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Combining levodopa and virtual reality-based therapy for the rehabilitation of upper limb after acute stroke: pilot study part II

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Singapore Med J 2016, 1–25

doi: 10.11622/smedj.2016111

Published ahead of print: 17 June 2016

Online version can be found at

<https://sma.org.sg/publications/index.aspx?ID=220>

ABSTRACT

Introduction: This study aimed to evaluate the safety and efficacy of a combination of levodopa and virtual reality (VR)-based therapy for the enhancement of upper limb recovery following acute stroke.

Methods: This was a pilot single-blinded case series of acute stroke patients with upper extremity hemiparesis randomised to standard care with concomitant administration of either levodopa alone (conventional therapy or control group) or combination therapy consisting of VR-based motivational visuomotor feedback training coupled with levodopa neuromodulation (combination therapy or VR group). Main clinical outcome measures were the Fugl-Meyer-Upper Extremity (FM-UE) assessment and Action Research Arm Test (ARAT). Kinematic measurements of the affected upper limb movement were evaluated as a secondary measure of improvement.

Results: Of 42 patients screened, four were enrolled in the VR group and four in the control group, from which two patients dropped out during the trial. Patients receiving combination therapy had clinically significant improvements in FM-UE assessment scores of 16.5 points compared to a 3.0-points improvement among control patients. Similarly, ARAT scores of VR group patients improved by 15.3 points compared to a 10.0-points improvement in the control group. Corresponding improvements were noted in kinematic measures, including hand-path ratio, demonstrating improved quality of upper limb movement in the VR group.

Conclusion: Our results suggest that VR-based therapy and pharmacotherapy may be combined for acute stroke rehabilitation. The bedside acquisition of kinematic measurements allows for an accurate assessment of the quality of limb movement, offering a sensitive clinical tool for quantifying motor recovery during the rehabilitation process after acute stroke.

Keywords: dopamine, kinematics, rehabilitation, stroke, virtual-reality

INTRODUCTION

Stroke is a debilitating condition affecting more than 15 million new patients worldwide annually.^(1,2) One in three affected persons remains permanently impaired due to persistent motor deficits, and this necessitates research into more effective treatments that can increase quality of life for these patients.⁽³⁾ Early rehabilitation is crucial in maximising functional recovery,^(4,5) yet the optimal treatment strategy is still not well defined.⁽⁶⁾ Based on the premise that neuroplasticity can be augmented to enhance the rehabilitative process, diverse modalities, including brain stimulation, robotics, virtual reality (VR) and pharmacotherapy, have been tried as adjunctive treatment for acute stroke, with varying efficacies.^(7,8)

Pharmacological modulation, through the use of dopaminergic agents, has been shown to be safe and potentially beneficial in modulating neuroplasticity though their efficacies as monotherapies have not been established.⁽⁹⁾ On the other hand, VR-based therapy offers high-intensity, repetitive, goal-oriented tasks in a stimulating and enjoyable environment.⁽¹⁰⁾ In some trials, VR has been shown to be more effective than conventional therapeutic interventions for improving arm function.⁽¹¹⁻¹³⁾ However, there is a paucity of research into the use of VR in the acute period after stroke. Few studies so far have attempted to look at the interaction between pharmacological and VR modalities in a mechanism-driven manner.^(10,11)

The majority of data from stroke rehabilitation trials have been obtained through clinical scales, such as the Fugl-Meyer-Upper Extremity (FM-UE) assessment; however, notable limitations, such as floor and ceiling effects, have been reported.⁽¹⁴⁾ This is a particular problem in acute stroke rehabilitation where commonly used scales may not be sensitive enough to detect improvements during a short inpatient rehabilitation stay.⁽¹⁵⁾ Extensive research exploring the clinical relevance and use of kinematic parameters as

outcome measurements has expounded them as being more sensitive and objective for the assessment of patients' rehabilitation potential.^(16,17)

We hypothesised that a two-week VR-based intervention for upper limb rehabilitation during the acute post-stroke period would optimise clinical and kinematic outcomes without prolonging the typical duration of post-stroke inpatient rehabilitation. Secondary aims were to: (a) explore the difference between improvements seen in patients receiving VR-based therapy and those undergoing a comparable amount of conventional occupational therapy; (b) establish the relevance of kinematic measures by investigating their correlation with clinical measures; and (c) assess the acceptance level and overall satisfaction of patients with the use of the VR-based rehabilitation modality.

METHODS

This pilot study was a single-blinded case series of acute stroke patients with upper extremity hemiparesis who were randomised to standard care with concomitant administration of either levodopa alone (conventional therapy or control group) or combination therapy consisting of VR-based motivational visuomotor feedback training coupled with levodopa neuromodulation (combination therapy or VR group). This study compared the tolerability and effectiveness of the combination of VR-based therapy and levodopa against a comparable duration of conventional therapy (i.e. levodopa only) in patients with hemiparesis due to a recent acute ischaemic stroke within 21 days of symptom onset.

Potential participants were screened from acute stroke patients transferred to an inpatient rehabilitation ward. The inclusion criteria were: (a) patients aged 25–99 years, with a first episode of ischaemic stroke within the last 7–21 days; (b) motor power deficit of the affected upper limb assessed using the Medical Research Council scale, with a minimum power of 2; and (c) ability to provide informed consent according to the Mini Mental State

Examination (MMSE), with a score of over 25. Patients were excluded if they were unable to understand study requirements or participate in therapy due to cognitive impairment or aphasia, or had pre-existing motor weakness due to other conditions. Patients with neglect of the affected side were also excluded from the trial. After obtaining informed consent, patients were randomised into the control or VR group using an independent internet-based random number generator.

All patients received standard 1-hour daily sessions of occupational and physiotherapy each. In addition, patients in the VR group received 30 minutes of VR-based therapy (with at least 15 minutes of active therapy) whereas patients in the control group received additional 30 minutes of conventional occupational therapy; each session was conducted daily five days a week for two weeks, as tolerated. The total duration of training in both groups was similar but we were unable to control the type and intensity of therapy administered during the additional occupational therapy sessions. Intervention sessions were targeted at the affected arm, with patients placed in a sitting position. Both groups were given the trial medication levodopa at 1–2 hours before the start of each trial therapy session to allow for adequate absorption and peak plasma levels to be reached by the time of commencing the intervention.

The pharmacotherapy administered was a single daily dose of 125 mg madopar (Roche Products Limited, Welwyn Garden City, UK), which consisted of a combination of 100 mg levodopa and 25 mg benserazide.⁽¹⁸⁾

VR-based therapy consisted of a specially developed software programme that encouraged active elbow flexion and extension movements of the affected arm by simulating the arm bringing as many food items to the mouth as possible within a 90-second interval (Fig. 1). The software interface was a custom-developed system coded using the 3D-game engine developed by Unity Technologies (San Francisco, CA, USA). This visuomotor

interface featured several built-in positive reinforcement signals in the form of an audiovisual feedback each time a successful attempt was made and encouragement to reach for food items at different locations (to increase the range of motion) through the use of a points system. Progression of therapy was encouraged through the ‘unlocking’ of new food items as the patient’s points reached varying levels and a score multiplier, which can be achieved by collecting combinations of food items.

Patients interacted with this programme via wireless inertial measurement units (IMUs) strapped to their affected arm and wrist (Fig. 2). We utilised IMU devices based on the InvenSense MPU-9150 chip (InvenSense, San Jose, CA, USA), a state-of-the-art integrated 9-axis motion tracking device combining a 3-axis MEMS (microelectromechanical systems) gyroscope (InvenSense, San Jose, CA, USA), 3-axis MEMS accelerometer (InvenSense, San Jose, CA, USA), 3-axis MEMS magnetometer (InvenSense, San Jose, CA, USA) and the InvenSense Digital Motion Processor™ (DMP™; InvenSense, San Jose, CA, USA) hardware accelerator engine. We selected these IMUs as they were small and easily wearable (each IMU weighed 15 g), and for their ability to sample a wide range of data. The device featured a user-programmable gyroscope with a full-scale range up to $\pm 2,000^\circ/\text{second}$ and an accelerometer with range up to 16 g force. For the purposes of this study, motion data was transmitted wirelessly to the receiver at a 50-Hz sampling rate. Captured kinematic data included angular velocity, acceleration and position in three-dimensional space. With this high sensitivity recording of minute movements of the elbow joint, the patient’s movement corresponded to the movement of an in-game virtual arm, creating a semi-immersive VR environment in which real-time x, y, z coordinates of the joints were continuously sampled for the calculation of kinematic measurements.

Patients in the VR group played a 90-second VR game ten times during each session for a total activity duration of 15 minutes. They were allowed to rest for up to five minutes

between sessions. Patients were instructed to rest between games to lessen the possibility of fatigue-induced bias. A study coordinator accompanied patients at all times to ensure patient safety in case of injury or photosensitivity-induced seizures from the virtual environment.

Before each therapy session, calibration was performed to record the range of motion of the patient's arm to account for individual and per session differences as the patient improved. Calibration also served to ensure that each session impelled the patient to perform at a skill level that was neither too challenging nor effortless, allowing for optimal motor learning. In addition, the virtual arm extended completely when the calibrated range was reached, even if the patient's arm was not. This observation of an ideal action provided augmented feedback and activated the mirror neuron system, which are recognised factors for motor learning.⁽¹⁸⁾

To track the efficacy of VR intervention with the gaming system, clinical and kinematic measurements were obtained at baseline and post intervention for all patients. To assess the patients' acceptance and satisfaction with the new rehabilitation modality, a short questionnaire was also administered for VR group patients before and after intervention. All measurements were taken at a mean 1.8 ± 0.5 days within the initiation or conclusion of the intervention course.

Clinical assessments were performed by an occupational therapist blinded to the assigned treatment arm. Two clinical measures were chosen to sensitively monitor improvements in different domains of the World Health Organization International Classification of Functioning, Disability and Health, namely that of body function (i.e. FM-UE assessment) and activity (Action Research Arm Test [ARAT]). These are clinically validated assessment tools for the analysis of stroke recovery.⁽¹⁹⁾ The FM-UE assessment score ranges from 0–66 and assesses reflexes, synergy of movements and coordination of upper limb movements. ARAT measures the ability to perform gross upper limb movements

and to grip, grasp and pinch objects with a maximum score of 57, and individual activity scores. For both scales, better ability is indicated by a higher score.

Kinematic assessments were obtained from raw data recorded by the wearable sensors, which consisted of timestamped position data (x, y, z coordinates) of the elbow and wrist joints. As the IMUs were sampled at a rate of 50 Hz, this translated into a large dataset of 4,500 data points for every 90-second game. To translate these data into meaningful kinematic measurements, the hand trajectories and velocity profiles were plotted out for visual inspection and were crosschecked to ensure accuracy. Kinematic measures calculated were: (a) handpath ratio (HPR); (b) number of velocity peaks (#velpeaks); (c) time taken to complete each flexion movement (timetaken); and (d) the total number of flexions performed during each game (#flexions).

HPR is a surrogate marker for movement quality, which is defined as the actual length of the path traversed divided by the shortest distance between the start and end points.⁽¹⁹⁾ A healthy person should have a HPR close to 1, choosing the most optimal path of a straight line to travel between two points. The same parameter has been used in prior literature under different terms,⁽²⁰⁾ and has been shown to approach a ratio of 1 as stroke patients recover.

The number of velocity peaks is another parameter that has been frequently used in the literature based on the understanding that stroke patients' movements tend to comprise multiple sub-movements or frequent correction attempts mid-movement due to a deficit in descending motor commands and ascending sensory feedback.^(16,17,19) Instantaneous velocities were computed, smoothed and transformed into velocity peaks (#velpeaks), which were defined as samples for which the two preceding and two succeeding smoothed samples were monotonically rising and falling, respectively.^(21,22) The number of velocity peaks present during each flexion movement was then summed up and tabulated.

At the end of the trial, a questionnaire was administered to patients in the VR group, which included questions on previous experience with computers, whether patients felt that VR therapy was beneficial and engaging, and if it should be part of routine therapy. Each question in the questionnaire was presented on a 5-point Likert scale.

RESULTS

From January to May 2014, 42 patients were screened for participation in the trial. However, 34 patients were excluded, as 24 did not meet the inclusion criteria and ten patients refused consent. As such, eight patients were enrolled, with four patients randomly assigned to each treatment group. None of the patients in the VR group complained of any discomfort from interaction with the virtual environment. In the control group, two patients dropped out after sessions 2 and 8, respectively, for personal reasons not related to the trial. The flow diagram of patients recruited is illustrated in Fig. 3.

Demographics of the study population are shown in Table I. The mean age of patients was 63.3 years, and mean time from stroke onset to enrolment was 8.7 ± 1.3 days. The mean number of therapy sessions received before discharge was 8.8 ± 0.9 in the VR group and 6.8 ± 1.0 in the control group.

Table I. Demographics of trial patients.

Group	Patient no.	Gender/age (yr)	Affected side	Stroke location	Clinical stroke classification	Duration between stroke and start of trial (day)	No. of therapy sessions completed
VR	2	F/72	L	Brainstem	Ataxic hemiparesis	12	10
	4	M/63	R*	Subcortical	Ataxic hemiparesis	6	6
	5	M/74	L	Subcortical	Pure motor	12	9
	7	M/60	R	Brainstem	Sensorimotor	5	10
Control	1	M/63	L	Subcortical	Ataxic hemiparesis	7	8

	3	M/67	R*	Subcortical	Ataxic hemiparesis	6	8 [†]
	6	M/68	L*	Subcortical	Pure motor	10	2 [†]
	8	M/39	R	Cortical	Pure motor	10	9

*Dominant hand affected. †Dropped out of trial. F: female; L: left-sided weakness; M: male; R: right-sided weakness; VR: virtual reality

VR group patients showed improvement in mean FM-UE score from 36.5 to 53.0 (an improvement of 16.5 points), approaching the maximum achievable score of 66. The control group demonstrated improvement in mean FM-UE score from 62.0 to 65.0. Mean ARAT score for the VR group improved from 15.5 to 30.8 (an improvement of 15.3 points). Comparatively, the control group showed improvement in mean FM-UE score from 62.0 to 65.0 (an improvement of 3.0 points) and mean ARAT score from 42.5 to 52.5 (an improvement of 10.0 points). The FM-UE and ARAT scores for both the control and VR groups are shown below in Fig. 4.

The minimal clinically important difference for FM-UE and ARAT scores have been established at 4.25–7.25⁽²³⁾ and 12–17 (for dominant and non-dominant hands affected) points, respectively.⁽²⁴⁾ The 16.5- and 15.3-point increases achieved in this trial for FM-UE and ARAT scores of VR group patients were thus clinically significant.

Based on clinical observation, two of the four VR group patients had great difficulty performing anti-gravity movements initially and required anti-gravity support at their elbows but were progressively able to play entire games without assistance. Their range of motion also increased, from originally only being able to reach the nearest virtual plate to freely traversing across all virtual plates. Manual motor power testing, as performed by an independent assessor at the start and end of the trial, is presented in Table II.

Table II. Individual patient differences in motor power before and after intervention.

Motor power	Patient no.							
	VR group				Control group			
	2	4	5	7	1	3	6	8
Pre-trial MMT	2	4+	4+	3	4+	3	2	4+
Post-trial MMT	4+	5	4+	4	5	NA*	NA*	5

*Patient dropped out of study. MMT: manual motor power testing; NA: not available; VR: virtual reality

Kinematic data showed corresponding improvements that matched the clinical data results (Fig. 5). For the VR group, mean HPR improved from 2.27 to 1.41 (improvement: -0.86 ± 0.29). The control group had an initial mean HPR of 1.17 and a post-intervention mean HPR of 1.18 (change: 0.02 ± 0.06), which was very close to the optimum HPR of 1 and suggested good movement of the affected limb both pre- and post-intervention. For the VR group, mean #velpeaks improved from 2.63 to 1.34 (change: -1.30 ± 0.23), mean timetaken for each flexion-extension movement improved from 0.59 seconds to 0.41 seconds and mean #flexions per 90-second game improved from 13.2 to 36.9. Correspondingly, for the control group, mean #velpeaks improved from 1.38 to 1.01 (change: -0.37 ± 0.70), mean timetaken improved from 0.40 seconds to 0.31 seconds and mean #flexions per 90-second game improved from 25.3 to 29.5.

Daily observation of patients undergoing VR therapy showed that patients enjoyed the sessions and looked forward to them. None of the patients had any prior experience with conventional gaming systems, and some of the patients aged ≥ 60 years were apprehensive about using computers initially. Despite this, feedback from the questionnaire was highly encouraging. Patients found VR therapy effective and engaging. Some requested for it to be part of routine therapy. When queried on being shown a visual trend of their daily improvement in kinematic measures, patients responded that they could tell how well they were performing each day. Selected responses from the questionnaire are shown in Fig. 6.

DISCUSSION

As observed in the patients undergoing combination therapy of levodopa and VR-based intervention, there was an improvement in the clinical measures of arm function, as assessed by FM-UE assessment and ARAT, despite the short intervention period (i.e. two weeks). In addition, by incorporating an IMU-based bedside VR rehabilitation system, we were able to objectively assess the patients' kinematic measures session by session. The HPR, #velpeaks, time taken and #flexions were found to improve, converging towards scores of the non-paretic arms by the end of the two-week intervention.

We compared our results with three other studies that have used VR-based rehabilitation in acute stroke patients. Kiper et al obtained improvements of 17.6% and 17.9% in FM-UE and Functional Independence Measure scores, respectively,⁽²⁵⁾ while Saposnik et al obtained a 20.1% clinical improvement on the Box and Block Test⁽²⁶⁾ and da Silva Cameirão et al attained a remarkable 46.0% improvement in FM-UE scores.⁽²⁷⁾ None of these studies used a neuromodulatory medication. Our intervention study group achieved a notable 45.2% improvement in FM-UE scores and 98.7% improvement in ARAT scores.

Statistical analysis of the corroboration of the clinical to kinematic data was not performed in view of the inadequate number of patients in our study. However, it is likely that the improvements seen during clinical testing were matched by quantitative improvements in movement quality, as measured by kinematics given that HPR, #velpeaks and time taken for each flexion-extension movement values became smaller, which indicated an enhanced quality of movement, and the FM-UE and ARAT scores improved.

Findings of our study have implications for the elucidation of neurobiological mechanisms that inform the optimal rehabilitation strategy in the acute post-stroke period. Levodopa may potentiate towards neuronal rewiring, as suggested by early reports that demonstrated its effectiveness,⁽²⁸⁾ but this effect may be highly reliant on the type of

rehabilitative intervention.⁽²⁹⁾ Since dopamine is a neurotransmitter that is associated with learning and memory of response-reward associations,⁽³⁰⁾ we postulated that other factors that increase motivation to participate in rehabilitation may synergise with dopaminergic neuromodulation, leading to enhanced motor learning. In this respect, our use of a simple VR gaming system accomplished this task by being able to: (a) train a purposeful massed movement (bringing food to one's mouth) in a semi-immersive environment; (b) provide direct feedback on quantifiable daily improvement in kinematic parameters; and (c) enhance positive reinforcement through the use of stimulating audiovisual visuomotor feedback. Therefore, it can be hypothesised that although pharmacologic neuromodulation may set the stage for brain plasticity, the optimal rehabilitation protocol has to incorporate factors such as visual, auditory and tactile feedback in order to be effective. While it is known that photosensitive epilepsy may be triggered by the visual stimulation from video games, seizures that occur after stroke are more closely associated with the severity of the stroke, location of stroke and haemorrhagic strokes.^(31,32) There is no significant evidence that stroke may lower the threshold for seizures but it may be prudent to be mindful of the risk of this occurring during the course of visual stimulation when using VR-based therapy.

Given the simple setup and ease of use of the VR environment presented herein, future studies investigating the integration of pharmacotherapy and VR-based therapy in stroke rehabilitation, with the aim to dissect the exact contributions made by each modality, are highly recommended.

The strong correlations between most kinematic measures obtained in this study and the clinical measurements are important contributors in the search for a more objective, quantitative way of tracking rehabilitation outcomes. Kinematic measures have been shown to correlate well with clinical measures of upper extremity function in previous studies.^(10,14,16) Individual kinematic parameters may represent certain aspects of neurological

function, such as motor function or coordination, but our results show that kinematic measures correlate more strongly with total FM-UE scores and thus represent overall function of the trained upper extremity.

To the best of our knowledge, kinematic outcome measures have not been integrated as a form of regular feedback to patients on their often overlooked or indiscernible daily improvements. One study developed a customised game that could adjust difficulty levels autonomously based on speed, range of movement and latency to movement onset but feedback on these parameters were not given to patients as testimony of their improvements.⁽²⁷⁾ Another study used kinematic measures in addition to clinical scales as baseline and post-intervention outcome measures for the effectiveness of VR rehabilitation in chronic stroke patients but there was no information on whether this data was communicated to patients.⁽³³⁾ By comparison, our system allowed for session-by-session graphical feedback to patients on their performance improvements during the game sessions.

With the increasing availability and development of wearable sensors that capture movement, there is compelling potential in the use of kinematic measures as outcome measures for stroke rehabilitation. Not only are these measures more sensitive and objective, their ability to quantitatively track progress while undergoing rehabilitation also simultaneously removes the need for therapists to perform additional evaluation sessions.

Based on the preliminary results provided by this study, we postulate that kinematic outcome measures may benefit all key players in rehabilitation – patients, clinicians, therapists and researchers; patients remain motivated with their visible daily improvements, clinicians and therapists obtain information necessary to intervene in a timelier manner, and researchers possess a more objective and quantitative way of tracking outcomes across different sites.

There were several limitations to our study. The clinical numbers too small to arrive at firm conclusions about the clinical significance and efficacy of VR-based therapy combined with pharmacotherapy in acute stroke rehabilitation. However, there was a trend toward improvement in the VR group and this needs to be verified in future studies. Patients' feedback suggested that many were uncomfortable with taking an additional pharmacological agent for the purpose of the trial and this likely contributed to the poor recruitment rate. Also, as a result of the small patient numbers and subsequent dropouts from the control group, the functional levels of the control group were high to begin with. This led to a ceiling effect on the rate of improvement that this group made.

A third control arm of patients not given any additional pharmacological or VR therapy to account for spontaneous recovery from stroke would have been ideal, but this was not undertaken because of manpower and time constraints. Instead, it was postulated that the trial control group would improve at least as much as patients undergoing a conventional stroke rehabilitation programme. Nonetheless, we are planning for a follow-up larger study with such a third arm to control for spontaneous recovery.

We were unable to fully control the type and intensity of the additional occupational therapy provided to control group patients, as the direction of therapy is often dependent on the interactions between the patient and therapist. Nonetheless, we instructed the performing occupational therapist to focus on arm flexion-extension exercises as far as possible so as to mimic the VR therapeutic intervention.

A specific limitation concerning the IMUs would be gyroscope drift due to the inherent design in small form-factor MEMS utilised in these types of studies. This is a challenging issue, as different drifting patterns are observed for individual sensors and algorithm refinements require further development. Lastly, patients were only followed-up for two weeks in this study, which was too short an evaluation period to determine if VR

therapy resulted in sustained improvements. Also, out of the ten patients recruited, only two patients returned for review at the third month after discharge.

In conclusion, this pilot study demonstrated that VR-based therapy and pharmacotherapy might be combined for acute stroke rehabilitation and objective data gathered for analysis. In addition, daily kinematic measurements were found to be a useful additional tool for tracking upper limb performance. Future studies with larger number of patients and longer follow-up would need to be performed to evaluate if VR-based therapy and pharmacotherapy in the acute stages after stroke significantly improves upper limb recovery both in terms of rate and degree of eventual recovery, and whether this effect is sustained and clinically significant in the long term.

ACKNOWLEDGEMENTS

This research was supported by the National Research Foundation, Prime Minister's Office, Singapore, under its IDM Futures Funding Initiative and administered by the Interactive and Digital Media Programme Office. This research is also part of an ongoing research initiative funded by the Singapore General Hospital's Department of Medicine 'Pitch For Funds' Grant.

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FIGURES



Fig. 1 Screen capture of the virtual reality-based game shows plates of local delicacies and the avatar arm reaching for the food items. Patient's total score for this session, remaining playing time and score multiplier indicator are visible in the upper portion of the screen.



Fig. 2 Photograph of the virtual reality rehabilitation setup shows a patient engaged in the virtual reality-based game. Two inertial measurement units are strapped to the patient's right arm (above the elbow) and forearm (above the wrist). A wireless receiver can be seen on the table adjacent to the laptop computer.

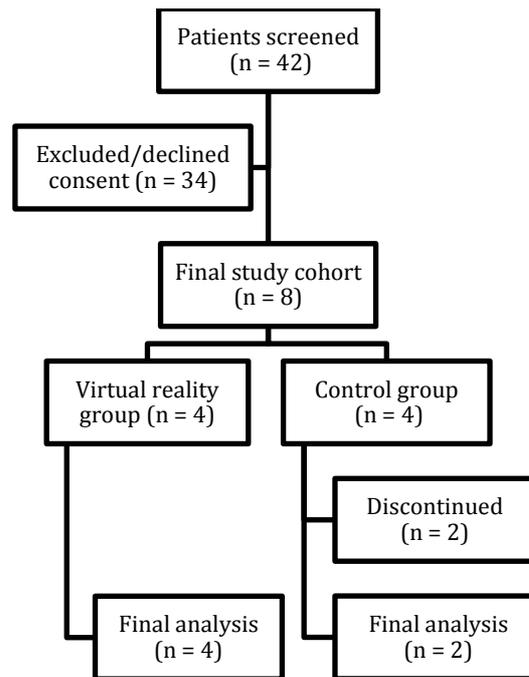


Fig. 3 Flow diagram shows the recruitment of patients into the virtual reality and control groups.

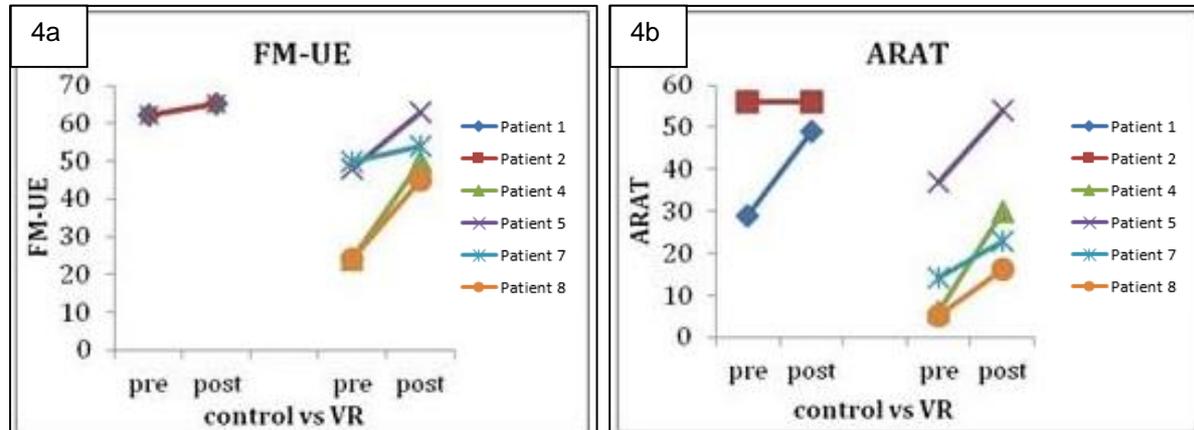
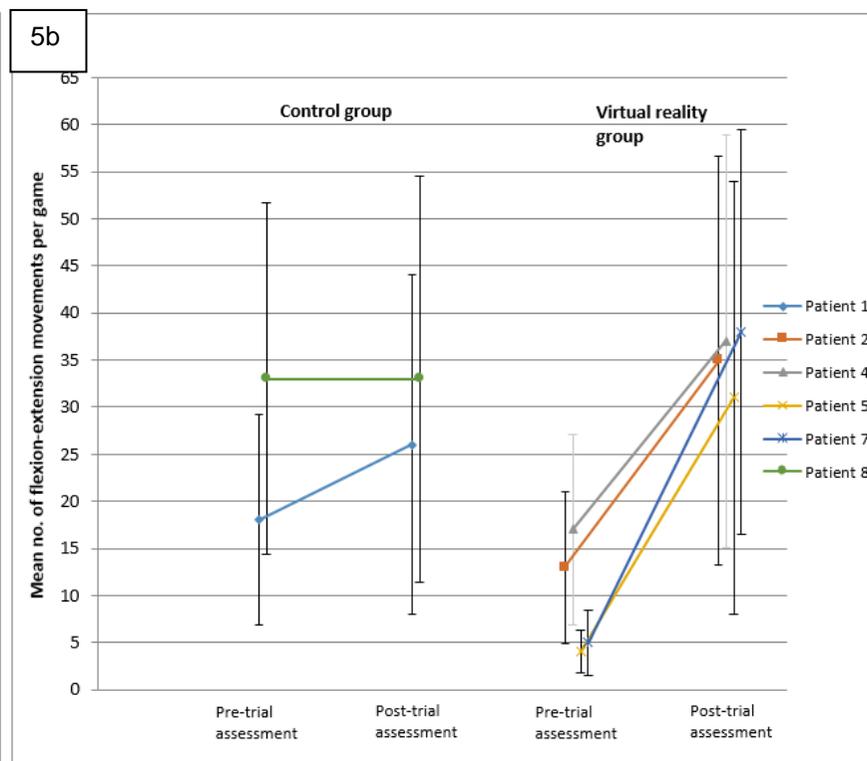
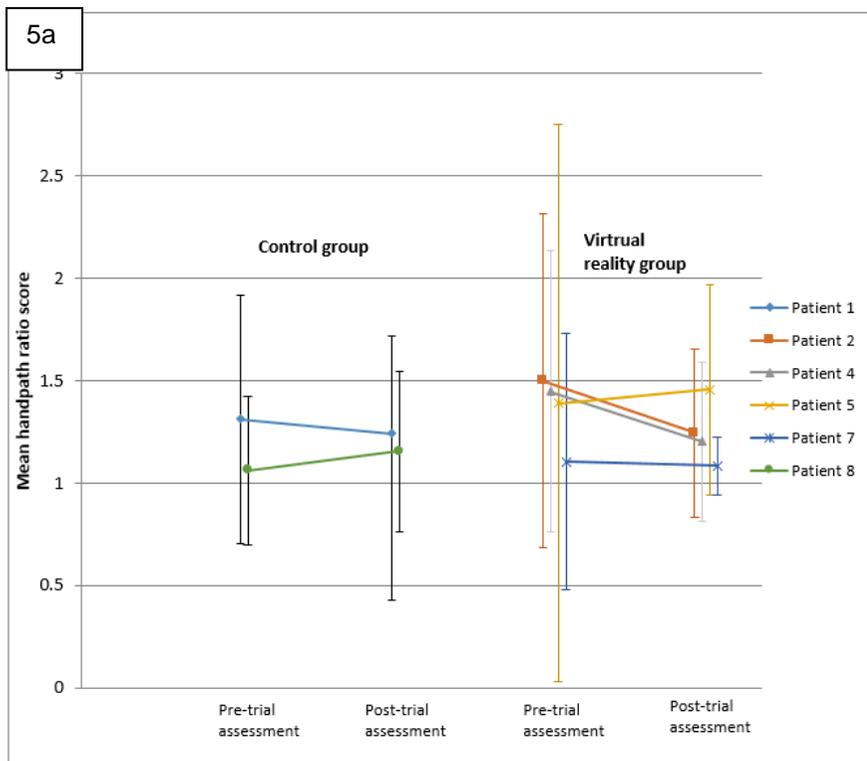


Fig. 4 Plot graphs show the (a) Fugl-Meyer-Upper Extremity (FM-UE) assessment and (b) Action Research Arm Test (ARAT) scores achieved by control and virtual reality (VR) group patients pre- and post-rehabilitation.



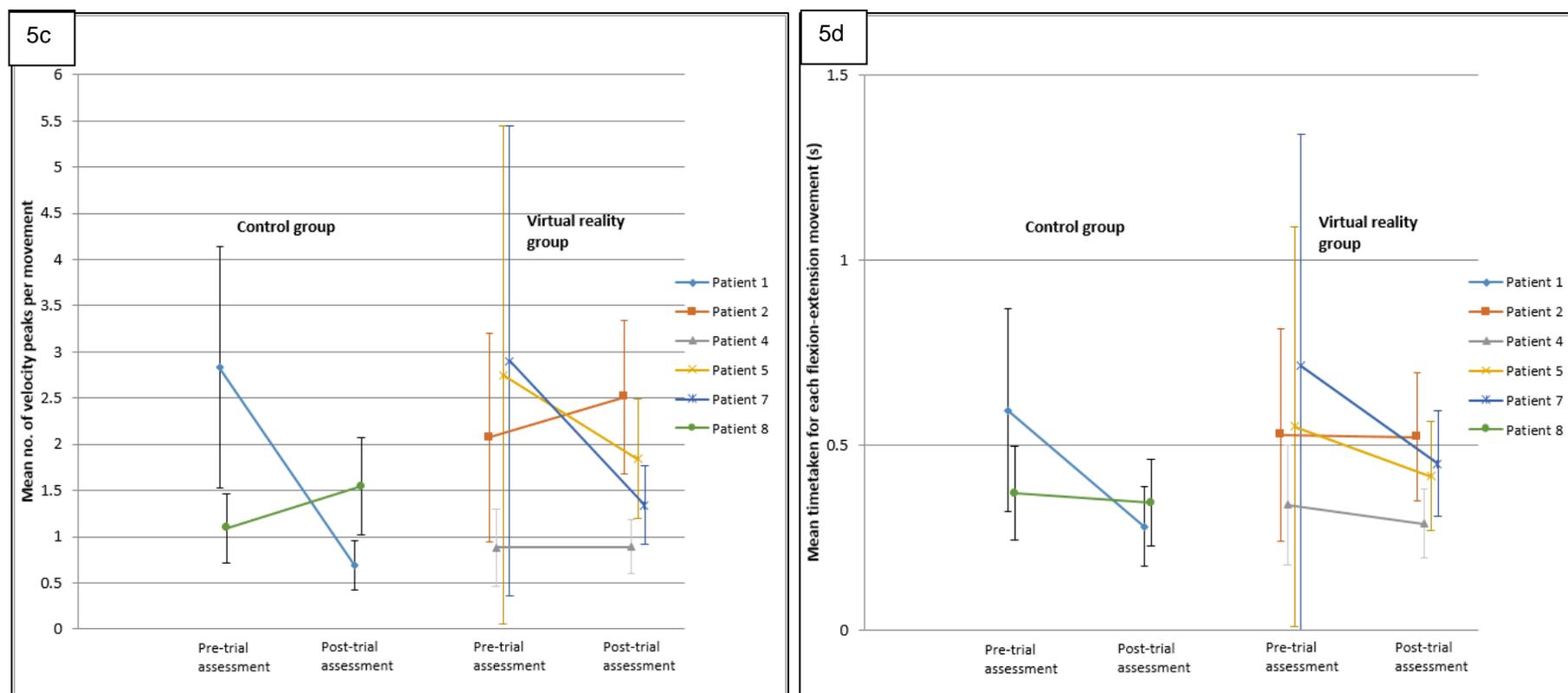


Fig. 5 Line graphs comparing pre- and post-trial assessment scores of the control and virtual reality group patients show changes in the kinematics of upper limb movement, as measured by mean (a) handpath ratio scores, (b) number of flexion-extension movements per game, (c) number of velocity peaks per movement, and (d) time taken for each movement, in patients who underwent combination therapy.

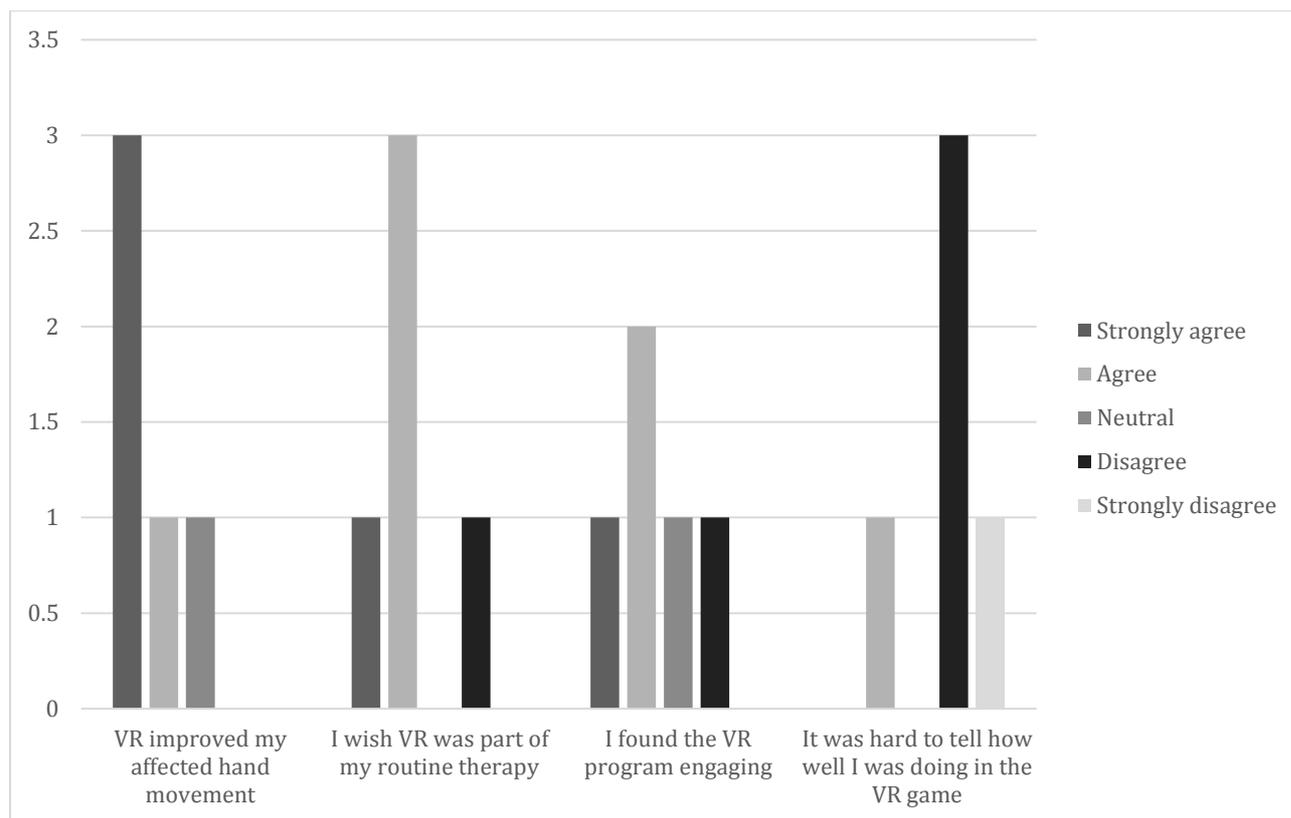


Fig. 6 Chart shows patients' responses to the questionnaire on the virtual reality (VR)-based game.