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Conjunctive Rehabilitation of Multiple Cognitive Domains for Chronic Stroke Patients in Virtual Reality*

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Abstract— **Classically, cognitive deficits have been studied and treated in isolation from each other. A stroke patient is classified as being memory impaired, having executive dysfunction or showing attentional deficits after which a dedicated rehabilitation therapy is given. Studies seldom looked at the relationship between these different cognitive domains and syndromes, although, there is evidence that they might share common neuronal substrates and do not occur in isolation. Here, we propose a novel rehabilitation method in virtual reality to treat cognitive deficits in conjunction and report the preliminary results of an ongoing randomized controlled clinical trial. The current results suggest that in a homogeneous patient group the cognitive deficits are correlated and that the individual impairment level can be optimally addressed through an adaptive training paradigm.**

I. Introduction

Cognitive deficits are common consequences after stroke, however, incident rates can vary from 35.2% [1] up to 78% [2], as the deficit definition and inclusion criteria vary from study to study [2]. Cognitive impairments have a severe impact on a person's activities of daily living [3]. In addition, cognitive disabilities are a predictor of poor functional outcome independent of the intensity of the rehabilitation attempt [4]. Although there are numerous dedicated cognitive therapies, most rehabilitation effects are limited to the task trained and do not generalize to everyday function or remain inconclusive [5], [6]. One reason for the absence of conclusive effects could be the narrow focus on patients that express a very specific syndrome or lesion location even though stroke patients typically express deficits in various cognitive domains [6]. Corbetta et al. showed that cognitive functions might depend on a highly distributed pattern of brain activation and are less sensitive to the lesion location, unlike motor or language impairments, that show a clear lateralization [7]. The authors tried to tie lesions from a large sample of heterogeneous stroke patients to impaired behavior in various domains. They found that a given lesion location could lead to cognitive impairments in several domains. Damaged regions that were linked to deficits in multiple domains are mainly subcortical and located in areas with high white matter overlap. They concluded that lesions cause a disturbance to the connections between regions impairing the processes necessary for higher cognitive functioning. The symptoms observed are a consequence of this disturbance. Hence, two inferences can be drawn. First, if rehabilitation studies focus too much on highly specific syndromes or lesion locations they might fail to uncover and treat the underlying impaired brain processes that account for the symptom observed. Second, if individual lesions can lead to impairment in various cognitive domains, then these domains should be trained in conjunction instead of putting the focus on rehabilitating them in isolation.

The current study tried to address these two aspects. To understand the underlying impaired processes, we developed an adaptive cognitive training in virtual reality (VR) that is independent of syndrome categorization. We focused on the four cognitive domains that are most often observed to be impaired after stroke: Spatial awareness (including neglect), executive function, memory and attention. Interestingly, interdependencies between these domains have been identified [8], [9]. For instance, a patient expressing executive dysfunction might also show impaired attention, and the same would hold true for spatial neglect and memory. An emerging body of studies supports this concept of a network of interrelated symptoms, identifying the frontoparietal network of brain regions as a candidate for attentional [10] and memory processes to emerge. This network might serve as a general-purpose hardware that can be flexibly employed in various tasks [11], [12], [13]. Regarding this network perspective, spatial neglect and executive dysfunction are two different syndromes whereas attention and memory are two distinct but interdependent brain processes.

We therefore assume that a lesion causes a disturbance to the frontoparietal network and affects the processes that underlie cognitive functioning, leading to deficits in various domains. Consequently, we built a rehabilitation system that trains these domains in conjunction and adapts automatically to the impairment level of the patient in each domain. The resulting individualized training protocols might lead to an enhanced improvement in the impaired domains. By measuring the development of the patient's impairment levels, we can examine the relationship between the domains and how the interaction modulates the syndromes observed. We believe that only VR enables us to effectively implement the requirements of an individualized conjunctive training, that includes a high-level of manipulation and control of the tasks a subject performs. For instance, automatized online adjustment of training levels cannot be based on human diagnosis and intervention for several reasons. In addition, VR assessments provide higher precision and resolution as

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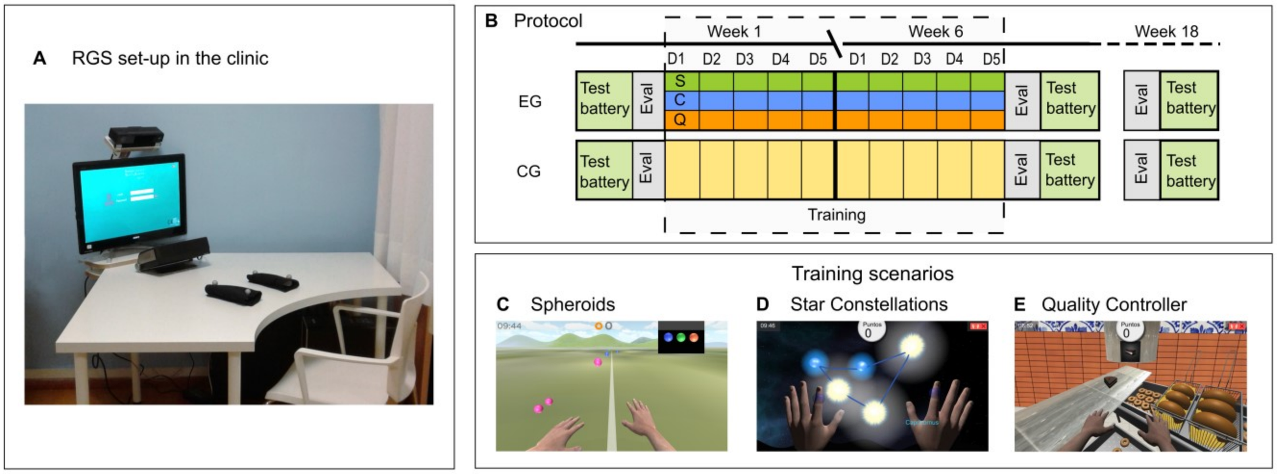

Figure 1. Experimental protocol and set-up. A) The RGS includes a 24 inch touch screen with an integrated CPU, a Microsoft Kinect Sensor that is placed above the screen, a Tobii Eytracker T120 and a table to support the arm. Reflective markers on the patients arms allow the Kinect to capture the movement of the limbs that move over the table and map them onto an avatar's limbs. The screen displays a first-person view of the gaming environment. B) Experimental protocol for both groups, green indicates the clinical assessments, EG: experimental group, CG: control group, S: Spheroids, C: Star Constellations, Q: Quality Controller. C-E) Screenshots of the three training scenarios as they are seen by the patient.

compared to standard clinical scales. We developed the new training scenarios using the Rehabilitation Gaming System (RGS), a VR-based rehabilitation tool (Fig. 1A). RGS has shown to be effective in inducing neural and behavioral changes [14], [15], [16]. It restores impaired motor contingencies by modulating perception, prediction and action through embodiment. The patient executes goal-oriented arm movements and observes them, mapped on an avatar's body, on a screen in front of him. This action-observation paradigm is based on the neurological rationale that capitalizes on the plasticity mechanisms of the brain. Affected brain areas can functionally reorganize if the activation of targeted brain areas, such as the ideomotor system, is facilitated [17], [18]. The same principles can be applied to cognitive rehabilitation, since cognitive processes are an integral part of goal-oriented behavior. Through conjunctive cognitive training we ultimately aim to extend our previous results in improving motor functioning to also ameliorating impaired cognitive functions in a heterogeneous group of stroke patients. This hypothesis is currently being tested in an ongoing longitudinal clinical trial with chronic stroke patients. Here we report the methods and preliminary results from this study. However, due to the small sample size of this preliminary pilot no statistically significant differences will be reported.

II. Methods

A. Patients

The current report includes data from 11 chronic stroke patients, (experimental group (EG) N=6, control group (CG) N=5), that were screened and recruited by the doctors from the rehabilitation unit at Hospital de l'Esperança in Barcelona. Patients were randomly assigned to the two groups by the experimenter using minimization in order to avoid group imbalances in all outcome measures. The patients' characteristics can be found in Table 1. All patients gave their written consent prior to participation. Inclusion criteria were as follows: a) cognitive impairment due to a first-ever stroke (Montreal Cognitive Assessment, MoCA < 26), b) no severe upper limb motor disability (Medical Research Council Scale, MRC > 2), c) age between 45 and 75 years old and d) chronic state (more than six months after stroke). Exclusion criteria were: a) severe cognitive incapacity that prohibits the execution of the experiment, b) severe impairments like spasticity, communication disabilities (aphasia or apraxia) and perceptual or physical impairments that would interfere with the correct execution or understanding of the experiment, c) history of serious mental-health problems in acute or subacute phase and d) presence of hemianopia. This study was approved by the local Ethical Committee at Parc de Salut Mar and registered at ClinicalTrials.gov (NCT02816008).

B. Experimental Protocol and Set-up

All patients underwent a six weeks long, daily training of 30 minutes (five times per week), either in an experimental or control condition (Fig. 1B). The experimental training consisted of three cognitive training scenarios with a duration of 10 minutes each using the RGS set-up that was stationary in the hospital (Fig. 1A). In two of the three scenarios, the difficulty automatically adapts to the patient's individual capabilities (description of method in [19]) to guarantee a performance level of 70 - 80%. A Tobii Eye Tracker T120 tracks the patient's eye movements during training in all three scenarios.

The *Spheroids* scenario (Fig. 1C) is a basic attention and memory training. The patient must intercept approaching spheres of different colors by following a given sequence indicated at the top of the screen. The patient has to keep the current position in the color sequence in memory. Errors are indicated with a tone. After completing the sequence three times correctly in a row, the patient is rewarded with a point and the sequence changes. The difficulty is fixed and equal for all patients, so the scores can serve as a control measure.

The *Star Constellations* scenario (Fig. 1D) trains spatial attention and spatial memory, as well as working memory load and memory delayed recall. The patient is shown a star constellation and some stars light up in a sequence. The patient has to remember the sequence and reproduce it after a delay period by touching the stars accordingly. If the sequence is reproduced correctly, the patient is rewarded with one point for each star in the sequence and the constellation lights up. If the order of the sequence is incorrect, the wrongly touched stars light up in red. This scenario has five difficulty descriptors: the complexity (i.e. network structure) and extension (i.e. spatial dispersion) of the constellation category, the number of stars to be remembered, the time interval between the appearance of the stars, and length of the delay period.

The *Quality Controller* scenario (Fig. 1E) trains selective, sustained and divided attention, alertness, spatial awareness, as well as components of executive function (planning, inhibition and error correction). The patient must take care of two concurrent tasks. In the right work space, doughnuts must be taken out of a fryer when their cooking time ends (indicated by a ringing clock) by moving the arm over the fryer. In the left work space, candies move over a conveyor belt. The currently produced candy is indicated on the machine at the top of the screen. Candies that do not match the indicated sample are considered defective and need to be pushed away. The patient is rewarded with a point for each correctly detected defective candy and cooked doughnuts, but loses a point when the doughnuts are touched too early/late or a non-defective candy has been touched. The difficulty is modulated by five parameters: the speed of the conveyor belt, the interval between candies and the amount of candies in a sequence, as well as the cooking time and the time given to save the doughnuts.

The control group receives a folder with 30 individual cognitive tasks (e.g. draw figures mirrored, complete sentences or word search puzzle etc.). They are asked to spend every day 30 minutes with one task. If they do not finish the task within 30 minutes they can continue with it or choose another task the next day. As these patients complete the tasks at home, they are asked to write down the date and the time spent on each started or completed task and bring the folder back after six weeks.

Before (T0) and at the end of the intervention period (T1) as well as at 3-months follow-up, a neuropsychologist assesses the patients through a neuropsychological test battery, additional clinical outcome scales and two virtual assessments (see *Outcome Measures*).

C. *Outcome Measures*

The neuropsychological test battery was put together with the neuropsychologist to cover all cognitive domains and consists of the following cognitive assessments: Trail Making Test A (TMT A), Trail Making Test B (TMT B) [20], Corsi Block Tapping Test Forward (Corsi F) [21] and Backward (Corsi B) [22], Wechsler Adult Intelligence Scale IV (WAIS) Digit Span Forward (WAIS F) and Backward (WAIS B) as well as Digit Symbol Coding (WAIS C) [23], Ray Auditory Verbal Learning Test Immediate (RAVLT I) and Delayed Recall (RAVLT D) [24], Frontal Assessment Battery (FAB) [25] and a star cancellation test [26]. The standard scoring, and, where available, Spanish versions were used. The additional clinical outcomes were selected to control for further effects of the treatment and consisted of: Fugl-Meyer Assessment for the upper limb (FM-UE), Barthel Index (BI) and Mini-Mental-State-Examination (MMSE).

The virtual assessments consist of two tests: the Bomb Cancellation task, a sustained attention and spatial awareness task where the patient must fixate his eyes on targets that appear at random locations on the screen, and the Validation Gate task, a visual attention task where the patient must detect discontinuities in the moving trajectory of circles on the screen.

TABLE I. PARTICIPANTS CHARATERISTICS AT BASELINE

	EG (N=6)		CG (N=5)		p-val	
Gender (female)	2		3		0.78	
Age, years	66.33 (6.80)		64.00 (7.00)		0.65	
Days after stroke	1’211.17 (1’116.57)		1’742.60 (2’309.99)		0.93	
Impaired limb (left)	3		3		1.00	
Type (ischemic)	3		4		1.00	
MoCA	21.33 (2.07)		19.8 (4.38)		0.67	
MRC	3.67 (1.03)		3.60 (0.89)		0.85	
	T0	**T1**	**T0**	**T1**	**T0**	**T1**
TMT A	79.00 (79.33)	74.67 (34.59)	63.60 (39.12)	55.40 (26.31)	0.54	0.43
TMT B	266.33 (154.83)	217.67 (131.22)	265.40 (187.41)	262.60 (190.89)	0.81	0.66
Corsi F	4.17 (1.72)	6.00 (2.28)	4.80 (2.17)	6.00 (1.41)	0.65	0.95
Corsi B	2.83 (1.72)	4.00 (1.09)	4.00 (2.00)	4.00 (1.87)	0.38	0.87
WAIS F	4.83 (0.98)	5.00 (1.41)	5.20 (0.45)	5.40 (0.89)	0.97	0.77
WAIS B	2.83 (1.17)	3.50 (1.05)	2.80 (1.30)	3.400 (0.89)	0.88	0.76
WAIS C	32.50 (14.15)	32.50 (14.09)	33.40 (19.96)	35.60 (21.33)	0.82	0.84
RAVLT I	27.17 (12.86)	28.00 (13.21)	34.80 (11.05)	35.40 (7.50)	0.35	0.45
RAVLT D	3.83 (3.18)	3.33 (2.73)	7.40 (1.94)	7.60 (1.67)	0.10	0.03
FAB	15.50 (1.64)	15.83 (2.79)	15.20 (3.42)	16.00 (1.58)	0.95	0.84
SC	48.00 (11.31)	53.50 (0.55)	52.00 (1.58)	53.60 (0.55)	1.00	1.00
MMSE	27.50 (2.34)	27.00 (1.10)	27.20 (1.64)	27.80 (2.39)	0.81	0.35
FM-UE	48.33 (13.63)	50.17 (12.83)	51.00 (27.97)	51.80 (26.19)	0.27	0.35
BI	90.00 (6.32)	88.33 (10.80)	95.00 (11.18)	95.00 (11.18)	0.18	0.16

Unless not indicated differently, mean (SD) is shown, EG: experimental group, CG: control group, MoCA: Montreal Cognitive Assessment, MRC: Research Council Scale, TMT: Trail Making Test A (TMT A) and B (TMT B), Corsi: Corsi Block Tapping Test Forward (Corsi F) and Backward (Corsi B), WAIS: Wechsler Adult Intelligence Scale IV Digit Span Forward (WAIS F) and Backward (WAIS B), Digit Symbol Coding (WAIS C), RAVLT: Ray Auditory Verbal Learning Test Immediate (RAVLT I) and Delayed Recall (RAVLT D), FAB: Frontal Assessment Battery, SC: Star Cancellation, MMSE: Mini-Mental-State-Examination, FM-UE: Fugl-Meyer Assessment for upper limbs, BI: Barthel Index, statistical test used: Wilcoxon rank-sum test.

D. *Statistical Analysis*

For this preliminary reporting of the ongoing trial, we will present results from the neuropsychological test battery (i.e. the composite scores that was created for each domain) and from the training scenarios Star Constellations and Quality Controller at baseline (T0) and after treatment (T1). The patients that are currently enrolled did not yet complete follow-up evaluations.

Differences between the two groups characteristics at T0 and T1 were assessed using the Wilcoxon rank-sum test. To analyze the neuropsychological test battery with regards to the cognitive domains, four composite scores were created: attention (Corsi F, TMT A and WAIS F), memory (Corsi B, RAVLT I, RAVLT D and WAIS B), executive function (TMT B, WAIS C and FAB) and spatial attention (star cancellation). Individual test scores for each cognitive assessment were converted to standard z-scores, using the mean and standard deviation (SD) of normative age-adjusted data [27], [28], [29], [30]. The individual z-scores were averaged to obtain the patient's average standardized composite score (ASCS) for a given domain.

Based on the ASCS, each patient's impairment in each domain was stratified into 'no impairment' (up to -1 SD from normative data), 'mild' (between -1 and -1.5 SD from normative data), 'moderate' (between -1.5 and -2 SD from normative data) and 'severe' (more than -2 SD from normative data). We adopted a finer gradient of impairment level as classically reported [31], [32]. However, due to the small sample size of this study, the moderate and the severe patients were combined in one stratum for the analysis of the difficulty adjustment. To evaluate reliability of the composed domain, we computed the Cronbach's α. We used Spearman's correlation to evaluate the relationship between ASCS at T0 and at T1 as well as ASCS and the performance in the scenarios.

III. Results

The baseline characteristics of the patients included in this preliminary analysis did not significantly differ between the two groups (Table 1). However, this finding was also true for the measures taken after treatment, revealing no effect of treatment on the outcome measures.

The composed cognitive domains had a mixed reliability, with executive function scoring the highest (Cronbach's α 0.85), followed by memory (Cronbach's α 0.62) and attention at last (Cronbach's α 0.58).

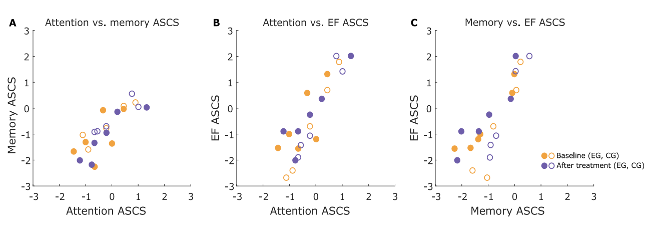

Figure 2. ASCS correlations. The ASCS positvely correlate at T0 (orange) and at T1 (violet) and between T0 and T1. Filled circles: data points for exerimental group (EG), empty circles: data points for control group (CG), EF: executive function.

The ASCS of all patients together correlated significantly between the domains attention, memory and executive function at T0 and at T1 (Table 2, Fig. 2). In addition, we found significant correlations between these domain's T0 ASCS and T1 ASCS (Table 3, Fig. 2). No correlation was found for the ASCS of spatial awareness. Overall, the T1 ASCS for the experimental group correlated with the patient's success rate at the end of the treatment in the Star Constellations scenario (attention T0 r = 0.71, ns and T1 r = 0.94, p<0.05, memory T0 r = 0.82, ns and T1 r = 1, p<0.01, executive function T0 r = 0.83, ns and T1 r = 0.94, p<0.05, star cancellation T0 r = 0.49, ns and T1 r = 0.29, ns). However, in the Quality Controller scenario, no significant correlation with the success rates was found.

TABLE II. Relationships between Domains

Time	Domains		
	Attention vs. Memory	*Attention vs. EF*	*Memory vs. EF*
T0 ASCS	r = 0.74*	r = 0.81**	r = 0.83**
T1 ASCS	r = 0.91***	r = 0.80**	r = 0.73*

* p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001, EF = executive function

TABLE III. Relationships between T0 and T1

T0 ASCS	T1 ASCS		
	Attention	*Memory*	*EF*
Attention	r = 0.83**	r = 0.75*	r = 0.73*
Memory	r = 0.80**	r = 0.91 ***	r = 0.78**
EF	r = 0.77**	r = 0.75*	r = 0.91***

* p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001, EF = executive function

In the experimental group, the impairment level in each domain seems to be reflective in the difficulty level of the Star Constellations and the Quality Controller scenarios. When stratifying the ASCS into the levels "moderate", "mild" and "no impairment", we observe that the patient's impairment level in the memory domain is the same as in the executive function domain. We can apply this stratification to the difficulty measures of the two scenarios and see that our system distinguishes between and adapts to the different impairment levels (Fig. 3). In addition, we observe that six out of the eleven included patients show an impairment in at least two domains.

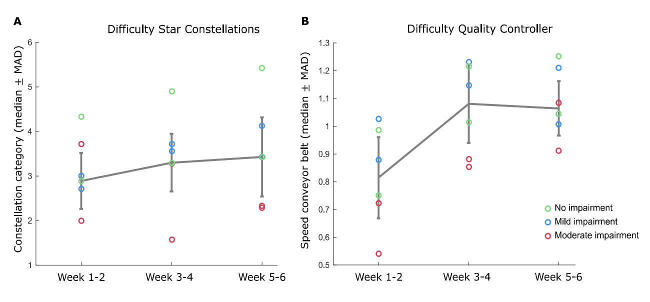

Figure 3. Relationship between impairment levels and performance. Difficulty achievment in the Star Constellations scenario (A) and in the Quality Controller scenario (B), solid line and errorbars represent median and median absolut deviation (MAD) per 10 sessions (equal to two weeks), circles represent individual data points stratified according to patient's impairment level in memory and executive function domain at baseline: moderate (red), mild (blue) and no impairment (green). Difficulty parameter in Star Constellations is the constellation category, in Quality Controller it is the speed of the conveyor belt.

IV. Discussion

To our knowledge this is one of the first attempts to provide a conjunctive training of several cognitive domains for a wide range of cognitively impaired stroke patients. The patients in our study spawn across all impairment levels, from severe to mildly impaired. Also, more than half of the patient faced an initial impairment in at least two of the included domains, showing that there is a need for methods that do not focus on one specific syndrome. In addition, given the high correlation between the assessments in three of the four domains, we expect synergistic recovery dynamics where training in one will be beneficial in the others. This is consistent with the idea the general cognitive functions are realized through an overlapping set of neuronal processes [31] and the Distributed Adaptive Control theory of mind and brain that has informed our interventions [32].

Our preliminary results suggest, that impairments in different domains in attention, memory and executive function are not independent. The positive correlation between these domains at baseline and at the end of the treatment and as well as between baseline and end of treatment, might indicate that patients that would have been classically ascribed to a specific syndrome seem to express deficits in other domains too. However, neither of these domains correlated with spatial awareness at any time point. Further analysis will show, whether this domain truly is affected in isolation and patients show a binomial deficit profile. In addition, the individual impairment levels seem to move in conjunction during the training period given the strong correlation between baseline and after treatment ASCS and the final success rate in the Star Constellations scenario. This could be an evidence that the training across several domains was indeed effective.

Stratifying the impairment level into categories that include a mild impairment (i.e. between 1 SD and 1.5 SD from a normalized mean), seems to reflect the performance variance in the training scenarios better. This finding suggests that our system can identify subtle impairments that might otherwise be seen as unimpaired if the standard categorization of previous studies would be applied [33], [34]. This notion is further supported by the fact that we relied on the MoCA to define the presence of a cognitive impairment. If we had applied the more widely used but less sensitive MMSE [35], only one of our patients would have been treated as cognitively impaired. The positive correlation between the cognitive domains and the performance results in the Star Cancellations scenario further supports this finding. The reason why we could not replicate this result in the performance measures of the Quality Controller Scenario might be found in the fact that subjects were not free in deciding which arm to use for which subtask. Therefore, the patient's motor impairment may have biased his or her cognitive performance.

Although these preliminary results are promising, they rely on a small sample size, therefore having limited statistical power. As we progress with the study we are planning to include a total number of 30 patients. This sample size is based on estimations by a power analysis with alpha of 0.05 and power of 70% using the data in [34]. We will then be able to conduct a factor analysis of the neuropsychological battery, partial correlations that account for age and motor impairment and finally estimate the improvement in each domain for each group. We expect that results from a factor analysis will uncover key rehabilitation principles for the clinical practice, such as which are the retention rates of VR-induced cognitive improvements, or which type of patients do benefit the most from this therapy.

V. Conclusion

The current study presents a novel rehabilitation approach that is suitable for patients with a wide range of cognitive deficits. The initial results suggest that the cognitive disabilities in different domains of a heterogeneous group of stroke patients are correlated. In addition, our proposed rehabilitation system is able to identify impairment levels and to adjust the difficulty of the training adequately, therefore leading to a better performance over time. Future research will show whether training various deficits in conjunction will be a more effective method to treat cognitive deficits than conventional approaches.

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References

[1] D. W. Desmond, J. T. Moroney, M. Sano, and Y. Stern, "Recovery of cognitive function after stroke," Stroke, vol. 27, no. 10, pp. 1798–1803, 1996.

[2] M. Lesniak, T. Bak, W. Czepiel, J. Seniów, and A. Czlonkowska, "Frequency and prognostic value of cognitive disorders in stroke patients," Dement. Geriatr. Cogn. Disord., vol. 26, no. 4, pp. 356–363, 2008.

[3] L. Mercier, T. Audet, R. Hébert, A. Rochette, and M. F. Dubois, "Impact of motor, cognitive, and perceptual disorders on ability to perform activities of daily living after stroke.," Stroke., vol. 32, no. 11, pp. 2602–2608, 2001.

[4] S. Paolucci, G. Antonucci, E. Gialloreti, M. Traballesi, S. Lubich, L. Pratesi, and L. Palombi, "Predicting Stroke Inpatient Rehabilitation Outcome: The Prominent Role of Neuropsychological Disorders," Eur. Neurol., vol. 36, no. 6, pp. 385–390, 1996.

[5] K. D. Cicerone, D. M. Langenbahn, C. Braden, J. F. Malec, K. Kalmar, M. Fraas, T. Felicetti, L. Laatsch, J. P. Harley, T. Bergquist, J. Azulay, J. Cantor, and T. Ashman, "Evidence-based cognitive rehabilitation: Updated review of the literature from 2003 through 2008," Arch. Phys. Med. Rehabil., vol. 92, no. 4, pp. 519–530, 2011.

[6] D. C. Gillespie, A. Bowen, C. S. Chung, J. Cockburn, P. Knapp, and A. Pollock, "Rehabilitation for post-stroke cognitive impairment: an

overview of recommendations arising from systematic reviews of current evidence.," Clin. Rehabil., 2014.
[7] M. Corbetta, L. Ramsey, A. Callejas, A. Baldassarre, C. D. Hacker, J. S. Siegel, S. V. Astafiev, J. Rengachary, K. Zinn, C. E. Lang, L. T. Connor, R. Fucetola, M. Strube, A. R. Carter, and G. L. Shulman, "Common Behavioral Clusters and Subcortical Anatomy in Stroke," Neuron, vol. 85, no. 5, pp. 927–941, 2015.
[8] R. J. Perry and J. R. Hodges, "Attention and executive deficits in Alzheimer's disease. A critical review," Brain, vol. 122, pp. 383–404, 1999.
[9] P. Malhotra, S. Mannan, J. Driver, and M. Husain, "Impaired Spatial Working Memory: One Component of the Visual Neglect Syndrome?," Cortex, vol. 40, no. 4, pp. 667–676, 2004.
[10] M. Corbetta and G. L. Shulman, "Spatial neglect and attention networks," Annu. Rev. Neurosci., vol. 34, pp. 569–599, 2011.
[11] R. Cabeza, E. Ciaramelli, I. R. Olson, and M. Moscovitch, "The parietal cortex and episodic memory: an attentional account.," Nat. Rev. Neurosci., vol. 9, no. 8, pp. 613–25, 2008.
[12] A. Gazzaley and A. C. Nobre, "Top-down modulation: Bridging selective attention and working memory," Trends Cogn. Sci., vol. 16, no. 2, pp. 129–135, 2012.
[13] P. F. M. J. Verschure, "Synthetic consciousness: the distributed adaptive control perspective.," Philos. Trans. R. Soc. Lond. B. Biol. Sci., vol. 371, no. 1701, pp. 263–275, 2016.
[14] M. S. Cameirão, S. B. I. Badia, E. D. Oller, and P. F. M. J. Verschure, "Neurorehabilitation using the virtual reality based Rehabilitation Gaming System: methodology, design, psychometrics, usability and validation.," J. Neuroeng. Rehabil., vol. 7, no. 48, p. 48, 2010.
[15] M. S. Cameirão, S. Bermúdez i Badia, E. Duarte, A. Frisoli, and P. F. M. J. Verschure, "The combined impact of virtual reality neurorehabilitation and its interfaces on upper extremity functional recovery in patients with chronic stroke," Stroke, vol. 43, no. 10, pp. 2720–2728, Oct. 2012.
[16] B. R. Ballester, M. Maier, R. María, S. Segundo, V. Castañeda, A. Duff, and P. F. M. J. Verschure, "Counteracting learned non-use in chronic stroke patients with reinforcement-induced movement therapy," J. Neuroeng. Rehabil., pp. 1–15, 2016.
[17] M. Franceschini, M. Agosti, A. Cantagallo, P. Sale, M. Mancuso, and G. Buccino, "Mirror neurons: action observation treatment as a tool in stroke rehabilitation," Eur. J. Phys. Rehabil. Med., vol. 46, no. 4, pp. 517–523, 2010.
[18] D. Prochnow, S. Bermúdez i Badia, J. Schmidt, A. Duff, S. Brunheim, R. Kleiser, R. J. Seitz, and P. F. M. J. Verschure, "A functional magnetic resonance imaging study of visuomotor processing in a virtual reality-based paradigm: Rehabilitation Gaming System," Eur. J. Neurosci., vol. 37, no. 9, pp. 1441–1447, May 2013.
[19] J. Nirme, A. Duff, and P. F. M. J. Verschure, "Adaptive rehabilitation gaming system: on-line individualization of stroke rehabilitation.," Conf. Proc. ... Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. IEEE Eng. Med. Biol. Soc. Annu. Conf., vol. 2011, pp. 6749–52, Jan. 2011.
[20] R. M. Reitan, "Trail Making Test: Manual for administration scoring and interpretation," Dept. of Neurology, Indiana Univ. Medical Center, 1958.
[21] E. H. F. de H. Kessels, R. P. C., Martine J. E. van Zandvoort, Albert Postma, L. Jaap Kappelle, "The Corsi Block-Tapping Task: Standardization and Normative Data," Appl. Neuropsychol., vol. 7, no. February 2015, pp. 252–258, 2000.
[22] R. P. C. Kessels, E. van den Berg, C. Ruis, and A. M. A. Brands, "The backward span of the Corsi Block-Tapping Task and its association with the WAIS-III Digit Span.," Assessment, vol. 15, no. 4, pp. 426–34, 2008.
[23] J. A. Amador Campos, "Escala de inteligencia de Wechsler para adultos-IV (WAIS-IV)," Fac. Psicol. Univ. Barcelona, pp. 1–21, 2013.
[24] A. Rey, "L'examen psychologique dans les cas d'encéphalopathie traumatique, " Archives de Psychologie, 28, 21, 1941.
[25] B. Dubois, A. Slachevsky, I. Litvan, and B. Pillon, "The FAB," Neurology, vol. 55, no. 11, pp. 1621–1626, 2000.
[26] B. Wilson, J. Cockburn, and P. Halligan, "Development of a behavioral test of visuospatial neglect", Archives of physical medicine and rehabilitation 68.2: 98-102, 1987.
[27] J. Peña-Casanova, S. Quiñones-Úbeda, M. Quintana-Aparicio, M. Aguilar, D. Badenes, J. L. Molinuevo, L. Torner, A. Robles, M. S. Barquero, C. Villanueva, C. Antúnez, C. Martínez-Parra, A. Frank-García, A. Sanz, M. Fernández, V. Alfonso, J. M. Sol, and R. Blesa, "Spanish multicenter normative studies (NEURONORMA project): Norms for verbal Span, visuospatial Span, letter and number sequencing, trail making test, and symbol digit modalities test," Arch. Clin. Neuropsychol., vol. 24, no. 4, pp. 321–341, 2009.
[28] W. Van der Elst, M. P. J. van Boxtel, G. J. P. van Breukelen, and J. Jolles, "Rey's verbal learning test: normative data for 1855 healthy participants aged 24-81 years and the influence of age, sex, education, and mode of presentation.," J. Int. Neuropsychol. Soc., vol. 11, no. 3, pp. 290–302, 2005.
[29] I. Appollonio, M. Leone, V. Isella, F. Piamarta, T. Consoli, M. L. Villa, E. Forapani, A. Russo, and P. Nichelli, "The frontal assessment battery (FAB): Normative values in an Italian population sample," Neurol. Sci., vol. 26, no. 2, pp. 108–116, 2005.
[30] S. Raspelli, F. Pallavicini, L. Carelli, F. Morganti, E. Pedroli, P. Cipresso, B. Poletti, B. Corra, D. Sangalli, V. Silani, and G. Riva, "Validating the Neuro VR-Based Virtual Version of the Multiple Errands Test: Preliminary Results," Presence Teleoperators Virtual Environ., vol. 21, no. 1, pp. 31–42, 2012.
[31] A. Hampshire, R. R. Highfield, B. L. Parkin, and A. M. Owen, "Fractionating Human Intelligence," Neuron, vol. 76, no. 6, pp. 1225–1237, 2012.
[32] P. F. M. J. Verschure, C. M. A. Pennartz, and G. Pezzulo, "The why, what, where, when and how of goal-directed choice: neuronal and computational principles," Philos.trans.r.soc.l. B Biol.Sci., vol. 369, no. September, p. 20130483, 2014.
[33] M. J. E. Van Zandvoort, R. P. C. Kessels, G. M. S. Nys, E. H. F. De Haan, and L. J. Kappelle, "Early neuropsychological evaluation in patients with ischaemic stroke provides valid information," Clin. Neurol. Neurosurg., vol. 107, no. 5, pp. 385–392, 2005.
[34] O. L. Lopez, J. T. Becker, W. J. Jagust, A. Fitzpatrick, M. C. Carlson, S. T. DeKosky, J. Breitner, C. G. Lyketsos, B. Jones, C. Kawas, and L. H. Kuller, "Neuropsychological characteristics of mild cognitive impairment subgroups.," J. Neurol. Neurosurg. Psychiatry, vol. 77, no. 2, pp. 159–65, 2006.
[35] Y. Dong, V. K. Sharma, B. P. L. Chan, N. Venketasubramanian, H. L. Teoh, R. C. S. Seet, S. Tanicala, Y. H. Chan, and C. Chen, "The Montreal Cognitive Assessment (MoCA) is superior to the Mini-Mental State Examination (MMSE) for the detection of vascular cognitive impairment after acute stroke," J. Neurol. Sci., vol. 299, no. 1–2, pp. 15–18, 2010.
[36] M. Lesniak, T. Bak, W. Czepiel, J. Seniów, and A. Czlonkowska, "Frequency and prognostic value of cognitive disorders in stroke patients," Dement. Geriatr. Cogn. Disord., vol. 26, no. 4, pp. 356–363, 2008.