An integrative virtual reality cognitive-motor intervention approach in stroke rehabilitation: a pilot study

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ABSTRACT

Stroke is one of the most common causes of acquired disability, leaving numerous adults with cognitive and motor impairments, and affecting patient's capability to live independently. In post-stroke it is imperative to initiate a process of intensive rehabilitation and personalized objectives to maximize functional cognitive and motor recovery. Virtual Reality (VR) technology is being widely applied to rehabilitation of stroke, however, not in an integrative manner. Like traditional rehabilitation, these new tools mostly focus either in the cognitive or in the motor domain, which can take to a reduced impact in the performance of activities of daily living, most of them dual-task. Assuming the existence of cognitive and motor recovery interdependence, RehabNet proposes a holistic approach. Here we present a one-month long pilot study with three stroke patients whose training was a game-like VR version of the Toulouse-Piéron cancellation test, adapted to be performed by repetitive arm reaching movements. A standardized motor and cognitive assessment was performed pre and post intervention. The first results on this intervention support a holistic model for rehabilitation of stroke patients, sustaining interdependence on cognitive and motor recovery. Furthermore, we observed that the impact of the integrative VR approach generalizes to the performance of the activities of daily living.

1. INTRODUCTION

Stroke is the second largest cause of death worldwide and remains one of the leading causes of acquired disability in adults (WHO, 2014). The impairments to neuromuscular performance such as fine and gross motor control, muscle strength, and power are the consequences of stroke that have the greatest impact on functional capacity (Odier and Michel, 2009). However, stroke derived cognitive deficits also affect a person's capability to carry out activities of everyday living and their ability to live independently (Langhorne, Bernhardt, and Kwakkel, 2011). Cognitive impairments following stroke are common, and are present in approximately 70% of patients in the acute stages of recovery (Morris, Hacker, and Lincoln, 2012). The nature and severity of cognitive deficits varies according to several factors, such as location and extension of the lesion, type of stroke, comorbidities, complications, and may include problems with memory, perception, language, attention and executive functioning (Nudo, 2007). There is not a consistent profile of cognitive deficits after stroke, though slower information processing and executive dysfunction tend to predominate (Cumming, Marshall, and Lazar, 2013).

Rehabilitation programs based on intensive and customized treatment are important for improved functional recovery (Ganguly, Byl, and Abrams, 2013). Particularly, the persistent repetition of specific learning situations, which is standard practice in stroke rehabilitation, has been shown to lead to the re-organization of damaged cortical networks (Saleh et al, 2011). However, traditional stroke rehabilitation has some limitations, such as being labour and resource-intensive, at times demotivating and often resulting in modest and delayed effects in patients (Langhorne, Coupar, and Pollock, 2009). The limitations of traditional methods have inspired the development of Virtual Reality (VR) tools to increase treatment adherence and promote neuroplasticity by enhancing the effectiveness of traditional treatments. VR technology provides one of the most advanced interactions between humans and computers and, in the last decade, interest in its application to rehabilitation has increased substantially (Laver, George, Thomas, Deutsch, and Crotty, 2012). In particular, training cognitive and motor domains by means of gaming approaches is gaining increased clinical acceptance in the therapy of patients post-stroke or traumatic brain injury because of the ability of these tools to motivate patients, as well as to promote sustained movement practice (Albert and Kesselring, 2012).

Rehabilitation after stroke can be compromised because of cognitive-motor interference (Plummer et al, 2013). That is, in the cognitive domain, motor impairments can make hard or impossible the completion of cognitive exercises and in the motor domain patients might have difficulties in understanding instructions due to cognitive impairments. Hence, simultaneous (dual-task) performance of a cognitive and a motor task can result in deterioration of performance relative to performance of each task separately (Plummer et al, 2013). Moreover, activities of daily living are rarely exclusively motor or cognitive but a combination of both. So, a diminished capacity for dual-task performance may significantly impede functional independence and community participation.

Despite of the reported interdependency between cognitive and motor domains (Kizony, Levin, Hughey, Perez, and Fung, 2010), current methods for their rehabilitation are generally done separately and by different health professionals, and sometimes even in different clinical departments. The same trend has been observed in VR rehabilitation, with most of the approaches focusing either on motor [*Video Game–Based Exercises for Balance Rehabilitation* (Betker, Szturm, Moussavi, and Nett, 2006); *Rehabilitation Gaming System* (Cameirão, Bermúdez i Badia, Duarte, and Verschure, 2011); SeeMe System (Sugarman, Weisel-Eichler, Burstin, and Brown, 2011); IREX System (Kim, Chun, Yun, Song, and Young, 2011)] or cognitive [*LabPsicom* (Gamito et al, 2012); *Virtual Action Planning - Supermarket* (Josman et al, 2014); *The Virtual Street Crossing System* (Navarro, Lloréns, Noé, Ferri, and Alcañiz, 2013)] rehabilitation, disregarding issues like dual-tasking, a key factor for the ecological validity of the task.

We argue that novel VR approaches should focus on integrative cognitive and motor therapy based on games that pose both cognitive and motor demands. Assuming the interdependency between the recovery process of cognitive and motor domains, we may provide a more ecologically valid rehabilitation tool. As a consequence, we may have a greater impact in the recovery of independence, with the consequent impact in the performance of the activities of daily living. Here we present the results of a pilot study with three stroke patients who went through one-month intervention with a cognitive-motor training system operationalized in VR, the RehabNet. RehabNet aims at building a neuroscience based interactive toolset for stroke rehabilitation (Vourvopoulos, Faria, Cameirao, and Bermudez i Badia, 2013), merging together the cognitive and the motor training, in a holistic approach. RehabNet enables users with disabilities to interact with virtual environments in a way that they would not be able to do in the real world. Through different interaction interfaces, it enables motor impaired patients to generate meaningful goal oriented motor actions to recruit the neural networks responsible for action recognition, the mirror neurons (Rizzolatti, Fabbri-Destro, and Cattaneo, 2009). RehabNet combines VR with a gaming approach to allow patients to be active agents in the rehabilitation process by providing a totally controlled environment and an intensive training targeted to their deficits.

2. METHODS

2.1 Participants

Participants were recruited at the Physical Medicine and Rehabilitation Department of Nélio Mendonça Hospital (Funchal, Portugal) based on the following inclusion criteria: chronic stroke; first event ischemic stroke; no hemi-spatial neglect; non-aphasic and with sufficient cognitive ability to understand the training task instructions, Mini-Mental State Examination (MMSE) ≥ 15 (Folstein, Folstein, and McHugh, 1975) Portuguese version (Guerreiro et al, 1994); and ≥ 2 years of schooling. The sample consisted of three stroke patients with both cognitive and motor deficits (Table 1). The study was approved by the Madeira Health Service Ethical Committee and all the patients gave previous informed consent.

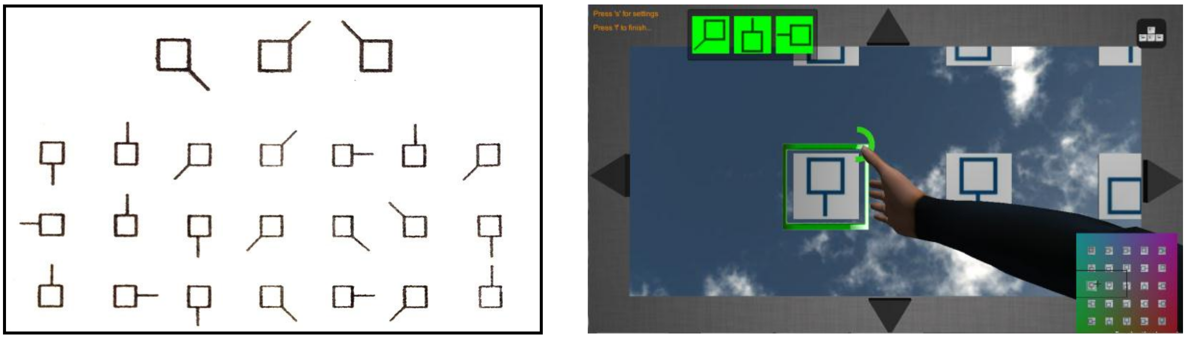
2.2 Cognitive-Motor Virtual Reality Task

Traditionally, motor rehabilitation of the upper-limbs focuses on strength, power, motor control and tonicity through a combination of physical and occupational therapy. On the other hand, cognitive rehabilitation is made through paper-and-pencil tasks, usually a specific task for each cognitive aspect, e.g. cancellation tests for selective attention. The Toulouse-Piéron (TP) test (Piéron, 1955) (Figure 1a) is among the most widely used cancellation tests to assess and/or train attention but, it can be of difficult or even of impossible execution for hemi-paretic stroke patients because of the motor deficits. Simulating some of the exercises used in traditional therapy, our training task consists of a game-like VR version of the TP test, (Figure 1b) adapted to be performed by repetitive arm reaching movements on a table top surface, and implemented by using the representation of the paretic arm for navigating and targeting symbols arranged in two dimensions.

Table 1. *Participant's demographics.*

	Patient 1	Patient 2	Patient 3
Age	47	72	46
Gender	Male	Female	Female
Schooling	4 years	2 years	6 years
Time after stroke	10 months	6 months	5 months
Hemisphere	Left	Left	Left

The training scenario has a build-in calibration function that is able to compute the active range of motion of the patient, normalizing the motor effort required to the skill set of the patient (Vourvopoulos et al, 2013). Two natural user interfaces [Kinect® (Microsoft Corporation, Washington, USA) for 3D movement and a custom made color tracking software (AnTS; Mathews, Badia, and Verschure, 2007) for 2D arm movements] and two pointing devices (mouse for 2D and airmouse for 3D movements) were used as interfaces by all patients in a random order. The four interfaces had the same selection method of the targets, which was a timer (Figure 1b). The intervention protocol entailed, in addition to conventional rehabilitation, twelve training sessions of twenty minutes, three times a week.



(a) *(b)*

Figure 1. *Representation of the paper-and-pencil (a) and virtual (b) modalities of the Toulouse-Piéron test.*

2.3 Cognitive and Motor Assessment

Before starting the intervention, cognitive and motor functions were assessed to obtain baseline measures. The same assessments were made at the end of the intervention. To capture the full scope of impairment and functionality, a number of cognitive and motor standard scales were used. All of them are widely applied clinically and in research to determine disease severity, describe cognitive and motor recovery, and to plan and assess intervention.

The analysis of the pattern of cognitive impairment was made through the Addenbrooke Cognitive Examination - Revised (ACE-R) (Mioshi, Dawson, Mitchell, Arnold, and Hodges, 2006) Portuguese version (Simões, Pinho, Sousa, and Firmino, 2011), a scale that covers a wide range of cognitive impairments by providing normative data for five subscales (attention, memory, verbal fluency, language and visuo-spatial capability), and also includes the MMSE (Morris et al, 2012). The task-related capabilities were assessed extensively with additional specific measures, such as: the Trail Making Test A and B (TMTA / TMTB) (Reitan, 1958) Portuguese version (Cavaco et al, 2013) for selective and divided attention, mental flexibility and motor speed; and the Coding subtest from the Wechsler Adult Intelligence Scale III (Wechsler, 2008) for visual-motor coordination, motor and mental processing speed and visual working memory. A short version of the TP test

(Piéron, 1955) was included to compare the performance on paper-and-pencil and the performance on the virtual environment. Performance was assessed with the following formula: TP = correct – (omissions + errors) / symbols x 100. The tests were delivered in the presented order, this is, we started by the screening scale, followed by the specific measures and finally, the paper and pencil TP.

A physician performed functional assessment such as the Fugl-Meyer assessment, the Barthel Index, the Functional Independence Measure (FIM) and the Medical Research Council (MRC) strength evaluation scale. The Fugl-Meyer assessment is a well-established measure of function impairment after stroke in 5 domains (motor, sensory, balance, joint amplitude and pain) of both upper and lower-limb, and can be adapted to evaluate the upper-limb (Gladstone, Danells, and Black, 2002). The Barthel Index and the FIM are commonly used scales to measure disability in activities of daily living (D'Olhaberriague, Litvan, Mitsias, and Mansbach, 1996), (Grimby et al, 1996). The MRC scale, which is widely used for Manual Muscle Testing (Paternostro-Sluga et al, 2008) was used for assessment of upper-limb muscle groups.

To assess patients' subjective opinions with respect to a number of aspects of the intervention with RehabNet, a 5-point Likert scale self-report questionnaire (Cameirão, 2010) was used at the end of the intervention.

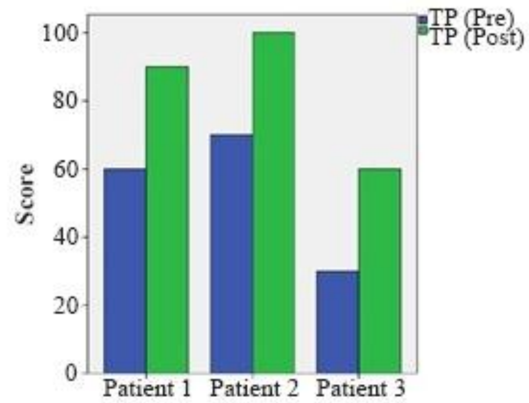
2.4 Data Analysis

The baseline measures of the cognitive and motor scales were quantitatively compared with the post-intervention results in all these clinical measures. Overall, the data analysis was qualitative because of the sample size.

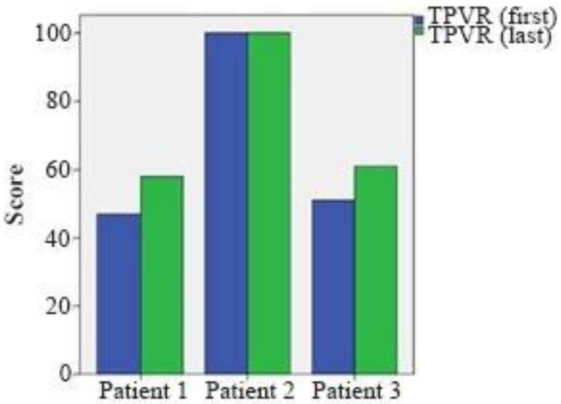
3. RESULTS

3.1 Can a paper and pencil assessment/training task be transferred to the virtual environment and have the same impact? Is training equivalent?

In order to overcome the motor limitations and allow the cognitive assessment and/or training, we had the TP test operationalized in virtual reality in the RehabNet system. All patients were exposed to all the interfaces in a random order. At the end of the one-month intervention, we observed improvements, from pre-intervention to post-intervention, in all patients when evaluated with the paper-and-pencil version of the TP test. Patient 1, 2 and 3 increased from 60% to 90%, 70% to 100%, and 30% to 60%, respectively (Figure 2a). These outcomes, together with the performance progress of patient 1 and 3 in the virtual task (patient 2 had already reached the maximum score in the first session and therefore can not improve any further) (Figure 2b), suggest that despite the necessary VR adaptations to embrace a motor-cognitive integrative training, there is a transfer between the gains in VR and the ones assessed by the paper-and-pencil. The improvements were higher in the paper-and-pencil task probably because in the VR task the motor deficits were mitigated by means of the interfaces and their calibration.



(a)



(b)

Figure 2. *Pre and post-intervention performance in the paper-and-pencil reduced version of TP test (a) and the first and last session performance in the VR version of the TP test (b).*

3.2 *Does training with the RehabNet cancellation task improve cognitive domains related and non-related to the task?*

In the cognitive domain, participants improved or reached the maximum score in memory and visuo-spatial ability, as assessed by the ACE-R, both domains targeted by RehabNet training task (Table 2). So, we can say there was a specific transfer of what participants have been training in VR to general improvements as assessed after the intervention by the cognitive assessment tools.

Table 2. *Cognitive assessment pre and post-intervention. Improvements are highlighted in bold.*

		Patient 1		***Patient 2***		***Patient 3***	
		Pre	*Post*	*Pre*	*Post*	*Pre*	*Post*
ACE-R	*Total*	**78**	74	93	**97**	57	**63**
	Attention	**18[1]**	15	18[1]	18[1]	16	**17**
	Memory	18	**19**	25	25	**11**	10
	Verbal Fluency	**7**	5	11	**12**	**6**	4
	Language	**25**	24	23	**26[1]**	13	**20**
	Visuo-Spatial	10	**11**	16[1]	16[1]	11	**12**
TMTA	*Time*	80	**76**	---	**66**	275	**137**
	Errors	0	0	---	**0**	4	**0**
TMTB	*Time*	257	**190**	---	**115**	---	**450**
	Errors	0	0	---	**1**	---	**3**
Coding (WMS)	*Coding*	12	**13**	---	---	**3**	**11**
	Learning	0	**6**	---	---	**0**	0
	Free Recall	2	**4**	---	---	**0**	**3**

1 Maximum score of the assessment instrument.

Participant 3 improved in attention/concentration, participant 2 had already reached the highest score in the pre-intervention assessment and participant 1 got a lower score. This last participant also did worse in language, whereas the other two participants improved in this domain that was not directly addressed by the RehabNet training.

At the pre-intervention assessment, participants 2 and 3 could not perform some of the cognitive scales because for the execution of these tasks they were required fine motor skills. Examples of these tasks are the TMTA and TMTB and the Coding from the WMS-III. In the TMT, which measures attention, mental flexibility and motor speed, participant 2 was not able to do it in the pre-intervention but did it in the post, needing a short time and making just one error. Participant 3 was not able to perform the TMTB in pre-assessment but did it in the post. The patient needed a short time and made 3 errors. Participant 1 performed very well in both assessments with this task, making better in the processing speed from the pre to the post-intervention. Participants 1 and 3 improved in the Coding task, which assesses visual-motor coordination and processing speed. Participant 2 was not able to perform the task in neither pre nor post-assessment. Participant 1 improved in the Incidental Learning and Free Recall tasks, which assesses visual working memory. Overall, these results suggest that our intervention improved some of the cognitive domains targeted by the system, and that for patients 2 and 3, we can say that there was a generalization of the rehabilitation process to cognitive domains non-related to the task.

In the motor domain, we can see general improvements for patients 2 and 3 (Table 3). Patient 2 and 3 had improved scores as assessed by the Fugl-Meyer scale in the upper-limbs and passive movement amplitude while patient 1 had a small recess. All patients improved or maintained in the Sensibility and in the Pain scores. In terms of arm strength, patient 1 improved it in the wrist flexion and extension, maintained in the shoulder flexion, extension and adduction with a small recess in the shoulder abduction, and also maintained in the elbow flexion and extension. Patient 2 was limited by pain in the pre and post-assessment of the shoulder, nonetheless, improved in the elbow and wrist both flexion and extension. Patient 3 was limited by pain in the pre-assessment of the shoulder, reaching the maximum score in the post-assessment. This patient maintained the maximum score for the elbow and wrist, flexion and extension, in both assessment moments. More importantly, all patients improved or maintained the score in the Barthel Index, meaning that this intervention had an impact in the performance of the activities of daily living in 2 of the 3 participants. Overall, these results suggest that our integrative intervention (Table 2 and 3) improved cognitive function – for some patients beyond the specifically trained domains – and also fine motor skills, which made possible the accomplishment of paper-and-pencil tasks that wasn't possible before.

Table 3. *Motor and Activities of Daily Living assessment pre and post-intervention. Improvements are highlighted in bold.*

		Patient 1		*Patient 2*		*Patient 3*	
		Pre	*Post*	*Pre*	*Post*	*Pre*	*Post*
Fugl-Meyer	*Upper-Limbs*	**50**	47	24	**38**	48	**59**
	Sensibility	8	**10**	7	**11**	12	12
	Passive Movement	**24**	23	20	**21**	23	**24**
	Pain	24	24	16	**18**	22	**24**
ADL's	*Barthel*	80	80	85	**95**	80	**95**
	FIM	114	113	113	**117**	115	**123**
MRC	*Shoulder flexion*	4	4	limited by pain	limited by pain	limited by pain	**5[1]**
	Shoulder extension	5[1]	5[1]	limited by pain	limited by pain	limited by pain	**5[1]**
	Shoulder abduction	5[1]	4	limited by pain	limited by pain	limited by pain	**5[1]**
	Shoulder adduction	5[1]	5[1]	limited by pain	limited by pain	limited by pain	**5[1]**
	Elbow flexion	5[1]	5[1]	3	**5**[1]	5[1]	5[1]
	Elbow extension	5[1]	5[1]	2	**5**[1]	5[1]	5[1]
	Wrist flexion	2	**3**	2	**3**	5[1]	5[1]
	Wrist extension	4	**5[1]**	4	**5**[1]	5[1]	5[1]

1 Maximum score of the assessment instrument.

3.3 Validity of the holistic cognitive-motor RehabNet approach

As already discussed, one of the main features of RehabNet system is the integration of the cognitive and motor training. All patients improved on specifically trained aspects of the task. Moreover, the two participants who improved in the overall ACE-R also had higher scores in the Fugl-Meyer (upper-limb) motor scores. Our data shows that the only patient that did not improve in the overall ACE-R did not improve either in the Fugl-Meyer. Our data shows congruent data in both motor and cognitive domains for all patients (Figure 3), being consistent with the premise of interdependency of recovery. Furthermore, it is common for patients to improve their scores on paper-and-pencil tests through practice, without showing an associated improvement in real life situations (Navarro et al, 2013). In our study, the improvements verified in the cognitive and motor scales also correlate with the improvement results in the Barthel Index, that is, in the performance of activities of daily living. Thus, our data is consistent with the idea that training both domains at the same time might have a boosting effect in the general rehabilitation process.

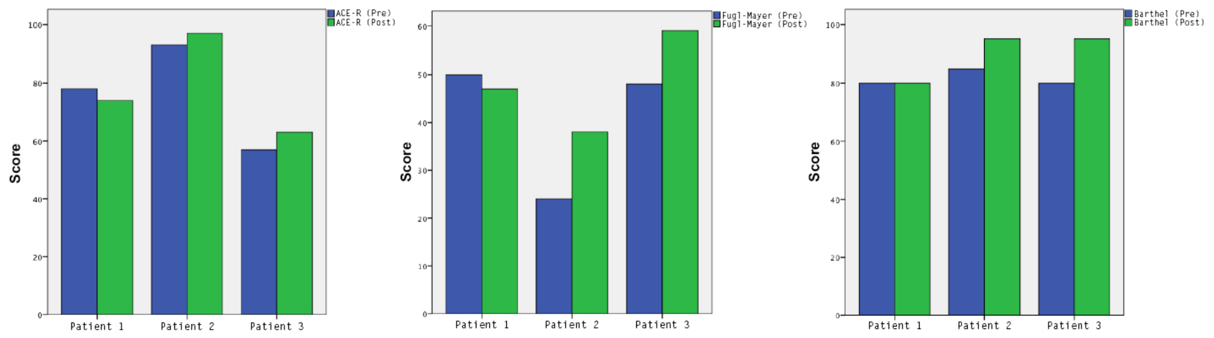


Figure 3. *ACE-R, Fugl-Meyer (upper-limbs) and Barthel Index results showing the interdependency between the cognitive, motor and functionality variables.*

4. DISCUSSION AND CONCLUSIONS

Here we presented a VR motor-cognitive dual training task and the results of a one-month intervention with 3 patients. In the cognitive domain, we find improvements in domains trained by the VR task, and the generalization of the improvements to other domains in 2 of the 3 patients. However, in the cognitive domain, these improvements were small (4 and 6 points) probably due to the low frequency and intensity of the training (12 sessions of 20 minutes). The improvements in the TP paper-and-pencil task are greater than those in the cognitive domain of the TPVR task, suggesting that cognitive and motor domain improvements are related. However this training rendered much greater improvements in the motor domain than in the cognitive domain. The results of this pilot are consistent with our hypothesis of a holistic model for rehabilitation of stroke patients. Further, we could observe in 2 patients that the integrative rehabilitation of both domains has an impact on the capacity of performance of activities of daily living.

We investigated further the case of patient 1, who even showed a recess in some assessment measures. While most patients are discharged from the rehabilitation programs six months after the stroke, at the moment of this paper, this patient is already at the Physical Medicine and Rehabilitation Department for fifteen months due to the poor impact of therapy. We found that patient 1 has a history of drug abuse, what might be one of the factors contributing for the unusual evolution.

Despite the limitations of the sample size and amount of training, the results of this study show improvements and emphasize the value of rehabilitation approaches that merge cognitive and motor domains in single tasks. In the future, we aim to increase the sample size to perform a more quantitative assessment of the impact of the RehabNet, and to implement more cognitive tasks targeting different cognitive functions, and assessing their impact in recovery following stroke by means of longitudinal clinical trials.

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