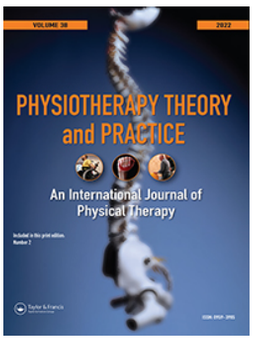

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Implementing technology enhanced real-time action observation therapy in persons with chronic stroke: A pilot study

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ABSTRACT

This pilot study examined a novel technology-enhanced real-time action observation therapy (TERTAOT) of symmetrical bilateral movements in survivors of chronic stroke regardless of their ability to move their paretic limb(s). The TERTAOT used a Kinect XBox One to project mirror images of non-paretic limbs as participants performed symmetrical bilateral motor tasks involving whole-body movements in sitting or standing. The participants received eight weeks of treatment consisting of 30-minutes of conventional physical therapy (balance training, gait training, neuromuscular reeducation, and generalized strength training) and 30-minutes of the TERTAOT protocol per session (three sessions per week for a total of 24 sessions). Ten Meter Walk Test (10MWT), Five Times Sit-to-Stand (5TSTS), Timed Up and Go (TUG), Motor Activity Log – Quality of Movement (QOM) and Amount of Use (AOU) were administered at baseline (pretest), 4 weeks (posttest 1) and 8 weeks (posttest 2) post-TERTAOT, and 3 months after TERTAOT ended (retention). A General Linear Model Repeated Measures (parametric test) or the Friedman Test (non-parametric test) was used to compare outcomes across time points, depending on the normality of data distribution. Bonferroni post-hoc corrections were applied. Seventeen participants completed >80% of TERTAOT sessions without adverse events. The effect of time was significant for 10MWT (p = .001), 5TSTS (p = .001), TUG (p = .005), QOM (p = .001), and AOU (p = .017). TERTAOT may be feasible to be implemented in an outpatient setting. Improvements in functional outcomes including gait, balance, and use of upper limbs were observed after eight weeks of conventional therapy and TERTAOT protocol in survivors of chronic stroke.

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Stroke; technology; rehabilitation

Introduction

Conventional rehabilitation, such as manual therapy, neuromuscular reeducation, strengthening, stretching, and task-oriented training have shown to promote motor recovery post-stroke (Borges et al., 2018; Lin et al., 2019; Livingston-Thomas et al., 2016; Perez-Cruzado, Merchan-Baeza, Gonzalez-Sanchez, and Cuesta-Vargas, 2017; Salazar et al., 2018; Thieme et al., 2018). Experimental interventions based on motor simulation, specifically action observation (AO) and mirror therapy (MT), are effective, easily accessible, and safe for stroke survivors (Borges et al., 2018; Lin et al., 2019; Thieme et al., 2018). Systematic reviews have found significant positive effects of AO and MT on improving motor function, motor impairments, and activities of daily living in stroke survivors (Lin et al., 2019; Perez-Cruzado, Merchan-Baeza, Gonzalez-Sanchez, and Cuesta-Vargas, 2017; Thieme et al., 2018; Zhang, Fong, Welage, and Liu, 2018).

AO requires the participant to watch a healthy individual performing a motor task in person or on a video, which is often followed by physically executing the same task (Borges et al., 2018). AO can be applied using the first-person perspective (1PP), as if the observer is performing the action themselves, or the third-person perspective (3PP), as if another person is performing it (Borges et al., 2018; Hsieh et al., 2020). Both 1PP and 3PP of AO are associated with similar patterns and extent of activation in the mirror neuron systems (Ge et al., 2018). Functional magnetic resonance imaging (fMRI) revealed that both AO and movement execution activate common brain areas, including the inferior parietal lobe, primary motor cortex, premotor cortex, and insula in stroke survivors and healthy individuals (Brunner, Skouen, Ersland, and Gruner, 2014; Buccino, 2014; Zhang, Fong, Welage, and Liu, 2018). Therefore, AO likely results in benefits similar to physical practice of

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a movement task. Using the fMRI, Ertelt et al. (2007) demonstrated that AO with concomitant physical training of the observed action improved motor skills in survivors of chronic stroke (>6 months post onset) by reactivating the motor system. Compared to survivors in the control group, those in the AO group had a significant increase in activity in bilateral premotor cortex, superior temporal gyrus, supplementary motor area, and the contralateral supramarginal gyrus after training (Ertelt et al., 2007). A positive effect of 4 weeks of AO on improving the motor performance was also observed in survivors of subacute stroke (Franceschini et al., 2012). A recent systematic review identifies strong evidence supporting the use of AO for rehabilitation of stroke survivors to improve upper limb function, walking ability and balance (Ryan et al., 2021). Taken together, AO is advantageous in enhancing the neural reorganization and clinical outcome of stroke survivors.

MT involves portraying visual stimuli through the observation of the participants' non-paretic body part as it carries out movements, while placing the paretic body part behind a mirror (Ramachandran and Altschuler, 2009). Compared to viewing the inactive limb directly, viewing the mirror image of the participant's active limb movement increases the excitability of neurons in the ipsilateral sensorimotor cortex and areas involved in attention and monitoring of movements (Deconinck et al., 2015; Guo et al., 2016). MT may assist in functional recovery post stroke by recruiting the mirror neuron system, facilitating reorganization of the affected primary motor cortex, and attenuating hemispheric asymmetry and interhemispheric inhibition (Bartur, Pratt, Frenkel-Toledo, and Soroker, 2018; Deconinck et al., 2015; Michielsen et al., 2011). When utilizing MT in survivors of stroke, MT likely provides the substitute of proprioceptive feedback from the paretic limb and creates a direct visual perceptual cue of the paretic limb moving normally (Deconinck et al., 2015; Ramachandran and Altschuler, 2009). One limitation of MT in stroke rehabilitation is that the individuals' movements may be restricted by the need to place the mirror in the middle of the individuals in order to reflect the image of the non-paretic limb. An alternative way to using a mirror in MT is creating a mirrored image using technology. Indeed fMRI studies have demonstrated that computer generated "mirrored" images of non-paretic limb movements recruit similar neural networks as the reflection of movements in a mirror and the real movement of the paretic limb (Adamovich, August, Merians, and Tunik, 2009; Tunik et al., 2011). Thus, stroke survivors may benefit from mirror therapy that utilizes technology to create realistic visual representations of the paretic side of the body.

AO and MT are typically used separately in rehabilitation of stroke survivors but are supported by similar neuroscience basis involving the mirror neuron system (Adamovich, August, Merians, and Tunik, 2009; Shih et al., 2017; Stevens and Stoykov, 2003). AO requires the participants to observe the normal motor action and then perform the same action, while MT involves observing the mirror reflections of the non-paretic limb. The technology that combines AO and MT remains to be developed. In the context of stroke rehabilitation, we proposed a novel approach combining AO and MT that allows the participants to observe the mirrored reflection of the non-paretic limb and the real image of the non-paretic limb at the same time as they perform the symmetrical bilateral movements. The researchers in this study created a technology to combine a third-person visual perspective (AO) with a first-person internal visual perspective (MT) using the Microsoft Kinect interface. Essentially, this novel technology allows the participants to observe the symmetrical bilateral movements that are under their volitional control, regardless of their ability to move the paretic limbs(s). The research questions were: 1) Is the eight-week therapy using the TERTAOT protocol safe and feasible to be implemented in survivors of chronic stroke at an outpatient setting; and 2) Can the participants improve motor function after the eight-week intervention? It was hypothesized that 1) The participants would attend ≥80% of the treatment sessions over eight weeks without adverse events; and 2) The intervention would increase the scores of outcome measures for mobility, balance, and movement quality and use of upper limbs at the end of intervention and at three-month retention post-intervention.

Methods

Design

This study was a single group repeated measures design.

Participants

We recruited patients receiving outpatient rehabilitation at Michigan Medicine to participate in the study. Inclusion criteria were adults aged ≥40 years; ≥ six months post onset of stroke at the time of study enrollment; able to follow commands in English; medically stable; without acute illness; without chest pain or

shortness of breath while walking or performing light activities; able to rise from and sit down on a standard height chair (16–18 inches) without assistance from another person; and able to stand or walk independently or moderate independently with an assistive device and/or an ankle foot orthosis. Exclusion criteria were adults with cognitive impairments as measured by a score <24/30 on Mini Mental State Examination; a diagnoses of cancer involving the nervous or musculoskeletal system; severe pain in the arms, legs, or spine measured by >6/10 using Verbal Numerical Pain Rating Scale; a diagnosis of other neurological diseases except for stroke; as well as individuals at the advanced stage of a disease and with less than 12 months to live. Regardless of the level of spasticity present and/or range of motion limitation of the paretic limbs, individuals meeting all other criteria were eligible to participate. All participants provided written informed consent. The study was approved by the Institutional Review Board of University of Michigan Medical School and registered Clinical Trial Registration Number: NCT03780296

Instrumentation

Real-time action observation of the entire participant's body with a mirrored image of the non-paretic side of each participant was created using the Microsoft Xbox One Kinect. The Kinect hardware sensor consists of an infrared light projector, time-of-flight depth-sensing camera, and a visible-light color video camera. The Kinect software, including the driver and software development kit, communicates with its hardware to recognize human profiles based on six-degree-of freedom pose data (x, y, z, roll, pitch, yaw) from 25 labeled joints (e.g. left elbow, right elbow, left knee, etc). The Kinect device does not require calibration for a participant in order to create a human profile. The pose location data from the non-paretic side of the body are used to create a mirrored image that replaces the actual image of the paretic side to simulate mirror therapy. This mirrored image and the actual image of the non-paretic side of the body are then used to create a three-dimensional avatar. This software for creating the avatar is an application of the University of Michigan's "Jugular" virtual reality system (Jugular 4.0 development). Figure 1 shows the setup of the Kinect during a treatment session. We used a gaming computer (Alienware CMIT ID: 2016AO4766) to run the Kinect software and projected the avatar on a 65" television screen placed 10.5 feet in front of the participant who performed the TERTAOT exercises while observing the avatar performing symmetrical bilateral movements in real-time.

Protocol

Each treatment session included 30-minutes of conventional physical therapy (i.e. balance training, gait training, neuromuscular reeducation, and generalized strength training) followed by 30-minutes of therapy using the TERTAOT. The participants attended three sessions per week at an outpatient clinic for eight weeks for a total of

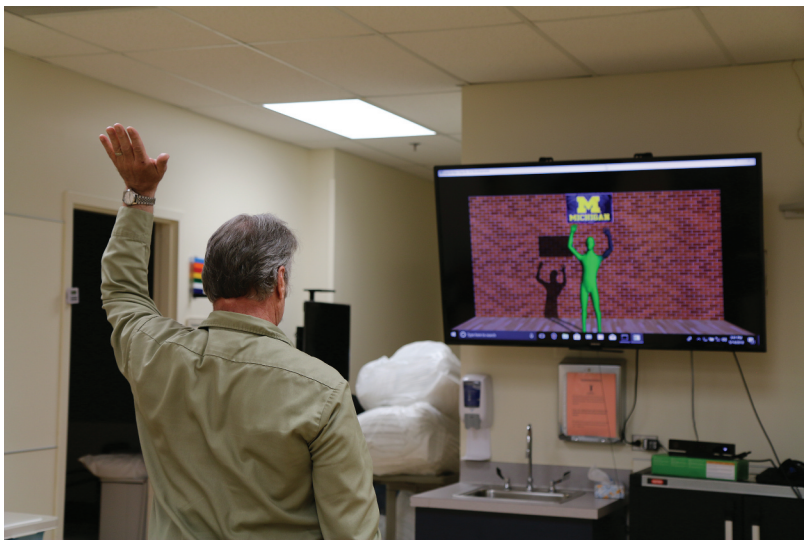

Figure 1. The set up for technology-enhanced real-time action observation therapy (TERTAOT) during a treatment session is shown. The Kinect Xbox One sensor (placed at 10 feet from the participant) captures the participant's pose data. The Jugular virtual reality system (Jugular 4.0 development) by the University of Michigan processes the Kinect pose data to create an avatar by replacing the image of the paretic limb/side of the participant with the image of the non-paretic limb/side. The Kinect application does not require preparation or calibration for the participant before each session. To begin the TERTAOT, the participant sat in a standard height chair at 10.5 feet away from the television screen and performed the TERTAOT exercises while observing the avatar performing symmetrical bilateral movements in real-time.

Table 1. TERTAOT exercise protocol.

UE Reaching Tasks in Sitting	LE Exercises in Sitting and Standing	UE Reaching Tasks in Standing
Seated reaching performing alternate repetitions of bilateral shoulder flexion and bilateral shoulder abduction	Seated leg kick with synchronous bilateral leg lift	Standing reaching performing alternate repetitions of bilateral shoulder flexion and bilateral shoulder abduction
Seated bilateral hands to head	Seated lower extremity abduction and adduction with uninvolved leg	Standing bilateral hands to head
Seated bilateral UE PNF D2 flexion pattern	Sit to stand (use assistive device if needed)	Standing bilateral UE PNF D2 flexion pattern
	Mini-squats	Standing reach to a flag

The exercise protocol was a circuit activity whereby the participants performed 3 sets 15 repetitions (up to 495 repetitions total in a session as some participants were faster and some were slower in completing the exercises). The participant performed each exercise in the circuit before beginning another set. A 15-second rest break was offered after each individual exercise set. Supervision from the investigator was given in the form of verbal and tactile guidance as well as contact guard assist to ensure safety and reduce fall risk.

TERTAOT, technology enhanced real-time action observation therapy; UE, upper extremity; LE, lower extremity; PNF, proprioceptive neuromuscular facilitation

24 sessions. After completing eight weeks of physical therapy, the participants were provided individualized home exercise programs and instructed to continue engaging the paretic limb/side for activities of daily living such as raising the paretic arm to apply deodorant or turning a doorknob. The study participant sat in a standard height chair approximately 10 feet from the Kinect sensor and 10.5 feet from the television screen to begin the exercise. The participants performed the TERTAOT exercises while observing the avatar at the same time. As soon as the participants began moving, the Kinect captured their pose data and displayed, in real-time, an avatar performing the same bilateral movement in a normal pattern. The exercises involved bilateral activities, including seated bilateral upper extremity reaching to a target flag on the screen, seated and standing bilateral lower extremity exercises, and standing bilateral upper extremity reaching exercises (Table 1). Supervision from one of the study's investigators was given in the form of verbal and tactile guidance as well as contact guard assist to ensure safety and reduce fall risk. If the participants could not perform the tasks, they were instructed to observe the avatar and executed the movement to the best of their ability.

Measurements

Recruitment, adherence, and adverse events

The numbers of participants who provided consent, completed TERTAOT and all the assessments were tracked. The research investigators monitored any adverse events throughout the study through interviewing and reviews of medical charts. Adverse events were defined as any unfavorable medical occurrence in a participant, including death, inpatient hospitalization, falls, or other serious medical conditions that may not result in deaths or hospitalization that were temporally associated with the participant's participation in the study.

Mobility, balance, and upper limb motor function

Measurements were conducted by one of the investigators at the initial evaluation (pretest), at one month (posttest 1) and at two months (posttest 2) after starting TERTAOT, and at three months after TERTAOT ended (retention). Posttest 1 reassessment at 30 days was designed to follow the conventional protocol in routine physical therapy care. Outcome measures that are highly recommended or recommended for use at the outpatient setting by the StrokEDGE task force of the Academy of Neurologic Physical Therapy (Sullivan et al., 2013) were selected.

10-meter walk test

The 10-Meter Walk Test (10MWT) was used to measure mobility by gait speed. The participants walked at their own comfortable pace over a 10-meter walkway (Watson, 2002). The participants were allowed to use their assistive device and/or ankle foot orthosis to complete the test. The time taken to walk the middle six meters from the 2-meter mark to the 8-meter mark was recorded to calculate gait speed. In stroke survivors, the minimal clinical important difference (MCID) (i.e. the smallest change of an outcome that a patient would identify as important and valuable) is 0.06 m/s for a small meaningful change and 0.14 m/s for a substantial meaningful change (Perera, Mody, Woodman, and Studenski, 2006). In survivors of chronic stroke, the minimum detectable change at 95% confidence level (MDC_{95}) (i.e. the minimal amount of change beyond random measurement errors) for comfortable gait speed were 0.10 m/s, 0.15 m/s, and 0.18 m/s for individuals with gait speed <0.40 m/s, 0.40 to 0.80 m/s, and >0.80 m/s, respectively (Lewek and Sykes, 2019).

Five times sit to stand

The Five Times Sit to Stand (5TSTS) was used to measure transfer mobility and functional strength of lower extremities (Mong, Teo, and Ng, 2010). The time taken

for the participants to stand up and sit down five times was recorded. The normative values of 5TSTS are 7.7 ± 2.6 s for individuals aged 50–59 years, 7.8 ± 2.4 for individuals aged 60–69 years, and 9.3 ± 2.1 for individuals aged 70–79 years (Bohannon et al., 2010). The cutoff score predictive of falls in older adults is 15 seconds (Buatois et al., 2008).

Timed up and go

The Timed Up and Go (TUG) was used to measure mobility and balance (Flansbjer et al., 2005; Podsiadlo and Richardson, 1991). The time taken for the participants to rise up from a chair, walk three meters, turn around, walk back to the chair and sit down was recorded. The participants used their assistive device and/or ankle foot orthosis as necessary during testing. The MDC95 for the TUG in survivors of chronic stroke is 2.9 s (Flansbjer et al., 2005).

Motor activity log

The Motor Activity Log (MAL) was used to measure the motor function of upper limbs (Taub et al., 1993). The MAL is a patient-reported measurement in the activity and participation domains. The participants were asked to rate, from zero to five, the quality of movement (QOM) and amount of use (AOU) of the weaker arm during 30 functional tasks, such as opening a drawer, picking up a phone, taking off socks, brushing teeth, or combing hair. The rating scale printed on a paper was placed in front of the participants during testing. If the participants could not perform the activity, a rating score of zero was entered. Higher scores indicate better movement control and more frequent use of the weaker arm. The MAL has two scales, QOM scale and AOU scale. The average of scores from all test items was calculated for both QOM and AOU scales. The responsiveness ratios (i.e. the ability of a test to detect a change after the intervention) are 2.0 for QOM scale and 1.9 for AOU scale (Van Der Lee et al., 2004). Responsiveness ratios were calculated as the effect size for the test normalized for the variability of test scores in a stable population or at the baseline before the intervention (Van Der Lee et al., 2004).

Statistical Analysis

Data were analyzed using IBM-SPSS Version 26. Descriptive statistics were calculated for participant characteristics and measurements. The Shapiro–Wilk test was used to examine the distribution of data. The data of TUG, MAL-QOM and MAL-AOU were not normally distributed and were analyzed using the non-parametric tests. To compare the scores of measurements across pretest, posttest 1, posttest 2, and retention, the General Linear Model Repeated Measures (GLM-RM) was used for the data of 10MWT and 5TSTS and the Friedman test (Kim et al., 2017) was used for the data of TUG, MAL-QOM and MAL-AOU. Bonferroni adjustment was applied to all post-hoc analyses to correct for multiple comparisons. For the GLM-RM procedure, the homogeneous distribution of the variances was tested with the Mauchly's Test of Sphericity. The sphericity assumption was violated for the data of 5TSTS and therefore, Greenhouse-Geisser correction was applied (Grieve, 1984). Effect size for pairwise comparisons of pretest with posttest 1, posttest 2, and retention test was estimated using η2p for GLM repeated measures (criteria: 0.01 = small, 0.06 = medium, and 0.14 = large) (Fritz, Morris, and Richler, 2012) and Kendall's W for Friedman test (criteria: 0.1 = small, 0.3 = medium, and 0.5 = large) (Cafiso, Di Graziano, and Pappalardo, 2013). Two-tailed significance level was $p < .05$.

Results

Recruitment, Adherence, Adverse Events, and Participant Characteristics

Patients with chronic stroke were recruited from an outpatient rehabilitation clinic over eight months. Individuals meeting the inclusion criteria were approached by three physical therapists at the clinic and provided with flyers and information about the study. Figure 2 shows the sample flowchart. A total of 18 survivors consented to participate and one participant dropped out prior to starting the TERTAOT intervention. One participant completed the eight-week intervention but was lost to follow-up and did not receive the retention assessment. The remaining participants completed all four assessments. Available data from all participants, including those from the participant who missed the retention, were included in the statistical analyses. All participants attended >80% of the TERTAOT sessions (23.5 ± 1.5 sessions; range = 20 to 24 sessions). All participants completed 12 treatment sessions at posttest 1. Only three participants attended less than 24 treatment sessions by the end of the eight-week intervention (one missed one session, one missed two sessions, and one missed four sessions). No adverse events,

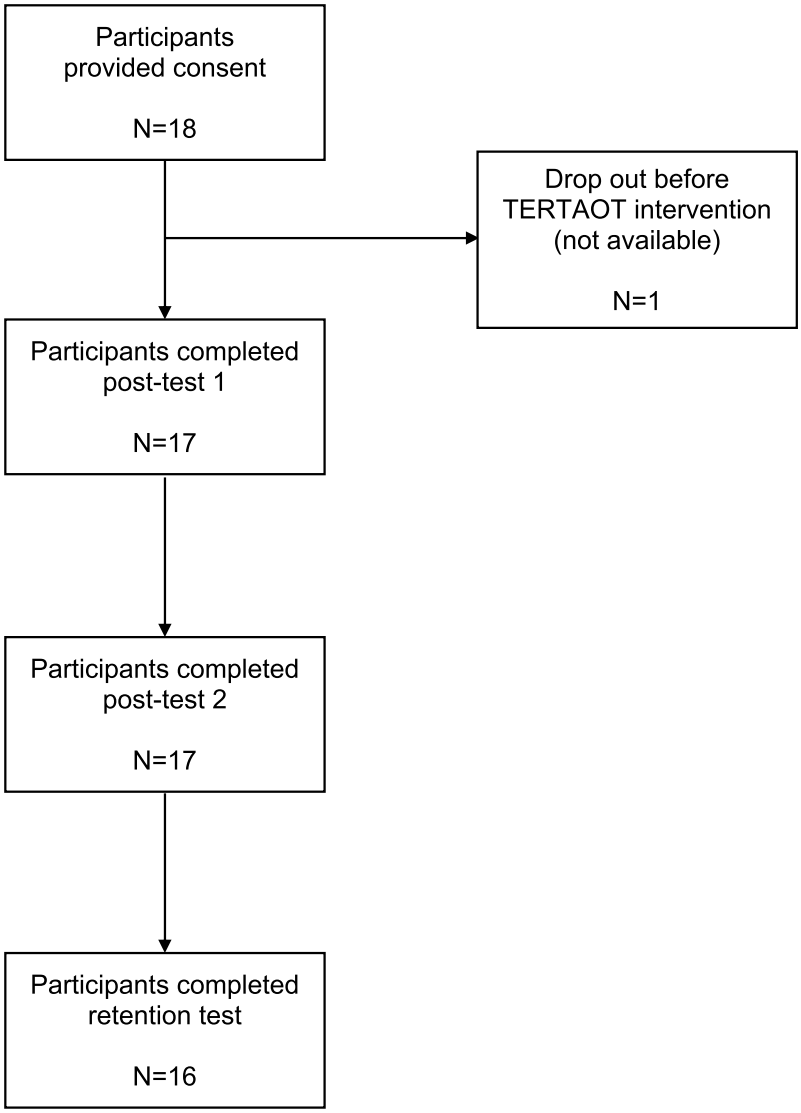

Figure 2. The flowchart of the study sample is shown.

Table 2. Participant characteristics.

Variables	Participant Characteristics
Male/Female	13/4
Age, years (SD)	63.76 (8.95)
Time since stroke, years (SD)	7.26 (5.05)
Mini-Mental State Examination (SD)	28.5 (2.89)
Type of Stroke	
Ischemic	15
Hemorrhagic	2
Hemiparetic side (Left/Right)	13/4
Spasticity present[a]	13

[a]Spasticity was measured based on the Modified Ashworth Scale. Spasticity present was defined as the score of Modified Ashworth Scale for the involved limbs >1; Values are expressed as number of subjects or mean (SD).

such as death, hospitalization, or falls were found during the study period. Table 2 presents the characteristics of the participants.

Meter walk test

The effect of time for 10MWT was significant (p = .001) (Table 3). Post-hoc analyses with Bonferroni correction showed that the participants significantly increased gait speeds by 0.07 m/s at the posttest 2 (p = .022; η^2p = .44) and by 0.083 m/s at the retention (p = .026; η^2p = .43) in comparison with the pretest.

Five Times Sit to Stand

The effect of time for 5TSTS was significant (p = .001) (Table 3). Post-hoc analyses with Bonferroni correction showed that the participants significantly reduced the

Table 3. Scores of outcome measurements.

	Pretest (N = 17)		Posttest 1 (N = 17)			Posttest 2 (N = 17)			Retention (N = 16)				
Measurement	Mean (SD)	95% CI	Mean (SD)	95% CI	Effect size	Mean (SD)	95% CI	Effect size	Mean (SD)	95% CI	Effect size	*p*-value	F value
10 Meter Walk Test, m/s	0.40 (0.24)	0.27, 0.53	0.46 (0.29)	0.31, 0.61	$\eta^2p = .35$	0.47 (0.31)[a]	0.30, 0.64	$\eta^2p = .44$	0.49 (0.30)[a]	0.33, 0.65	$\eta^2p = .43$	0.001	6.11
5 Times Sit to Stand, s	17.6 (8.9)	12.9, 22.3	14.1 (6.9)[a]	10.4, 17.8	$\eta^2p = .45$	12.6 (6.3)[a]	9.2, 16.0	$\eta^2p = .45$	11.9 (4.2)[a]	9.7, 14.1	$\eta^2p = .46$	0.001	9.72
Timed Up and Go, s	24.1 (18.6)	14,7, 34.9	22.9 (20.4)	14.2, 34.0	W = 0.17	21.7 (22.3)	12.0, 33.8	W = 0.17	22.6 (23.4)[a]	10.1, 35.1	W = 0.56	0.005	12.74
Motor Activity Log – Quality of Movement	1.16 (1.69)	0.26, 2.06	1.71 (1.91)[a]	0.69, 2.73	W = 0.72	1.82 (1.81)[a]	0.86, 2.78	W = 0.59	1.60 (1.86)[a]	0.61, 2.59	W = 0.70	0.001	24.08
Motor Activity Log – Amount of Use	1.22 (1.61)	0.25, 1.95	1.66 (1.91)[a]	0.54, 2.46	W = 0.94	1.76 (1.67)[a]	0.80, 2.40	W = 0.42	1.45 (1.67)	0.65, 2.35	W = 0.34	0.017	17.62

Measurements were administered before starting the intervention (pretest), 4 weeks (posttest 1) and 8 weeks (posttest 2) after starting the intervention, and three months after completing the intervention (retention). Values are expressed as mean (SD); *p*-values correspond to the effect of time across four time points; [a] Indicates statistically significant difference in pairwise comparison with pretest after Bonferroni correction.
Effect size for pairwise comparisons of pretest with posttest 1, posttest 2, and retention test is estimated using η2p for parametric General Linear Model Repeated Measures (criteria: 0.01 = small, 0.06 = medium, and 0.14 = large) and Kendall's W for non-parametric Friedman test (criteria: 0.1 = small, 0.3 = medium, and 0.5 = large).

time of 5TSTS at the posttest 1 (p = .02; η^2p = .45), posttest 2 (p = .019; η^2p = .45), and retention (p = .017; η^2p = .46) in comparison with the pretest.

Timed Up and Go

The TUG time differed significantly by time (p = .005) (Table 3). Post-hoc analyses with Bonferroni correction showed that the participants significantly reduced the TUG time at the retention compared to the pretest (p = .01; W = 0.56).

Motor Activity Log

The effect of time was significant for QOM (p < .001) and AOU (p = .001) (Table 3). Post-hoc analyses with Bonferroni correction revealed that the QOM increased significantly at the posttest 1 (p = .003; W = 0.72), posttest 2 (p = .001; W = 0.59) and retention (p = .001; W = 0.70) in comparison with the pretest, and the AOU improved significantly at the posttest 1 (p = .016; W = 0.42) and posttest 2 (p < .001; W = 0.34) compared to the pretest.

Discussion

This pilot study demonstrated that the TERTAOT was a safe intervention without adverse events and the adherence for intervention was >80% among survivors of chronic stroke at an outpatient physical therapy clinic. The participants significantly improved mobility in gait speed, ability to transfer, and motor function of the upper limbs after eight-weeks of combined conventional therapy and TERTAOT and the improvements were retained for up to three months after the intervention ended. This pilot study did not aim to delineate the effects of conventional therapy versus the TERTAOT protocol. Instead, current results suggested that it may be feasible to implement the TERTAOT protocol in a typical outpatient setting and that the physical practice from conventional therapy and TERTAOT together resulted in positive outcomes in the participants.

The improvements in gait speed after TERTAOT exceeded the MCID of 0.06 m/s for gait speed (Perera, Mody, Woodman, and Studenski, 2006). The changes in gait speed were clinically meaningful and retained for up to three months. The participants reduced 5TSTS scores to less than 15 seconds after completing one month of TERTAOT and at three-month retention, indicating a reduced risk of falls (Buatois et al., 2008) that was sustained after completing TERTAOT. Compared to the pretest, the TUG time was reduced by 1.5 seconds at the retention. This change is smaller than the minimal detectable change of the TUG (2.9 seconds) in survivors of chronic stroke (Flansbjer et al., 2005). The gains in QOM and AOU among the participants were statistically significant but did not reach responsiveness ratios for MAL (Van Der Lee et al., 2004).

Research of MT or AO with asynchronous physical practice has reported benefits in improving motor function in survivors of chronic stroke (Adamovich, August, Merians, and Tunik, 2009; Harmsen et al., 2015; Shih et al., 2017; Stevens and Stoykov, 2003; Sugg et al., 2015). Unlike previous studies, the TERTAOT protocol provided the AO with synchronous physical practice while the participants observed the MT-based image of whole-body movement. A study compared the effects of AO involving watching videos of motor tasks followed by immediate physical practice versus physical practice alone in survivors of chronic stroke using a single group design (Sugg et al., 2015). AO and physical practice together resulted in significant improvements in motor function of upper limbs after four weeks and the gains were sustained for at least eight weeks after the intervention ended (Sugg et al., 2015). These results indicate that physical practice plays an important role in addition to AO in enhancing the motor outcome. One unique feature of the TERTAOT protocol is the synchronous physical practice of bilateral symmetrical movements during AO. Another study used mirror imagery of the non-paretic limbs in AO and found improvements in motor skills of the paretic upper limb among survivors of chronic stroke (Harmsen et al., 2015). The participants receiving the MT-based AO observed mirrored videos of reaching movements performed by their non-paretic limb, which is similar to observing the avatar movements in the TERTAOT. The participants in the control group observed photographs of landscapes (Harmsen et al., 2015). It was found that the MT-based AO resulted in significantly faster reaching movements performed by the paretic limb. Unlike previous studies focusing on rehabilitation training of upper limbs focusing on unilateral limb (Adamovich, August, Merians, and Tunik, 2009; Harmsen et al., 2015; Stevens and Stoykov, 2003; Sugg et al., 2015), the TERTAOT involved bilateral symmetrical whole-body movements performed from sitting or standing. In this study, the treatment benefits of the TERTAOT in addition to conventional therapy likely included more frequent use and better control of the paretic upper limb during daily activities and improved mobility tasks involving walking and transferring.

Several neurophysiological mechanisms likely mediate the effects of TERTAOT. Observing the mirrored images of non-paretic limbs created by the Kinect would potentially recruit the brain areas involved in the control

of the paretic limbs (Saleh, Adamovich, and Tunik, 2014; Zhang, Fong, Welage, and Liu, 2018). The participants were able to perceive bilateral motor activities regardless of motor capabilities of their paretic limbs, which likely enhanced bilateral cortical activities during movements of bilateral limbs (Cheng et al., 2019; Takeuchi, Tada, Matsuo, and Ikoma, 2012). The avatar in the TERTAOT provided visual and temporal cues for bilateral movements as the participants practiced the tasks, which likely increased the participants' engagement with the training activities and directed their attention toward the movements being carried out (Deconinck et al., 2015; Dohle et al., 2009). Some researchers consider MT as a type of motor imagery (Mi) (Bello, Winser, and Chan, 2020; Polli et al., 2017), while others view MT and MI as two separate techniques (Hebert et al., 2016; Lee and Cha, 2019; Lin et al., 2019). MI is defined as the internal visual and/or kinesthetic simulation of movement without overt action that is carried out either implicitly or explicitly by instruction (Deconinck et al., 2015; Lin et al., 2019; Ruffino, Papaxanthis, and Lebon, 2017). Research has shown that AO combined with MI resulted in greater activations of the motor system than the application of AO or MI independently (Eaves, Riach, Holmes, and Wright, 2016; Nedelko et al., 2012). Although no specific instruction about practicing MI was given in this study, it may be possible that current participants had engaged MI by kinesthetically and/or visually internalizing the observed mirrored image during or after the TERTAOT exercises. In stroke survivors, MI combined with synchronous AO was found to enhance the activities of sensorimotor cortex and the motor function more effectively than MI followed by asynchronous AO (Sun et al., 2016). The role of MI as related to the TERTAOT on improving motor function remains to be investigated.

The adherence to TERTAOT was high without adverse events, supporting its safety and feasibility as an intervention at an outpatient clinic. In order to broaden the applications of TERTAOT to other populations, future research involving survivors of acute or subacute stroke may be necessary. fMRI data before and after the TERTAOT may be used to provide direct evidence of neuroplastic changes with the treatment, in addition to functional measures. Variations in the TERTAOT protocols need to be explored to establish the appropriate dose and parameters.

Findings from this study may inform the implementation of a randomized controlled trial. An extended recruitment time beyond eight months would likely result in a sufficient sample size for adequate statistical power. Based on the current results and the 10MWT as the primary outcome, we estimated that the sample size for a future randomized controlled trial of the TERTAOT would be a total of 32 participants using G*Power (Faul, Erdfelder, Lang, and Buchner, 2007) (2 groups including the control and TERTAOT groups; 4 repeated measurements with 1 pretest, 2 posttests, and 1 retention; alpha level = 0.05; power = 0.95; effect size of $\eta 2p = .28$ from 10WMT).

This study has limitations. The TERTAOT was conducted in a busy outpatient setting and environmental distractions were possible. However, the setup reflects the real-world practice environment and substantiates the external validity of the TERTAOT intervention. Quality of life measurements were not administered in this study although the participants reported improved quality of life, such as improvements using the paretic limb to carry out personal hygiene practices and bilateral activities including driving. Using a measurement, such as the Stroke Impact Scale (SIS) (Mulder and Nijland, 2016), would have assisted the clinicians in gauging the impact of the TERTAOT intervention on health-related quality of life among the participants. The sample size was small and only a single group was examined. However, this pilot study revealed large effect sizes for outcome measurements and provided important information for a larger randomized controlled trial. Prior to the retention test, the exercise and activity were not monitored after the participants completed the weight-weeks of TERTAOT intervention. This pilot study lacked a control group and thereby, the results of the outcome measures could not be solely attributed to the TERTAOT protocol. Lastly, MI as an important tool for stroke rehabilitation (Hebert et al., 2016; Lin et al., 2019) likely played a role in the TERTAOT application but was not examined in this study. Future research is warranted to delineate the potential influence of MI, including the kinesthetic, haptic, and/or visual modality frames and the first – or third-person perspective of imagery (Ruffino, Papaxanthis, and Lebon, 2017) in the TERTAOT application. fMRI investigation may differentiate the neural mechanism underlying MI associated with AO and MT in TERTAOT for stroke rehabilitation.

Conclusion

The TERTAOT may be a safe and feasible novel technology for rehabilitation of chronic stroke survivors at an outpatient rehabilitation setting. In this pilot study, the intervention including conventional therapy and the TERTAOT had good adherence and resulted in significant and meaningful gains in gait speed,

reduction in fall risks, and increased participation of the paretic limb during daily activities.

Disclosure statement

The authors reported no conflict of interest.

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