

Virtual Reality with Customized Positive Stimuli in a Cognitive-Motor Rehabilitation Task

A feasibility study with subacute stroke patients with mild cognitive impairment

Mónica S. Cameirão^{1,2,*}, Fábio Pereira², Sergi Bermúdez i Badia^{1,2}

¹Faculdade de Ciências Exatas e da Engenharia, Universidade da Madeira

²Madeira Interactive Technologies Institute
Funchal, Portugal

*monica.cameirao@m-iti.org

Abstract—Virtual Reality applications for integrated cognitive and motor stroke rehabilitation show promise for providing more comprehensive rehabilitation programs. However, we are still missing evidence on its impact in comparison with standard rehabilitation, particularly in patients with cognitive impairment. Additionally, little is known on how specific stimuli in the virtual environment affect task performance and its consequence on recovery. Here we investigate the impact in stroke recovery of a virtual cognitive-motor task customized with positive stimuli, in comparison to standard rehabilitation. The positive stimuli were images based on individual preferences, and self-selected music (half of the sessions). 13 participants in the subacute stage of stroke, with cognitive and motor deficits, were allocated to one of two groups (VR, Control). Motor and cognitive outcomes were assessed at end of treatment (4-6 weeks) and at a 4-week follow-up. Both groups showed significant improvements over time in functional ability during task performance, but without changes in motor impairment. Cognitive outcomes were modest in both groups. For participants in the VR group, the score in the task was significantly higher in sessions with music. There were no statistical differences between groups at end of treatment and follow-up. The impact of VR therapy was lower than in similar studies with stroke patients without cognitive deficits. This study is a first step towards understanding how VR could be shaped to address the particular needs of this population.

Keywords—virtual reality; stroke rehabilitation; cognitive-motor; positive stimuli; music

I. INTRODUCTION

During the last few years there has been increasing interest in using Virtual Reality (VR) stroke rehabilitation paradigms that combine motor and cognitive training instead of addressing these domains separately [1], [2]. The main reasoning relies on the increasing evidence of the existence of an interaction between cognitive and motor deficits and recovery [3]–[5]. Studies have shown differential patterns of motor outcomes in stroke survivors depending on their cognitive deficits [6], [7]. In addition, a comprehensive rehabilitation program that combines both motor and cognitive demands could be more effective [8], [9]. We hypothesize that this combined approach may be particularly beneficial in patients with cognitive impairment after stroke. Clinical studies with VR for simultaneous motor and cognitive rehabilitation have shown the potential of such

approaches, but the evidence is still modest [1], [2], [10], [11]. Hence, further investigation is needed on this topic.

VR scenarios for stroke rehabilitation have mainly focused on training specific movements, cognitive tasks, or Activities of Daily Living (ADL), with specific tasks developed for that purpose. Surprisingly, little work has been done on investigating the impact of the type of content that is being used in the VR scenarios. For example, color of specific stimuli can influence performance in a virtual environment in users with Attention Deficit Hyperactivity Disorder (ADHD), but also in healthy participants [12]. There is also evidence that affective valence (pleasantness of a given stimulus) of elements in tasks influences performance. In a visual search task, patients with neglect took significantly more time to find targets on the left hand side when initially exposed to negative images in comparison to positive images [13]. Valence has also an effect in memory, with positive and negative content being more easily remembered [14]. In a recent study, chronic stroke survivors that performed a cancellation task with images of specific valence (neutral, positive, and negative) showed decreased attention, reduced visual search and more false memories when negative images were presented as targets [15]. These results suggest that the impact on stroke recovery of cognitive rehabilitation paradigms based on positive stimuli for the training of attention is worth exploring.

Besides visual elements, there is also the potential effect of sound and music. A study by Särkämö *et al.* showed that self-selected daily music listening in addition to standard stroke rehabilitation lead to improved verbal memory, focused attention, and mood [16]. Music and sonification based interventions have also shown benefits in the motor domain in acquired brain injury [17], [18]. In fact, a recent fMRI study with stroke patients undergoing music supported therapy showed enhanced activation in auditory and motor areas, which was accompanied by improvements in the paretic upper extremity [19].

Here we present the results of a pilot study where we explore the feasibility of a VR cognitive-motor task that uses personalized positive stimuli for rehabilitation in a sample of subacute stroke survivors with Mild Cognitive Impairment (MCI). In VR studies, the effect of motor rehabilitation in patients with MCI is an understudied area [20]. Our paradigm

uses a cancellation task for the training of attention, memory, and reaching movements of the upper limb. The task consists of finding and reaching for positive target images in a pool of neutral distractors. In some trials, the targets need to be memorized first. The target images have been personalized based on the individual preferences of each participant. In addition, we have included music selected by the user in alternating sessions. We compare the impact of such approach to time matched standard rehabilitation activities. Our first hypothesis is that the proposed rehabilitation paradigm will result in improved motor and cognitive outcomes when compared to patients in the standard rehabilitation condition. As a second hypothesis, we predict that performance in the VR task will be superior in the sessions with music when compared to sessions without.

II. METHODS

A. Experimental Setup and VR Task

The setup consists of a PC (OS: Windows 7, CPU: Intel core 2 duo E8235 at 2.80GHz, RAM: 4Gb, Graphics: ATI mobility Radeon HD 2600 XT), a PlayStation Eye camera (Sony Computer Entertainment Inc., Tokyo, Japan) and a customized handle with a tracking pattern. The user works on a tabletop, facing a LCD monitor (24") (Fig. 1). In sessions with music, headphones are used. The user moves the handle with his/her paretic arm on the surface of the table, and 2D upper limb reaching movements are captured through a camera-based Augmented Reality (AR) pattern tracking software (AnTS) [21] (<http://neurorehabilitation.m-iti.org/tools/ants>).

The VR scenario has a built-in calibration function that considers the active range of motion of the user, and normalizes the motor effort required in the task to the skillset of the user. The user's arm movements are then mapped onto the movements of a virtual arm on the VR environment. The cognitive-motor virtual task is an adaptation of the Reh@Task, which is described in detail elsewhere [1]. Reh@Task is a VR adaptation of traditional cancellation tasks that has been modified to incorporate both the training of attention and memory, as well as upper limb reaching movements. The task consists of finding target elements within a pool of distractors. In the memory variant, the target(s) must be memorized first. The Reh@Task has incremental difficulty and is adjusted to the individual performance of each user. The progression of difficulty is made by manipulating the number of targets and distractors, the available time to solve the task, and, in the memory variant, the available time for memorization of the target image (see [1] for a detailed description of the difficulty adjustment algorithm). The adjustment of difficulty is done independently for attention and memory trials, which are presented to the user alternatively. An accumulative score is presented to the user throughout the training session. The score is computed based on correctness and timeliness of task completion.

For the purpose of this study, target and distractors were pictures of specific affective valence. The target pictures had positive valence and were personalized to the individual preferences of each individual user; the distractors had neutral valence. For customizing the task stimuli to each user,

participants were asked about things that they like (places, food, shows, animals, etc...). This information was used to create a database of an average of 161 pictures for each participant. To confirm the positivity of the selected images, 10 pictures were randomly selected from the database, and the participants were asked to rate their valence using a 9-points Self-Assessment Manikin (SAM) along the dimensions of affective valence (ranging from unpleasant to pleasant). If the mean valence score was of at least 6, the database was used as it was. Otherwise, a new database of pictures was created and the process was repeated. Neutral images were selected from the International Affective Picture System (IAPS) [22] and had valence between 4.5 and 5.5. To reduce repetition, the researchers extended the database of neutral pictures with visually similar images to increase the number of distractors to 800 images.

B. Participants

170 patients with a diagnostic of stroke were admitted to rehabilitation units of the Madeira Health System, SESARAM (Serviço de Saúde da Região Autónoma da Madeira), in Portugal between June of 2015 and December of 2016. Out of these, 18 stroke survivors were included and randomized for participation in this study as described in Fig. 2. The following were inclusion criteria: 1) ischemic or hemorrhagic stroke within the first 6 months post-stroke; 2) motor impairment of the upper extremity but with a minimum score of 28 in the Motricity Index (MI) [23] (elbow flexion and shoulder abduction domains combined score); 3) cognitive deficit but with enough capacity to understand the task and follow instructions with a minimum score of 11 over 17 in the Token Test [24]; and 4) able to read. Exclusion criteria included: 1) previous motor and/or cognitive deficits; 2) normal cognitive functioning with a score above 26

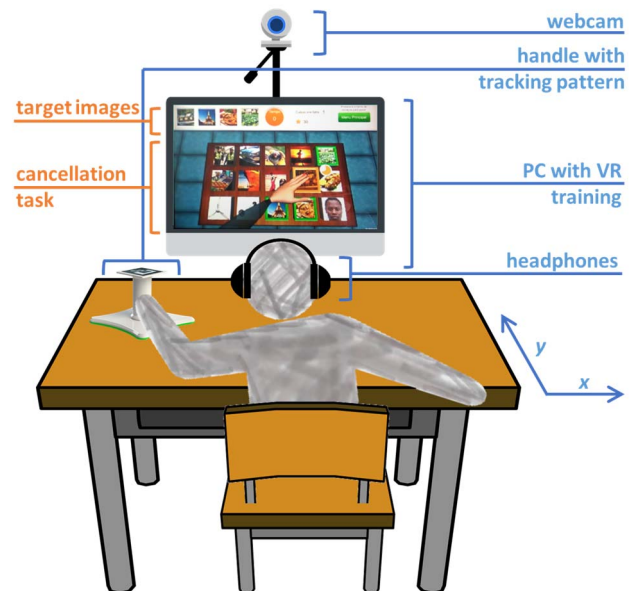


Fig. 1. Experimental setup. The user works on a tabletop and performs a VR based cancellation task with customized positive stimuli. The movements of the upper extremity are captured by AR pattern tracking and mapped onto the movements of a virtual arm on the screen. In sessions with music, the user wears headphones.

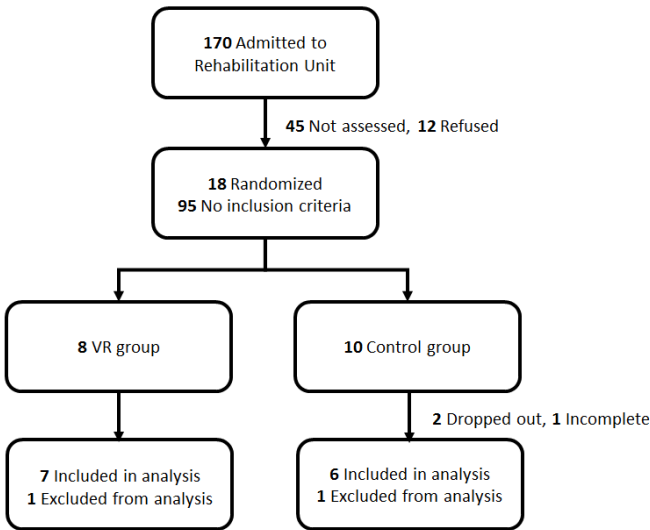


Fig. 2. Flowchart of the recruitment process, including attrition and exclusion from data analysis.

points in the Montreal Cognitive Assessment (MoCA) [25]; 3) unilateral spatial neglect; 4) moderate to severe depressive symptomatology with a score above 20 points in the Geriatric Depression Scale (GDS) [26]; and 5) vision disorders that could interfere with the execution of the task. After randomization, 2 participants dropped out, 1 did not complete the intervention within the required period, and 2 were not included in the analysis because image scans revealed that these participants had not suffered a stroke. 13 participants completed the protocol and were included in the analysis (TABLE 1). The study was approved by the ethics committee of SESARAM, and all participants signed an informed consent. This study is registered in ClinicalTrials.gov with number NCT02539914.

C. Experimental Protocol

This study followed a between-subjects design. The participants of the study were randomly assigned to one of two groups: VR or Control. For both groups, the intervention comprised 12 sessions of 45 minutes during 4-6 weeks, in addition to the standard rehabilitation program. The intervention of the VR group consisted of training with the individually customized Reh@Task, both with visual stimuli and music preferences. To assess differences of task performance with and without music, training sessions had or not music, alternatively. The tasks of the Control group included standard rehabilitation activities that train the same competences as those trained with Reh@Task. Examples of activities are color and image sequencing, association of pairs of images, memorization of image sequences, range of movement training on the surface of the table, just to refer a few. Participants underwent motor, cognitive and functional assessment through a number of standardized clinical scales, at baseline, end of treatment and 4-weeks follow-up. All participants continued with their standard rehabilitation program after the 12 training sessions, except for 3 participants (IDs: 1, 2, and 15).

D. Outcome Measures

Primary outcome measures in this study are change from baseline in: upper extremities part of the Fugl-Meyer Assessment Test (FM-UE) [27] for motor and joint functioning of the paretic upper extremity; Chedoke Arm and Hand Activity Inventory (CAHAI) [28] for functionality of the paretic upper extremity in task performance; and Montreal Cognitive Assessment (MoCA) for cognitive domains. Secondary outcome measures are change from baseline in: Barthel Index (BI) [29] for independence in activities of daily living; Motricity Index (MI) for muscle power of the paretic upper extremity; Modified Ashworth Scale (MAS) [30] for spasticity; and Bells Test (BT) [31] for visual scanning.

E. Data Analysis

Because of the small size, nonparametric statistical tests were used. Hence, central tendency and dispersion measures of the clinical outcome measures are presented as median and interquartile range (IQR), respectively. For improvements in clinical scores, we also show the mean and standard deviation (SD) for an easier comparison with the literature. Differences between groups in demographic and clinical data at baseline were assessed using a Mann-Whitney U test in interval and ordinal variables, and a Pearson's chi-square (χ^2) test in nominal variables. For within-group changes over time across the three evaluation moments (baseline, end of treatment, and follow-up), a Friedman test for related samples was used. The Wilcoxon's T matched pairs signed ranks (one-tailed because we predicted improvement over time in both groups) was used for further related pairwise comparisons with respect to baseline. No correction was applied to account for the number of pairwise comparisons as nonparametric tests are already considered conservative. To compare groups at the end of treatment and follow-up, for each group we computed the improvement with respect to baseline. We used a one-tailed Mann-Whitney U test to test the hypothesis that improvements in the VR group were superior against the control group.

To assess improvements in Range of Movement (ROM) over time in the VR group, the average improvements in x and y components of the movement (Fig. 1) of the last 3 sessions were compared against the average of the 3 first sessions with the one-tailed Wilcoxon's T matched pairs signed ranks test. To compare performance in the Reh@Task between sessions with or without music, the mean score in the task was computed for each participant in each condition. The Wilcoxon's T matched pairs signed ranks (one-tailed) was used to test the hypothesis that performance was significantly better in sessions with music. Effect sizes are reported on the pairwise comparisons.

For all statistical tests, a significance level of 5% ($\alpha=0.05$) was set. Data were analyzed using Matlab (MathWorks Inc., Natick, MA, USA) and IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp).

III. RESULTS

The results are presented in two sections, as to address the two research hypotheses. In the first section, we report on the comparison between the two groups in terms of primary and secondary outcomes. In the second section, we compare task

TABLE I. DEMOGRAPHIC INFORMATION OF PARTICIPANTS

Group	ID	Sex	Age	Schooling ^a	Days post-stroke	Type of stroke ^b	GDS	Lesion location
<i>VR</i>	1	F	57	4	139	I	20	Left temporal lobe
	6	M	57	4	51	I	18	Right middle cerebral artery
	7	M	59	4	32	H	5	Right internal capsule-lenticular nucleus
	12	F	67	3	38	H	16	Right striatocapsular area
	14	M	70	5	35	I	12	Right lateral lenticulostriate arteries
	15	M	83	4	35	I	17	Bilateral lenticular nucleus
	17	M	60	8	30	I	18	Paramedian thalamic region
<i>Control</i>	2	F	66	4	10	I	20	Middle cerebellar peduncles
	5	M	63	5	30	I	11	Left middle cerebral artery
	8	M	42	4	30	I	9	Left temporal lobe
	11	F	64	4	39	-	14	-
	16	F	86	7	117	I	10	Bilateral striatocapsular and thalamic region
	18	M	52	4	57	I	10	Left middle and anterior cerebral arteries
<i>VR</i>		5/2	64.7±9.5	4.6±1.6	51.4±39.2	5/2	15.1±5.1	
<i>Control</i>		3/3	62.2±14.8	4.7±1.2	47.1±37.4	5/0	12.3±4.1	

^a Number of years of education^b I = ischemic, H = hemorrhagic

performance in the Reh@Task in training sessions with or without music.

A. The impact in outcome measures

1) *Balance of groups at baseline*: 7 participants from the VR group and 6 from Control completed the protocol and were included in the analysis. On the demographic data at baseline (TABLE I), groups were balanced in sex ($\chi^2(1, 13)=0.63$, $p=0.43$, $\Phi=0.22$), age ($U=19.0$, $p=0.78$, $r=0.08$), years of schooling ($U=18.5$, $p=0.68$, $r=0.11$), days post-stroke ($U=18.0$, $p=0.67$, $r=0.12$), type of stroke ($\chi^2(1, 12)=1.71$, $p=0.19$, $\Phi=0.38$), and GDS ($U=12.5$, $p=0.22$, $r=0.34$). However, for sex and type of stroke, we have cells with expected frequencies less than five, what weakens the interpretation of the result. On the scores in clinical scales at baseline (TABLE II), the groups were balanced in all scores [FM-UE ($U=20.5$, $p=0.94$, $r=0.02$); CAHAI ($U=18.0$, $p=0.67$, $r=0.12$); MoCA ($U=19.0$, $p=0.77$, $r=0.08$); BI ($U=20.0$, $p=0.89$, $r=0.04$); MI ($U=16.5$, $p=0.52$, $r=0.18$); MAS ($U=20.0$, $p=0.88$, $r=0.04$)], except in the number of errors in the Bells test ($U=5.0$, $p=0.042$, $r=0.59$). The VR

group did significantly more errors in this test at baseline when compared to the control group.

2) *Within and between group analysis of outcome measures*: an analysis of the scores over time for each group, considering the 3 evaluation moments (baseline, end of treatment, and follow-up), showed a significant impact on the functional ability of the paretic arm and hand to perform tasks, and cognitive domain in both groups (TABLE II). Specifically, in CAHAI [VR: $Fr(2)=9.6$, $p=0.008$; Control: $Fr(2)=8.0$, $p=0.018$], and MoCA [VR: $Fr(2)=6.0$, $p=0.050$; Control: $Fr(2)=6.0$, $p=0.050$]. The specific impact on activities of daily living was more prominent in the VR group, who displayed a significant evolution over time in BI [VR: $Fr(2)=9.6$, $p=0.008$; Control: $Fr(2)=2.8$, $p>0.05$]. There was no significant impact across time for both groups in FM-UE [VR: $Fr(2)=3.9$, $p>0.05$; Control: $Fr(2)=3.7$, $p>0.05$], MI [VR: $Fr(2)=3.6$, $p>0.05$; Control: $Fr(2)=1.4$, $p>0.05$], MAS [VR: $Fr(2)=3.7$, $p>0.05$; Control: $Fr(2)=3.0$, $p>0.05$], and BT [VR: $Fr(2)=4.4$, $p>0.05$; Control: $Fr(2)=4.3$, $p>0.05$]. Further pairwise comparisons with

TABLE II. PRIMARY AND SECONDARY OUTCOME MEASURES AT BASELINE, END OF TREATMENT, AND FOLLOW-UP

Outcome Measure ^c	Virtual Reality (N=7)				Control (N=6)			
	Baseline	End	Follow-up	p^d	Baseline	End	Follow-up	p
Primary								
FM-UE (max = 66)	52.0 (36.0)	54.0 (34.0)	57.0 (30.0)	0.142	42.0 (27.0)	47.0 (19.0)	46.0 (19.0)	0.154
CAHAI (max = 91)	61.0 (51.0)	73.0 (69.0)^e	75.0 (63.0)^e	0.008	62.5 (44.0)	70.5 (38.0)^e	76.5 (26.0)^e	0.018
MoCA (max = 30)	20.0 (3.0)	20.0 (5.0)	21.0 (6.0)	0.050	21.0 (5.0)	23.0 (5.0)	23.0 (4.0)^e	0.050
Secondary								
BI (max = 100)	60.0 (15.0)	70.0 (30.0)	80.0 (10.0)^e	0.008	65.5 (69.0)	87.5 (35.0)	87.5 (39.0)	0.241
MI (max = 99)	51.0 (27.0)	61.0 (27.0)	71.0 (24.0)	0.167	57.5 (41.0)	63.5 (39.0)	64.0 (33.0)	0.504
MAS (max = 4)	1.0 (2.0)	1.0 (1.5)	0.0 (1.0)	0.156	1.0 (1.6)	1.0 (1.6)	1.0 (1.3)	0.223
BT - Errors	8.0 (9.0)	8.0 (9.0)	3.0 (5.0)	0.112	2.0 (6.0)	1.0 (2.0)	2.0 (4.0)	0.113

^c Scores presented as median (IQR)^d p = p -value, Friedman test. Bold indicates a significant effect ($p<0.05$) over time^e Significant one-tailed pairwise comparison with respect to baseline ($p<0.05$)

TABLE III. IMPROVEMENT AT END OF TREATMENT AND FOLLOW-UP

Outcome Measure ^f	End		Follow-up	
	VR	Control	VR	Control
<i>FM-UE</i>	2.0 (2.0) 0.3 (5.3)	3.5 (11.2) 2.3 (6.1)	1.0 (7.0) 3.0 (6.9)	2.5 (15.7) 5.7 (9.7)
<i>CAHAI</i>	5.0 (14.0) 6.6 (8.0)	2.0 (15.0) 6.0 (7.9)	5.0 (16.0) 11.1 (11.9)	7.0 (27.7) 14.2 (19.5)
<i>MoCA</i>	0.0 (2.0) -0.9 (1.7)	1.0 (4.0) 1.4 (2.3)	1.0 (5.0) 1.7 (2.4)	3.0 (2.0) 2.6 (1.1)
<i>BI</i>	5.0 (20.0) 7.9 (11.1)	12.5 (38.7) 16.7 (19.7)	10.0 (10.0) 15.0 (6.4)	20.0 (31.2) 15.8 (15.3)

^fImprovements presented as median (IQR), and mean (SD) in the second row

respect to baseline indicated that in the CAHAI both groups showed a significant improvement in time at end of treatment [VR: $T=2.5$, $p=0.046$, $r=0.45$; Control: $T=0.0$, $p=0.033$, $r=0.53$], and follow-up [VR: $T=0.0$, $p=0.014$, $r=0.59$; Control: $T=0.0$, $p=0.034$, $r=0.53$]. For the BI in the VR group, the effect across time results from a significant improvement at follow-up ($T=0.0$, $p=0.008$, $r=0.64$), but not at the end of treatment ($T=1.5$, $p=0.052$, $r=0.53$), although there is a trend. Finally, in MoCA, both groups did not differ significantly from baseline at end of treatment [VR: $T=8.5$, $p=0.197$, $r=0.34$; Control: $T=3.0$, $p=0.223$, $r=0.38$]; at follow-up, the control group showed a significant improvement, and the VR group only a trend [VR: $T=1.5$, $p=0.051$, $r=0.44$; Control: $T=0.0$, $p=0.021$, $r=0.64$].

No significant differences ($p>0.05$) were found in the between-groups analysis, when comparing the improvements in the VR group with those of the control group in all tested outcome measures at end of treatment and follow-up.

3) *Extent of improvement in outcome measures*: we analyzed the improvement with respect to baseline in clinical scores for the primary outcome measures where we observed a significant within-group effect over time (TABLE III).

a) *FM-UE*: For both groups, the improvement was on average below the Minimally Clinically Important Difference (MCID) according to Page et al., which should be between 4.25 and 7.25 [32]. At follow-up the control group showed a meaningful change with respect to baseline, but not significant (TABLE II).

b) *CAHAI*: The mean improvement was similar in both groups at end of treatment and follow-up. At the end of treatment, these improvements were borderline of what is considered a Minimal Detectable Change (MDC) according to Barreca et al., which should be 6.3 [33], but improved at follow-up.

c) *MoCA*: The VR group showed no improvement in MoCA at end of treatment, and a limited one at follow-up. Results were also modest for the control group at end of treatment and follow-up, but better on average than those observed in the VR group.

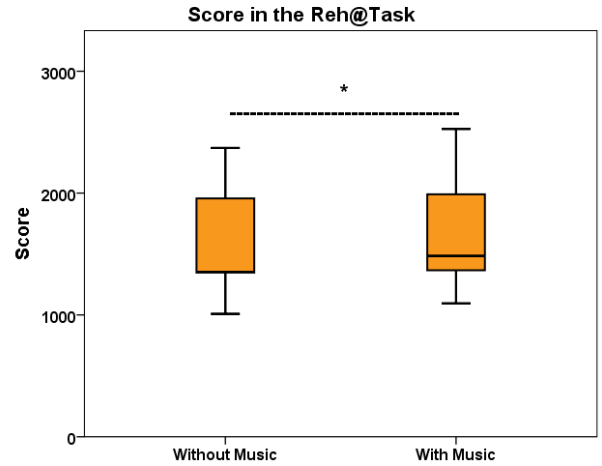


Fig. 3. Score in sessions of the Reh@Task with and without music. The score was significantly higher in sessions with music.

d) *BI*: For both groups, the average improvement at end of treatment and follow-up was substantially larger than what is considered a MCID according to Hsieh et al., which should be 1.85 [34].

B. Analysis of in-game measures

1) *Effect of training in ROM*: Using as measure of ROM the calibration data of each training session, a significant mean improvement of 18.2% was found in the x component ($T=2.0$, $p=0.02$). In the y component there was a nonsignificant improvement of 1.5%.

2) *Effect of music on task performance*: The comparison of the mean total score between sessions with or without music showed that the score was approximately 4% higher in sessions with music, being this difference significant ($T=3.0$, $p=0.031$, $r=0.50$) (Fig. 3).

C. Correlation analysis of outcome and baseline measures

To understand the implications of motor function, cognitive function and depressive symptomatology on the impact of the interventions, we performed an exploratory correlation analysis of baseline assessments with the improvements in outcome measures at the end of intervention (FM-UE, CAHAI, MoCA, BI and GDS). In this analysis, the data of both groups were merged. The only significant correlation found was between GDS at baseline and improvement in MoCA ($\rho=-0.65$, $p=0.022$). That is, the higher the depressive symptomatology, the worse the cognitive improvements.

IV. DISCUSSION AND CONCLUSIONS

This study aimed to assess the impact in recovery of a cognitive-motor VR training task customized with positive stimuli, compared to time-match conventional rehabilitation in the subacute phase of stroke. To this end, a VR system that trained attention, memory and reaching movements was

developed, the Reh@Task. Positive stimuli, namely visual and musical, were selected according to each patient's preferences. The reasoning behind this decision is that valence attributed to visual stimuli, music or general experiences is highly variable and influenced by personality [35], [36], gender [37]–[39], age [39], [40], personal experience [41], and culture [35], [37]. For example, in a study in which young and older adults had to rate pictures on valence and arousal after a specific task, results showed that older adults rated positive and negative images more extremely [40]. Hence, considering the personal subjectivity of perceived valence, any intervention based on positive stimuli should be customized to each user based on personal preferences.

Effects over time were found for VR (CAHAI, MoCA and BI) and Control (CAHAI and MoCA) groups. However, pairwise comparisons showed significant improvements at the end of treatment only in CAHAI. In-game data also revealed a significant improvement of 18% in ROM for the VR group at the end of treatment. No statistical differences were found between groups. Although statistically significant, the attained improvements at end of treatment were in general small. Groups reached clinically relevant improvements only in CAHAI and BI.

Overall, we did not find important differences between groups and improvements were limited, except for the improvements in ADLs. This is particularly surprising taking into account that the patient population was in average within the first 2 months after stroke. Indeed, our findings contrast with previous studies using a similar protocol on a chronic population, where we found larger improvements [1]. There are multiple reasons that can have influenced these results. First, our target population had both cognitive and motor deficits. There is evidence suggesting that cognitive deficits may interfere with motor recovery [4]. According to the last Cochrane review, most of the studies performed in upper limb motor rehabilitation exclude patients with low cognitive function [20]. In our case, the average MoCA was of 20 and 21 for VR and Control groups, respectively. These scores are well below what is considered normal function (26) [25], and indicate MCI. Hence the importance of this study. Second, although patients trained specific motor and cognitive competences, the larger gains were in assessments that relate to ADLs. This could indicate that a combined cognitive-motor training may be more effective at improving tasks that involve both domains that each domain separately. Third, although we excluded patients with high depressive symptomatology, our analysis revealed a significant correlation between GDS and the improvements in cognitive function at the end of treatment. Thus, the reduced improvements in MoCA could be explained by the existence of patients indicative of having mild depressive symptomatology. Finally, there is evidence that shows that MCI affects dual task performance [42], [43]. Although our training is single task, it combines both motor and cognitive components. It is possible that patients with MCI have more difficulties in rehabilitation targeting both components simultaneously. Finally, our participants had a limited number of years of education (4.6 in average), a factor that has been also associated with an increased risk for cognitive decline [44].

With respect to the role of the addition of personalized positive stimuli and music, we can conclude that music had a measurable positive effect in task performance (4%). In previous research, we reported on a similar positive impact when using images with positive stimuli [15]. Given the small sample size and results attained, it is unclear to what extent this improved task performance translated to actual recovery.

The results of this study contribute to a better understanding of the impact of VR therapy in a poorly studied population, stroke patients with MCI. Our findings show that a VR intervention is as effective as conventional. However, both VR and conventional interventions had a reduced impact in this population. This means that effective VR therapies in stroke patients may not be as effective when applied to patients with MCI in the subacute phase. Hence, this implies that further studies need to be conducted to understand which protocols may be more effective. Specific attention should be given to the role of combined or separate cognitive motor training, and the impact of dual task training. These experimental decisions need to be further addressed, and VR allows us addressing them in a systematic way.

ACKNOWLEDGMENT

We would like to thank SESARAM and the participants of this study. We would also like to thank Teresa Paulino for the development of the Reh@Task. This work was supported by the European Commission through the RehabNet project - Neuroscience Based Interactive Systems for Motor Rehabilitation - EC (303891 RehabNet FP7-PEOPLE-2011-CIG); by the Fundação para a Ciência e Tecnologia through UID/EEA/50009/2013 and Augmented Human Assistance project (CMUPERI/HCI/0046/2013); and by the INTERREG program through the MACBIOIDI project (MAC/1.1.b/098).

REFERENCES

- [1] A. L. Faria, J. Couras, M. S. Cameirão, T. Paulino, G. M. Costa, and S. Bermúdez i Badia, "Impact of combined cognitive and motor rehabilitation in a virtual reality task: an on-going longitudinal study in the chronic phase of stroke," in *11th ICDVRAT, Los Angeles, USA, Sept. 20-22, 2016*, 2016.
- [2] G. House *et al.*, "Integrative rehabilitation of residents chronic post-stroke in skilled nursing facilities: the design and evaluation of the BrightArm Duo," *Disability and Rehabilitation: Assistive Technology*, vol. 11, no. 8, pp. 683–694, Nov. 2016.
- [3] S. Verstraeten, R. Mark, and M. Sitskoorn, "Motor and Cognitive Impairment after Stroke: A Common Bond or a Simultaneous Deficit?," *Stroke Research & Therapy*, 2016.
- [4] A. A. Mullick, S. K. Subramanian, and M. F. Levin, "Emerging evidence of the association between cognitive deficits and arm motor recovery after stroke: A meta-analysis," *Restorative Neurology and Neuroscience*, vol. 33, no. 3, pp. 389–403, Jun. 2015.
- [5] G. Pichierri, P. Wolf, K. Murer, and E. D. de Bruin, "Cognitive and cognitive-motor interventions affecting physical functioning: a systematic review," *BMC Geriatr*, vol. 11, p. 29, 2011.
- [6] U. Pählman, C. Gutiérrez-pérez, M. Sävborg, E. Knopp, and E. Tarkowski, "Cognitive function and improvement of balance after stroke in elderly people: the Gothenburg Cognitive Stroke Study in the Elderly," *Disability and Rehabilitation*, vol. 33, no. 21–22, pp. 1952–1962, Jan. 2011.
- [7] L. Čengić, V. Vuletić, M. Karlić, M. Dikanović, and V. Demarin, "Motor and Cognitive Impairment after Stroke," *Acta Clinica Croatica*, vol. 50, no. 4, pp. 463–467, Dec. 2011.

- [8] N. Theill, V. Schumacher, R. Adelsberger, M. Martin, and L. Jäncke, "Effects of simultaneously performed cognitive and physical training in older adults," *BMC Neuroscience*, vol. 14, p. 103, 2013.
- [9] J. H. Choi, B. R. Kim, E. Y. Han, and S. M. Kim, "The Effect of Dual-Task Training on Balance and Cognition in Patients With Subacute Post-Stroke," *Annals of Rehabilitation Medicine*, vol. 39, no. 1, pp. 81–90, Feb. 2015.
- [10] I.-W. Lee, Y.-N. Kim, and D.-K. Lee, "Effect of a virtual reality exercise program accompanied by cognitive tasks on the balance and gait of stroke patients," *Journal of Physical Therapy Science*, vol. 27, no. 7, pp. 2175–2177, 2015.
- [11] D. Rand, P. L. (Tamar) Weiss, and N. Katz, "Training Multitasking in a Virtual Supermarket: A Novel Intervention After Stroke," *Am J Occup Ther*, vol. 63, no. 5, pp. 535–542, Sep. 2009.
- [12] A. P. Silva and A. F. Frère, "Virtual environment to quantify the influence of colour stimuli on the performance of tasks requiring attention," *BioMedical Engineering OnLine*, vol. 10, p. 74, 2011.
- [13] N. Oren, N. Soroker, and L. Y. Deouell, "Immediate effects of exposure to positive and negative emotional stimuli on visual search characteristics in patients with unilateral neglect," *Neuropsychologia*, vol. 51, no. 13, pp. 2729–2739, Nov. 2013.
- [14] E. A. Kensinger, "Remembering emotional experiences: The contribution of valence and arousal," *Reviews in the Neurosciences*, vol. 15, no. 4, pp. 241–252, 2004.
- [15] M. S. Cameirão, A. L. Faria, T. Paulino, J. Alves, and S. Bermúdez i Badia, "The impact of positive, negative and neutral stimuli in a virtual reality cognitive-motor rehabilitation task: a pilot study with stroke patients," *Journal of NeuroEngineering and Rehabilitation*, vol. 13, p. 70, 2016.
- [16] T. Särkämö *et al.*, "Music listening enhances cognitive recovery and mood after middle cerebral artery stroke," *Brain*, vol. 131, no. 3, pp. 866–876, Mar. 2008.
- [17] W. L. Magee, I. Clark, J. Tamplin, and J. Bradt, "Music interventions for acquired brain injury," in *Cochrane Database of Systematic Reviews*, John Wiley & Sons, Ltd, 2017.
- [18] D. S. Scholz *et al.*, "Sonification of Arm Movements in Stroke Rehabilitation – A Novel Approach in Neurologic Music Therapy," *Front. Neurol.*, vol. 7, 2016.
- [19] P. Ripollés *et al.*, "Music supported therapy promotes motor plasticity in individuals with chronic stroke," *Brain Imaging and Behavior*, vol. 10, no. 4, pp. 1289–1307, Dec. 2016.
- [20] K. E. Laver, S. George, S. Thomas, J. E. Deutsch, and M. Crotty, "Virtual reality for stroke rehabilitation," in *Cochrane Database of Systematic Reviews*, John Wiley & Sons, Ltd, 2015.
- [21] Z. Mathews, S. B. i Badia, and P. Verschure, "A novel brain-based approach for multi-modal multi-target tracking in a mixed reality space," in *Proceedings of 4th INTUITION International Conference and Workshop on Virtual Reality*, 2007.
- [22] P. Lang, M. Bradley, and B. Cuthbert, "International affective picture system (IAPS): Affective ratings of pictures and instruction manual," University of Florida, Gainesville, FL, Technical Report A-8, 2008.
- [23] G. Demeurisse, O. Demol, and E. Robaye, "Motor Evaluation in Vascular Hemiplegia," *Eur Neurol*, vol. 19, no. 6, pp. 382–389, Jul. 1980.
- [24] A. De Renzi and L. A., "Token test: A sensitive test to detect receptive disturbances in aphasics," *Brain: A Journal of Neurology*, vol. 85, pp. 665–678, 1962.
- [25] Freitas, M. R. Simões, L. Alves, and I. Santana, "Montreal Cognitive Assessment (MoCA): normative study for the Portuguese population," *Journal of Clinical and Experimental Neuropsychology*, vol. 33, no. 9, pp. 989–996, 2011.
- [26] J. A. Yesavage *et al.*, "Development and validation of a geriatric depression screening scale: A preliminary report," *Journal of Psychiatric Research*, vol. 17, no. 1, pp. 37–49, 1983.
- [27] A. R. Fugl-Meyer, L. Jaasko, I. Leyman, S. Olsson, and S. Steglind, "The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance," *Scand J Rehabil Med*, vol. 7, pp. 13–31, 1975.
- [28] S. Barreca *et al.*, "Development of the Chedoke Arm and Hand Activity Inventory: theoretical constructs, item generation, and selection," *Top Stroke Rehabil*, vol. 11, pp. 31–42, Fall 2004.
- [29] F. I. Mahoney and D. W. Barthel, "Functional Evaluation: The Barthel Index," *Md State Med J*, vol. 14, pp. 61–5, Feb. 1965.
- [30] R. W. Bohannon and M. B. Smith, "Interrater reliability of a modified Ashworth scale of muscle spasticity," *Phys Ther*, vol. 67, pp. 206–7, Feb. 1987.
- [31] L. Gauthier, F. Dehaut, and Y. Joanette, "The Bells Test: A quantitative and qualitative test for visual neglect," *International Journal of Clinical Neuropsychology*, vol. 11, no. 2, pp. 49–54, 1989.
- [32] S. J. Page, G. D. Fulk, and P. Boyne, "Clinically Important Differences for the Upper-Extremity Fugl-Meyer Scale in People With Minimal to Moderate Impairment Due to Chronic Stroke," *PHYS THER*, vol. 92, no. 6, pp. 791–798, Jun. 2012.
- [33] S. R. Barreca, P. W. Stratford, C. L. Lambert, L. M. Masters, and D. L. Streiner, "Test-Retest Reliability, Validity, and Sensitivity of the Chedoke Arm and Hand Activity Inventory: A New Measure of Upper-Limb Function for Survivors of Stroke," *Archives of Physical Medicine and Rehabilitation*, vol. 86, no. 8, pp. 1616–1622, Aug. 2005.
- [34] Y.-W. Hsieh, C.-H. Wang, S.-C. Wu, P.-C. Chen, C.-F. Sheu, and C.-L. Hsieh, "Establishing the minimal clinically important difference of the Barthel Index in stroke patients," *Neurorehabil Neural Repair*, vol. 21, no. 3, pp. 233–238, Jun. 2007.
- [35] P. Kuppens *et al.*, "The Relation Between Valence and Arousal in Subjective Experience Varies With Personality and Culture," *J Pers*, p. n/a–n/a, May 2016.
- [36] J. K. Vuoskoski and T. Eerola, "Measuring Music-Induced Emotion: A Comparison of Emotion Models, Personality Biases, and Intensity of Experiences," *Musicae Scientiae*, vol. 15, no. 2, pp. 159–173, Jul. 2011.
- [37] J. Huang *et al.*, "Affective reactions differ between Chinese and American healthy young adults: a cross-cultural study using the international affective picture system," *BMC Psychiatry*, vol. 15, p. 60, 2015.
- [38] R. Kato and Y. Takeda, "Responses to affective pictures depicting humans: late positive potential reveals a sex-related effect in processing that is not present in subjective ratings," *Exp Brain Res*, vol. 235, no. 1, pp. 193–204, Jan. 2017.
- [39] P. Gomez, A. von Gunten, and B. Danuser, "Autonomic nervous system reactivity within the valence–arousal affective space: Modulation by sex and age," *International Journal of Psychophysiology*, vol. 109, pp. 51–62, Nov. 2016.
- [40] D. Grünh and S. Scheibe, "Age-related differences in valence and arousal ratings of pictures from the International Affective Picture System (IAPS): Do ratings become more extreme with age?," *Behavior Research Methods*, vol. 40, no. 2, pp. 512–521, May 2008.
- [41] C. Pulido, A. Mok, S. A. Brown, and S. F. Tapert, "Heavy drinking relates to positive valence ratings of alcohol cues," *Addiction Biology*, vol. 14, no. 1, pp. 65–72, Jan. 2009.
- [42] S. Schaefer and V. Schumacher, "The Interplay between Cognitive and Motor Functioning in Healthy Older Adults: Findings from Dual-Task Studies and Suggestions for Intervention," *Gerontology*, vol. 57, no. 3, pp. 239–246, Oct. 2010.
- [43] T. J. Buracchio *et al.*, "Executive function predicts risk of falls in older adults without balance impairment," *BMC Geriatrics*, vol. 11, p. 74, 2011.
- [44] L. B. Zahodne, Y. Stern, and J. J. Manly, "Differing effects of education on cognitive decline in diverse elders with low versus high educational attainment," *Neuropsychology*, vol. 29, no. 4, pp. 649–657, 2015.