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Machine Learning role in clinical decision-making: Neuro-rehabilitation video game

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ABSTRACT

In this study, we investigated the potential use of Machine Learning algorithms (ML) to predict the outcome of home-based neuro-rehabilitation video game intervention and its advantage in supporting clinical decision-making. We adopted Support Vector Machines (SVM) and K-Nearest Neighbors (KNN) to develop multidimensional functions (multi-variable Kernel functions) since both algorithms were considered significant and active analysis agents for prediction and classification. Supervised SVM and KNN algorithms were trained using the upper extremity (arm, forearm, and hand) joints' kinematic data and hand gestures of participants while interacting with the developed video games. Data collected from healthy and Multiple sclerosis (MS) participants were compared and used to develop the predictive algorithm. Pre- and post-rehabilitation data of MS subjects were investigated and used to assess the subject's functional improvements following the program. Bayesian optimization, Sigmoid, polynomial, and Gaussian Radial Basis functions were utilized for training and predicting outcomes. The results showed that the first two kernel regressions had the best performance regarding predictability and cross-validation loss. KNN's prediction accuracy was exceeded by 91.7% versus SVM, which was 88.0%. The effectiveness of the rehabilitation program was assessed through Spatiotemporal control and motor assessment scale presenting 40% improvement. Our findings suggest that ML has a great potential to be used for decision-making in neuro-rehabilitation programs.

1. Introduction

Multiple sclerosis (MS) is the most prevalent autoimmune disease affecting the nervous system and motor control (Steinman, 1996). Motor control is a mechanism by which individuals use their cognition to stimulate and coordinate the muscles and limbs involved in the administration of a motor ability (Benedict et al., 2005). Based on numerous studies, continuous inpatient or outpatient rehabilitation could lead to intensification inactivity and overall ability to engage in society with optimal improvement and functionality (Jonsdottir et al., 2018). According to Kwakkel et al. (2019) UE, recovery probably occurs through an aggregate of inevitable and learning-dependent manners, including reestablishing the quality of movement and learning ways to use their residual capacity in the most practical way to accomplish a task.

MS casualties often do not adhere to recommended exercise by clinicians due to lack of motivation (Giusti et al., 2006). However, there is substantial evidence of the feasibility and effectiveness of using serious games for rehabilitation (Esfahlani, Thompson, Parsa, Brown and Cirstea, 2018; Jonsdottir et al., 2018; Tannous, 2018), which encourage participants' retention and incentive to practice.

A study by Jonsdottir et al. (2018) showed the clinically significant enhancements in MS people's arm function following interaction with a serious game for rehabilitation. Bettger and Stineman (2007) also suggested that regular exercises and automatic assessment of the upper extremity through home-based rehabilitation could be advantageous for people with motor control impairment and MS condition.

To facilitate a home-based rehabilitation program for MS casualties, we developed mini video games using the principle of modified constraint-induced movement theory (mCIMT) and mirror image therapy. The game's difficulty level was adjusted using the Monte Carlo Tree Search algorithm, examined in our previous studies (Esfahlani, Butt, & Shirvani, 2019; Esfahlani, Muresan, Sanaei and Wilson, 2018). ML has received less attention in supporting clinical decision-making

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Abbreviations

The following abbreviations are used in this manuscript:

ML	Machine Learning
mCIMT	Modified Constraint-Induced Movement Therapy
SVM	Support Vector Machine
KNN	K-nearest neighbors
UE	Upper Extremity
RBF	Radial Basis Function
EMG	Electromyography
IMU	Inertial Measurement Unit
BLE	Bluetooth Low Energy
LOO	Leave one out
AUC	Area Under the curve
LDA	linear discriminant analysis
ROC	Receiver Operating Characteristics
PCA	Principal Component Analysis

and predicting rehabilitation of upper extremity (UE) outcomes. Machine Learning (ML) algorithms were integrated to automate the process of analyzing 3D kinematics of the UE movements and classify its patterns based on data obtained from sensors (Microsoft Kinect, Leap Motion, and Myo armband devices). KNN and SVM ML algorithms were utilized due to their high accuracy and good theoretical guarantee of overfitting.

Support Vector Machines (SVMs) and k-Nearest-Neighbors (KNNs) are the non-probabilistic ML algorithms, which represent different approaches to learning as active analysis agents for prediction and classification. These algorithms function based on a statistical learning procedure demonstrated to have high accuracy (Derie et al., 2020; Stetter, Krafft, Ringhof, Stein, & Sell, 2020). The algorithm could predict the players' arm function following the rehabilitation program and classify the arm and hand pattern and gestures. We obtained a view-invariant representation of the 3D positions and orientation of the skeleton joints of UE, an arm's muscle actions, and hand gestures. Participant's with MS condition was distinguished from healthy subjects with the algorithm followed by predicting the motor function improvement following the intervention.

2. Background

ML has been successfully applied to several applications; ranging from face identification (Heisele, Ho, & Poggio, 2001) to text categorization (Joachims, 1998), and pattern recognition and classification problems (Hosomi et al., 2012; Levinger, Lai, Webster, Begg, & Feller, 2007). The application of SVM to classify gait patterns of Knee osteoarthritis was conducted by Levinger et al. (2007) to investigate whether ML can assess gait improvement following knee replacement surgery. Zhang, McCullagh, Nugent, Zheng, and Baumgarten (2011) investigated optimal model selection for posture recognition through a supervised classification and training of a multiclass ML. They classified nine everyday postures from a belt-worn smartphone's accelerometer data. Lau, Tong, and Zhu (2009) explored the use of ML to classify different walking conditions for hemiparetic subjects. The participants walked in five different conditions in that two portable sensor units, comprising an Accelerometer and Gyroscope, were attached to the lower limb on the shank and foot segments to measure the kinematic data. Their results showed that the SVM classification method could be applied as a tool for pathological gait analysis, pattern recognition, and activity monitoring during the rehabilitation of daily exercises. They also suggested that the performance of an SVM was superior to other ML methods. Begg, Palaniswami, and Owen (2005) integrated SVM to perform an automated recognition of gait changes among young and senior participants. It was used to identify the aging influence on gait patterns and locomotor balance with the advantage of early identification of at-risk gait and monitoring the progress of treatment outcomes. They recommended that SVMs function as an efficient gait classifier to recognize young and elderly gait patterns. Fleury, Vacher, and Noury (2010) used a health smart home in that a wearable kinematic sensor was utilized to collect postural transitions using pattern recognition and walk periods frequency analysis. The data collected from various sensors used to classify each temporal frame using SVM. Long et al. (2016) utilized an online SVM optimized by particle swarm optimization to identify different locomotion modes to realize a smooth and automatic transition. Their experimental results show the effectiveness of the SVM algorithm with high accuracy. Oskoei, Hu, et al. (2008) showed that the SVM is computationally an efficient algorithm for classification using electromyogram inputs.

3. Materials and methods

The task in ML involves separating data into training and testing sets. Each instance in the training set contains one target value and several attributes. ML produces a model based on the training data, which predicts the target values of the test data given only the test data attributes (Boser, Guyon, & Vapnik, 1992). In this study, ML Matlab Toolbox was used to map the input into a high-dimensional space.

3.1. Support vector machines (SVM)

SVM constructs an optimal hyperplane as a decision surface to maximize the margin of separation between the two classes. An iterative training algorithm must construct an optimal hyperplane, which is managed to minimize an error function. Based on the error function, SVM models can be classified into four distinct types (Joachims, 1998), categorized as classification and regression models. The algorithm finds optimal locations of the decision surface by using a set of mathematical functions involving classification and regression models (Cortes & Vapnik, 1995). Training for the algorithm has two phases; (I) Remodel predictors (input data) to a high-dimensional feature space where the data is never explicitly transformed into the feature space. (II) Solve an optimization problem to fit an optimal hyperplane to classify the transformed features into two classes. The number of support vectors determines the number of transformed features, and the process of rearranging the objects is known as mapping or transformation.

Given a training set of instance-label pairs (x_i, y_i), i = 1, …,l where $x_i \in R^n$ and $y \in \{1, -1\}^l$, the SVM require the solution for equations listed in Table 1. Table shows two classification and two-regression types; C-SVM and ν-SVM, and ϵ-SVM. $C \in [0, \infty]$, $\nu \in [0, 1]$ and $\epsilon \in [0, 1]$ are regulation parameters that supports implementing a penalty on the misclassifications that are performed while separating the classes. It helps in improving the accuracy of the output. The regularization parameters control the trade-off between the slack variable penalty (misclassifications) and the width of the margin. Small value makes the constraints be ignored, which leads to a large margin. Large value allows the constraints difficult to be ignored, which leads to a small margin. ϕ is the kernel function which maps x_i to $\phi(x_i)$. ζ is the slack variable that allows regression errors to exist up to the value of ζ_i and ζ_i^*, yet still satisfy the required conditions. $w \in R^n$ is inversely proportional to margin, hence to maximize the margin, we will have to minimize w, $b \in R$.

K function estimates the functional dependence of the dependent variable y on a set of independent variables x (Cortes & Vapnik, 1995). Kernel functions are distinguished mainly based on the localization and boundary between different classes to determine finite response across the entire range of features. Linear, polynomial, radial basis function (RBF), and sigmoid kernel functions were adopted, which accompanied

Table 1
SVM algorithm with the error functions and constraints.

Classification SVM	Regression SVM
1: C-SVM classification	**3: epsilon-SVM regression**
$min_{w,b,\zeta} \quad \frac{1}{2}w^T w + C\sum_{i=1}^{l}\zeta_i$ **Subject to the constraints :** $y_i(w^T\phi(x_i)+b) \geqslant 1-\zeta_i$ $\zeta_i \geqslant 0,\ i=1,\dots,l$	$min_{w,b,\zeta} \quad \frac{1}{2}w^T w + C\sum_{i=1}^{l}\zeta_i + C\sum_{i=1}^{l}\zeta_i^*$ **Subject to the constraints :** $w^T\phi(x_i)+b-y_i \leqslant \varepsilon+\zeta_i^*$ $y_i - w^T\phi(x_i)-b \leqslant \varepsilon+\zeta_i$ $\zeta_i,\zeta_i^* \geqslant 0,\ i=1,\dots,l$
2: nu-SVM classification	**4: nu-SVM regression**
$min_{w,b,\zeta} \quad \frac{1}{2}w^T w - \upsilon\rho + \frac{1}{l}C\sum_{i=1}^{l}\zeta_i$ **Subject to the constraints :** $y_i(w^T\phi(x_i)+b) \geqslant \rho-\zeta_i$ $\rho \geqslant 0,\ \zeta_i \geqslant 0,\ i=1,\dots,l$	$min_{w,b,\zeta} \quad \frac{1}{2}w^T w - C(\upsilon\varepsilon + \frac{1}{l}C\sum_{i=1}^{l}(\zeta_i+\zeta_i^*))$ **Subject to the constraints :** $(w^T\phi(x_i)+b)-y_i \leqslant \varepsilon+\zeta_i$ $y_i-(w^T\phi(x_i)+b) \leqslant \varepsilon+\zeta_i^*$ $\zeta_i,\ \zeta_i^* \geqslant 0,\ i=1,\dots,l$

by Bayesian optimization to map data, illustrated in Eq. (1). Dot product in the equation acts as a transformer to map input data points to the higher dimensional feature space, and γ is kernel function's adjustable parameter (Joachims, 1998).

$$K(X_i,X_j)=\phi(X_i)\cdot\phi(X_j)\begin{cases}X_i\cdot X_j & Linear\\ (\gamma X_i\cdot X_j+C)^d & Polynomial\\ exp(-\gamma\mid X_i-X_j\mid^2) & Gaussian\ RBF\\ tanh(\gamma X_i\cdot X_j+C) & Sigmoid\end{cases} \tag{1}$$

3.2. K-nearest neighbor

Inputs in KNN consist of k closest training examples in the feature space. The output depends on whether KNN is qualified for classification or regression. In regression, the output is the object's property value that is the average of the KNNs values. KNN regression's output is the object's property value that an average of the values of CNN's. In KNN classification, the output is a class membership where a majority vote of the neighbors classifies objects. KNN classifier or weighted nearest neighbor classifier could be perceived as assigning the K-Nearest Neighbors a weight $\frac{1}{k}$. Given a X set of n points and a distance function, KNN search finds the k most adjacent points in X to set of points Y. The choice of K is essential and needs to be selected carefully, i.e., if K is too large or small, some of the neighbors used to make prediction will no longer be similar to the foreseen one, which will bias the prediction (Hastie, Tibshirani, & Friedman, 2009). In the study, an optimal K is selected empirically, examining cross-validation procedure on the training set (Hastie et al., 2009).

Given the covariate vector of a new observation, x_0, the goal is to predict its response, y_0. For every observation x_i in the training set, let $s_i = s(x_0, x_i)$ be its similarity to x_0. Then the similarities are put in an order $s_{(i)}$, that is, $s_{(1)} \geqslant s_{(2)} \geqslant \cdots \geqslant s_{(n)}$. Similarly, if $s_j = s_{(k)}$, where x_j is the kth most similar observation in training set to x_0 then the set of KNNs of x_0; $N(x_0, K)$, could be described as all observations whose similarities to x_0 are at least $s_{(K)}$; $N(x_0,K) = x_i : s_i \geqslant s_{(K)}$.

$$\hat{p} = \frac{\sum_{x_i\in N(x_0,K)} y_i}{|N(x_0,K)|} \tag{2}$$

KNN algorithm estimates the probability of $y_0 = 1$, $|N(x_0,K)|$ is the number of items contained in the set $N(x_0,K)$. It generally equals K but may exceed it depending on how ties are treated. The response is then predicted to be one if $\hat{p} \geqslant c$, where c is a prespecified threshold parameter. The overall error rate in KNN decreases as K increases and levels off at around $K = 20$. In a few cases, we can see that the overall error rate commences increasing again as K, increasing further; thus, we chose K to be 20.

3.3. Video game & modified constraint-induced movement therapy

Constraint-Induced Movement Therapy (CIMT) is a physical rehabilitation strategy that uses operant training techniques applied in the context of rehabilitation medicine (Kwakkel, Veerbeek, van Wegen, & Wolf, 2015), developed by Taub, Crago, and Uswatte (1998). Its principle is to continue stretching motor capacity gradually beyond an attained achievement level. CIMT emphasizes massed practice with the affected upper limb by restraining the less affected limb and training the affected one by shaping movements. CIMT is exhaustive, possibly resulting in non-compliance with the protocol. It devotes six hours or more of therapy while constraining the intact arm for 90% of waking hours per day throughout two weeks (Kwakkel et al., 2015). Thus, a modified version of it - mCIMT has been formed by Page, Levine, Leonard, Szaflarski, and Kissela (2008) to overcome such complexity. The mCIMT intends to overcome learned non-use in chronic hemiparesis, which is the behavioral conquest of purposive movement of the more affected UE in daily living exercises. Two to three weeks of mCIMT for stroke patients' rehabilitation have shown significant improvements in the spontaneous use of the paretic limb in the live setting, in comparison with placebo control therapy or usual and customary care (Wolf et al., 2006). Mark et al. (2008) also suggested that slowly progressive MS conditions could take advantage of mCIMT and achieve promising progress. Since chronic UE hemiparesis occurs in MS casualties (Cowan, Ormerod, & Rudge, 1990), we hypothesized that such patients could manifest learned non-use and favorably respond to the therapy. Therefore, in this study, the mCIMT principle was paired with mirror image therapy to acquire mini video games. It was developed based upon repetitive task practice and the application of behavioral techniques known as shaping. Shaping involves matching the difficulty of tasks performed to the improvements the patients make and providing encouraging feedback immediately after any gain in function (Corbetta, Sirtori, Castellini, Moja, & Gatti, 2015). Shaping in conventional mCIMT is determined by therapists based on individual movement deficits at specific skeleton joints (joint movements) that have the most potential for improvement according to a therapist's judgment (Taub et al., 2006). Whereas in our design, the process and decision-making are conducted automatically by the algorithm. The progression of movement tasks is made systematically, quantified, and parametric way on personalized tasks for a patient. Duration of intervention in conventional mCIMT could vary from [2-10] weeks. Furthermore, the treatment time could be modified from thirty minutes to three hours per session (Yen, Wang, Chen, & Hong, 2005). Thus, therapy sessions are designed as follows:

1. Therapy sessions of one hour, five days a week for ten weeks.
2. Restraining the use of a non-paretic upper limb to promote the use of the more impaired limb during sessions.
3. Adherence-enhancing behavioral methods designed to transfer the gains obtained in the clinical setting to the patients' real-world environment.
4. Each task was practiced for at least five minutes before starting the formal session.

Table 2 lists the mini-video-game tasks developed for this study with the devices used to interact with the therapy/game. Further explanations on devices and the game setting are followed.

1. forearm to the table, participants' forearm reaches the highlighted areas presented in the virtual environment.
2. Forearm to the virtual button, and hold it in that position for three seconds, while the visual feedback and timer are activated.
3. Extend an elbow to press the virtual button.
4. Hand to the table and press the virtual button at the same time.
5. Hand to the virtual button and hold it for three seconds.
6. Collect virtual boxes and place them on top of each other.

Table 2
Task-specific use of devices and computer supervised mini-video games for the rehabilitation.

Mini video games	Devices		
	Myo	Kinect	Leap Motion
1. Forearm to the table	✓	✓	·
2. Forearm to the virtual button and hold for three sec	✓	✓	·
3. Extended Elbow	✓	✓	·
4. Hand to table	✓	✓	·
5. Hand to the virtual button and hold for three sec	✓	✓	·
6. Reach virtual boxes on the table collect and place them	✓	✓	✓
7. Lift the virtual box to 10 cm	✓	✓	✓
8. Pull the virtual rubber string to hit virtual objects	✓	✓	·
9. Grab the virtual fruit	✓	✓	·
10. Lift the virtual pencil and put it on the virtual box	✓	✓	✓
11. Stack the virtual boxes (up to 4)	✓	✓	✓
12. Flip the cards	✓	✓	✓
13. Grip strength	✓	✓	✓
14. Turn the key in the virtual lock	✓	✓	·
15. Reach virtual fruits and place them in the basket	✓	✓	·

7. Lift virtual boxes to 10 cm (identified by highlighted areas in the game).
8. Pull the virtual rubber sling and release it to smash/hit virtual boxes.
9. Grab virtual objects that are spawned randomly in the space to collect them.
10. Lift a virtual pencil and put it on the virtual box.
11. Stack virtual boxes (up to four boxes),
12. Flip the virtual cards.
13. Grip/hold an object firmly,
14. Turn a key in a virtual lock.
15. Reach virtual fruits and place them in the basket.

The video game in this work provides participants with graphical feedback, positive rewarding and scoring system to encourage the continuation of tasks and retention. The player acts as a controller of the game in that body actions are transferred into the 3D environment using the mirroring effect via Kinect and Leap Motion.

3.3.1. Myo armband

Myo armband by Thalmic Labs is a low-cost consumer-grade EMG device integrating an ARM Cortex-M4 based microcontroller unit, a set of eight dry EMG electrodes, a nine-axis inertial measurement unit (IMU), and a Bluetooth Low Energy (BLE) module (Phinyomark, Khushaba, & Scheme, 2018). The Myo is non-intrusive, as the electrodes allow users to slip the bracelet on and off (Côté-Allard et al., 2018; Esfahlani, Thompson et al., 2018). EMG and IMU data, were collected for hand gestures. The optimal position of the armband placement is determined by conducting various examinations and placed on the widest part of the forearm (right or left). For optimal results and a strong connection to the arm muscles, the Myo armband was warmed up for five minutes (Phinyomark et al., 2018).

3.3.2. Microsoft kinect V2

Kinect v2 has an Infrared (IR) camera with 512 × 424 pixels. Its RGB camera resolution is 1920 × 1080 pixels. It has a field of view (FoV) of 70 × 60° and a frame rate of 30 Hz. Kinect was located on top of the screen within [1.5–2.0] meters from the player. It was elevated 45° in front of the subject (tilted toward the subject). Kinect was used to transfer the players' body joints to the game environment. Skeleton joints were also used for classification and regression analysis. To measure the dynamic range of motion of the UE joints, we employed a sequential kinematic model based on the joint coordinate system (JCS), which was proposed by the Standardization and Terminology Committee (STC) of the International Society of Biomechanics (ISB) (Wu et al., 2005). The coordinates were defined where the coronal axis of the patient is the X-axis, the sagittal axis is the Y-axis, the vertical axis is the Z-axis, and the idle position is the origin of the joint coordinates (Butler, Ladd, LaMont, & Rose, 2010).

3.3.3. Leap Motion

Leap Motion peripheral uses two monochromatic IR cameras and three IR LEDs. It observes a roughly hemispherical area to a distance of about one meter. Leap Motion was located on the desk using a projective interaction mode within 0.4 to 0.6 meters below the player's hands. Fig. 1-a, Fig. 1-b, and Fig. 1-c are the screenshots of task number six using Leap Motion. The player should reach virtual boxes to interact with them. In this scenario, both hands are involved in completing the task where mirrored therapy is used in a 3D environment. The boxes must be picked up and placed on the pads matching the cube's color. At the more advanced level, the player should stack boxes on top of each other. Fig. 1-d, -e, and -f is the screenshot of task number eight from mini-game, according to Table 2.

Fig. 1-e, and -f both show that the player should only use the left hand to interact with the virtual ball and the elastic sling.

Fig. 2 illustrates the location of virtual fruits, task number fifteen in Table 2, spawned in the 3D environment. Monte Carlo Tree Search algorithm was used to spawn objects relative to the position of the player's body joints and their performance. According to the figure, the player only can interact with objects using the right hand. Left-hand could not be used to collect things to promote the use of the affected hand/arm. Fig. 2 displays various planes in which the objects are spawned; abduction/adduction, forward flexion/extension, external/internal rotation and horizontal flexion/extension.

4. Calculation

4.1. Data pre-processing and feature extraction

Myo armband, Microsoft Kinect, and Leap Motion devices enable the player to act as a controller. Kinect collects the player's body joints orientation, and position, Leap Motion transfers fingers and hand movements into the game environment.

EMG signals are formed via the superimposition of individual action potentials generated by irregular discharges of functioning motor units in a muscle fiber. Thus, amplitude and frequency both represent the level of activity of motor units in the fiber. EMG raw signals are transformed into a classification set of features following (feature extraction). There were three types of features in a different domain; Time, Frequency, and Time–Frequency distribution (Nazmi et al., 2016).

Data pre-processing method of baseline correlation was performed using a 4th-order Butterworth bandpass filter with different cut-off frequencies to improve the signal-to-noise ratio (SNR) of the signals. Savitzky–Golay filter was integrated to remove noise from the IMU signals. The 50 Hz notch power line noise removed using a 3 dB passband, amplitude normalization followed by wavelet method to localize both time and frequency segments (Phinyomark et al., 2018).

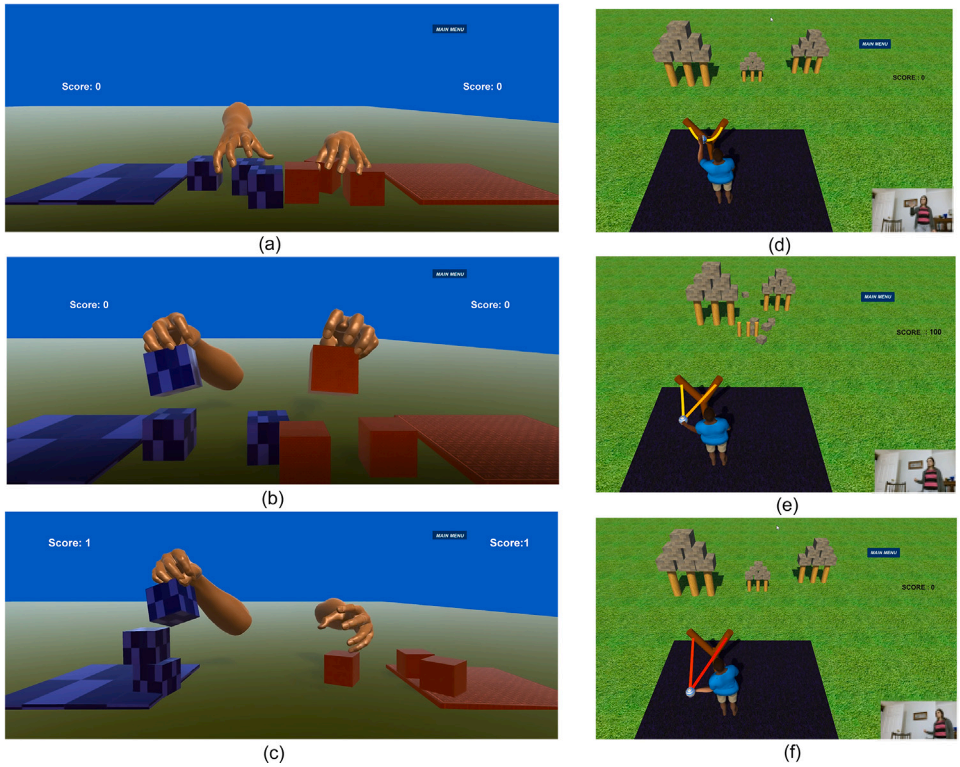


Fig. 1. (a), (b) and (c) 6th Video game task with virtual hands following the physical hands using Leap Motion. (d), (e) and (f) Rubber sling to knock down virtual boxes (right).

EMG signals were recorded at 200 Hz with a high-pass 20 Hz cut-off and low-pass of 500 Hz cut-off at the time domain and frequency of 24 and 2.

The EMG raw signal features were extracted for each type of hand movement from the denoised data. Waveform length time-domain feature extraction method was used to present the characteristics of signals for hand movements due to its high rate of accuracy and stability to changes in segmentation method (Oskoei et al., 2008).

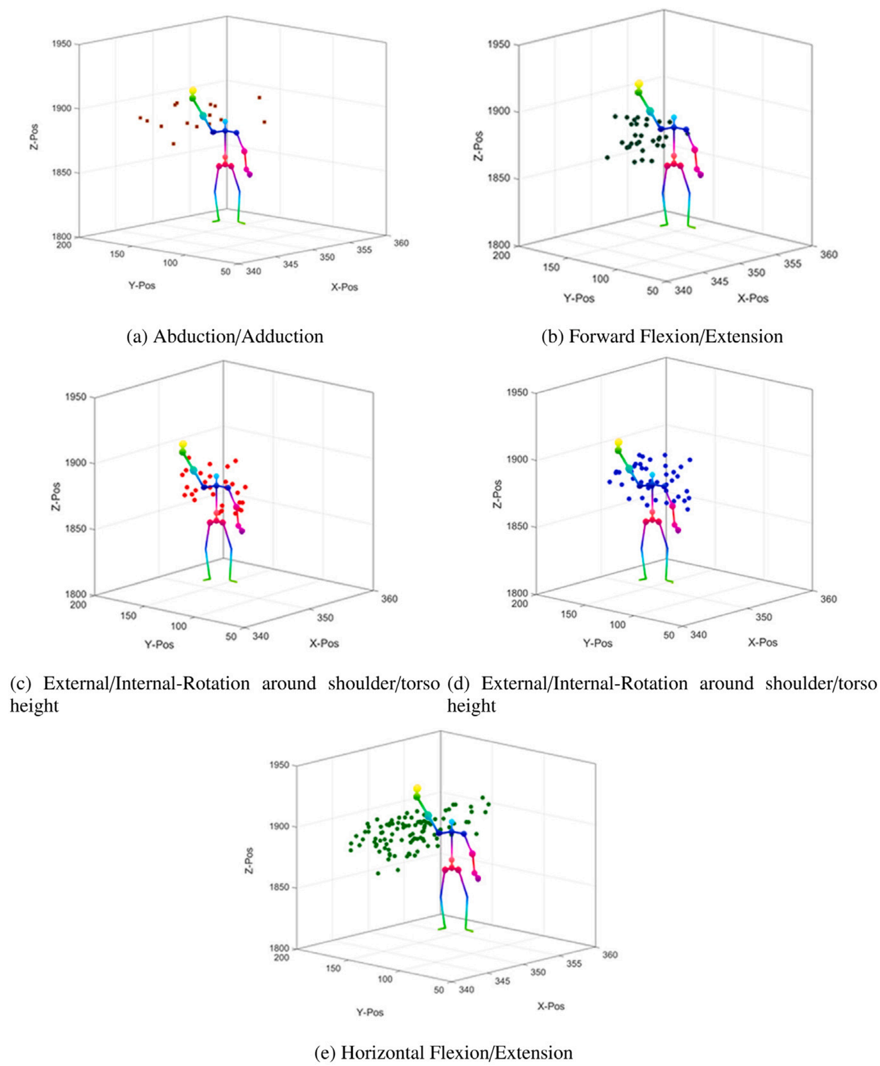
Four hand gestures were segmented using KNN and dynamic time warping algorithms. Each segment consisted of 500 data points taken from the armband. The armband's angular and linear movements were obtained from its Inertial Measurement Units (IMU: Gyroscope, Accelerometer, and Magnetometer) sensor. The Gyroscope determines the roll/pitch, and the magnetometer measures the yaw in various directions. After collecting data at the local sampling frequency, linear interpolations were performed to create a constant sampling interval while maintaining time and frequency domain signal integrity to achieve an identical sampling frequency. The signals were averaged over a hundred and twenty readings to manage high-dimensional data sets efficiently. Acceleration creates a force that is captured by the force detection mechanism of the accelerometer, which measures acceleration indirectly through a force applied to its axis. Linear acceleration was measured in ($G = 9.81\ \frac{m}{s^2}$) along each axes considering static (gravity) and dynamic (sudden starts/stops) acceleration. The Gyroscope's readings were collected in ($\frac{^\circ}{s}$) to calculate the angular velocity of the orientation. The Myo armband first placed on a level tabletop and then was slid along a straight line for a distance of one meter. The noise in data was filtered to adjust the initial and final velocities to zero. The velocity was obtained by integrating accelerometer measurements once, and the position was obtained by integrating the velocity. The sensor moved a distance of one meter, the estimated distance obtained by double integration.

Data from the game engine was registered based on the Unity game development platform frame-rates (60fps) and transferred to the computer's hardware in excel format. The average time required to perform each movement was found to be around 500 (ms) to estimate signal features (Lang, Bland, Bailey, Schaefer, & Birkenmeier, 2013).

4.2. Subjects

Fifty-two participants were recruited for the study (forty with MS and twelve MS-free). Twelve MS patient's data were excluded from analysis as five (four male, one female) could not complete the therapy sessions, and seven patients decided to leave the study. Forty subject's data were used for decision-making and prediction; twenty-eight MS casualties and twelve healthy with age ranged [28,62]. Table 4 summarizes the demographic and clinical characteristics of the forty MS participants at the time of admission. The patients diagnosed with relapsing–remitting MS, secondary progressive MS (47%), and primary progressive MS (53%). The institution (ARU) Research Ethics committee- a UK Research Integrity Office (UKRIO), approved the research. The research was performed following the Belmont principle. Informed consent was obtained from all participants or their legal guardians with a complete explanation of the research process. The explicit motor learning conditions were implemented with guidance to complete the motor tasks and learn them. It relies on maintaining attention, processing information, reflecting and maintain awareness, and working memory capacity. Participants were interviewed following each rehabilitation session to receive feedback. 83% of the MS participants had the previous experience of undertaking conventional physical and occupational therapy with discontinuation due to the lack of motivation. The eligibility criteria for MS patient's participation in the study are; slow primary and secondary progressive MS, at least 20° active wrist extension, 10° active finger extension, and minimal sensory or cognitive deficits (Dunham, Dunham, & Goldenson, 1978).

The healthy subjects' data also were used to train the algorithm accompanying MS casualties to measure the joint's range of motion (ROM) and hand gestures. Joint flexibility at a joint is measured by the number of degrees from the starting position of a segment to its final position at the end of its full range of movement. The measurements were performed using a double-armed goniometer and Kinect devices. In goniometer measurement, a stationary arm holding a protractor was placed parallel with a stationary body segment, and a movable arm



(a) Abduction/Adduction

(b) Forward Flexion/Extension

(c) External/Internal-Rotation around shoulder/torso height

(d) External/Internal-Rotation around shoulder/torso height

(e) Horizontal Flexion/Extension

Fig. 2. 15th video-game scenario of Table 2 with the location of the fruit which is spawned in the virtual environment relative to the player's performance (right hand).

moves along a movable body segment while the axis of the goniometer was placed over the joint (Hamilton, 2011). Table 3 displays the UE ROM collected from healthy subjects in degrees, using both goniometer and Kinect devices. The control groups' data are also used to identify four-hand gestures through the Myo armband, where each movement was held fixed for five seconds, and the signals were registered. The identified four gestures are; 1. Wave hand for reach or move to a target, 2. Fist for grasp or hold on to an object (to carry virtual objects from point A to B), 3. Release an object using the stop hand sign (spread fingers), and 4. Idle or relaxed hand gestures.

Motor Assessment Scale (MAS) with the scale of [0,6] was conducted pre-treatment, post-treatment, and four weeks follow up-treatment for upper arm function and hand movement. Participants performed each task three-time; only the best performance was recorded. Two therapists supervised and obtained the participant's MAS score. If the patient could not complete any part of a section, the score is zero, and if they complete it, the score is six.

The tasks in games are designed to incorporate the major joints of the upper body and represent functional tasks that are feasible yet challenging enough to engage UE and reveal motor deficits. The game difficulty, the score, and critical timing to finish each task were set initially through the game menu, which was consistent for all participants.

We performed supervised ML by supplying a known set of observations of input data (predictors) and known responses by using observations to train a model that generates predicted responses for new input data. As previously mentioned, the control subject's data were used to classify hand and arm patterns while players engage with the program. These data were utilized as a reference to compare the patterns generated by casualties pre and post-treatment and feature identification. The control subjects' within and between-session coefficients of variation were assessed ($\frac{\sigma}{\mu}$) while associated with virtual objects and completed the tasks in the games. The repeatability coefficient represents the absolute difference between two repeated test results with a probability of 95%. The dispersion of the variables was ranged [42–89]%, indicating excellent repeatability. Thus, control subjects' data was adequate to identify various patterns of hand and arm movements and compare data. The reliability of quantitative functional tests in patients with MS was considered to be varied by <20% of individual mean scores on repeated testing (Schwid, Goodman, McDermott, Bever, & Cook, 2002), to determine the range of measurement variability when patients are clinically stable.

5. Results

5.1. Data collection and analysis

To develop a control strategy and prediction model of the rehabilitation, ML was executed in that data were collected from Myo

Table 3
Kinematic data of upper extremity average ROM collected from healthy subjects.

Joint/Segment	Movement	Goniometer ROM°	Kinect ROM°
Wrist	Extension (Dorsiflexion)	55	64
	Flexion (Palmar flexion)	75	80
	Radial deviation	20	22
	Ulnar deviation	32	35
Elbow	Flexion	145	143
	Hyperextension	8	7
Forearm	Pronation	85	84
	Supination	85	83

Table 4
Demographic characteristics of the participants.

Variables	Results
Age	48.58 (8.52)[a]
Male vs Female	26 vs. 14
Time since the outset of MS symptoms in MS casualties (months)	59.9 (14.8)[a]
Subjects with Right upper-limb impairment	17 vs. 11
MAS: Hypotonus (low muscle tone)	3 (2.3)[a]

[a]Mean (SD).

armband and Kinect devices while the players were interacting with the game setting. The features considered for the SVM classification are as follows: Shoulder joint orientation (flexion/abduction), Elbow joint orientation and position (flexion/extension), and Wrist joint orientation and position (flexion/extension) from Kinect (30fps), Forearm pronation/supination (50 Hz), Hand gestures and data from 8-EMG Electrodes (200 Hz) from Myo armband. The UE joint orientation from the control groups helped identify the upper limb patterns while interacting with the game. The application of SVM classification was used to classify arm patterns pre-treatment, post-treatment, and four-month follow-up to investigate whether SVMs could be used to predict UE improvement following rehabilitation. A total of twelve parameters (six-upper arm function and six-hand movement) scores give a score between [0, 72], where 72 points represent a well-aligned upper arm and hand function and full UE range of motion. Three sets of data were created taken from each subject for the analysis resulting in a total data size of 105.

The MS people were labeled +1, and −1 demonstrated healthy people for arrangement and relapse ML utilizing lower arm developments and MAS scores. The region of the receiver operating characteristics (ROC) curve for single highlights was utilized to get a quantitative proportion of individual element distinguishableness. ROC zones were numerically approximated utilizing the trapezoidal guideline, where more considerable qualities inferred better straight component distinguishableness. The exhibition of the ML models at recognizing healthy subjects from MS people with restricted UE was portrayed by the affectability and particularity esteems. The ROC bend territory is evaluated by utilizing the trapezoidal guideline for approximating zones under bends. The order result of the ML was additionally contrasted and linear discriminant investigation (LDA).

As mentioned in the previous section, data were recorded as the participants interacted with fifteen mini video games. The control subjects used their dominant arm, and the MS casualties interacted with the more impaired limb. The orientation, velocity, and muscle activity of the forearm, hand position, and the average MAS score of hand and upper arm (pre/post and four-month-followup-treatment) were used for the classifications. The set of good models was determined by a leave one out (LOO) procedure which is a robust metric for determining the quality of the models. All models were trained using the linear, polynomial, Radial Basis Function (RBF), and Sigmoid kernels. Bayesian optimization was employed to optimize the prediction. Features were excluded randomly from the training data set and used as a test sample. The trial sets were divided into training test sets (75:25), while the test set was not included in the training. This was repeated until all training examples were individually tested on the models. Our test results showed that SVM and KNN are both efficient algorithms with reasonable accuracy. They could successfully classify data, identify individuals, and predict the improvement following the rehabilitation program. The mean period of completing tasks for people with MS condition was approximately twice as long as the control group (75 ± 0.6 s versus 35 ± 0.76 s).

Scatter plots and confusion matrix, and parallel coordinates plots were combined with observing data and assessing the accuracy of the classifier. Kernel functions with ROC areas close to unity indicated high accuracy and robustness to variations of classification inception and better overall execution.

The accuracy of the classifier was also identified as the rate of correct classification to all data. It was used as the primary index to illustrate the performance of the classification. Besides, statistical analyses were performed to interpret the Spatiotemporal results using a t-test in SPSS Statistics 24. The test made a statistically significant difference with the mean standard error of MSE = 0.17.

Spatiotemporal data used were; movement duration, hand trajectories, velocities, the linear distance between the start and endpoint, and the shoulder position during forward and upward reaching. Data were collected, although some participants experienced difficulties in completing some tasks, including wrist flexion, elbow extension/supination, and excessive shoulder elevation in forwarding/upward reaching and grasp. Participants with MS performed tasks over a higher duration than MS-free subjects 49.7% with $P < 0.001$. Furthermore, MS participants demonstrated reduced movement stability in terms of adjustment 5.5 vs. 1.8 (mm) and a less smooth movement in terms of frequency of direction changes 4.2 (Hz) vs. 3.1 (Hz). The Spatiotemporal data comparing pre and post-treatment showed a significant improvement in real-world motor ability for at least four weeks post-treatment, and 1.65 s improved movement speed. The maximum speed progressed to 1.7 m/s, and the timing of maximum velocity increased by 32%. Table 5 illustrates twenty-eight participant's MAS average upper arm function and its standard deviation (SD). <20% change on the test result is considered the threshold that reliably indicates an actual change in function for an individual with MS. An unbiased training set was derived using a leave-one-out cross-validation method in that; an arbitrary example was excluded from the training data and used as a test sample. This was repeated until all training samples were individually tested on the SVM. The average accuracy is the leave-one-out accuracy and is a robust metric for determining the quality of the SVM model.

The features included in the classification were; Wrist, Elbow, Forearm's joint/segment Orientation, Velocity, Position, EMGs, MAS Scores, and Time. MS patients were identified by −1 and healthy subjects as +1. The five-fold cross-validation and holdout validation classifier were used to overcome data overfitting. Five-fold cross-validation partitions the data into five disjoint sets and trains the model using the out-of-fold observations. It assesses the model's performance using in-fold data by studying the average test error overall folds. Table 6 lists the standardized kernel functions and RMSEs in that the overall error rate was used as the guiding criterion for performance. The Kernels scale mode was set to both automatic and manual. The automatic scale uses a heuristic procedure to select the initial kernel parameters, which the initial values were specified in manual one.

The automatic Gaussian kernel function has the best fit with RMSE = 0.056. The manual Gaussian kernel function with the box constraint = 1.483, epsilon = 0.148 and scale = 21 resulted in the RMSE = 0.079. The features were reduced to Elbow, Forearm's joint/segment Orientation, Velocity, EMGs, MAS Scores, and Time in that the classification was improved. The residuals plot was investigated to check model performance considering the difference between the predicted and true responses. The kernel functions determine the correlation in the response as a function of the distance between the predictor values.

Table 5
MS participant's average UE function ability.

Upper arm	Pre-treatment		Post-treatment		Four-week follow-up	
	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
1	2.29	0.85	3.14	0.71	3.36	0.62
2	2.39	0.96	3.39	0.69	3.39	0.63
3	3.00	0.77	3.86	0.65	3.75	0.65
4	2.75	0.97	3.79	0.57	3.75	0.70
5	2.79	0.74	3.82	0.61	4.00	0.72
6	2.46	0.84	3.57	0.57	3.75	0.59
Hand movement	Pre-treatment		Post-treatment		Four-week follow-up	
	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD
1	2.93	0.66	3.39	0.74	3.39	0.57
2	2.82	0.72	3.96	0.74	3.61	0.57
3	2.71	0.81	3.93	0.72	3.71	0.60
4	3.25	0.64	3.75	0.65	3.64	0.56
5	3.14	0.65	3.43	0.58	3.54	0.51
6	2.90	0.92	3.39	0.63	3.79	0.63

Table 6
SVM regression learner models using cross-validation and holdout-validation.

Binary	Features	Cross-validation		Holdout-validation	
		RMSE (%)	R^2	RMSE (%)	R^2
SVM kernel function					
Linear (Automatic Epsilon mode)	27/27	12.4	0.98	14.8	0.97
Quadratic	27/27	12.4	0.98	14.8	0.97
Cubic	27/27	11.9	0.98	14.3	0.97
Fine Gaussian (Automatic Epsilon mode)	27/27	76.4	0.22	71.9	0.26
Medium Gaussian (Automatic Epsilon mode)	27/27	14.7	0.97	14.1	0.97
Coarse Gaussian (Automatic Epsilon mode)	27/27	6.4	0.99	7.3	0.99
Coarse Gaussian (Epsilon = 0.148; Kernel Scale = 10)	27/27	8.7	0.99	7.5	0.99
Coarse Gaussian (Epsilon = 0.148; Kernel Scale = 18)	27/27	6.1	1.00	7.8	0.99
PCA: Component reduction criteria					
Linear (Automatic Epsilon mode)	10/27	8.1	0.99	7.8	0.99
Quadratic (Automatic Epsilon mode)	10/27	10.1	0.99	11.8	0.98
Cubic (Automatic Epsilon mode)	10/27	10.7	0.98	12.6	0.98
Fine Gaussian (Automatic Epsilon mode)	10/27	63.0	0.47	62.3	0.48
Medium Gaussian (Automatic Epsilon mode)	10/27	14.3	0.97	14.1	0.97
Coarse Gaussian (Automatic Epsilon mode)	10/27	6.4	0.99	19.3	0.95
Coarse Gaussian (Epsilon = 0.148; Kernel Scale = 10)	10/27	6.7	0.99	6.4	0.99
Coarse Gaussian (Epsilon = 0.148; Kernel Scale = 18)	10/27	10.5	0.99	10.4	0.99

We adopted linear, polynomial, RBF, Sigmoid kernel functions, and Bayesian Optimization to build SVM and compared the outcomes. The Bayesian Optimization was employed to optimize the SVM classifier fit.

Five-fold cross-validation and 25% holdout validation were utilized to partition the data set into folds, estimate the training data accuracy, and avoid over-fitting. The results indicated that the SVM could successfully identify individuals with MS from the healthy using the data collected from sensors and predict rehabilitation outcomes. The out-of-sample misclassification rate was 5% which indicated a reasonable classification. 25% holdout validation classifier was used in that medium Gaussian radial basis function had the highest accuracy, 83.8% as displayed in Table 7. Fig. 3 shows the 3D model of the objective functions that are used to perform optimization. The optimal values of the decision variables result in the best possible value of the objective function to find an input that results in the minimum/maximum cost of a given objective function. Bayesian optimization offers a principled technique based on the Bayes Theorem to supervise a search of a global optimization problem that is efficient and effective. It starts by building a probabilistic model of the objective function, known as the surrogate function, then searched efficiently with an acquisition function before applicant samples are collected to evaluate the actual objective function. As illustrated in figure thirty, Objective Evaluations and Sigmoid kernel function were adopted to train the classifier. The results showed a good fit and low cross-validation loss of the pairs using Bayesian Optimization. The characterization takes a shot at areas of focuses from a Gaussian blend model with base focuses produced arbitrarily and freely.

6. Discussion

Multiple Sclerosis (MS) is a degenerative neurological issue influencing casualties freedom of everyday life; hence, causing dependency on others (Taylor & Griffin, 2015). Studies have shown the advantage of continuous rehabilitation and its role in a patient's brain plasticity and recuperation at various phases of the disease (Thomas et al., 2017). Plasticity is the capacity of the sensory system to adjust to the ever-changing states of the environment, experienced during improvement and learning (Prosperini, Piattella, Giannì, & Pantano, 2015). This study integrated the Human Machine Interface platform to facilitate exercise and rehabilitation programs for MS casualties to reduce the limitations resulting from the neurological deficit. ML was used for data exploration and to gain the experience required to develop predictive models, classify patterns, and reduce dimensionality in human UE movement analysis. The application of ML methods to human posture and movement classification was studied to assess the movement quality in response to the intervention. The study demonstrated the application of KNN and SVM to predict the outcome of the home-based neuro-rehabilitation video game and its effectiveness in supporting clinical decision-making. KNN and SVM have the advantage of high accuracy, good theoretical guarantees regarding overfitting. SVM performs well where base feature and kinematic data are interconnected and are not linearly separable. KNN is a high variance classifier and demonstrates robustness towards noisy training data.

NN and SVM both showed having the ability to recognize complex and noisy patterns available in UE (upper extremity) data. SVM and

Table 7
Binary classification using SVM and KNN algorithms.

SVM classifier	95% PCA	Linear	Quadratic	Cubic	Fine Gaussian RBF	Medium Gaussian RBF	Course Gaussian RBF
Cross-validation							
	Accuracy (%)	74.8	79.7	66.1	88.0	76.6	74.8
	AUC of ROC	0.56	0.82	0.64	0.93	0.83	0.81
Holdout validation							
	Accuracy (%)	74.9	79.5	61.0	87.8	77.2	74.9
	AUC of ROC	0.66	0.83	0.57	0.92	0.83	0.80
KNN classifier	95% PCA	Fine	Medium	Coarse	Cosine	Cubic	Weighted
Cross-validation							
	Accuracy (%)	91.6	90.1	84.6	87.6	90.3	91.7
	AUC of ROC	0.88	0.95	0.90	0.92	0.95	0.96
Holdout validation							
	Accuracy (%)	90.4	90.2	83.2	88.8	89.5	91.6
	AUC of ROC	0.87	0.95	0.90	0.92	0.95	0.96

Area Under the curve (AUC);
Receiver Operating Characteristic (ROC).

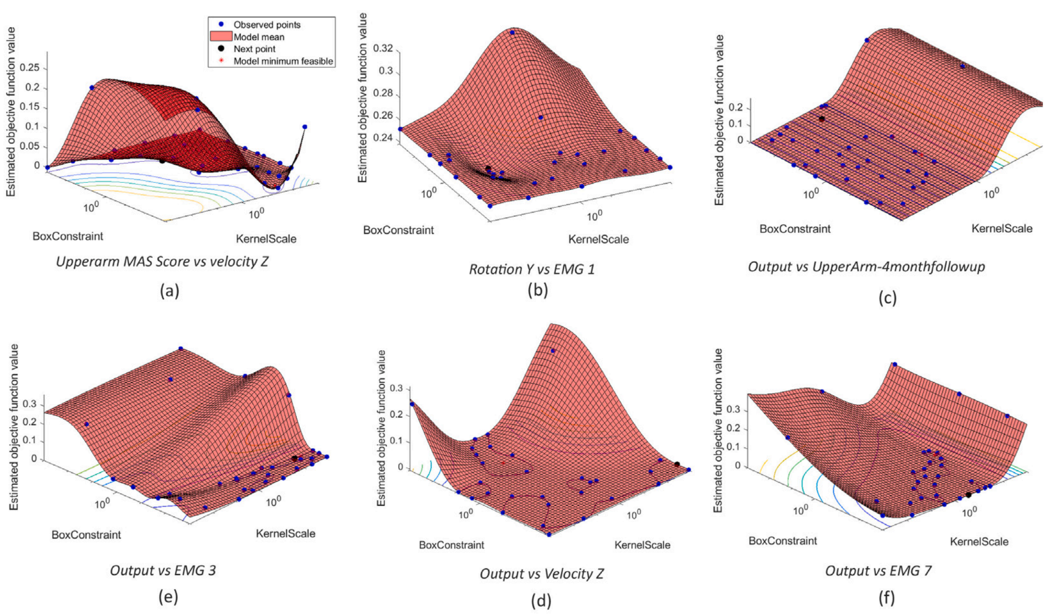


Fig. 3. Optimized SVM classifier fit using Bayesian Optimization. The output and input pairs' of objective function model.

KNN are both efficient while using cross-validation and holdout validation. The algorithm could identify individuals with a motor deficit from healthy participants, recognize the patterns created by joint kinematics (both healthy and MS casualties) and create a regression model that predicts the rehabilitation advantages post-treatment.

The prediction accuracy was in the range of [61% to 91.7%], where Gaussian KNN exceeded other kernel functions. Bayesian optimization resulted in an excellent classifier fit.

Spatiotemporal control and motor assessment scale used to assess the effectiveness of the rehabilitation program. Our findings suggest that ML has a great potential to be used for decision-making in neuro-rehabilitation programs. It is suggested that more accurate targeting of rehabilitation programs could result in the more efficient and effective use of health care resources, which results in the reduction of health care costs. The outcomes also illustrate that repetitive movement of the affected UE enables neuro-plasticity in MS casualties. Real-time graphical feedback provided in the invention offered a suitable platform for self-assessment, suggested prescriptive input about what to do following a mistake/dysfunction, thus, reducing the cognitive load. The participants agreed that the video game platform increased their motivation and retention compared to their experiences with conventional therapies. The theory and mechanism behind the improvements in outcomes following the interaction with the rehabilitation program indicated the adequacy of computer games and visual-input practices in improving parity in MS patients.

7. Conclusion

With the expanded use of standardized information systems in many parts of the health system, there is great potential for enhanced use of sophisticated computer modeling and statistical analysis techniques to inform clinical decision-making and health system planning (Zhu, Chen, Hirdes, & Stolee, 2007). Data selection to train SVM and KNN models requires randomly selected large samples to achieve satisfactory models. However, many training data will raise the computation cost for model training and data testing. Thus, it is crucial to reduce the training dataset without degrading the final classification result. The results showed that to train a multiclass support vector machine (SVM), a small training set is sufficient since an initial model is improved iteratively and incrementally, which complies with the study of Zhang et al. (2011). It is important to choose the right parameters to achieve testing accuracy rather than using conventional models with large sample sizes. Our models were evaluated and validated against the classification approach in literature; Fleury et al. (2010), Keerthi and Lin (2003) and Lau et al. (2009). The classification derived from the small training set improved computational efficiency by 28%.

The use of the proposed rehabilitation study could be considered experimental in MS people. Thus further research with rigorous methodology and reliable outcome measures could be beneficial to provide higher-level support of the effectiveness of the intervention for MS people. The future work will focus on using the classification data to achieve a dynamical coupling between a player and a prosthetic armor artificial limb. This could lead to an expansion of ML functionality in developing advanced online training schemes to support the long-term operation.

CRediT authorship contribution statement

Shabnam Sadeghi Esfahlani: Methodology, Software, Validation, Formal analysis, Investigation, Data curating, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Hassan Shirvani:** Validation, Investigation, Writing – review & editing, Visualization. **Javaid Butt:** Formal analysis, Investigation, Project administration. **Iraj Mirzaee:** Resources. **Karim Sadeghi Esfahlani:** Conceptualization, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Samples of data are available at; Supplementary Material.

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Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.eswa.2022.117165.

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