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RESEARCH ARTICLE

Presenting a New Muscle Synergy Analysis Based Mechanism to Design a Trackable Visual Biofeedback Signal: Applicable to Arm Movement Recovery After Ischemic Stroke

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ABSTRACT This study aimed to evaluate the effect of a novel underlining mechanism of visual biofeedback based on muscle synergy pattern on upper extremity motor functions for subacute stroke patients. The experimental studies were conducted on 12 participants in the control group and 24 subjects with ischemic stroke. In the first step, a visual biofeedback trajectory designed for rehabilitation was produced using the patterns extracted from the muscle synergy of arm movement using the hierarchical alternating least squares (HALS) method and with the help of nonlinear autoregressive with exogenous inputs (NARX) from the family of recurrent neural networks and was evaluated on healthy participants. In the second step, all patients received conventional therapy for the upper extremity, 2 times per week for 5 weeks. The interventional group additionally received training with the proposed visual biofeedback system for 30 minutes per session. The evaluations were performed regarding modeling performance, trackability, and clinical efficacy. In terms of modeling performance, the results showed that the NARX method has the best performance compared to other conventional models. Regarding trackability, the analyses based on computing the correlation coefficient showed significant improvement in the trackability from baseline to post-treatment in both the interventional and the control groups. In terms of clinical efficacy and based on analyzing the NIHSS, Fugl-Meyer, and MRS scores, the findings showed that the proposed visual biofeedback mechanism along with the conventional therapy may have supplemental benefits for stroke survivors.

INDEX TERMS Biofeedback, muscle synergy pattern, surface EMG signal, stroke survivors, upper extremity.

ABBREVIATION LIST

ANOVA	Analysis of variance.
CC	Correlation Coefficient.
CNS	Central Nervous System.
EMG	Electromyography.
FES	Functional Electrical Stimulation.
FMA-UE	Fugl-Meyer Assessment for Upper Extremity.
GUI	Graphical User Interface.
HMI	Human-Machine Interface.
HALS	Hierarchical Alternating Least Squares.
MCA	Middle Cerebral Artery.
MMSE	Mini-Mental State Exam.
MRS	Modified Rankin Scale.

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MSE	Mean Squared Error.
NARX	Nonlinear Autoregressive with Exogenous inputs.
NIHSS	National Institutes of Health Stroke Scale.
RCT	Randomized Clinical Trials.
STD	Standard Deviation.
VR	Virtual Reality.

I. INTRODUCTION

Stroke is one of the main causes of disability in adults [1]. In addition, stroke survivors mostly require receiving long term rehabilitative therapies [2], [3]. Intensive motor training, exercise, and physiotherapy are the staple of the rehabilitation approaches for stroke patients [4]. But in most conventional methods, the recovery time is very long and tedious [5], [6], [7]. Thus, developing new rehabilitation approaches with higher efficacy and shorter recovery time is an inevitable need [8]. For more than a decade, approaches like assistant robot systems [9], functional electrical stimulation (FES) [7], [10], and biofeedback [11], or a combination of these [12], [13], [14], [15], have been recommended for the neurorehabilitation of stroke survivors. According to studies, rehabilitation programs that are designed based on the principles of motor learning, such as heavy repetition of goal-oriented and task-specific exercises, and cognitive participation, could give rise to neuroplasticity and long-term changes in motor function in stroke survivors [16], [17], [22]. Among the well-known rehabilitation methods, biofeedback-based approaches are more prone to be designed based on the principles of motor learning. In addition, the biofeedback-based approaches has several advantages, including non-invasiveness, impact on neuroplasticity, user-friendliness, increasing motivation, and patient adherence [18], [19], [20]. Therefore, biofeedback-based neurorehabilitation has become a popular approach to improve the physical capabilities and independence of individuals with functional disabilities [11]. Biofeedback can be unimodal, such as: auditory [21], [22], visual, tactile [23], and electromyography (EMG) based [24], [25], [26], or a bimodal or multimodal combination of these approaches [27], [28], [29]. In visual biofeedback methods, a graphical interface in the form of diagrams, numbers, or simple video games provides a feedback loop with the user [30], [31], [32]. Nowadays, motion-enabled video games have become more popular as an adjunct to physiotherapy, demonstrating their potential as a viable and effective post-stroke treatment option [33]. Using the virtual reality (VR) training could be also effective [34]. Although they are effective in the rehabilitation of stroke patients, the complexity and high cost due to using VR systems [35], [36], or even game consoles, impedes the use of this device [39].

Compared with other biofeedback approaches, the use of EMG signals has specific advantages. The EMG signal contains critical information about the muscle activation pattern that determine the quality of movement [37], [38], [39], [40]. Despite all the outstanding work in the development of sEMG-based biofeedback systems, few researches have been published regarding the design of optimal visual biofeedback trajectories. For example, Zadnia et al. [41] provides an approach for selecting the most suitable characteristics from wrist muscles sEMG data to create a predictable visual biofeedback signal for stroke patients' wrist movement rehabilitation. The results were promising, but no experimental evaluations on stroke patients were reported in that work. Thus, design of informative and traceable visual biofeedback signal is yet an open research problem. The authors believe that a visual guide trajectory has to bear information regarding the correct muscle synergy pattern. Because the correct muscle coactivation pattern will gradually emerge when trying to track the displayed trajectory. In other words, recovering the muscle synergy means recognizing the correct movement patterns in performing a functional activity [42], [43], [44], [45]. Therefore, in this study, we present a fundamental method for designing visual biofeedback based on muscle synergy pattern analysis for the neurorehabilitation of stroke survivors. The trajectory generated according to the proposed method is such that, tracking it by the patient can lead to the regeneration of correct synergy patterns in all muscles.

According to the organization of the paper, in section II, the data recording protocol, the proposed method of visual feedback signal design, and the assessment approaches are elaborated. In section III, the results of the evaluations performed in terms of different aspects have been reported. In section IV, different aspects of the results are discussed, and finally, concluding remarks are given in section V.

II. MATERIAL AND METHODS

A. PARTICIPANTS

This study included two general stages. First stage, design and training of the model with twelve healthy participants (8 men, 4 women, age range: 24–70 years old, right-hand dominance) without any history of disease or other skeletal disorders or cognitive problems. Second stage, the clinical evaluation of the model with twenty-four volunteers (11 men, 13 women, age range: 32–83 years old, right-hand dominance) with Arterial Ischemic Stroke (AIS) of the Middle Cerebral Artery (MCA), and right-side hemiplegia. The MCA was selected because it is the largest cerebral artery and the most commonly affected vessel in cerebrovascular accidents [46]. The procedures were approved by the Local Research Ethics Committees. Therefore, all of the participants were informed about every step of the protocol and signed a written informed consent before participating in the study. If the individual lacked capacity, a relative was asked as a proxy. The demographics and clinical characteristics of the second-stage participants are illustrated in TABLE 1. Inclusion criteria for study participants were as follows: (1) Right-handed dominance, (2) The patients with AIS of the MCA stroke within 1 and 5 days of stroke symptom onset (subacute phase), (3) medically stable enough condition so

TABLE 1. Participants' demographic and clinical characteristics.

Variables		The Experimental Group (n =12) (mean±SD)	The Control Group (n =12) (mean±SD)	P-Value
Age (years)		63.25 ± 15.53	64.16 ± 15.43	0.57
Education (years)		5.41 ± 5.21	5.16 ± 5.25	0.42
Duration After Stroke (days)		3.16 ± 1.40	2.91 ± 1.44	0.34
MMSE Score		25.25 ± 2.30	25.16 ± 2.16	0.43
Gender	Female	6(50%)	7(58%)	0.50
	Male	6(50%)	5(42%)	

Abbreviations: MMSE, Mini-Mental State Exam; Values are expressed as mean ± standard deviation; There were no significant differences (P< 0.05).

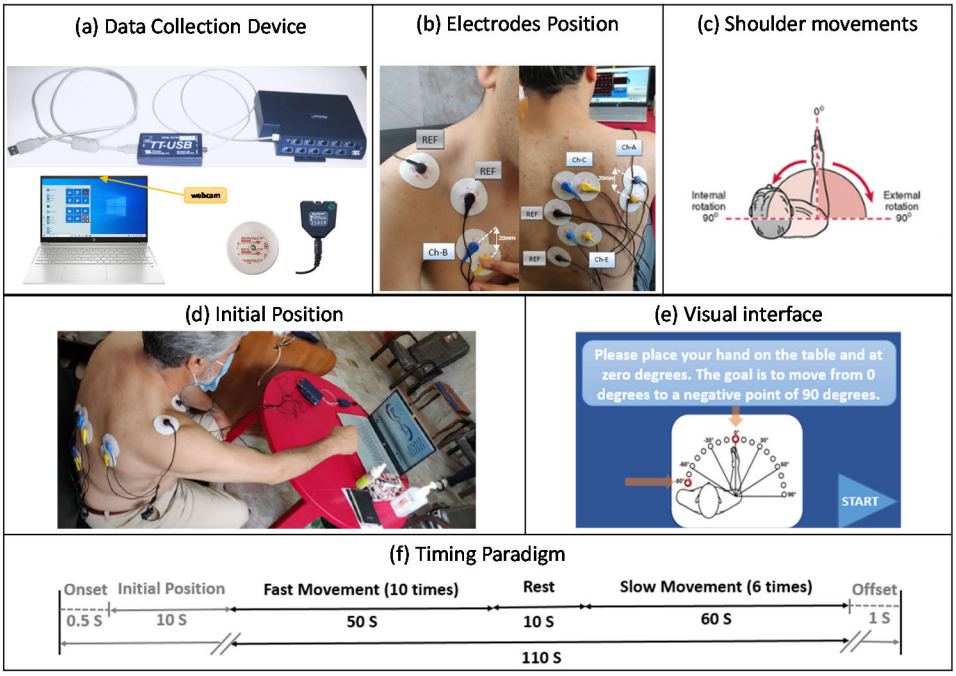

FIGURE 1. a) The data collection devices [79]. b) Electrodes placement in the PD, PM, MT, and LT muscles. c) Shoulder movements [80]. d) Initial position of the participants in the recording setup. e) Visual interface. f) Timing paradigm.

that they can be active in rehabilitation, (4) The first episode of stroke with right side hemiparesis with no musculoskeletal disorders prior to the stroke, (5) There should be no problems with auditory or visual functions, (6) examination mini-mental state (MMSE) total score of 23 or greater [47], as it is illustrated in FIGURE 5 participants enrolment consort flow diagram. A double-blind randomized controlled trial was applied to all participants.

B. THE MODEL BASED DESIGNED INTERVENTION

1) DATA ACQUISITION

For healthy participants in the first stage of the experiment it was required that the participants sat on a chair during the experiment. The visual interface monitor was within one meter of the chair. As shown in FIGURE 1, the participant moved his or her right hand horizontally with internal rotation. To record sEMG data, total of four pairs of surface bipolar Ag–AgCl electrodes (Skintact - Fannin Ltd, F-55 ECG electrodes) were placed on the Posterior Deltoid (PD), Pectoralis Major (PM), Middle Trapezius (MT), and Lower Trapezius (LT) muscles of each individual, separated by 20 millimeters [32]. Electrode placement was carried out according to the guidelines provided by SENIAM [51], Electromyography and Neuromuscular Disorders [33]. For better recording the surface EMG signal, electrodes were placed on the belly of the muscles, and before installation of electrodes, the skin of the desired area was exfoliated with an abrasive gel and cleaned with an alcohol pad. The reference electrodes are placed on the thoracic spine bone. After that, shoulder movement EMG signals were recorded by a commercial Flex-Comp Infiniti amplifier (10 high-speed channels, T7555M, Canada) from Thought Technology

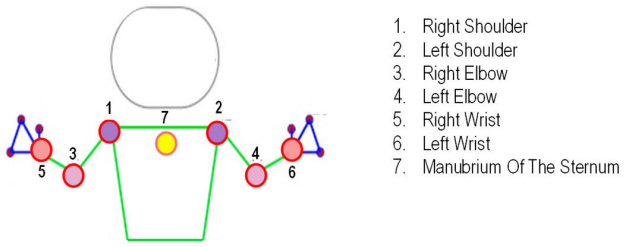

FIGURE 2. Modified BlazePose key points topology for the upper limb [81].

at a sampling frequency rate of 2048 Hz. The target task consisted of shoulder movement with internal and external rotation. According to [35] and [36], the standard range of internal shoulder rotation is 0° ∼ 90°. Before starting the recording, the participants practiced the procedures once and any possible questions and ambiguities were answered. We recorded five fast movements (duration time: 10 seconds) and three slow movements (duration time: 20 seconds) with a 10-second break between them to prevent muscle fatigue, but only slow movements that resembled normal motion pattern were used. FIGURE 1 illustrates the detail of the experimental setup. The raw EMG signals were band-pass filtered in the range of 40 and 400 Hz to reduce the Direct Current (DC) offset and motion artifacts as much as possible (3rd-order Butterworth digital, cutoff frequency of 20 Hz, roll-off rate of 12 dB/decade) [37]. However, our main solution was to avoid noise sources by using portable devices with battery power supply. Subsequently, the signals were rectified and outliers were removed. Finally, a low-pass filter was applied with a cutoff frequency of 4 Hz (4rd-order Butterworth digital, 12 dB/decade roll-off rate), which resulted in EMG envelopes [38], [39], [40]. For muscle synergy-related analyses, the extracted envelops have to be used. Simultaneously to record upper limb joints position data, we used an HD webcam built into the laptop that was capable of recording video at 30 frames per second (FPS). Also, as shown in FIGURE 2, we used the modified MediaPipe algorithm [41] to estimate the joint position. The proposed algorithm uses BlazePose topology. Which includes 33 key points with three DOFs (x, y position and view) with an input RGB image size of 256 × 256×3 on the human skeletal system and includes a set of topologies COCO [42], BlazeFace [43] and BlazePalm [44].

By developing the basic algorithm, we have added another point called the manubrium of the sternum joint (MOS) to it as the 34th key point. The MOS point was used as a reference point and the positions of all points were computed relative to the position at this point. In this manner, the computed positions of the joints would not be affected due to inevitable unintentional motions. Finally, the key points RW, RE, RS and MOS were selected for the movement of the participants' right arm. Due to the difference in the frequency rate of the input data, a reliable synchronization function was designed based on the reduction of the sampling rate and the time paradigm. For better performance, the data were normalized using the min-max method. To increase the processing speed and create suitable inputs for the neural network, both signals were vectorized by the Numpy library to match the dimensions.

2) THE MODEL DESIGN AND TRAINING STRATEGY

A visual biofeedback signal has to be not only informative but also trackable by the participant. If a motion-related visual biofeedback signal could not be trackable by different participants, it could not be applied to a biofeedback-based rehabilitation system. The basic hypothesis was to use muscle synergy patterns to design the visual biofeedback trajectory. These patterns contain essential information on movement quality, and they seem to be able to indirectly alter patients' synergy patterns and thus help restore movement quality [48]. The visual biofeedback training tool used in this study, as shown in FIGURE 4, was designed and evaluated using sEMG data and kinematic information from healthy individuals. Unlike other EMG-based biofeedback approaches, participants do not need online or offline EMG recording data [24], [49]. As shown in FIGURE 4, the EMG signal was collected from four muscles involved in the arm movement of healthy participants, and the muscle synergy patterns related to that movement were extracted using Hierarchical Alternating Least Squares (HALS) algorithm [50], [51].

$$M = [W][C]^T \tag{1}$$

where M is the preprocessed EMG signals in an m by n matrix, where m is the number of time series, n is the number of EMG channel inputs, $C = [c1,\ldots, c_j]$ is the synergy set, where j is the number of synergies and $c_j = [c1, \ldots, c_n]^T$ represents a single set of synergies, where c_n is the coactivation coefficient of EMG n, and W is the coactivation coefficient of the synergy in m by j matrix [52]. Once the synergy model is developed, learning algorithm techniques are used to iterate equation (2) and II-B3 several times, with k (1, 2,…, j) denoting the label of synergies [52]. C and W matrices were generated using a single set of shoulder movement EMG data.

$$[C_k] \leftarrow [C_k] + \frac{([M][W]^T - [C][W]W^T)_K}{[W_k][W_k]^T} \tag{2}$$

$$[W_k] \leftarrow [W_k]^T + \frac{([M]^T[C] - [W]^T[C]^T[C])_K}{[C_k]^T[C_k]} \tag{3}$$

Finally, a nonlinear model designed based on an artificial neural network as a machine learning algorithm called nonlinear autoregressive with exogenous inputs (NARX) was identified in a manner that could predict the desired arm movement trajectory. The NARX neural network is a recurrent neural network (RNN). The RNNs have internal memory. Thus, these neural networks could be used to model the dynamic process such as biological processes.

There are two approaches to train the NARX network. The first approach is the parallel (P) mode, where the output of the feedforward neural network is fed back to its input as part

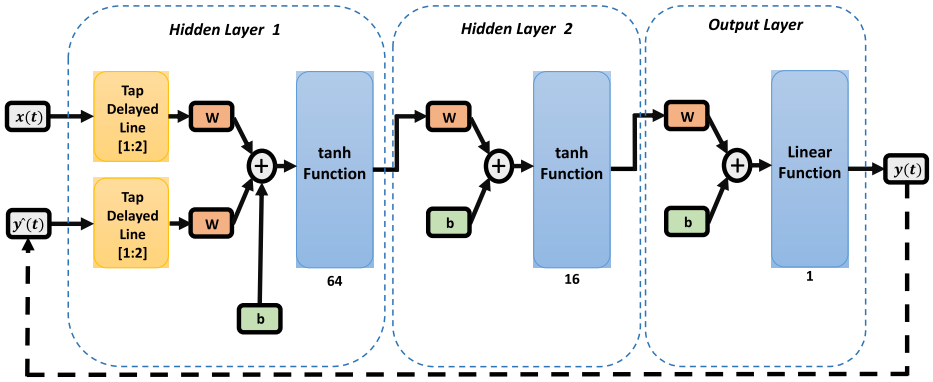

FIGURE 3. The proposed NARX structure with two hidden layers. Where x and y are the input and the output and $\hat{y}$ is the target, b is a bias term and W is a weight term.

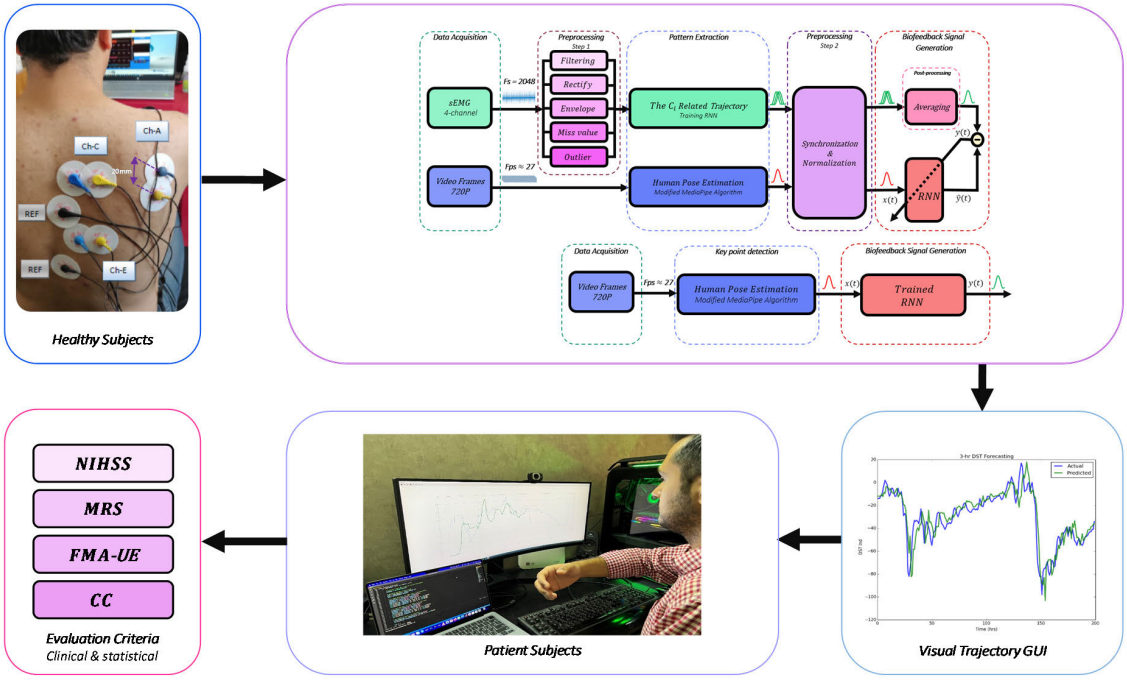

FIGURE 4. A block diagram representing the proposed visual biofeedback based training protocol.

of the typical NARX architecture. The second approach is the series-parallel (SP) mode, where the actual output is used instead of the estimated output feedback [53], [79].

In this research, the SP mode NARX network is designed for training, then turned to P mode to do the prediction. We can express NARX mathematically as [54]:

$$y(n+1) = f\left[y(n), \cdots, y\left(n-d_y+1\right); u(n-k), u(n-k+1), \cdots, u(n-d_u-k+1)\right] \quad (4)$$

where $u(n) \in R$ and $y(n) \in R$ is the model's input and output at discrete time step n, respectively, and $du \geq 1$ and $dy \geq 1, du \leq dy$, respectively, are the input and output memory order. Process dead-time parameter $k(k \geq 0)$ is a delay term. Without lack of generality, we always assumed $k = 1$ in this study, thus obtaining the following NARX model:

$$y(n+1) = f\left[y(n), ; u(n-k)\right] \quad (5)$$

The predicted trajectory was being displayed to the patient as a visual biofeedback signal. The actual motion trajectory was being displayed concurrently. The patient was asked to try to perform the arm movement in a manner that the displayed actual trajectory tracks the displayed desired trajectory. Figure 3 shows a summary related to the implemented training protocol designed based on presenting the visual biofeedback.

3) THE EXERCISE PROTOCOL

Both the interventional and the control group underwent 60 minutes of conventional physical therapy 2 days per week for a total of 5 weeks. Participants allocated to the

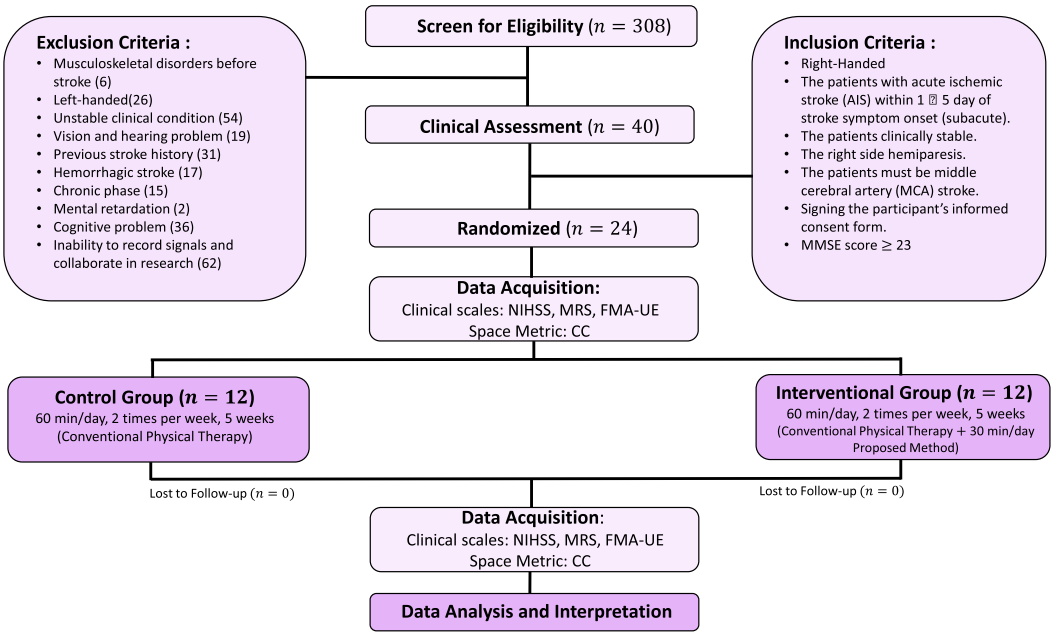

FIGURE 5. The CONSORT flowchart shows the process from enrolment to data analysis.

interventional group received 60 minutes of conventionally physiotherapy in addition to 25 minutes of training with our proposed biofeedback method. Also, a 5-minute warm-up exercise with the patient's recommended system was performed before the main training session to allow the patient to adapt to how the system works. Whereas participants allocated to the control group received 60 minutes of conventional physiotherapy of the same type as the interventional group. Conventional physiotherapy aimed to normalize movement patterns and minimize spasticity [55], [56]. Physiotherapy included static and dynamic control of position, motor-skill exercises, mobility training, balance skills, weight shift, and activities of daily living [57]. In addition, physiotherapists choose the intensity of rehabilitation exercises based on the needs of each patient. During each training session using the designed biofeedback based protocol, the patients sat on a wheelchair or stable chair at 1 meter from the laptop. Patients were informed about the task before the training session started and they were shown how to do it. The task is to ask the patient to perform the movements in a way that is following the reference trajectory taken from the healthy participant's patterns. In this approach, the patient indirectly tries to adjust and modify the muscle synergy patterns. Patients during the trajectory tracking task actively performed lateral internal and external rotation shoulder movements. Internal shoulder rotation inward causes the upper arm to rotate toward the front of the torso, and external rotation causes the upper arm to spin away from the front of the torso [58].

4) THE ASSESSMENT APPROACHES

a: CLINICAL ASSESSMENT

In this study, the motor function of the upper extremity was evaluated using the upper extremity subscale of the

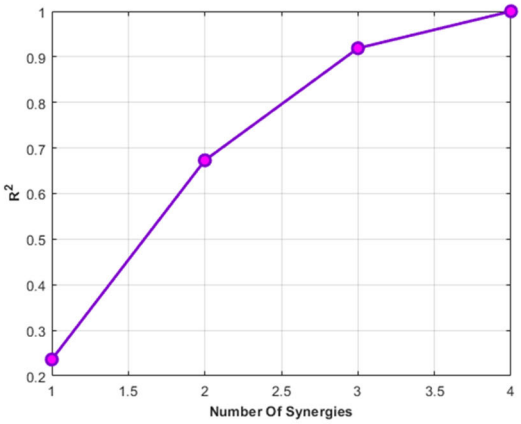

FIGURE 6. The mean calculated R^2 value according to the number of synergy matrices extracted from the EMG signal.

Fugl-Meyer Assessment (FMA-UE) at the first and last rehabilitation session for all participants [59], [60]. The National Institutes of Health Stroke Scale (NIHSS) is a common criterion to assess the side effects of stroke. In this study, this measure was evaluated on all participants in the first and last rehabilitation session [61], [62]. In addition, the Modified Rankin Scale (MRS) was evaluated as a measure of global disability reported by physicians and as a widely used criterion for evaluating post-stroke recovery at the first and last rehabilitation session for all participants in this study [63], [64].

b: THE TRAJECTORY TRACKING ASSESSING

In this study mathematical and statistical measures were used to evaluate patients' ability to track the displayed visual trajectory [65], [66]. The correlation coefficient (CC) is a

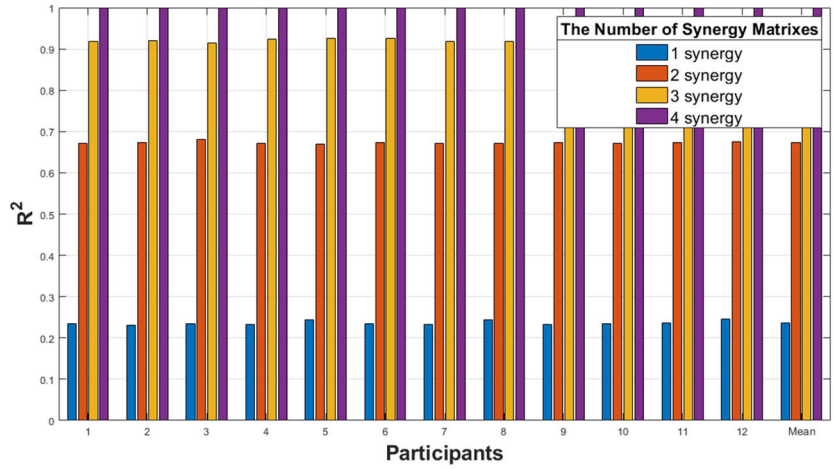

FIGURE 7. R^2 index variation for healthy participants and mean of all vs. concerning the number of synergy matrixes.

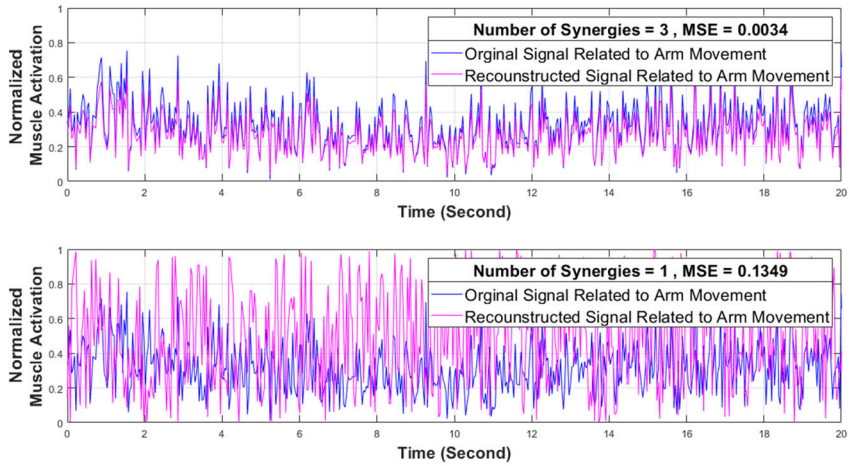

FIGURE 8. The muscle activation patterns and the reconstructed signals that have been obtained with two different numbers of muscle synergy patterns related to a healthy participant (AZ).

statistical indicator of how close two variables are to each other. The range of values is -1 to 1. A correlation of 1 indicates a perfect positive correlation, whereas -1 indicates a perfect negative correlation. No linear link exists between the movements of the two variables, as shown by a correlation of 0 [67]. Thus, the quantity of CC between the actual and desired trajectory could illustrate the patients' capability for tracking the shown visual signal. The quantity of CC could be computed using the Eq. (1) and (2).

$$H = h_1, h_2, \cdots, h_i, \cdots, h_n$$
$$P = p_1, p_2, \cdots, p_i, \cdots, p_n \tag{6}$$
$$CC(H,P) = \frac{\sum \left(h_i - \bar{h}\right)(p_i - \bar{p})}{\sqrt{\sum \left(h_i - \bar{h}\right)^2 \sum (p_i - \bar{p})^2}} \tag{7}$$

where, H is the actual motion trajectory and P stands for the desired motion trajectory. The n shows the time step of the trajectories.

5) STATISTICAL ANALYSIS

The normality and homogeneity of the variances were evaluated using the Shapiro Wilk and Levene Tests. Since the conditions for non-parametric test were met, the Mann-Whitney U test and Wilcoxon test were used for intra-group data analysis, while one-way Analysis of variance (ANOVA) test was used for intra-group data analysis. The t-test was also used to analyze the computed differences between two groups. Chi-square and Fisher's exact tests were used to assess categorical data. When the expected frequencies were less than 20%, we used the ''Monte Carlo Simulation Method'' to incorporate any minor frequencies in the study. The tests were considered statistically significant if the P value < 0.05.

III. RESULTS

A. EXTRACTING THE SYNERGY PATTERNS

To get a better understanding of the output performance of the HALS algorithm, we used the R^2 index. Using R^2 the optimal

TABLE 2. Evaluation of performance with MSE for different RNN models.

Model	MSE
Elman	5.16e-04
LSTM	3.83e-04
NARX	1.63e-05

TABLE 3. Evaluation of performance with the Pearson correlation coefficients of different RNNs.

Model	Pearson Correlation Coefficient
Elman	0.912781
LSTM	0.953445
NARX	0.98992

number of synergy matrixes can be determined. In Eq. 8, SSE is the residual sum of squares, and SST is the sum of the remaining squares of the mean activation vector ($\bar{m}$) [68].

$$R^2 = 1 - \frac{SSE}{SST} = 1 - \frac{\sum_s \sum_{k=1}^{k_s} \left\| m^s(t_k) - \sum_i c_i^s w_i \left(t_k - t_i^s\right) \right\|^2}{\sum_s \sum_{k=1}^{k_s} \|m^s(t_k) - \bar{m}\|^2} \quad (8)$$

In the data collection section, we recorded the EMG signal of four muscles, then three muscle synergy matrices were extracted using the HALS method. Best R^2 value was considered with 3 synergy matrices. The result of R^2 variations concerning the number of synergy matrixes have been shown in FIGURE 6 and FIGURE 7. Also, FIGURE 8 shows the mean values of Mean Squared Error (MSE) values after reconstructing the muscle activation pattern using the extracted C and W synergy matrices. The muscle synergy extracted method could be acceptable because the mean value of MSE was 0.0037. According to the range of the extracted muscle activation pattern (0-1), the computed MSE is so low compared to the data range that the reconstruction performance could be acceptable.

B. THE PERFORMANCE OF THE NARX MODEL

For different RNN models, MSE values and correlation coefficient performance are reported in TABLE 2 and TABLE 3. Though the low values of the computed MSEs could be attributed to the MES-related averaging, the MES-related results are in conformity with CC-related results. Because the computed CCs are near one (TABLE 3).

C. THE TRACKABILITY

Before carrying out the interventions on the patients, the trackability of the designed visual biofeedback signal was first evaluated. The healthy participants took part because the aim was to assess the maximum trackability of the designed visual biofeedback trajectory. According to Eq. (1) and (2),

TABLE 4. The mean value of the computed CC for healthy participant.

Participant ID	Correlation Coefficient
AZ	0.865
SS	0.810
HR	0.764
MR	0.833
SH	0.757
HM	0.891
EM	0.812
HN	0.863
JZ	0.810
KZ	0.763
TZ	0.783
MS	0.762

the results of following the visual trajectory for healthy participants and in the training stage of the model are according to TABLE 4. The results show that the average correlation coefficient (CC) is between 0.76 and 0.87. These values can convince us that the designed path can be followed by healthy participants. Despite the fluctuation of the displayed trajectory geometry, healthy participants could produce a movement-related trajectory that was reasonably correlated with the reference trajectory.

D. ASSESSING THE DESIGNED EXERCISE PROTOCOL

A total of 308 stroke patients were screened for the study. 40 participants met the inclusion criteria, of which 24 were randomly selected and divided into 2 groups. The experimental studies conducted on 12 participants in the control group and 24 subjects with ischemic stroke. The 24 patients who completed the study included 11 women and 13 men. The demographic and clinical characteristics of the patients are shown in TABLE 1. Age, gender, dominant hand, paretic hand, lesion type, and time after the stroke were not statistically different across the groups ($P > 0.05$). Both groups were similar in terms of MMSE score ($P > 0.05$). At post-treatment, a statistically significant increase was found in both groups in terms of the FMA-UE, NIHSS, and MRS score ($P < 0.001$). No statistically significant difference was found between the two groups regarding the NIHSS and FMA-UE scores as shown in TABLE 5. However, the inter-group analyses showed significant changes in the quantities of the NIHSS, FMA-UE, MRS, and especially CC computed before and after intervention as shown in TABLE 5 and FIGURE 10. Finally, as shown in TABLE 5, the follow-ups continued until

TABLE 5. The computed quantitative measures before, after the intervention and after the follow-up, as well as the average difference of values in both intervention and control groups.

Parameters		The Intervention group (N =12)			The Control group (N =12)		
		Mean±SD	F-Value	P-Value	Mean±SD	F-Value	P-Value
NIHSS Score	Pre-treatment (day 0)	8.41 ± 3.55	0.37	0.772	7.66 ± 3.98	0.15	0.927
	Post-treatment (5 weeks)	7.50 ± 3.55			6.83 ± 4.54		
	Follow-up 1(3 Months)	7.33 ± 3.52			6.83 ± 4.54		
	Follow-up 2 (6 Months)	6.91 ± 3.70			6.50 ± 4.50		
	Delta - NIHSS Score	0.91 ± 0.00	Not Applicable	Not Applicable	0.83 ± 0.56	Not Applicable	0.41
MRS Score	Pre-treatment (day 0)	3.25 ± 0.62	4.11	0.054	3.08 ± 0.66	2.08	0.162
	Post-treatment (5 weeks)	2.66 ± 0.77			2.58 ± 0.99		
	Delta - MRS Score	0.58 ± 0.15	Not Applicable	Not Applicable	0.50 ± 0.32	Not Applicable	0.33
FMA-UE Score	Pre-treatment (day 0)	21.66 ± 7.37	6.92	0.015	21.91 ± 6.51	7.01	0.014
	Post-treatment (5 weeks)	35.16 ± 16.16			35.83 ± 17.00		
	Delta - FMA-UE Score	13.50 ± 8.79	Not Applicable	Not Applicable	13.91 ± 10.49	Not Applicable	0.45
CC	Pre-treatment (day 0)	0.428 ± 0.068	124.29	$1.611e^{-10}$	Not Applicable	Not Applicable	Not Applicable
	Post-treatment (5 weeks)	0.695 ± 0.046					
	Delta- CC	0.26 ± 0.02	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; MRS, Modified Rankin Score; FMA-UE, Fugl-Meyer Assessment for Upper Extremity; CC, Correlation Coefficient. Values are expressed as the mean ± standard deviation; F-values and p-values from one-way ANOVA and P-values from t-test for analyzing the computed differences.

three and six months later than the last sessions. In TABLE 5, the ''Delta'' notation shows the difference between the computed measures related to two groups.

IV. DISCUSSION

Developing motor programs, motor learning, and new cognitive experiences cause restructuring of the Central Nervous System (CNS). Goal-oriented, repetitive, and reinforce safe movement patterns are performed with biofeedback systems. Increased muscle strength, especially in the damaged upper extremity, with patient functional activity [69]. However, the design of biofeedback signals has often been based on simple motion analysis of a single joint or single muscle [9], [66]. But we believe that overcoming the mentioned obstacle requires proposing new approaches to design biofeedback signals. Our hypothesis is that biofeedback signals contain enough information about muscle activation patterns and can be considered as a Graphical User Interface (GUI). In the traditional method of electromyographic biofeedback, the muscle activation patterns of muscles are usually used as the biofeedback signals to only increase the voluntary muscle activation level [26], [28]. While increasing the muscle activation level merely could not be a guarantee for a normal movement recovery. Because without recovering the muscles' synergy patterns the quality of the restored movement may not be proper. Therefore, mapping muscle synergy to movement-related trajectory becomes a secondary challenge. In this study, we propose and evaluate an underlying mechanism for creating a visual biofeedback intervention for arm movement based on kinematics. Using muscle synergistic patterns, the trajectory related to kinematics was extracted. Tracing such a trajectory by humans is crucial in addition to being informative. A patient must be able to track a visual biofeedback trajectory. In order to compare the generated trajectory by our model with the displayed trajectory, CC was calculated. This method allowed us to measure the level of covariance between the two trajectories. The results show that the average CC is between 0.76 and 0.87. These values can convince us that the designed path can be followed by healthy participants. Despite the fluctuation of the displayed trajectory geometry, healthy participants could produce a movement-related trajectory that was reasonably correlated with the reference trajectory. Also, based on Adams' closed-loop theory, the process of motor learning works with the

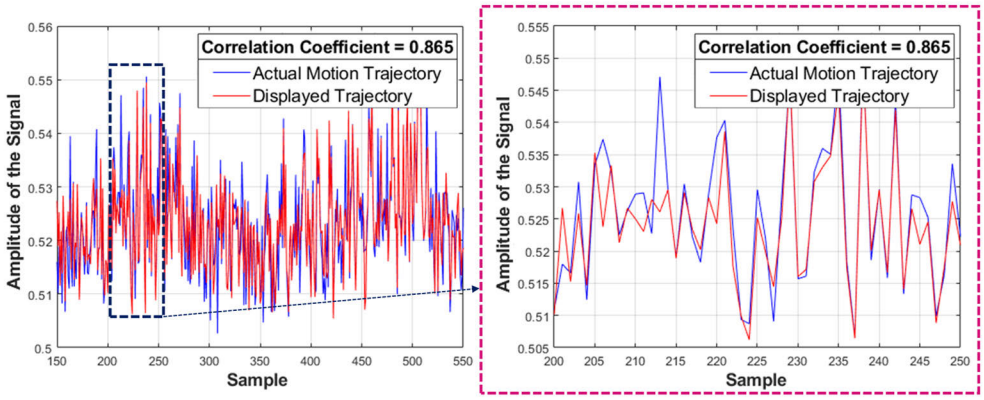

FIGURE 9. Tracking quality related to a healthy participant (AZ).

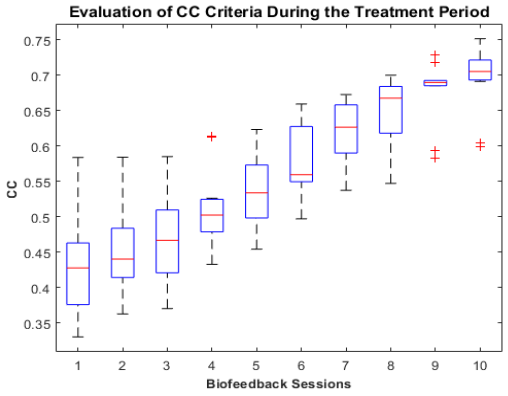

FIGURE 10. The quantities of the computed CC's for each biofeedback session in the interventional group.

help of sensory feedback to detect and correct errors, and its basis is the gradual increase of correct perceptual tracking and the reduction of incorrect perceptual tracking [70]. Therefore, based on the clinical evidence of the studies and this theory, biofeedback-based techniques can revive motor recovery in patients with motor impairments by repeating and strengthening correct perceptual tracking [71], [72]. According to this theory, internal and external feedbacks play a critical role in motor learning.

This study included two main stages. Thus different assessment indexes related to each stage were used. The first stage was modeling based on muscle synergy analysis. In this stage, only evaluating the model performance was essential. In the second stage, the experimental evaluations were performed. For the healthy participants, only trackability of the designed biofeedback trajectory was essential. In addition, the clinical effectiveness was evaluated for the stroke patients using some clinical indexes in a pre-intervention and post-intervention assessment manner. The results showed a statistically significant improvement in upper extremity NIHSS and FMA-UE scores in the intervention group compared to the control group. Also, the results showed that there was a significant change in the CC score of the intervention group during the experiment. Additionally, the intervention group's MRS scores were higher than the corresponding scores in the control group. According to prior studies, the visual biofeedback group showed more motor improvement in the upper extremity groups than the control group [26], [31], [33], [35], [73], [74], [75].These results may be explained by the fact that the participants in the intervention group received higher scores in terms of clinical evaluation than those in the control group. Similarly, an increase in post-treatment FMA-UE scores of the upper extremity in this study also supports the improvement in the CC scores. These results may be related to the use of the proximal portion of the arm in EMG-based visual biofeedback training. The expected lack of improvement in the NIHSS and MRS index can also be justified. Because there is a mismatch between the intended target and the evaluation parameters.

In our study, the NIHSS, MRS, and FMA-UE scores of the patients in both groups improved compared to pretreatment. However, although the intervention group showed significant changes in NIHSS and CC scores, the changes in FMA-UE scores for the intervention group were not significantly higher than the control group. Unfortunately, this is a point in our study about which we have no definitive explanation but, there was a significant relationship between age, level of education, MMSE score, MRS score, and NIHSS score. Both groups were similar at baseline in terms of NIHSS, MRS, and FMA-UE scores, however, the NIHSS scores after follow-up evaluation were significantly better in the intervention group. This may be the reason why the FMA-UE scale may be insufficiently sensitive to record the change in high-functioning individuals. On the other hand, changes of 4–7 points for chronic stroke and 9–10 points for subacute stroke are considered to be clinically important [76], [77]. Other reasons may be inadequate sample size, short treatment duration, and short follow-up. Our results also showed a significant increase in the FMA-UE scores after treatment in both groups, but there

was no statistically significant difference between the groups. No significant changes were observed in some patients who were older with more severe stroke and lower education level.

According to the observations remarked on and reported by the neurologists who collaborated on the study, it seems that the proposed method is more effective for patients with mild to moderate degrees of injury. It seems that extending this task into more interesting video games and combining it with auditory biofeedback can be helpful [30]. This study has faced some limitations. The first limitation was that the duration of treatment in the study group was longer than in the control group because the proposed biofeedback technique was added to conventional rehabilitation. The longer time of rehabilitation training can affect functional results. The second limitation was that this study was performed on all right-handed individuals.

In future work, by recording EMG from the normal side of the patient's body, a biofeedback mechanism can be designed for the paretic side according to the specific physiological and anatomical characteristics of the individual. In addition, the low patient diversity included in the study also prevents the generalization of results. In addition, despite the wide age range of participants, the impact of age was not considered. This issue has to be addressed in future studies.

V. CONCLUSION

In this study, a proposed mechanism for the design of a visual biofeedback signal related to upper extremity rehabilitation was evaluated in terms of different aspects. First of all, the trackability of such signals by the participants had to be assessed. The low values of MSE alongside the near-one values of CC proved an acceptable trackability of the designed trajectory. In the next step, the efficacy of the exercise therapy using the implemented biofeedback system on stroke patients was assessed. According to the achieved results, the NIHSS and FMA-UE scores in the intervention group have significantly improved compared to the control group. Furthermore, the results proved that there was a significant change in the CC value of the intervention group. Thus, the results show that the designed underlying mechanism in this study based on analyzing the muscle synergy patterns extracted from EMG signal information helps along with the conventional rehabilitation and could improve the movement and function of the upper extremity in patients with subacute stroke hemiplegia. This treatment was not significantly superior to the control group in improving Activities of Daily Living (ADL), but these results may change with longer follow-up. However, according to the authors' knowledge, no study has used muscle synergy patterns to design visual biofeedback for the upper extremity of a stroke survivor. Nevertheless, evaluating more patients, incorporating attractive components such as video games, and working on visual feedback scenarios could guarantee brain reorganization are the future steps of this research.

AUTHORS' CONTRIBUTIONS

Seyyed Ali Zendehbad performed data recording experiments on the participants and helped implement the proposed method. Hamid Reza Kobravi administered and designed the protocol, coordinated the study, and contributed to data analysis and writing of the original draft and review and editing preparation. Mohammad Mahdi Khalilzadeh assisted in the design of the computer vision section and assisted in the analysis of the result and the preparation of the version. Athena Sharifi Razavi and Payam Sasan Nezhad helped select and evaluate stroke patients, data curation, supervision and validation, and complete clinical trials. All authors read and approved the final manuscript.

ETHICAL APPROVAL

The procedures were approved by the Research Ethics Committees Mazandaran University of Medical Sciences (IR.MAZUMS.REC.1398.902) and the Iranian Registry of Clinical Trials (IRCT20200914048720N1) [78].

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