Can Action Observation Therapy be an Alternative to Robotic Rehabilitation to Improve Upper Extremity Functions in Stroke Patients?: A Protocol of Randomized Controlled Study

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Abstract

Aim: Approximately two-thirds of stroke patients have upper extremity involvement after the disease. Traditional and innovative rehabilitation programs are needed to restore of the upper extremity motor movements. This clinical trial aims to investigate and compare treatment effects robotic rehabilitation (RR) and action observation therapy (AOT) on upper-limb motor function, independence and quality of life in subacute stroke.

Method: The estimated sample of the study is 30 subacute stroke patients. Participants will be randomized into two groups (RR and AOT). All participants will receive conventional treatment for 60x3x8 minutes/day/week. In addition to conventional methods, robotic rehabilitation will be applied to the RR group, and the AOT protocol will be applied to the other group for the same duration. Assessments will be repeated at the baseline, end of the 4th and 8th weeks.

Conclusion: This paper will be the first study that compares the effects of AOT and RR on upper extremity motor functions on stroke. In addition, this study will be a reference source for systematic review or meta-analysis studies that investigate the effectiveness of AOT.

Keywords: Stroke, robotic rehabilitation, action observation therapy, motor function

Özgün Araştırma Makalesi (Original Research Article)
Geliş / Received: 21.06.2023 & **Kabul / Accepted:** 11.12.2023
DOI: https://doi.org/10.38079/igusabder.1317876
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ETHICAL STATEMENT: This randomized controlled study was approved by the Marmara University, Faculty of Medicine, Clinical Research Ethics Committee with protocol number 09.2022.649 and registered on clinicaltrials.gov with NCT05590156 reference number. The study will be conducted in accordance with the Declaration of Helsinki.

İnme Hastalarında Üst Ekstremite Fonksiyonlarını İyileştirmek İçin Hareket Gözlem Terapisi Robotik Rehabilitasyona Alternatif Olabilir mi?: Randomize Kontrollü Çalışma Protokolü

Öz

Amaç: İnme hastalarının yaklaşık üçte ikisinde hastalıktan sonra üst ekstremite etkilenimi meydana gelir. Bu sebeple, üst ekstremite motor hareketlerini restore etmek için geleneksel ve yenilikçi rehabilitasyon programlarına ihtiyaç vardır. Bu klinik araştırma, robotik rehabilitasyon (RR) ve hareket gözlem tedavilerinin (AOT) subakut inmeli hastalarda üst ekstremite motor fonksiyonları, bağımsızlık ve yaşam kalitesi üzerindeki tedavi etkilerini araştırmayı ve karşılaştırmayı amaçlamaktadır.

Yöntem: Çalışmanın tahmini örneklem büyüklüğü 30 subakut inmeli hasta olacaktır. Katılımcılar randomizasyon yöntemiyle iki gruba (RR ve AOT) ayrılacaktır. Tüm katılımcılar 60x3x8 dakika/gün/hafta konvansiyonel tedavi alacaklardır. RR grubuna konvansiyonel yöntemlere ek olarak robotik rehabilitasyon, diğer gruba ise aynı süre boyunca AOT protokolü uygulanacaktır. Değerlendirmeler başlangıçta, 4. ve 8. haftaların sonunda tekrarlanacaktır.

Sonuç: Bu makale AOT ve RR'nin inmeli hastalarda üst ekstremite motor fonksiyonları üzerindeki etkilerini karşılaştıran ilk çalışma olacaktır. Ayrıca bu çalışma, AOT'nin etkinliğini araştıran sistematik inceleme veya meta-analiz çalışmaları için bir referans kaynağı olacaktır.

Anahtar Sözcükler: İnme, robotik rehabilitasyon, hareket gözlem terapisi, motor fonksiyon.

Introduction

Stroke is defined as a clinical picture wherein cerebral function is impaired without any factor other than a vascular cause and focal/global symptoms lasting longer than 24 hours occur as a result of this deterioration[1]. While the prevalence of stroke, the second leading cause of death in the world, is increasing day by day, the prevalence of the disease has been reported to be between 0.9% and 4.1% in the Turkish population[2]. The cost of acute, subacute, and chronic treatment processes of stroke increases due to the high prevalence[3]. Rehabilitation services constitute a significant part of the cost[4]. Within physiological possibilities long-term rehabilitation programs are needed to restore the sensory and motor losses of the upper and lower extremities that occur after cerebral involvement[5]. Especially the fact that 80% of motor recovery takes place within the first six months makes it necessary to start the rehabilitation process as soon as possible[6].

A 55-75% of stroke patients have upper extremity involvement, and only 38% of these patients show partial recovery in the first six months[7]. Due to the selective motor control being affected, patients have to cope with a decrease in the daily functional activities of the upper extremity and their individual quality of life[8,9]. Effective and efficient rehabilitation programs are needed to overcome all these problems and to develop selective motor control[10]. Stroke rehabilitation programs are planned to be individual-specific. However, intensive rehabilitation programs cannot be implemented at the desired level due to a lack of resources and personnel[7,11]. Alternative

treatment methods such as virtual reality, restrictive motion therapy, mirror therapy, robotic devices, and motion observation therapy (AOT) have become widespread in recent years, and patients have been allowed to participate in more intensive programs than traditional methods with these techniques[10,12]. These treatment methods cause improvement in motor functions thanks to the neuroplasticity that develops due to repeated experiences in the damaged hemisphere.

Brain plasticity can be defined as adaptive changes in the morphological, neuronal network structures and functions of the brain as a result of new neuronal connections, neurogenesis and neurochemical changes[13]. These changes occur when the preserved axonal sprouts in the denervated region establish new circuits by the induction of multiple repetitive activities[14]. However, the movement must not only be repetitive but also learnable for neuroplasticity. Learning of the–movement directly affects the cortical reorganization process[15]. Both robot-assisted rehabilitation and AOT, which are used in addition to traditional stroke treatments, can help the recovery process through mechanisms of neuroplasticity[12,16].

AOT is a neuroscientific-based treatment method aimed at functional recovery with cognitive strategies. The basis of this approach is to provide motor learning with the mirror neuron activitation[17]. Mirror neurons are activated both during the observation and practice of a movement[18]. During AOT, patients are usually asked to carefully observe the actions performed by a healthy person in the videos and then try to imitate the same actions. This intervention helps to develop the patient's motor skills. Neural reorganization and motor relearning develop in response to visual feedback[17]. Because there are not enough studies about AOT involved in the treatment methods of patients with stroke yet, a consensus has not occurred on the optimal parameters for this technique[19].

Video games can induce neuroplasticity and contribute to repetitive, aimed-target movements[14]. Also, modules are important for rehabilitation, such as rewards, challenges, and goals in-game content. For this purpose, game-assisted robotic devices are also frequently used in stroke rehabilitation, and it is recommended that they be applied in addition to conventional therapy methods[20]. Robotic systems also allow the patient to perform highly repetitive activities, which are the basic elements of motor learning, interactively[21]. Although there are many studies in the literature on robotic rehabilitation, unlike AOT, the effectiveness results differ. This is because the characteristics of the devices, protocols, and participants used in the study are different[20].

Objectives:

- Primary Research Aim: The first aim is to investigate and compare the effects of the AOT and robot-assisted rehabilitation protocols on upper limb motor function in sub-acute stroke survivors.

- Secondary Research Aims: The secondary aims of the study are to compare the effects of

AOT and robotic rehabilitation on the independence and quality of life in stroke.

Methods

Study Design and Ethics

This randomized controlled study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee with protocol number 09.2022.649 and registered on clinicaltrials.gov with NCT05590156 reference number. The study will be conducted in accordance with the Declaration of Helsinki. Individuals will be verbally informed, and their written consent will be obtained before the study. This research complies with The SPIRIT 2013 Statement.

Subjects

Individuals aged 18-80 who resided in Istanbul during the treatment and had a stroke in the last six months will be included. Other inclusion criteria are:

- Having a Mini-Mental Status Evaluation score of over 24 points,
- Ability to sit independently,
- Presence of at least half of the range of motion of all joints for the upper extremity,
- Spasticity level less than or equal to 2 based on the Modified Ashworth Scale,
- Having 20-60 points based on The Fugl-Meyer Assessment for Upper Extremity Scores,
- Without severe visual impairment,
- Having normal communication and cooperation.

Also, the exclusion criteria are:

- Having another secondary neurological disease,
- Having any orthopedic injuries that may affect the upper limb functions,
- Taking neuropsychiatric and neuroleptic pills,
- Having Botox history or tendon surgery,
- Being afflicted with ataxia
- Having less than 80% adherence to total sessions.

Power and Sample Size

Gpower 3.1.9.7 software was used for sample size calculation. At least 30 patients will be included in this study; when the alpha error is determined as 5%, the power as 80%, and the effect size as 1.29. The studies of Lima and Christofoletti were taken as references for calculating the effect size[22].

Randomization and Groups

Participants will be assigned to groups by an independent physiotherapist based on a 1:1 allocation ratio. Randomization will be performed via the online randomization software (www.randomizer.org).

- Robotic Rehabilitation Group: Robotic rehabilitation will be performed in addition to conventional rehabilitation.

- Action Observation Therapy Group: AOT will be performed in addition to conventional rehabilitation.

Procedure

- Conventional Rehabilitation: All participants will be included in a personalized, customized conventional rehabilitation program in line with their needs, functions, and expectations. This program will be applied for 60x3x8 min/day/week. The additional rehabilitation methods (robotic rehabilitation or AOT) will be applied to the patients according to their assigned groups after the conventional program.

- Robotic Rehabilitation: This program will be performed with a device named Exo Rehab X (Houston Bionics, Inc.) for 60x3x8 minutes/day/week. This device is a computer-assisted upper extremity robotic rehabilitation system that works with the active participation of patients. The avatar on the screen moves via the sensors embedded into the device during the patient's movements and provides visual feedback that helps the patient perform the relevant activities and movements. There are ten games inside the system to fulfill different purposes. The device does not create any resistance as long as the resistance attachments are not added during the movements. The speed of the movement and the number of repetitions can be regulated, if necessary. Exercise can be carried out between the desired range of motion and resistance with resistance attachments.

Robotic rehabilitation protocol and intervention will be as follows:

1. The patient will be seated in a specially designed chair with his feet touching the ground,

2. Then, the patient's upper extremity will be placed on the upper extremity robot,

3. The patient will be taken to a suitable viewing angle in front of a 43” television,

4. The robotic exercise program will be implemented to include the movements of all parts of the upper limb along all directions. The resistance and velocity modules of the device will be adjusted by considering the patient's characteristics.

There are three different ways to regulate the intensity of robotic rehabilitation in stroke patients. The first is controlling the number of repetitions, which requires a lot of effort. Due to the complexity of human movements, it is costly in terms of time to have each movement performed

separately. The second method is how long the treatment program will continue. The third method, the duration of therapy, is more convenient in terms of use. When the difficulty level is kept constant in task-oriented training, the patient's participation in the active movement for minutes is directly related to the number of repetitions. For this reason, using protocols depending on the treatment time is suitable for adjusting the robotic rehabilitation intensity[23].

Each of the games can be used in accordance with the movements of all parts of the upper extremity in all directions in the ExoRehab X. In the study, the region/regions that the rehabilitation program will focus on will be determined according to the functional status and needs of the affected upper limb of the stroke survivors. The rehabilitation will be applied to the areas forming the focus of the rehabilitation program for eight weeks, three days a week, with a daily session duration of sixty minutes. During the treatment, different games for the same purpose will be used in the rehabilitation process to maximize program adherence and patient participation. If more than one joint is included in the rehabilitation program in a session, each joint's treatment time will be equal. The pace of the games will be adjusted, taking into account the patient's individual situation.

- Action Observation Therapy (AOT): Thirty-one video content aimed at improving functional activities will be produced within the scope of the AOT protocol. The video of the function appropriate to the clinical and functional status of the patient will be selected and added to the conventional treatment sessions. In practice, the patient will first watch the video of the function for 3 minutes and then try to imitate the exercise in the video with the hemiparetic side for 3 minutes. AOT sessions will continue with the watching-performing cycle, and each session will be completed in 60 minutes with ten cycles. Simple functions will be performed in ten loops with a single video. Simple functions will be performed in ten loops with a single video. More complex functional movements (for example, drinking water) will be divided into their components, and videos of each component (for example, reaching the glass, grasping the glass, and bringing the glass to the mouth) will be watched and performed separately. At the last stage, after watching the video containing the whole movement, it will be requested to perform it. Whether functional activities are watched in a single video or separate videos divided into components, the season will always be ten loops of six minutes and will complete sixty minutes. The monitoring-performing time of the components will be obtained by dividing one or more of the component numbers by sixty. The stages will also be voiced in the videos so that the patients can perform the movements correctly. Patients will complete the program by watching a functional video weekly for six weeks. The video contents of the functional activities are shown in Table 1.

AOT treatment will be performed in a hospital setting under the physiotherapist's supervision. In this way, it aims for the patient to understand, perform the movement correctly, and eliminate ambiguities.

Table 1. Contents of Videos Belong to AOT

1. Reaching Object on Desktop	**17.** Using Mobile Phone
2. Reaching Shelf at Eye Level	**18.** Opening the Shoe Box
3. Reaching for an Object Near the Body	**19.** Combing the Hair
4. Bringing the Hand to the Mouth	**20.** Carrying Books
5. Grasp-Release Cup on Desktop	**21.** Zipper Pull
6. Putting the Empty Glass to the Mouth	**22.** Washing Hands
7. Wiping the Table with a Napkin	**23.** Keeping the Credit Card
8. Folding the Napkin	**24.** Shoulder Protraction-Retraction
9. Grasping and Lifting the Water Bottle	**25.** Shoulder Flexion-Extension
10. Filling a Glass with a Water Bottle	**26.** Elbow Flexion-Extension
11. Putting the Apple in the Mouth	**27.** Forearm Pronation-Supination
12. Emptying 5 cm Cubes	**28.** Wrist flexion-extension
13. Stacking 4 Cubes of 5 cm	**29.** Wrist Circumduction
14. Dip Fork in a Hard Vegetable	**30.** Wrist Ulnar-Radial Deviations
15. Opening and Closing the Drawer	**31.** Finger Abduction-Adduction
16. Opening the Unsealed Jar	

Assessments

Patients will be assessed three times: baseline, 4th, and 8th week. Blinding is not possible for the participants and the physiotherapist who will conduct the treatment program because of the study nature. An independent researcher will do statistical analysis as a single-blind. Summary information about the assessment and treatment process is shown in Figure 1.

Figure 1. Summary Flowchart of Research Process

	RESEARCH PROCESS			
	PREPARATORY PHASE	INTERVENTION PHASE		
TIMELINE	$-T_{1\text{-week}}$	$T_{0\text{-week}}$	$T_{4\text{-weeks}}$	$T_{8\text{-weeks}}$
ENROLMENT:				
Eligibility Screen	♦			
Informed Consent	♦			
Allocation	♦			
INTERVENTIONS:				
Conventional Therapy		●	●	●
Action Observation Therapy		●	●	●
Robotic Rehabilitation		●	●	●
ASSESSMENTS:				
Demographic Data Form		♦		
FMA-UE		♦	♦	♦
WMFT		♦	♦	♦
FIM		♦	♦	♦
SSQOL		♦	♦	♦
BBT		♦	♦	♦

BBT: Box and Block Test; FIM: Functional Independence Measure; FMA-UE: The Fugl-Meyer Assessment for Upper Extremity; SSQOL: Stroke Specific Quality of Life; WMFT: Wolf Motor Function Test

- *Demographic Data Form:* The form will contain information such as age, height, weight, gender, stroke onset time, lesion side, dominant extremity, stroke type, education level, and spasticity level.

- *Fugl Meyer Assessment for Upper Extremity:* The scale is an objective and disease-specific assessment method designed to assess recovery in hemiplegic patients[24]. The assessment includes subsections assessing shoulder, elbow, forearm, wrist, and hand movements, coordination, and reflex activities and is done in a sitting position. A high score indicates good motor activity.

- *Wolf Motor Function Test:* The test consisted of 17 items and is used to assess the motor skills of the upper extremity[25]. The scoring is performed on a 5-point Likert scale. A high score represents the fine motor function. While data is collected in the fields of functional skill and performance time for 15 items, muscle strength is evaluated in the other two items[26]. The strength assessment section will not be used.

- *Functional Independence (FIM):* The scale indicates the degree of independence of the person in daily physical-cognitive activities with 18 items. Items are scored between 0-7. A 6-7 points are considered independent, 3-5 points semi-dependent, and 1-2 points dependent. The maximum score that can be obtained in FIM motor is 91 points, and the maximum score that can be obtained in FIM cognitive is 35 points. The total FIM score can vary between 18 and 126 points[27].

- *The Stroke-Specific Quality of Life Scale (SS-QoL):* The SS-QoL will be used to assess the quality of life. This scale consists of 12 subsections such as energy, family roles, language, mobility, mood, personality, self-care, social roles, thinking, upper extremity function, vision, and

work productivity. It is graded with a Likert-type score ranging from 1 to 5[28]. The higher the score means the higher the quality of life for stroke survivors.

- Box and Block Test: The test has been developed to assess gross motor skills for hands. A box and small wooden blocks are used for the test. Small wooden blocks are all placed on one side of the box. The patient is asked to move the wooden blocks from side to side for 60 seconds as fast as possible. The test is applied to both hands, and the number of blocks moved gives the total score[29]. The number of blocks collected per unit of time indicates fine hand function.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS v11.5) statistical software will be used for qualitative and quantitative statistical methods. The data will be evaluated at the 95% confidence interval and the significance level of $p<0.05$. The Shapiro-Wilk test and histogram curves will be used to question the normal distribution. Appropriate statistical tests will be applied depending on the provision of parametric or non-parametric test conditions. When the data has a normal distribution, One-way ANOVA, the Independent Sample T-test and Paired Sample T-test will be used. In other conditions; Kruskal Wallis, the Mann-Whitney U test and the Wilcoxon Signed Rank Test will be used.

Discussion

The effects of AOT and robotic rehabilitation methods applied in addition to conventional techniques will be investigated with this research protocol and compared in terms of improving upper limb motor activity, independence, and life quality in patients with subacute stroke.

It is seen that upper extremity impairments that affect daily life and require referral to a rehabilitation program occur in approximately 85% of stroke patients in the acute period and 50% in the chronic period[30]. The high number of patients with upper extremity involvement also increases the importance of rehabilitation services. The recovery time of rehabilitation programs applied to the lower and upper extremities is different from each other. Longer-term rehabilitation programs are needed, especially for the recovery process of the upper extremity[31]. This situation requires the use of different effective techniques and the support of the process as much as possible to maximize the benefits obtained from upper extremity rehabilitation services. Because the gains will affect not only the productivity of the patient in daily life but also the functional status, independence, economic status, and quality of life of stroke patients[32].

In the literature, it is possible to come across studies that include different treatment approaches to restore and minimize the upper extremity motor effects of stroke. These studies mostly focused on comparing robot-assisted systems with other therapeutic approaches[33–35]. However, no study has been found comparing the efficacy of robotic rehabilitation and AOT. Therefore, the primary aim of our study is to examine the effects of robotic rehabilitation and AOT on upper extremity motor function and compare their effectiveness in subacute stroke patients. The secondary aim is

to compare the effects of these treatment modalities on functional independence and quality of life. While this research is being conducted, both robotic rehabilitation and AOT will be applied in addition to the conventional rehabilitation program. It is emphasized that the intervention of robotic rehabilitation not alone but in addition to conventional techniques causes more motor gain according to literature[36]. Regarding AOT, no such recommendation was found. Since it is assumed that the treatment period will have a positive effect on the rehabilitation gains methodologically, the AOT technique will be applied with the same therapy time as the robotic rehabilitation in addition to the conventional methods.

Robotic rehabilitation activates the brain's plasticity pathways by allowing the high-intensity execution of purposeful activities. In this way, it causes improvements in motor functions. On the other hand, AOT allows the restoration of motor movement due to the activation of mirror neurons in the brain. Both methods trigger healing by activating different brain mechanisms. In the literature, both treatment methods are used to achieve motor recovery. However, studies on robotic rehabilitation take up much more space than AOT. Because the philosophy of AOT was put forward after the introduction of robotic rehabilitation systems. For this reason, there are limited studies on AOT compared to robotic rehabilitation. However, studies of AOT show that this technique is suitable for development, dissemination, and combination with other treatment methods.

Limitations

The Robotic rehabilitation or the AOT treatment methods added to conventional methods also means that the treatment period is prolonged according to our methodology. In this way, we think that the maximum effect will be achieved. This is the strength of our research. Also, this study may have several limitations that we foresee. First, more than one hundred and forty different systems are used in robotic rehabilitation in the literature. This study will follow the rehabilitation process with the Houston ExoRehab X (HoustonBionics, Inc.) device. The use of different systems has led to a discussion of different results in the literature, and at this point, we cannot do anything. On the other hand, thirty-one different video content will be produced in this research. The rehabilitation program will be continued with the videos most suitable for the patient's functional state. Although there are more functional activity videos in this study compared to other AOT studies in the literature, it may be necessary to expand the video pools of functional movements for future studies.

Conclusion

Studies on stroke indicate that the performing of robotic rehabilitation added to conventional techniques plays an active role in improving upper extremity functions. The AOT technique is an accessible, diversifiable, easy-to-apply, and lower-cost method compared to robotic rehabilitation

systems. Also, while the treatment process progresses depending on a system and clinic in robotic rehabilitation, a rehabilitation program can be maintained as a clinic-free in AOT technique. If this study is concluded positively in favor of the AOT technique, this qualified randomized controlled study will contribute to the literature. In addition, our results may provide methodological guidance for possible clinical trials in the future. On the other hand, we think that AOT intervention can be included in the scope of primary care services thanks to its simple design and potential to reach more cases that can be supported with the remote access model. If the results of the robotic rehabilitation are found to be better, the effectiveness of the relevant device and the applied protocol will be supported and may be the starting point for the design of new protocols. If our results show that both treatments are equally effective, clinical use recommendations and widespread use of them can be developed by planning new studies on cost-effectiveness.

Implications for Physiotherapy Practice: As a result of this study, the effects of two different rehabilitation techniques (RR and AOT) on upper extremity motor function will be examined in motor loss based on subacute stroke.

Funding: None.

Declarations of interest: None.

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