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The effectiveness of reinforced feedback in virtual environment in the first 12 months after stroke

Skuteczność terapii w środowisku wirtualnym w pierwszych 12 miesiącach po udarze mózgu

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Abstract

Background and purpose: Reinforced feedback in virtual environment (RFVE) therapy is emerging as an innovative method in rehabilitation, which may be advantageous in the treatment of the affected arm after stroke. The purpose of this study was to investigate the impact of assisted motor training in a virtual environment for the treatment of the upper extremity (UE) after stroke compared to traditional neuromotor rehabilitation (TNR), studying also if differences exist related to the type of stroke (haemorrhagic or ischaemic).
Material and methods: Eighty patients affected by a stroke (48 ischaemic and 32 haemorrhagic) that occurred at least 1 year before were enrolled. The clinical assessment comprising the Fugl-Meyer UE (F-M UE), modified Ashworth (Bohannon & Smith) and Functional Independence Measure scale (FIM) was administered before and after the treatment.
Results: A statistically significant difference between RFVE and TNR groups (Mann-Whitney U-test) was observed in the clinical outcomes of F-M UE and FIM (both $p < 0.001$), but not Ashworth ($p = 0.053$). The outcomes of F-M UE and FIM improved in the RFVE haemorrhagic group and in the TNR haemorrhagic group with a significant difference between groups (both $p < 0.001$), but not for Ashworth ($p = 0.651$). Comparing the RFVE ischaemic group to the TNR ischaemic group, statistically significant differences emerged in F-M UE ($p < 0.001$), FIM ($p < 0.001$), and Ashworth ($p = 0.036$).

Streszczenie

Wstęp i cel pracy: Terapia w środowisku wirtualnym (*reinforced feedback in virtual environment* – RFVE) staje się nowatorską metodą w rehabilitacji, której zastosowanie może mieć korzystny wpływ w leczeniu porażonej kończyny górnej u chorych po udarze mózgu. Celem pracy było zbadanie wpływu terapii RFVE w leczeniu kończyny górnej po udarze mózgu w stosunku do tradycyjnej rehabilitacji neurologicznej (TRN) oraz określenie występowania różnic zależnych od rodzaju udaru mózgu (krwotoczny, niedokrwienny).
Materiał i metody: Badaniom poddano 80 chorych (48 pacjentów po udarze niedokrwiennym i 32 pacjentów po krwotocznym udarze mózgu) z niedowładem połowiczym w okresie do roku po przebytym udarze mózgu. Funkcje kończyny górnej oceniano na początku i po zakończeniu badania. Ocena kliniczna obejmowała skalę Fugl-Meyer dla kończyn górnych (F-M UE), zmodyfikowaną skalę Ashworth (Bohannon & Smith) i skalę *Functional Independence Measure* (FIM).
Wyniki: Zaobserwowano istotne różnice między grupami RFVE i TNR (test U Manna-Whitneya) w ocenie w skalach F-M UE i FIM ($p < 0,001$ dla obu różnic), nie stwierdzono natomiast różnicy w skali Ashworth ($p = 0,053$). Wyniki w skali F-M UE i FIM poprawiły się w grupie chorych z udarem krwotocznym po terapii RFVE i TNR z istotną różnicą pomiędzy grupami ($p < 0,001$ dla obu różnic), nie stwierdzono natomiast różnicy w skali Ashworth ($p = 0,651$). Istotne różnice odnotowano również, porów-

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Conclusions: The RFVE therapy in combination with TNR showed better improvements compared to the TNR treatment only. The RFVE therapy combined with the TNR treatment was more effective than the TNR double training, in both post-ischaemic and post-haemorrhagic groups. We observed improvements in both groups of patients: post-haemorrhagic and post-ischaemic stroke after RFVE training.

Key words: stroke, rehabilitation, motor learning, virtual reality.

nując grupę chorych z udarem niedokrwiennym po terapii RFVE oraz po terapii TNR w skalach F-M UE ($p < 0{,}001$), FIM ($p = 0{,}001$) i Ashworth ($p = 0{,}036$).

Wnioski: Zastosowanie RFVE połączonej z TNR prowadzi do większej poprawy niż leczenie wyłącznie za pomocą TNR. Terapia w środowisku wirtualnym połączona z TNR była skuteczniejsza niż TNR prowadzona dwa razy intensywniej niż zwykle, zarówno u chorych po udarze niedokrwiennym, jak i krwotocznym. Poprawa po RFVE dotyczyła nie tylko chorych po udarze niedokrwiennym, lecz także krwotocznym.

Słowa kluczowe: udar mózgu, rehabilitacja, nauka motoryki, rzeczywistość wirtualna.

Introduction

Stroke is one of the main causes of death and disability in all classes and ethnic origins worldwide. Disability and motor deficit could be particularly evident in upper extremities. Indeed, the loss of mobility of the upper extremity is a major source of impairment in neuromuscular disorders, frequently preventing effective occupational performance and autonomy in daily life [1].

Recent studies demonstrated that the traditional concept of one-to-one rehabilitation [2], where the physical therapist (or more frequently several ones) interacts directly with a single patient, could be advantageously implemented with the use of strategies based on specific kinematic feedback to improve the motor performance [3-7]. Patients affected by a stroke represent a considerable number among those patients suffering from nervous system disorders who need rehabilitation. Epidemiological data indicate a mortality rate of 30% in the first month after stroke independently from the type of cerebrovascular accident, while 10% of patients were discharged from the hospital without serious functional impairment [8]. At least 60% of patients affected by stroke present severely reduced ability to perform activities of daily living (ADL), with persistent symptoms of focal brain lesion [1,8,9].

Reinforced feedback in virtual environment (RFVE) for arm motor training, as demonstrated in previous studies [3,4,6,10-16], represents a possibility in the field of the motor learning based technique for the upper limb. The treatment in the virtual environment with augmented feedback promotes learning in normal subjects and in some post-stroke patients with motor deficit involving the upper extremity [3,16,17]. After a stroke, patients can improve movement ability with regular, intensive and supervised training [2,12,18-20].

The central nervous system (CNS) shows regenerative capacities in post-stroke patients [21,22]. It is also noted that the plasticity of the CNS, thus its adaptability to natural developmental changes, is maintained throughout all the life of a subject regardless of age [23]. Magnetic resonance (MR) imaging and transcranial magnetic stimulation tests in humans provide evidence for functional adaptation of the motor cortex following injury [1,21,24-27]. Neuroimaging has shown evidence of cortical plasticity after task-oriented motor exercises [24,26,28]. Furthermore, many studies have demonstrated that neuroplasticity can occur even in the chronic phase after stroke [1,25,29].

Our study aims to investigate whether the repetition of tasks (intended as oriented movements of the upper extremity performed in interaction with a virtual environment) could improve motor function in post-ischaemic and post-haemorrhagic stroke subjects with hemiparesis, in comparison to the traditional neuromotor rehabilitation (TNR) treatment. The first aim of the study was to determine the effectiveness of RFVE therapy combined with TNR training compared to the double TNR in the treatment of patients after stroke. The second objective was to study the effect of the RFVE therapy, depending on the kind of stroke (haemorrhagic, ischaemic), between patients undergoing the RFVE and TNR therapy compared to the double TNR training.

Material and methods

The study group included inpatients of the Institute of Neurorehabilitation I.R.C.C.S 'San Camillo' in Venice. In the present study, patients affected by a stroke occurring in the period no longer than 1 year before the enrolment (mean time 5.7 ± 3.5 months) and scoring higher than 24 points in the Mini-Mental State Examination (MMSE) were considered. The group consisted of 80 patients (46 men and 34 women); 48 were affected by an ischaemic stroke, 32 by a haemorrhagic stroke, and the mean age was 64.0 ± 16.4 years. For all the participants, the RFVE therapy for upper limb training and/or assessments were first time applied.

Subjects with clinical evidence of cognitive impairment, such as apraxia (score lower than 62 points in the De Renzi test), neglect, language disturbances interfering with verbal comprehension (more than 40 errors in the Token test), upper extremity complete paralysis, upper limb sensory disorders, or post-traumatic injury, which prevented the execution of exercises, were excluded from the study.

All patients were informed about the aims and procedures of the study and written informed consent was obtained from all participants. Approval for this study was obtained from the local ethical committee.

The 80 patients were split randomly into two groups, stratified by the kind of stroke (ischaemic or haemorrhagic) during the recruitment. The RFVE training group consisted of 40 patients who underwent a TNR and the RFVE treatment (including 24 patients with ischaemic stroke and 16 patients with haemorrhagic stroke). The TNR training group included 40 patients who were undergoing TNR training with further treatment dedicated to the upper extremity (including 24 patients with ischaemic stroke and 16 patients with haemorrhagic stroke).

Both treatments lasted 1 hour a day, five days weekly for four weeks. During the experiment, patients in the RFVE training group received 1 hour of TNR treatment and 1 hour of RFVE therapy. The TNR training group patients were treated totally for two hours daily by means of a TNR programme. At the beginning and at the end of the treatment, four weeks thereafter, the motor deficit and the functional activities of the upper extremity were assessed with the Fugl-Meyer scale for the upper extremity (F-M UE) [30]. The spasticity of the arm was determined with the modified Ashworth scale [31]. In addition, a functional assessment was performed with the Functional Independence Measure (FIM) [32].

The patients were undergoing virtual training using a PC (PC workstation: Pentium IV 1.2 GHz, 256 MB RAM, video graphics card 32 MB, LCD projector with high resolution – 1200 Ansi Lumen, 3D motion tracking system-position signal 0.76 mm RMS; orientation signal 0:15 RMS; range resolution of 0.0005 cm/cm and 0025°/°; latency of 4 ms unfiltered; sampling frequency of 120 Hz – Pohlemus 3Space Fastrack, Vermont, USA) and a rehabilitation system called 'Virtual Reality Rehabilitation System (VRRS)' originally developed by the Massachusetts Institute of Technology, Cambridge USA.

During the virtual therapy the subject was seated in front of the wall screen grasping a sensorized real object (ball, disc or cube) with the affected hand. If the grasp was not possible the sensors were fixed on a glove worn by the patient (Fig. 1).

The virtual environment target objects were displayed on the wall screen. The real object held by the subject, equipped with electromagnetic sensors, was matched to the virtual handling object (Fig. 2). The sensor contained in the real object (end-effector) recorded the arm movements by means of a magnetic receiver. The virtual scenarios could be created by the physiotherapist, recording the movements carried out grasping the same sensorized object (for example an envelope, a glass, etc.) used for the patients. Afterwards, the system software displayed a virtual representation (virtual object) of the real object that changed position and orientation on the screen in response to the receiver movement. Hence, the physiotherapist created a sequence of virtual tasks that the patient had to perform on his workstation. Virtual tasks consisted mainly of simple movements, e.g. pouring water from a glass, using a hammer, turning around the centre of a doughnut, etc. The physiotherapist determined the complexity of the task, tailored to the patient's motor deficit. Thereafter, the patient moved the real object (envelope, carafe, hammer) following the trajectory of the corresponding virtual object displayed on the computer screen in accordance with the requested virtual task (Fig. 3).

The TNR programme was based on traditional rehabilitation following stroke, in accordance with the rehabilitative principles to reduce the degree of disability, improve quality of life and reduce direct and indirect costs related to stroke. The patients were asked to perform the exercises of postural control, exercises for hand pre-configuration, manipulative and functional skills exercises, proximal-distal exercises coordination with physiotherapist assistance and without it. The upper limb motions were trained with progressive complexity. To achieve the requested goal (in a horizontal or vertical plane) patients performed various movements, for example: shoulder flexion and extension, shoulder abduction and adduction, shoulder internal and external rotation and shoulder large circular movement, elbow flexion and extension, forearm pronation and supination, hand grasping-release and clenching into a fist. The rehabilitation programme was planned in accordance

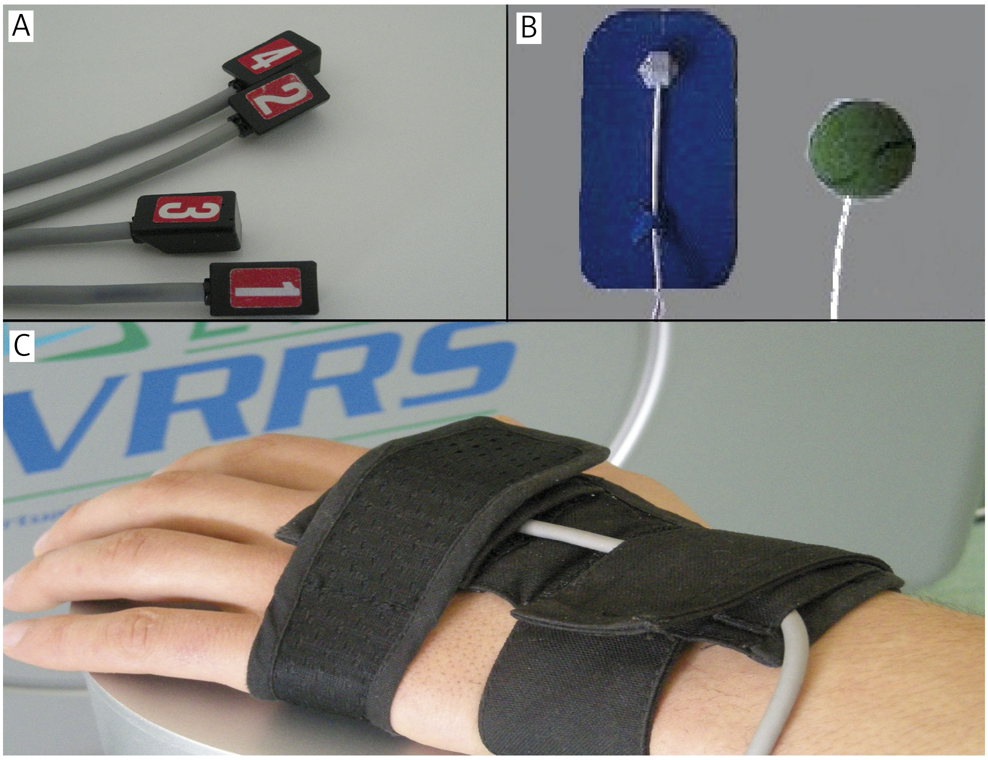

Fig. 1. (A) the receiver types; (B) application of the receivers to objects for performing the required tasks; (C) the glove for the application of the receiver in case of severe motor deficit

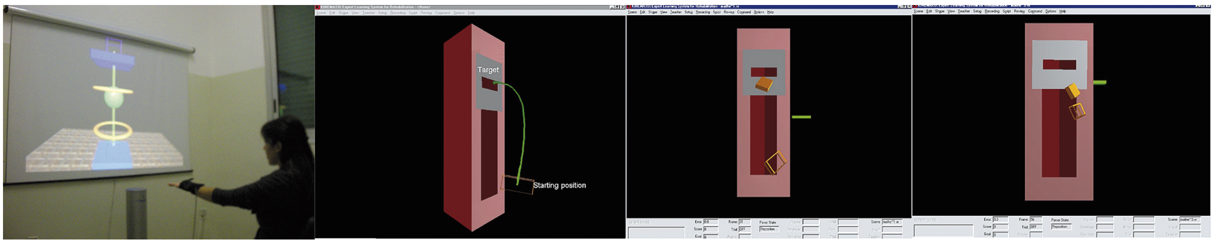

Fig. 2. The location of the starting position, the target and the other objects, virtually represented in the arm workspace, determines the type and the difficulty of movement requested. For example, in a scene where the task consists of posting an envelope in the mailbox, which has different orientation slot positions, the patient is forced to use different muscle synergies to perform the requested movement

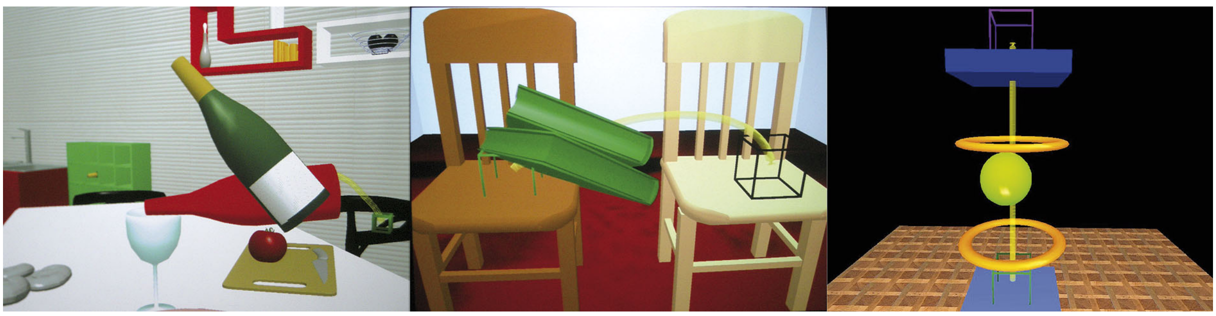

Fig. 3. The therapist could add virtual obstacles (for example a donut, a glass, a ball, etc.) to increase the task complexity

with the patients' current capacity. The individual exercises for each patient were selected (passive, active-assisted or active).

Statistical analysis

The Wilcoxon test was used to determine the statistical significance of the differences in the FM UE mean score, the FIM scale score and the modified Ashworth scale score before and after the therapy in each treatment group and the Mann-Whitney U-test was used for testing the statistical significance of the differences between the groups (RFVE vs. TNR). The normality of the distribution was examined with the Kolmogorov-Smirnov test. Statistical significance was considered at $p \le 0.05$.

Results

All 80 patients completed the study. No patient complained about any discomfort provoked by the RFVE due to interaction with the virtual world, such as cyber-sickness (nausea, vomiting, dizziness, headache, disorientation) [33]. In both groups (RFVE, TNR), all the scale parameters were similar at the beginning, as demonstrated by the absence of any statistical difference in the comparison (F-M UE $p = 0.10$, FIM $p = 0.11$, Ashworth $p = 0.41$).

After a comparison of groups of patients treated with TNR and RFVE training (independently from the kind of stroke), it can be observed that the performed tests, apart from the modified Ashworth scale ($p = 0.053$) showed significant differences between the patients' results (F-M UE $p < 0.001$; FIM $p < 0.001$). The RFVE therapy group showed improvements in the F-M UE scale (24.9%), FIM scale (16.9%) and the modified Ashworth scale (31.2%), respectively. The TNR therapy group demonstrated smaller score improvements in the F-M UE scale (3.7%) and in the FIM scale (4.3%), respectively, but worsening in the modified Ashworth scale (–14.0%) was noted (Table 1).

Significant differences in F-M UE and FIM scales were noted between RFVE and TNR groups among patients after haemorrhagic stroke ($p < 0.001$ for both differences); the difference was not significant in the modified Ashworth scale ($p = 0.651$) (Table 2). The percentage of improvement in clinical scales between RFVE and TNR groups was as follows: F-M UE 24.1% vs. 5.0%; FIM 25.2% vs. 5.1%; modified Ashworth scale 18.4% vs. 12.9%.

Significant differences in all clinical scales were noted between RFVE and TNR groups among patients after ischaemic stroke (F-M UE $p < 0.001$; FIM $p < 0.001$; modified Ashworth $p = 0.036$) (Table 3). The RFVE group of patients after ischaemic stroke demonstrated an improvement in the functional scales (F-M UE 25.5%; FIM 12.5%; and modified Ashworth scale 42.9%). Modest improvement was noted in the TNR group of patients after ischaemic stroke in the F-M UE scale (2.9%) and FIM (3.8%). The modified Ashworth scale showed marked deterioration among those patients (–46.1%).

Finally, we compared results between the RFVE patients training in post-haemorrhagic and post-ischaemic groups. No significant difference was found (F-M UE $p < 0.761$; FIM $p < 0.112$; modified Ashworth $p < 0.281$). We noted improvements in both groups, regardless of the kind of stroke.

In the RFVE training group, 32 of 40 patients demonstrated motor improvement of more than 10% in F-M UE. We observed that differentiation by age did not influence the motor improvements among patients trained in a virtual environment (post-haemorrhagic stroke group: F-M UE $r^2 = 0.096$; FIM $r^2 = 0.002$;

Table 1. Motor and functional performance of post-stroke patients undergoing reinforced feedback in virtual environment (RFVE) and traditional neuromotor rehabilitation (TNR) therapy

Functional scales	Before RFVE	After RFVE	*P*-value	Before TNR	After TNR	*P*-value
Fugl-Meyer Upper Extremity score; mean ± SD	39.1 ± 17.0	48.9 ± 15.2	< 0.001*	44.8 ± 17.4	46.4 ± 17.1	0.003*
Functional Independence Measure score; mean ± SD	90.7 ± 24.3	106.0 ± 19.8	< 0.001*	98.6 ± 20.9	102.9 ± 18.2	< 0.001*
Ashworth scale score; mean ± SD	2.0 ± 2.3	1.3 ± 1.6	0.005*	1.4 ± 1.8	1.6 ± 2.1	0.569

SD – standard deviation

**Significant difference within groups before and after therapy (p ≤ 0.05)*

Table 2. Motor and functional performance of post-haemorrhagic stroke patients undergoing reinforced feedback in virtual environment (RFVE) and traditional neuromotor rehabilitation (TNR) therapy

Functional scales	Before RFVE	After RFVE	*P*-value	Before TNR	After TNR	*P*-value
Fugl-Meyer Upper Extremity score; mean ± SD	39.6 ± 18.8	49.1 ± 16.1	< 0.001*	43.5 ± 18.9	45.6 ± 18.5	0.022*
Functional Independence Measure score; mean ± SD	78.6 ± 28.2	98.4 ± 25.0	< 0.001*	99.8 ± 18.5	104.9 ± 17.1	0.004*
Ashworth scale score; mean ± SD	2.3 ± 2.5	1.9 ± 2.1	0.138	1.9 ± 2.5	1.6 ± 2.3	0.554

SD – standard deviation
**Significant difference within haemorrhagic groups before and after therapy ($p \leq 0.05$).*

Table 3. Motor and functional performance of post-ischaemic stroke patients undergoing reinforced feedback in virtual environment (RFVE) and traditional neuromotor rehabilitation (TNR) therapy

Functional scales	Before RFVE	After RFVE	*P*-value	Before TNR	After TNR	*P*-value
Fugl-Meyer Upper Extremity score; mean ± SD	38.8 ± 16.1	48.7 ± 15.0	< 0.001*	45.6 ± 16.7	47.0 ± 16.4	0.055
Functional Independence Measure score; mean ± SD	98.7 ± 17.8	111.1 ± 13.8	< 0.001*	97.8 ± 22.4	101.6 ± 19.1	0.021*
Ashworth scale score; mean ± SD	1.7 ± 2.3	1.0 ± 1.1	0.017*	1.0 ± 1.1	1.5 ± 2.1	0.213

SD – standard deviation
**Significant difference within post-ischaemic stroke groups before and after therapy ($p \leq 0.05$).*

Ashworth $r^2 = 0.055$; post-ischaemic stroke group: F-M UE $r^2 = 0.073$; FIM $r^2 = 0.0002$; Ashworth $r^2 = 0.009$). We also compared patients who previously had rehabilitation against those subjects who had rehabilitation for the first time. We did not note any correlation (post-haemorrhagic stroke group: F-M UE $r^2 = 0.236$; FIM $r^2 = 0.127$; Ashworth $r^2 = 0.047$; post-ischaemic stroke group: F-M UE $r^2 = 0.002$; FIM $r^2 = 0.203$; Ashworth $r^2 = 0.0000$).

Discussion

In the present study, we demonstrated the therapeutic effect of the RFVE treatment, and stated that RFVE therapy could usefully integrate the TNR treatment. Comparison between the TNR and the RFVE treatment showed significant differences after the application of one of these therapies, in favour of the latter. Indeed, the RFVE therapy group showed better improvement than patients treated with TNR in each scale (F-M UE, FIM, modified Ashworth). In addition, we demonstrated that the kind of stroke does not limit the application of the RFVE therapy. Both post-ischaemic stroke and post-haemorrhagic stroke patients showed improvement of arm function. The results point to the effectiveness of RFVE therapy in patients after ischaemic and haemorrhagic stroke.

In our study, the process of motor recovery after a stroke seems to take advantage from the innovative rehabilitation technique. We confirmed that a virtual reality had a great positive impact on upper limb mobility. Also, the TNR treatment may speed up the processes of recovery, but to a lesser extent. Additionally, some subjects showed positive changes in the F-M UE test of arm function. The changes that we found could be due to either the nature or intensity of the RFVE training or the nature of intensity of the real-world tasks. Because both were incorporated into the study, it is currently not clear whether these improvements were due to the RFVE training, the TNR treatment, or the combination of both.

We also measured how much the RFVE activity could influence a patient's autonomy in activities of daily life (FIM test). The improvement in FIM was significant within both groups and between the groups (RFVE vs. TNR). The modification of the test score underlined the validity of both the RFVE and TNR training for functional gains.

In the first period after a stroke, some neurological mechanisms enforce the attempt to restore the brain functions spontaneously. In the immediate post-acute phase of stroke, indeed, motor function improvement is mostly attributed to the phenomenon of spontaneous recovery and, only in part, to rehabilitation therapies [3]. Several data indicate that plastic changes in the motor cortex of stroke patients occur even after a training session of only 1.5 hours [22]. A single session of physiotherapy produces a use-dependent enlargement of motor cortex representations paralleled by an improvement of motor function in stroke patients [22]. Jang *et al.* [26] suggest that a cortical reorganization in patients with a primary motor cortex (M1) infarct occurs after executing hand grasp-release movements [26]. You *et al*. [29] hypothesize that exercise in a virtual world could induce cortical reorganization of the neural locomotor pathways. Also Carey *et al*. [34] reported significantly greater activation of cortical area M1 during precision-demanding tracking movements than during simple repetitive movements. The effect is probably due to the increased use of the affected hand during the training. It is possible that functional plasticity will likely underlie many of the effects that could be gained by means of virtual reality based rehabilitation. Modalities of feedback are important for motor recovery improvement. Namely, the early predictive phase of movement depends on object shape, regardless of visual feedback availability, and in the late responsive phase the kind of feedback could optimize motor learning [35]. In the specific case, the reinforced feedback has a positive impact on post-stroke recovery and could help enhancing the cortical changes. However, the reinforced feedback in virtual environment treatment, composed of repetitive movements, may indeed have favoured the acquisition of new motor abilities [36]. During the treatment in a virtual environment, the patient could see his motor performance and through the feedback derived from the action could adjust the movements according to the task requirements.

Kahn *et al*. [5], using a robotic device called Assisted Rehabilitation and Measurement (ARM) Guide, suggested that the repetitive movement attempts by the patient are the primary stimuli to recovery. Training with virtual reality also confirmed the efficacy in motor rehabilitation for fine manual dexterity treatment and suggests usefulness in training of cognitive impairments [37-39]. Another study using rehabilitative conventional training to enhance motor recovery following stroke combined with intensive robot-assisted therapy showed improvement. Aisen *et al*. [40] noted that the benefits of the additional robot-assisted therapy could be due to the effect of the intensity of the training and they suggested that 'more therapy is better'.

An important factor contributing to the subjects' learning of the movements may be the specificity and frequency of feedback provided by the system regarding both the knowledge of their performance (KP) and the knowledge of the results of their actions (KR). Augmented feedback in the form of either KP (feedback related to the nature of the movement pattern that was produced) or KR (feedback related to the nature of results produced in terms of the movement goal) is known to enhance motor skill learning in younger adults [13], in the older healthy population [41] and in individuals after stroke [42]. Feedback provides information about the success of the action by the movement of the end-effector in virtual representation and it informs the subjects' perception to adjust the motion errors. Moreover, the motor task correctness was supplied to the patient in the form of simple scores and by displaying arm trajectory morphology on the screen. Therefore, improving the correctness of arm trajectories combined with the novelty and the originality of the RFVE therapy motivated the patients to participate in the rehabilitation session. The great advantage for the physiotherapist of using exercises in a virtual environment is the wealth of objective measures of a patient's performance.

Reinforced feedback in virtual environment is an expensive but also cost-effective system providing intensive rehabilitation treatment. Some data indicate that patients with moderate to severe motor disabilities have better outcomes when treated in more costly inpatient rehabilitation facilities with an intensive rehabilitation programme [43].

The results of this study provide support for future studies of RFVE in order to optimize functional interventions. An important question is whether the improvements seen in virtual environment exercise transfer to changes in activities of daily living. Future studies may explore the implications of these results in a larger cohort of patients of various clinical subcategories.

Conclusions

1. Reinforced feedback in virtual environment therapy in combination with TNR showed better improvements compared to TNR treatment only.
2. Reinforced feedback in virtual environment therapy combined with TNR treatment was more effective than TNR double training, both in patients after ischaemic and after haemorrhagic stroke.

3. Improvements after RFVE training were noted both in patients after ischaemic and after haemorrhagic stroke.

Disclosure

The authors report no conflict of interest.

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