated by attention in stroke patients with USN (Becker & Shapiro, 1980), and its assessment further corroborates our clinical findings. Indeed, S-VIT recovered the reduced amplitude of the P300 to contralesional targets, (that refer to the ipsilesional targets), while P300 amplitude increase correlated with the improvement in cognitive function scores and time in the standard neglect tests. These results suggest a link between a recovery of attentional dysfunction and the improvement in stimulus processing, which was strengthened by using S-VIT.

Conclusion

Virtual Reality technologies offer impressive opportunities for both the rehabilitation and assessment of different cognitive deficits, including USN. In particular, the combined rehabilitative treatment of SCT with S-IVT by using the BTS-NIRVANA System may be a promising approach in improving attention process and spatial cognition, which was as also demonstrated by the neurophysiological data. However, future studies are needed to examine the persisting effects of such treatment.

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