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Research Report

A novel digital approach for post-stroke cognitive deficits: a pilot study

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Abstract.

Background: Cognitive dysfunctions after a brain stroke have a huge impact on patients' disability and activities of daily living. Prism adaptation (PA) is currently used in patients with right brain damage to improve lateralized spatial attentional deficits. Recent findings suggest that PA could also be useful for rehabilitation of other cognitive functions.

Objective: In the present study, we tested for the efficacy on cognitive rehabilitation of a novel device in which the procedure of prism adaptation is digitized and followed by cognitive training of attention and executive functions using serious games.

Methods: Thirty stroke patients were randomly assigned to two groups: an experimental group of 15 patients, which performed the experimental rehabilitation training using the novel device in 10 consecutive daily sessions; a control group of 15 patients, which performed the routine cognitive training in 10 consecutive daily sessions. Both groups were tested before and after the rehabilitation program on neuropsychological tests (digit and spatial span forward and backward, attentional matrices, Stroop task) and on functional scales (Barthel index and Beck Anxiety Index).

Results: The main results showed that only patients who received the experimental rehabilitation training improved their scores on tests of digit span forward, spatial span backward, attentional matrices and Stroop. Moreover, patients of the experimental but not of the control group showed a significant correlation between improvement on some tasks (mainly spatial span backward) and improvement on activities of daily living as well as with reduction of anxiety levels.

Conclusions: These results suggest that combining digital PA with cognitive training using serious games may be added in clinical settings for cognitive rehabilitation of stroke patients, with beneficial effects extending in promoting independency in activities of daily living and reduction of psychiatric symptoms.

Keywords: Stroke, cognition, rehabilitation, digital medicine, prism adaptation

1. Introduction

Cognitive dysfunction after stroke is an unfavorable factor for long-term functional independence. In particular, attentional and executive dysfunctions reverberate over other cognitive functions, as well as on activities of daily living and psychological components such as anxiety and depression (Mukherjee et al., 2006; Kliem et al., 2022). The ongoing care and support needs required by stroke patients affected by these cognitive deficits dramatically increase the physical, psychological, and economic burden on

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family caregivers and on society (Bordet et al., 2017). Therefore, innovation in rehabilitation procedures for cognitive deficits is a hot topic in stroke cognitive rehabilitation.

Recent reviews addressed this issue by investigating whether stroke patients receiving cognitive rehabilitation show better outcomes and have a better functional recovery than those given no treatment or treatment as usual (Cramer et al., 2023). The main results of these studies show contradictory findings. Indeed, while there seems to be an immediate effect of rehabilitation on cognitive variables, there are not convincing data on the influence of rehabilitation on functional measures such as mood and quality of life (Skidmore et al., 2023).

Prism adaptation (PA) is traditionally known as a method to improve spatial attention deficits in right hemispheric stroke patients (Li et al., 2021). Prisms deviating the visual field during the execution of pointing movements towards visual targets induce a pointing terminal error in the direction of prism deviation, because patients are not able to point at the visual target in its real position. PA refers to the progressive patient's adaptation to this visual distortion, such that the initial terminal errors are progressively compensated for as the pointing trials go on. After PA, removing optical prisms leads to a phenomenon of spatial attentional deviation towards the side of space contralateral to that of the induced deviation: patients submitted to rightward prism deviation will deviate towards the left space and vice-versa, a phenomenon called aftereffect (Magnani et al., 2014). A large literature documents that this procedure alleviates deficits of spatial attention towards the left hemispace in right hemispheric stroke patients with spatial neglect (Rossetti et al., 1998; Frassinetti et al., 2002). To date, no studies have investigated the effects of prism adaptation on cognitive deficits other than spatial attention in patients with stroke.

In a recently developed device, the procedure of PA is digitized, and the patient is asked to point towards visual targets randomly presented in different spatial positions of a tablet (Danesin et al., 2023). In this protocol, PA is followed by cognitive training of attentional and executive functions using an application of serious games challenging planning, set-shifting, and go-no-go abilities. The rationale behind the protocol is provided by studies showing that PA increases the excitability of a fronto-parietal network ipsilateral to the side of spatial deviation (Magnani et al., 2014; Bracco et al., 2017, 2018; Turriziani et al., 2021). Increased excitation of the affected hemisphere is considered a positive marker for rehabilitation improvement in stroke patients (Cicinelli et al., 2003). Therefore, we hypothesized that increasing cortical excitation in the affected hemisphere using PA and coupling it with a cognitive training could provide a new non-invasive mean for accelerating cognitive recovery in stroke patients. Among cognitive trainings, serious games represent a novel approach able to enhance patients' involvement in their rehabilitation process as well as patients' motivation and compliance with the treatment (Mubin, 2022). Indeed, compared to traditional cognitive therapies, these games allow for a more dynamic rehabilitation process while the digitalization of the procedure (included in the above-mentioned novel device) guarantees an easier administration of PA also in acute hospitalized stroke patients. The possibility of non-invasively modulating brain activity to enhance the beneficial effects of cognitive trainings represents an open challenge in the field of neurorehabilitation.

Here, we present data from a clinical pilot study aimed to explore whether PA integrated with digital cognitive training has a cognitive-enhancing effect and to investigate its feasibility for rehabilitation in right and left hemispheric acute stroke patients. Furthermore, we wanted to investigate whether any cognitive enhancing effects correlated with improvement of functional measures such as anxiety, quality of life and activities of daily living.

2. Materials and methods

The study was conducted in the neurorehabilitation unit of Ospedale Giglio in Cefalù (Italy). The protocol was approved by the Ethical Committee of Palermo 1 (n° 06/19) and it was conducted in compliance with the Declaration of Helsinki. Exclusion criteria were: age below 18 years, previous ischemic or hemorrhagic stroke, presence of comorbid neurological or psychiatric disorders, severe vigilance deficits, severe verbal comprehension deficits restricting the ability to comprehend neuropsychological tests and instructions (as assessed preliminarily with AAT task), impaired motor control of both hands. Patients were enrolled in the study during their hospitalization for rehabilitation and were randomly assigned to one of two groups. A single-blind randomized controlled design was adopted.

Patients of the control group received a routine cognitive rehabilitation program, adjusted to their clinical status, with 10 consecutive sessions distributed over a mean of two weeks: in patients with neglect the training comprehended visuospatial scanning training, reading, and copy of sentences with 10 levels of difficulty, copy of drawings, picture description; in left brain damaged patients the training comprehended speech rehabilitation (e.g. conversational therapy, reading, and writing); all patients performed a training focused on processing speed, attention, executive functions, and problem solving ability, mainly based on goal management.

Patients of the experimental group received an experimental training using a medical device that integrates PA and serious games. The protocol lasted 10 sessions, about 40 minutes each, distributed over a mean of two weeks.

Both control and experimental groups received daily physiotherapy and occupational therapy.

All patients were assessed with a battery of neuropsychological tests at T0 (before standard or experimental training), and at T1 (after rehabilitation).

In addition to neuropsychological tests, measures of anxiety (Beck Anxiety Inventory) and independency in activities of daily living (Barthel Index) were assessed at T0 and T1.

2.1. Stroke patients

Patients were consecutively enrolled according to their hospital admission. A total of 30 patients were included in the study, based on a priori power calculation to detect an effect of rehabilitation (with a statistical power (1 - b) of 0.80 and a significance level (a) of 0.05 (G*Power 3 software).

Fifteen patients were included in the control and 15 in the experimental group. There were no drop-outs in either the control or the experimental group.

Patients' demographics and clinical characteristics are reported In Table 1.

No significant differences between groups were observed at baseline regarding age (t(28)=1.9, $p > 0.05$), lesion side (t(28)=1.2, $p > 0.05$), ischemic vs. hemorragic etiology (t(28)=1.47; $p > 0.05$), time from stroke occurrence (t(28)=0.04; $p > 0.05$).

The two groups differed as to the education (t(28)=6.22, $p < 0.05$), patients in the control group being more educated than those in the experimental group.

Structural information on brain lesions was obtained from MRI or computed tomography.

Table 1

Demographic and some clinical characteristics of the two patients' groups. Mean (and standard deviation) or frequencies are reported in cells

	Experimental Group	Control Group
Age (years)	65.1 (14.6)	56.9 (12.4)
M/F	7/8	9/6
Education (years)	5.9 (3.2)	13.7 (3.6)
Time since the event (days)	53.5 (29.6)	53.9 (29.7)
Time from T0 to T1 (days)	24.4 (5.2)	19.3 (5.9)
Ischemic stroke (N)	10	6
Haemorragic stroke (N)	5	9
Left hemisphere (N)	5	2
Right hemisphere (N)	10	13
Cortical/subcortical (N)	9/6	10/5
Neglect (N)*	4	8

*Contralesional spatial neglect evaluated with Albert's line cancellation and line bisection tasks.

2.2. Experimental rehabilitation program

In each session, the training started with the digitized PA session. Patients were guided by a neuropsychologist to wear prismatic lenses with a power of 10 dioptries. Based on previous neurophysiological results documenting an increase of cortical excitability in frontal areas of the hemisphere ipsilateral to prismatic deviation (Magnani et al., 2014), right-brain-damaged (RBD) patients wore rightward prism lenses and left-brain-damaged (LBD) patients wore leftward prism lenses. The adaptation procedure was performed using an 11" tablet, horizontally oriented, that was positioned at a distance of 53 cm from the patients' eyes, with a position aligned to the patient's sagittal midplane. Visual targets represented by black squares of 1° of visual angle were randomly presented on a white background in one of three spatial positions of the tablet's screen: in the centre of the screen or with a lateralization of 21° to the right or the left space. After the presentation of each target, patients were asked to point as fast and as accurately as possible towards the target, trying not to correct the movement during its trajectory, using the ipsilesional hand. The visual targets persisted on the screen until patients' touch or after a fixed interval of 1 sec.

In the pointing procedure, 30 targets were randomly presented. According to recent studies, this number of presentations allows for the correction of the initial pointing deviation due to prism lenses, leading to the phenomenon of error reduction that is the basis of prism adaptation (Danesin et al., 2023).

Following this adaptation phase, prismatic lenses were removed, and the patient started the cognitive training with a sequence of 7 serious games.

2.3. Serious games

Serious games in the adopted device have been planned to train sustained and divided attention, working memory, interference control, inhibition, and planning.

All games were implemented using a dynamic difficulty algorithm, i.e. adapting the speed of stimulus presentation and the game difficulty to the single patient's performance. This 'dynamic difficulty' not only affects the difficulty of the gameplay but also the calculation of the score. In fact, each difficulty brings with it a 'multiplier' consistent with the level of difficulty. This results in higher scores for a correct answer at a higher difficulty and lower scores for a correct answer at a lower difficulty. A visual feedback (thumb up for correct and thumb down for incorrect responses) was presented following each trial of the game.

In all games patients responded using their ipsilesional hand. All games were executed with the supervision of a neuropsychologist.

2.3.1. Game 1: Sustained attention and monitoring task

Patients have to catch target stimuli while avoiding catching non-target ones (i.e. bombs).

The scene is composed of simple geometric icons (regular circles and hexagons covering an area of about 160x160 pixels on 1920x1200 screens) and irregular figures (for example, bombs and hearts with colors and volumes that can be superimposed on the regular geometric shapes described,) that move from the top of the screen to the bottom with variable speed and directionality within the current difficulty level.

The target interaction space (where touch and interaction from the end user are required) is a rectangular space that covers the entire horizontal line of the bottom of the screen.

Stimuli last on the screen from the time they originate until they reach the end of the screen or they are intercepted by the user within the response bar.

2.3.2.. Game 2: Visual search task

Patients have to find a single target differing for single or multiple characteristics (shape, colour, texture) from a group of distractors.

The target stimuli are composed of 5 geometric figures (triangle, square, circle, pentagon, and hexagon, respectively) presented in 4 coloring variations, for a total of 20 different combinations between shapes and color. In addition, stimuli can be differentiated for a texture presented above the stimulus, which varies its appearance. There are 60 different combinations of icons of stationary and moving stimuli.

As the difficulty increases, more perceptually similar stimuli are presented. The final result is indicated by a score corresponding to the number of correct answers, weighted by the difficulty multiplier (the score may vary depending on the level of difficulty).

2.3.3. Game 3: Planning and Switching

The patient is asked to prepare coffee shop orders, after these orders are presented on the screen. As the difficulty increases, more orders are presented at the same time. More complex orders result in a higher score. The final result is indicated by a score corresponding to the total number of completed orders, weighted by the difficulty multiplier (the score may vary depending on the complexity of the orders or the level of difficulty).

Stimuli remain on the screen until delivered to the response area, generating new orders that are presented in a left-to-right alignment at the bottom of the screen.

2.3.4. Game 4: Go-NoGo

The patient is asked to click on the screen, in the target area, when the visual stimuli presented are identical and to perform no action when the visual stimuli are different. As the difficulty increases, more perceptually similar stimuli are presented. The final result is indicated by a score corresponding to the number of correct answers, weighted by the difficulty multiplier (the score may vary depending on the difficulty level).

The stimuli last on the screen for 1000 ms or until the subjects respond on the touch screen. The intertrial interval is 500 ms.

2.3.5. Game 5: Visual working memory

The gameplay consists of a stimulus presentation part (irregular icons of real objects and tools) that persists on the screen for varying amounts of time depending on the current difficulty (from 1500 ms for standard to 800 ms for the highest level), with a 500 ms intertrial interval.

The patient is asked to rearrange the icons in reverse order of presentation. As the difficulty increases, longer series are presented. The final result is a score corresponding to the number of correct answers, weighted by the difficulty multiplier (the score may vary depending on the difficulty level).

2.3.6. Game 6: Math speed and digit working memory

The patient is asked to perform a mathematical calculation with basic operations, while keeping the result in mind and continuing to perform other calculations. As the difficulty increases, more complex mathematical operations will be presented. The final result is a score corresponding to the number of correct answers, weighted by the difficulty multiplier (the score may vary depending on the level of difficulty).

2.3.7. Game 7: Semantic associations

The patient is asked to associate icons representing professional figures with icons representing their working tools. As the difficulty increases, more distracting stimuli will be presented. The final result is a score corresponding to the number of correct answers, weighted by the difficulty multiplier (the score may vary depending on the level of difficulty).

Target stimuli are icons representing objects of particular trades or ethnic-cultural classifications (e.g. policeman, singers, Mexican) for a total of 31 categories. Each category is represented by 4 iconic objects (e.g. a police cruiser for policeman) for a total of 124 target icons.

The patient must respond by dragging the target icon within a hollow circle corresponding to the semantic category indicated by a large icon. The stimulus remains on the screen until complete user interaction with the stimuli.

2.4. Outcome measures

Two types of outcome measures were analyzed to quantify the effect of training: performance on neuropsychological tests and scores on functional scales.

A neuropsychological test battery assessed short-term and working memory using Digit span forward and backward and Corsi span forward and backward (Monaco et al., 2013), attention using Attentional matrices (Spinnler & Tognoni, 1987), and executive functions using Stroop test (Caffarra et al., 2002). Standard scores corrected for age and education were considered for the analyses.

The Barthel Index (Mahoney, 1965) was used for functional analysis of activities of daily living; the Beck Anxiety Inventory (Beck & Steer, 1990) was used as a measure of anxiety symptoms.

2.5. Data analysis

Statistical analyses were conducted using Statistical Package for the Jamovi.

According to the Shapiro-Wilk test, the neuropsychological measures of digit span, spatial span, and Stroop tests were not normally distributed, while the scores of attentional matrices were not significantly different from a normal distribution. Therefore, in order to examine significant differences in scores between T0 and T1, paired t tests for attentional matrices and Wilcoxon signed-rank test for digit, spatial spans and Stroop tests were computed, separately for each group (experimental vs. control).

The effect sizes for pre-test –post-test control group designs were estimated, based on the mean pre–post change in the treatment group minus the mean pre–post change in the control group, divided by the pooled pretest standard deviation (Morris, 2018).

T1-T0 differences of the corrected test scores were correlated with T1-T0 differences in BAI and Barthel index scores using Pearson correlations, separately for each group (experimental vs. control).

p-values<0.05 were considered statistically significant.

3. Results

Table 2 reports the mean scores and standard deviations for each test and group, at T0 and T1.

Baseline (T0) performances at each test and functional scales were similar in the experimental vs. control group.

Patients of the experimental but not of the control group showed a significant improvement at T1 relative to T0 in the Attentional Matrices [experimental group: t(14)=4.63, $p < 0.01$; control group: t(14)=1.88, $p > 0.05$), in the Digit Span Forward (experimental group: $W = 4$, $p < 0.05$; control group: $W = 15.5$, $p = 0.9$), in the Spatial Span Backward (experimental group: $W = 4$, $p < 0.05$; control group: $W = 5.50$, $p = 0.2$), in the Stroop test considering Time of execution (experimental group: $W = 101$, $p < 0.05$; control group: $W = 60.5$, $p = 1$).

Both experimental and control group patients showed a significant improvement at T1 relative to T0 in the Spatial Span Forward (experimental

Table 2

Means and standard deviations for Pre- (T0) and Post-rehabilitation (T1) sessions

	Experimental Group		Control Group	
	T0	T1	T0	T1
Digit span forward	3.9 (1.8)	4.6 (1.7)	4.5 (1.7)	4.5 (1.4)
Digit span backward	2.5 (1.4)	2.5 (1.2)	2.4 (0.9)	2.4 (1.2)
Spatial span forward	2.8 (1.5)	3.7 (1)	2.1 (1.7)	3.4 (1)
Spatial span backward	1.4 (1.9)	2.4 (1.9)	1.5 (1.7)	2.2 (1.9)
Attentional matrices	22.7 (15.1)	28.7 (15.1)	13.4 (14.7)	16 (13.9)
Stroop task (Time)	57.1 (49.9)	33.4 (18)	38.5 (24.1)	44.5 (29.9)
Stroop task (errors)	6.5 (7.8)	4.4 (5.2)	5.4 (6.3)	4.4 (5.1)
Barthel Index	29.3 (25.6)	39 (30.1)	32.1 (26.6)	50 (30.2)
BAI scale	13.4 (12)	6.7 (6.7)	15.4 (13.6)	7.6 (6)

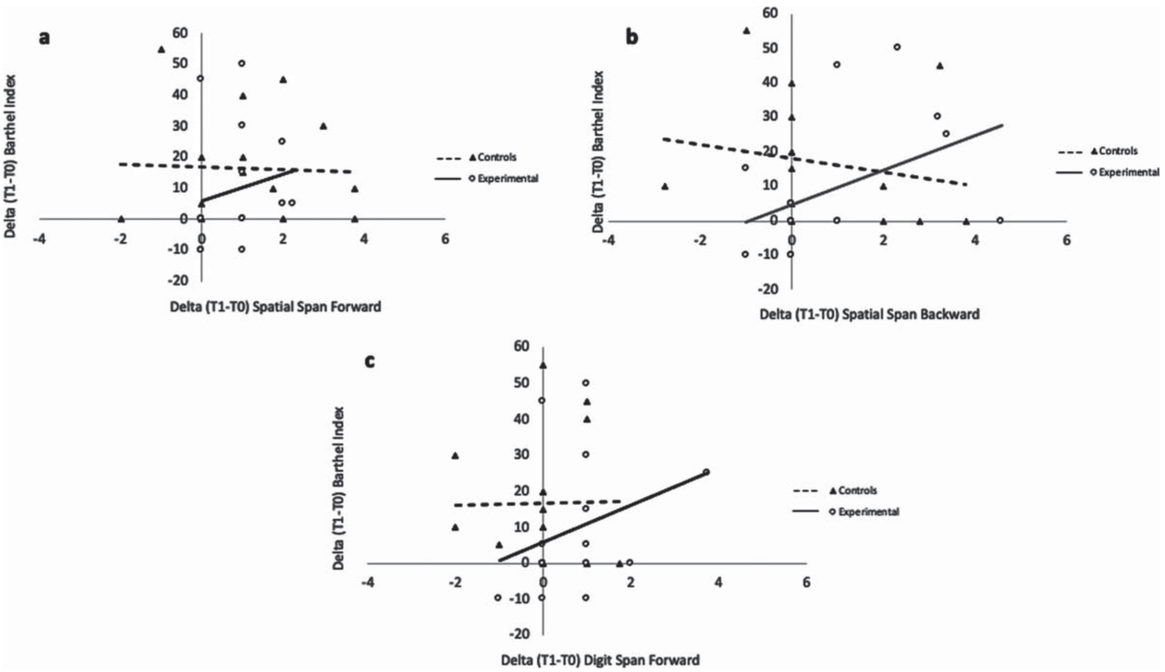

Fig. 1. Correlation between T1-T0 difference (delta) of scores of Spatial Span forward (a), Spatial Span Backward (b) and Digit Span Forward (c) and T1-T0 difference (delta) of scores of the Barthel Index in patients of the control and of the experimental group.

group: $W = 0.00$, $p < 0.01$; control group: $W = 9.50$, $p < 0.05$). There were no significant improvements in the Digit Span Backward (experimental group: $W = 24.5$, $p = 0.8$; control group: $p = 1$) and Stroop test considering errors (experimental group: $W = 82.5$, $p = 0.2$; control group: $W = 56$, $p = 0.2$).

In the experimental group, the group effect size on the post–pre comparison was larger than 0.4 in the Digit span forward ($d = 0.56$) and in the Stroop interference for Time ($d = 1.12$). None of the tests showed a larger positive change in the control group.

Scores on the functional scales revealed significant improvements from the hospital admission to the discharge for both groups (Barthel index: experimental group t(14)=2.15, $p < 0.05$; control group t(14)=3.55, $p < 0.01$; BAI: experimental group: $W = 89.5$, $p < 0.01$, control group; $W = 91.5$, $p < 0.05$). Seven patients in the experimental group and seven patients in the control group underwent an improvement in the Barthel index above the minimal detectable change expected in test–retest assessment [Morris, 2008].

When analyzing correlations between T1-T0 difference in neuropsychological test scores and T1–T0 difference in the Barthel Index score, there was a significant correlation in the experimental but not in the control group for Spatial Span Backward (experimental group: $r = 0.45$, $p = 0.04$; control group: $r = -0.19$, $p = 0.5$) as well as a trend towards significance for Digit Span Forward (experimental group: $r = 0.4$,

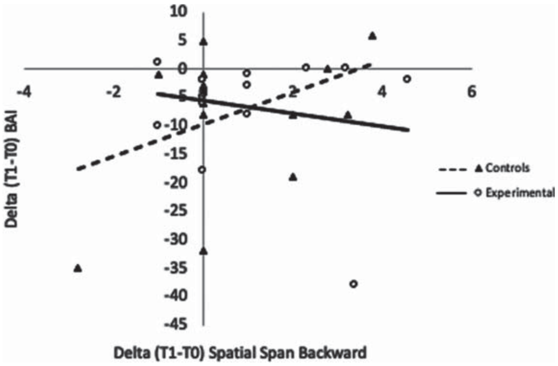

Fig. 2. Correlation between T1-T0 difference (delta) of scores of Spatial Span Backward and T1-T0 difference (delta) of scores of the Beck Anxiety Index in patients of the control and of the experimental group.

$p = 0.08$; control group: $r = 0.01$; $p = 0.9$) and Spatial Span Forward (experimental group:=0.4, $p = 0.07$; control group: $r = -0.03$, $p = 0.9$) (Figure 1 a-c). The difference in the correlation coefficients between experimental vs. control group was significant for the Spatial Span Backward test ($p < 0.05$).

These results suggest that, specifically for the patients of the experimental group, the more they improved in the Spatial Span Forward, Spatial Span Backward and Digit Span Forward tasks, the more they improved in functional activities of daily living along the two weeks rehabilitation period.

When analyzing correlations between T1-T0 difference in neuropsychological test scores and T1-T0 difference in the BAI scale scores, there was a significant correlation in the experimental but not in the control group for Spatial Span Backward (experimental group: r=- 0.46, $p = 0.04$; control group: $r = 0.40$, $p = 0.1$). The difference in the two correlation coefficients between the experimental vs. control group was significant for this test ($p < 0.05$; Figure 2). This result suggests that the more the patients of the experimental group improved in the Spatial Span Backward task, the more they showed a reduction in the anxiety levels along the two weeks rehabilitation period.

4. Discussion

The main results of the present study can be summarized as follows: prism adaptation using prismatic lenses that deviate the visual field to the same side of the affected hemisphere, combined with a digital cognitive training using serious games, improved verbal and spatial working memory, attention and a measure of inhibition (Stroop test) in subacute stroke patients more than standard rehabilitation therapy. Improvements in activities of daily living and in the anxiety levels following rehabilitation were correlated with improvements in some working memory measures, particularly in spatial span backward tasks, selectively in the experimental group.

Prism adaptation is known in the neurorehabilitation literature for its effects on spatial attention in right brain-damaged patients with left neglect. The present results suggest that prism adaptation could also be used in combination with cognitive training for the rehabilitation of other, non-directly spatial, cognitive functions. An explanation of the observed results could be that an improvement of spatial attention induced by prism adaptation (at least in right-brain-damaged patients) could reverberate on other cognitive functions, such as working memory and other executive functions. Indeed, previous studies reported spatial attention effects on other cognitive functions, such as language and executive functions (Chatterje et al., 1995, 1999; Turriziani et al., 2009). However, in the present study, the use of a concurrent exposure prism adaptation procedure, with vision of the arm performing the pointing movements, prevented the development of measurable spatial aftereffects in both right and left brain-damaged patients.

We therefore think that the mechanism underlying the rehabilitative effects is not strictly dependent on the modulation of spatial attention. Related to this, it is worth noting that in the present study, the distribution of patients with neglect at Albert's cancellation and line bisection tasks was unbalanced, with a greater number of neglect patients in the control group. Despite this, the baseline performance on each neuropsychological test and functional scale was similar in the experimental vs. control group. Moreover, the limited number of neglect patients in the experimental group makes it unlikely that any effect of prism adaptation on neglect could explain the cognitive enhancing effects of the procedure on the other neuropsychological tests.

Prism adaptation can increase cortical excitability of the hemisphere ipsilesional to prism deviation, with an effect comparable to that of anodal transcranial direct current stimulation (Magnani et al., 2014; Bracco et al., 2017, 2018). This effect has been observed following either rightward or leftward prism adaptation and it leads to behavioral effects that vary according to the hemisphere being "modulated" by prism adaptation. Consistent with this view, leftward but not rightward prism adaptation selectively increases phonological fluency, i.e. a cognitive function presenting a selective association with left hemispheric frontal circuits (Turriziani et al., 2021). Another example is provided by the finding that leftward but not rightward prism adaptation facilitates reward-based learning, a function more associated with the activation of left hemispheric basal ganglia circuits (Schintu et al., 2018).

Recovery from stroke has been associated with increased cortical excitability (i.e. reduced inhibition) of the affected hemisphere (Cicinelli et al., 2003). Therefore, a selective increase of cortical excitability of the affected hemisphere in stroke patients, induced by rightward prism adaptation in right brain damaged patients and leftward prism adaptation in left brain-damaged ones could be a mechanism promoting cognitive recovery.

This proposed mechanism of action would be similar as that of non-invasive brain stimulation in stroke patients. Previous studies extensively documented that increasing excitation of the affected hemisphere or reducing excitation of the unaffected one induces cognitive recovery of modality specific functions associated to the affected hemisphere, such as language in left-brain-damaged patients or spatial neglect in right-brain-damaged ones (Miniussi et al., 2008; Xu et al., 2022). In this line, the logic behind the improvement of cognitive functions following prism adaptation integrated with digital cognitive training could be similar as that reported for brain stimulation integrated with cognitive training (Myoung-Hwan et al., 2022). The use of digital cognitive training following PA would sustain, rather than directly determine, cognitive effects, exploiting the background of modulation of cortical excitability induced by prisms. Following this logic, in each rehabilitation session, serious games were applied in a temporal window immediately following that of prism adaptation.

In addition to producing effects on cortical excitability, it has been demonstrated that prism adaptation modulates functionally interconnected brain regions of either the hemisphere ipsilateral or contralateral to visual field deviation (Schintu et al., 2020). At a network level, the effects of prism adaptation are subserved by a parietal–temporal network, associated to sensorimotor aftereffects, and by a fronto-cerebellar network, responsible for cognitive aftereffects (Panico et al., 2022). The crucial role of the cerebellum in cognition, for both implicit and explicit processes (Giustiniani et al., 2019, 2021; Oliveri et al., 2007) and the usefulness of stimulation of cerebellar circuits for cognitive rehabilitation in stroke patients (Manto et al., 2022) are further arguments supporting a role for PA, if confirmed by future larger studies, as an additional neuromodulation procedure in stroke.

The mechanism of action based on priming cortical excitability in order to make it more responsive to cognitive training, could operate as a general mechanism in support, rather than as an alternative, of whatever theoretical model of cognitive training.

A main result of the present study is the significant correlation between improvement on some tasks and improvement of activities of daily living, as tested with the Barthel Index, in the experimental but not in the control group. It is well known that the improvement of executive functions in stroke patients is a main target of cognitive rehabilitation. Amelioration of working memory, planning, decision-making and inhibition is likely to generalize to other cognitive and behavioral abilities, making the recovery of functioning stable across time.

The translation to activities of daily living of the benefits of the training with PA and serious games would confirm the hypothesis that training of functions subserved by frontal circuits supports a generalized improvement of other abilities in different neurological diseases, regardless of the specific pattern of brain damage and of cognitive/ impairment (Karbach & Kray, 2009; Weicker et al., 2016; Burgio et al., 2018; Nikravesh et al., 2021; Tarantino et al., 2022).

Another main result of the present study is the correlation between improvement on some tasks and reduction of anxiety levels in the experimental but not in the control group.

Neuropsychiatric symptoms, especially anxiety and depression, are major problems affecting stroke survivors (Deb-Chatterji et al., 2022). Unfortunately, these symptoms are often underdiagnosed in community settings. In particular, the presence of anxiety in the acute phase of a stroke can predict long-term outcomes of the disease in patients with more severe impairments (Kim et al., 2023), although the cognitive impairment six months following a stroke seems to be more related to depression (Williams OA et al., 2021). Therefore, the development of non-pharmacological treatment strategies that address anxiety is an emerging field with likely long-term impact on neurorehabilitation (De Luca et al., 2018; Zhou et al., 2022). Anxiety symptoms in stroke patients are associated with attentional and executive deficits (Kliem et al., 2022). Treatments able to address both attentional/executive deficits and neuropsychiatric symptoms are likely to operate on a common pathophysiological background, i.e. the lack of frontal control on subcortical limbic structures, through neuromodulation of excitability of a brain network involving frontal lobes. According to the neurophysiological and neuroimaging data already discussed, PA modulates large cerebellar-frontal networks. The addition of serious games with executive components to PA could consolidate this neuromodulation effect and generalize it towards behavioral and psychological symptoms associated with defective cortico-limbic control. Further dedicated studies with larger patients' samples and longer follow up times will better address this issue.

In conclusion, although the results of the present study are preliminary given the relatively low sample sizes, they suggest that digital PA and computerized cognitive trainings can offer a new tool for cognitive neurorehabilitation in stroke patients, extending its effects to functional and psychological abilities.

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