The Rehabilitation Gaming System: a Review

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Abstract. Stroke will become one of the main burdens of disease and loss of quality of life in the near future. However, we still have not found rehabilitation approaches that can scale up so as to face this challenge. Virtual reality based therapy systems have a great promise for directly addressing this challenge. Here we review different approaches that are based on this technology and their assumptions and clinical impact. In particular we will focus on virtual reality based rehabilitation systems that combine hypotheses on the aftermath of stroke and the neuronal mechanisms of recovery that directly aims at addressing this challenge. In particular we will analyze the, so called, Rehabilitation Gaming System (RGS) that uses non-invasive multi-modal stimulation to activate intact neuronal systems that provide direct stimulation to motor areas affected by brain lesions. The RGS is designed to engage the patients in task specific training scenarios that adapt to their performance, allowing for an individualized training of graded difficulty and complexity. Although RGS stands for a generic rehabilitative approach it has been specifically tested for the rehabilitation of motor deficits of the upper extremities of stroke patients. In this chapter we review the main foundations and properties of the RGS, and report on the major findings extracted from studies with healthy and stroke subjects. We show that the RGS captures qualitative and quantitative data on motor deficits, and that this is transferred between real and VR tasks. Additionally, we show how the RGS uses the detailed assessment of the kinematics and performance of stroke patients to individualize the treatment. Subsequently, we will discuss how real-time physiology can be used to provide additional measures to assess the task difficulty and subject engagement. Finally, we report on preliminary results of an ongoing longitudinal study on acute stroke patients.

Keywords. Virtual reality, stroke, acute phase, rehabilitation, cortical plasticity, gaming, individualized training.

Introduction

In the last decade there has been a growing interest in the use of Virtual Reality (VR) based methods for the rehabilitation of cognitive and motor deficits after lesions to the nervous system. Stroke patients have become one of the main target populations for

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these new rehabilitative methods (see [1-3] for reviews). This is due to stroke being one of the major causes of adult disability worldwide [4], with restoration of normal motor function in the hemiplegic upper limb being observed in less than 15% of patients with initial paralysis [5]. This has a strong impact on the degree of independence of these patients and leads to high societal costs in rehabilitation expenses. In addition, we should take into account the psychological impact as many of these patients regress into depression [6].

Rehabilitation following stroke focuses on maximizing the restoration of the lost motor functions and on relearning skills for the performance of the activities of daily living (ADLs). Most of the newest rehabilitation techniques rely on the fact that motor function can be recovered by cortical plasticity [7-9]. The ability of the brain to reorganize itself after a brain injury has been observed by a remapping of the surrounding areas of the lesion [10] and in other cases as a functional shift to the contralateral hemisphere [11]. To maximize brain plasticity, several rehabilitation strategies have been proposed that rely on a putative promotion of activity within surviving motor networks (see [12] for review). Among those strategies we can find intensive rehabilitation [13], repetitive motor training [14, 15], techniques directed towards specific deficits of the patients [16], mirror therapy [17], constraint-induced movement therapy [18], motor imagery [19], action observation [20], etc.

More recently, growing evidence of the positive impact of virtual reality techniques on recovery following stroke has been shown [1, 2]. These systems allow for the integration of several of the above mentioned rehabilitation strategies. Different paradigms have been used, which we can group in different categories: learning by imitation [21, 22], reinforced feedback [23, 24], haptic feedback [25, 26], augmented practice and repetition [27, 28], video capture virtual reality [29], exoskeletons [30, 31], mental practice [32], and action execution/observation [33-35]. The major findings of these studies show that virtual reality technologies will become a more and more essential ingredient in the treatment of stroke and order disorders of the nervous system. Indeed, with VR we can have well controlled training protocols within specifically defined interactive scenarios that are customized towards the needs of the patient. However, it is not yet clear which characteristics of these systems are effective for rehabilitation. Unfortunately, the quantification of the impact of these novel rehabilitation technologies on patient's recovery and well being is in general still very anecdotal. One problem is that most of the reported studies are performed on small numbers of chronic stroke patients [1, 2] although most of the cortical reorganization happens in the first few months after stroke [36-38]. Since plasticity is a requirement for functional recovery, intervention at early stages of stroke should be pursuit more vigorously.

The Rehabilitation Gaming System (RGS) is a VR based system that is targeted for the induction and enhancement of functional recovery after lesions to the nervous system using non-invasive multi-modal stimulation. Currently RGS is tested in the context of the rehabilitation of motor deficits of the upper extremities after stroke. RGS assumes that neuronal plasticity is a permanent feature of the CNS and that conditions for recovery can be induced by activating areas of the brain that are affected by a lesion through de use of non-invasive multi-modal stimulation. In the specific case of the rehabilitation of motor deficits after stroke, the working hypothesis of RGS is that action execution combined with the observation of correlated movements in a virtual environment may activate undamaged primary or secondary motor areas recruiting alternative networks that will improve the conditions for functional reorganization.

Indeed, it has been shown that VR stimulation can activate these motor areas [39]. One candidate network that can provide the interface between multi-modal stimulation and motor execution is the, so-called, mirror neuron system [40-42]. The mirror neurons have been shown to be active during the execution of hand, foot and mouth goal oriented movements and also during the observation of these movements while performed by others. This implies that we can recruit this system not only during action execution but also during the observation of actions. We will in detail analyze the impact of RGS on acute stroke patients [33, 35, 43].

The RGS provides VR tasks performed in a first-person perspective where users control the movement of two virtual arms with their own arm movements. The choice of the first-person perspective relies on the fact that it has been shown that observation of hand movements produces an increase in cortical excitability modulated by the orientation with respect to the observer [44]. In particular, those experiments showed stronger responses when both the orientation of the hand and the orientation of the observer coincide. This suggests that a first-person perspective could be more effective than a third-person perspective in driving cortical activation during the performance of virtual tasks. Furthermore, the first-person perspective can recruit the motor system to a greater extent and allows for the integration of kinesthetic information [45] that can result in a higher degree of identification with the virtual representation and thus more effective functional reorganization.

In addition to the above described neuronal principles, the RGS incorporates a number of features that make it a very well suited system for rehabilitation. It proposes tasks of graded complexity and difficulty. The varying complexity of the tasks allows the user to re-construct the different elements of instrumental activities of daily living (IADL) from overall stability to precision movements. In addition, RGS controls the individual task performance using a psychometric model of the training scenario. This model is derived from the game performance data from a large group of both patients and healthy control subjects. As a result RGS can adapt the difficulty of the task to the capabilities of the individual user, providing individualized training while following a single rule for all users. This is relevant since it reduces the effect of external uncontrolled influences in choosing game parameters and training protocols, eliminating important sources of error. For the same reason, the game instructions are automatically provided by the system in written and auditory form.

In this chapter we will in detail analyze RGS as a general paradigm for functional rehabilitation after lesions to the CNS. Our specific examples will be taken from results of a number of pilot studies we have performed with stroke patients that address issues such as the transfer of movements, deficits and training from real to virtual environments. We will assess the validity of the psychometric difficulty model implemented in the system by investigating the affective responses of the users. Additionally, we will report on preliminary results of an ongoing clinical study with acute stroke patients. Here the diagnostic and monitoring capabilities of the RGS will be discussed as well as the effect of the training paradigm compared to the performance of two control groups. Finally, we will try to extract which general principles are behind the impact of RGS.

1. Methods

1.1. The Rehabilitation Gaming System

The RGS has intentionally been designed with standard, out of the box and inexpensive components to provide stroke patients with the option to have this system at their homes for further training and monitoring after discharge from the hospital.

The RGS consists of a standard PC (Intel’s Core 2 Duo Processor, Santa Clara, California, USA) running the Linux operating system, a 3D graphics accelerator (nVidia GeForce Go 7300, Santa Clara, California, USA), a 19” 4:3 LCD monitor, a video camera (VGA) and a pair of data gloves (5DT, Pretória, South Africa) (Figure 1). Arm movements are tracked by means of a vision based tracking system (AnTS) that detects color patches located on the wrists and elbows (see section *1.2*). The finger flexion is captured by optic fiber data gloves that integrate seamlessly with our system via a USB connection. The lycra textile of the gloves adapts to a wide range of hand sizes and offers little resistance to finger bending. As many patients don’t have the ability to support their arms against gravity, the task is purposely in 2D and is performed on a table surface.

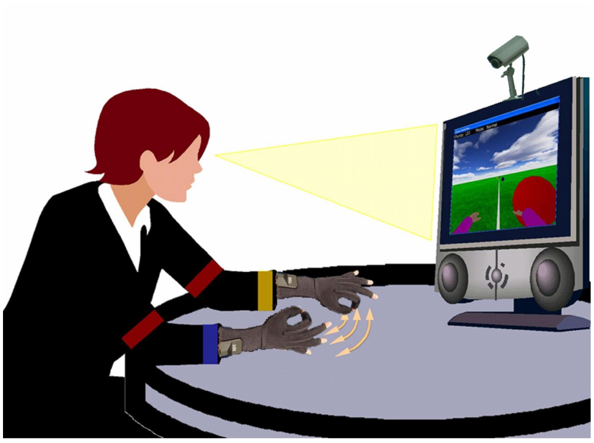

Figure 1. The Rehabilitation Gaming System (RGS). The subject, resting the arms on a table surface, faces the computer screen. The movements of the arms are visually captured by a camera positioned on top of the display that detects color patches located on wrists and elbows. A pair of data gloves measure finger flexure. An avatar moving according to the movements of the user performs a task in the virtual scenario. Adapted from Cameirão et al. [46].

1.2. AnTS

A vision based tracking system called AnTS has been adapted to track the movements of the arms of patients during the training period at an update frequency of 35 Hz [47, 48]. The basic processing stream of AnTS starts with the acquisition of images from the video camera that is placed on top of a computer screen (Figure 1). In this case, the goal is the reconstruction of arm motion. Therefore, the head of the subject and a set of color patches positioned on elbows and wrists are tracked. To locate those objects, a set of noise filtering and image segmentation techniques based on color, shape and size features are used. Color detection is performed by transforming the Red, Green and Blue (RGB) data of the input images to the Hue, Saturation and Value (HSV) color space, which encodes more robustly the identity of colors in dynamic environments (changing light conditions, shadows, etc). Thereafter, Bayesian inference techniques are used to locate the center of mass of objects using a model based on the Hue value, velocity vector, object size and position that improves performance during occlusions and target loss [48]. The position of the head and the color patches is subsequently fed to a biomechanically constrained model of the upper body, and the joint angles are computed. The biomechanical model imposes restrictions on the possible joint angles and allows for a 3D approximation of arm movements using a single camera setup.

1.3. The Environment

The Torque Game Engine (www.garagegames.com), a popular, versatile and multi-platform 3D engine has been chosen to implement the VR tasks. Torque provides both a 3D rendering and a physics engine that allows generating high resolution and realistic VR scenarios.

Our environment consists of a spring-like natural highland where the user interacts in a first-person perspective. A human avatar is rendered in the world in such way that only its arms are displayed on the screen. The joint angles captured by the tracking system and the finger flexure provided by the data gloves are mapped to the corresponding joints of the avatar skeleton. In this way, the user observes on the screen two virtual arms that move according to his/her own movements.

1.4. Tasks

The task protocol consists of three different stages: two stages of calibration (see below) and the training game. Both calibration phases allow measuring the properties of the movements in the real and virtual worlds, making possible the analysis of transfer between both worlds. The training game is the core task of the RGS intervention, and it deploys an exercise that is individualized for each subject depending on its performance. All the intervention tasks provide automated written and auditory instructions to minimize the influence of the human operator.

1.4.1. Real Calibration

The real calibration consists of performing a set of motor actions starting from a resting position, i.e. positioning the palm of the hand on a randomized sequence of numbered positions on the table surface (Figure 2, left panel). The patient receives auditory and written instructions during the process, which lasts approximately 2 minutes. This task allows recording every session basic properties of arm movement such as speed, reaching distance, precision and reaction time.

1.4.2. Virtual Calibration

The user is asked to perform the same randomized sequence as in the real calibration task but this time using the virtual arms and a virtual replica of the table displayed on the screen (Figure 2, right panel). To prevent the patients of using the numbered positions in the physical table top as external cues, the table surface is covered during this phase. This calibration phase allows for a comparison on how the movements of the real calibration phase are performed in a virtual world. Together with the analysis of real-to-virtual movement transfer, the main role of the virtual calibration is to daily set the starting game parameters of the training task.

Figure 2. Real and virtual calibration phases. Left panel: on the table surface, numbered dots are located at specific positions on the left and right hand sides. The user is asked to place the palm of his/her hand on the numbered dots in a randomized order. Right panel: the same setup is replicated in the virtual environment and the user is asked to perform the same task with the virtual arms. The figure text reads “Place your right hand palm above the number 2 and wait…”.

1.4.3. Training

The main task of the user is to intercept spheres that are flying towards him/her by hitting them with his/her virtual arms (‘Hitting’). We have purposefully taken a relatively constrained task since it allows us to fully control all aspects of the training scenario and understand its impact on recovery. The difficulty of the task is determined by three gaming parameters: the speed of the spheres, the time interval between consecutive spheres and the range of dispersion of the spheres. When the game starts, the difficulty baseline is set by using the parameters measured during the virtual calibration phase. The system automatically updates the task difficulty during the game, depending on the performance of the subject. To be able to adjust the difficulty level in an objective fashion, a difficulty model was developed based on experimental data on the performance of stroke patients with random game parameters. With such a model, the parameters are continuously adapted to keep the performance level at around 70%, keeping patients at a challenging difficulty level but within their capabilities to sustain motivation.

Starting from the ‘Hitting’ task, the RGS sequentially introduces tasks of graded difficulty that require movement execution with increasing complexity and scoring, ranging from arm extension/flexion to a coordination task that combines arm movement with grasp and release (‘Hitting’, ‘Grasping’ and ‘Placing’) (Figure 3). First, the initially described ‘Hitting’ task consists on intercepting approaching spheres. Successful interception sum 10 points to an accumulated score. Second, in the ‘Grasping’ task, the intercepted spheres have to be simultaneously grasped through finger flexure. The correct execution sums 20 points to the game score. Finally, in the ‘Placing’ task, the spheres have to be grasped and then released in a basket that matches their corresponding color. Here, a correct grasp and later release sums 20 + 10 points respectively to the accumulated score. During the game, visual and sound effects provide online feedback on the performance of the subject.

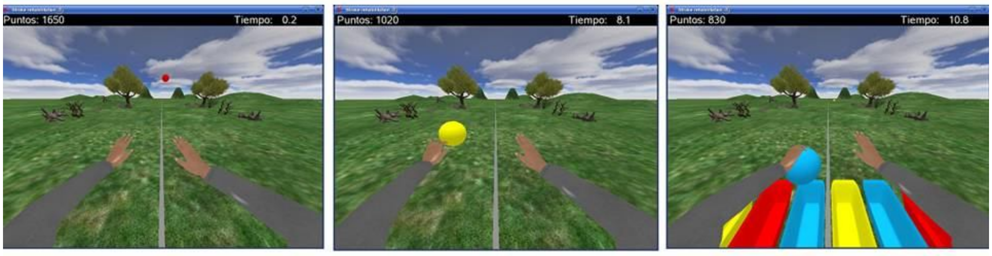

Figure 3. The 3 RGS training tasks of graded complexity. Left panel: 'Hitting' to train range of movement, movement speed, and arm and shoulder stability. The approaching virtual spheres have to be intercepted with the movements of the virtual arms. Middle panel: 'Grasping' to exercise finger flexure on top of movement range, speed, and arm and shoulder stability. Now, the intercepted spheres can be grasped by flexing the fingers. Right panel: 'Placing' to train not only grasp but also release. The grasped spheres can now be released in a basket of correspondent color. Adapted from Cameirão et al. [33].

1.5. Physiology

The Yerkes-Dodson law specifies that there is an optimal relationship between arousal and performance [49]. Hence, the RGS paradigm aims at modulation the task difficulty with respect to the arousal of the subject. In order to achieve this RGS capitalizes on the availability of portable real-time physiology systems. Moreover, this will allow us to analyze if specific game events trigger changes in the affective state of the subjects. Heart rate (HR), heart rate variability (HRV), and galvanic skin response (GSR) are measures that are widely used to address this question. Specifically, it has been described that HRV can reflect the valence of stimuli [50, 51] and that the GSR directly relates to stress and arousal [52].

The g.MOBIlab (www.gtec.at) signal acquisition system has been integrated with the RGS. The g.MOBIlab system allows signal visualization, data logging and online biosignal processing. We acquired single channel Electrocardiograms (ECG) and GSR at a sampling frequency of 256 Hz. To measure physiological responses to single events, the training game was restricted to the 'Hitting' task configured in such a way that every 10 seconds a single sphere is delivered at a random position of the screen at high speed. From the point of insertion, the sphere takes approximately 2 seconds to reach the avatar. During these experiments, the beginning of the task is preceded by a resting period of 15 seconds. 31 spheres are delivered during the experiment, which results in a total duration of 320 seconds. HR and GSR have also been recorded while performing the 'Hitting' task with a random combination of game parameters, resulting in a random difficulty level.

1.6. Clinical Study

In order to investigate the impact of the RGS in the early stages after stroke, a randomized longitudinal study with controls is being conducted at the "Hospital de

L'Esperança" in Barcelona, Spain. The selected patients are within the first 3 weeks post-stroke (acute/sub-acute stroke), presenting a first time stroke, with a severe to mild deficit of the paretic upper extremity (2≤MRC≤4 [53]), showing no aphasia or other cognitive deficits (assessed by the Mini Mental State Examination [54]) and age ≤ 80.

Patients are randomly assigned to one of three groups: RGS and two control groups (Control A or Control B). Patients in the RGS group perform the three tasks of the system ('Hitting', 'Grasping' and 'Placing') that are gradually introduced during the intervention period. Patients assigned to Control A group perform the same type of motor tasks (range of movement, grasping and object manipulation) as required by the RGS but without the virtual feedback. This group controls for the effect of the first-person perspective VR feedback. Finally, to control for the gaming effect and motivational aspects, patients in the Control B group perform non-specific games, such as Big Brain Academy® and Trivial Pursuit®, with the Nintendo Wii (Tokyo, Japan). Intervention for all groups has a duration of 12 weeks plus a 12-week follow-up period (Figure 4), with 3 weekly sessions of 20 minutes. The patients are evaluated at admittance, week 5, week 12 (end of the treatment) and week 24 (12 weeks follow-up).

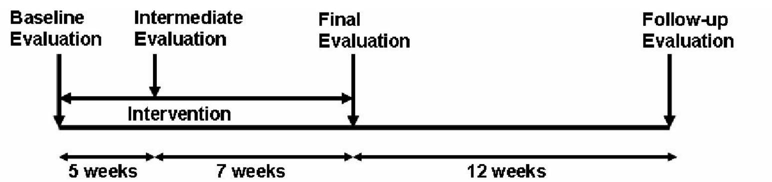

Figure 4. Timeline of the study. The intervention period has a duration of 12 weeks plus a 12 weeks follow-up period. The clinical evaluation of the patients is performed at several stages of the process.

To have objective and quantitative arm movement data for an inter-group comparison, patients from both control groups also perform the real calibration task once per week (see section *1.4.1*).

The standard clinical evaluation scales for motor and function assessment that we use include the Functional Independence Measure [55] and Barthel Index [56] for outcome assessment; the Motricity Index [57] for the arm and the Fugl-Meyer Assessment Test [58] for upper extremities for assessment of motor and joint functioning; the Chedoke Arm and Hand Activity Inventory [59] for the functional assessment of the recovering paretic upper limb; and the 9-hole Pegboard Test [60] for the assessment of finger dexterity and coordination.

2. Results

2.1. Real vs Virtual

A crucial aspect for our research, and consequently for the possible benefits it can provide users with, is to understand the responses of the patients to these new VR technologies and the correspondence between task execution in real and virtual worlds. Therefore, an analysis of how movements were transferred to the virtual world when performing the same task as in reality is pivotal. These issues were addressed in a pilot study with 6 naive right handed stroke patients with left hemiparesis, mean age of 61 years (range 32-74), Brunnstrom Stage for upper extremity ranging from II to V [61], and Barthel Index from 36 to 72 [35]. These naïve patients performed single trials of the real and virtual calibration tasks (see section *1.4*). Out of these 6 patients, two were excluded from the analysis since they did not complete the execution of the real and/or virtual tasks within the given time. From the real and virtual tasks we extracted reaching distance and the speed information from the movements. The reaching distance is measured as the farthest position the patients were able to reach from the resting position, and the speed is computed as the mean speed of all the movement sequences performed by each arm individually.

The measurements performed during the real calibration phase show that the task is a valid method to quantitatively analyze the performance differences between paretic and non-paretic arms. Thus, the calibration tasks are well suited to evaluate and monitor the evolution of patients over sessions, independent of the specific training they are exposed to (Figure 5). In addition, this allows for a direct comparison between the performance in both real and virtual tasks.

The results for the real and virtual tasks show that the behavior in the virtual environment is consistent with the one in the real world. This means that the RGS is able to assess from both tasks the degree of impairment. This is measured in both the reaching distance (Figure 5, left panel) and the movement speed, with the only difference that naive patients display slower movements in the VR environment for both the paretic and healthy arms (Figure 5, right panel). This could be due to an adaptation effect to the virtual environment. Nevertheless, the relative differences between paretic and non-paretic arms are conserved in real and virtual worlds, meaning that motor deficits are transferred (Figure 5, right panel). This strongly suggests that improvements measured within the RGS virtual tasks will translate to measurable improvements in real world tasks.

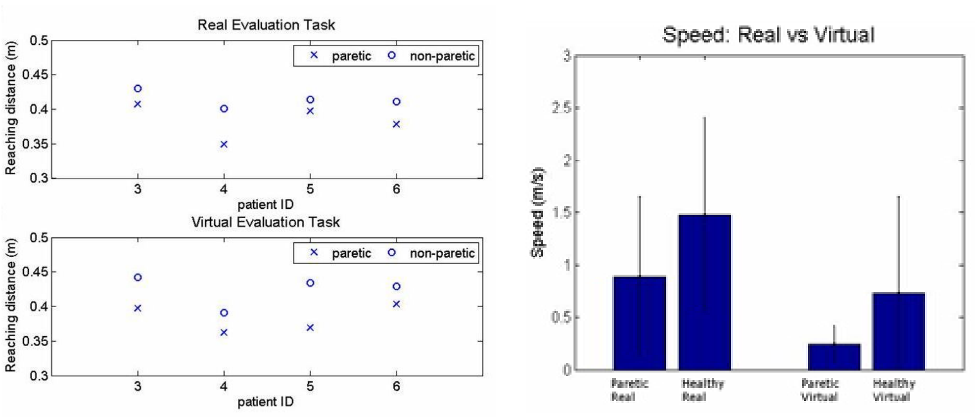

Figure 5. Real vs virtual reaching distance and speed of the movements. Left panel: maximum reaching distance across patients for the paretic and non-paretic arms in real (up) and virtual (bottom) worlds. Adapted from Cameirão et al. [35]. Right panel: mean speed for the paretic and non-paretic arms of all the patients in real and virtual worlds. Vertical bars indicate the standard deviation.

2.2. Game Data Analysis

In addition to the data extracted from the calibration phases, the gaming scenario of the RGS provides data about the movements of the arms of the patients synchronized with all the game events that take place during the 20 minutes of training. At the end of every single RGS session, the data of the goal oriented motor actions (i.e. 'Hitting', 'Grasping' and 'Placing') are available for each patient (Figure 6).

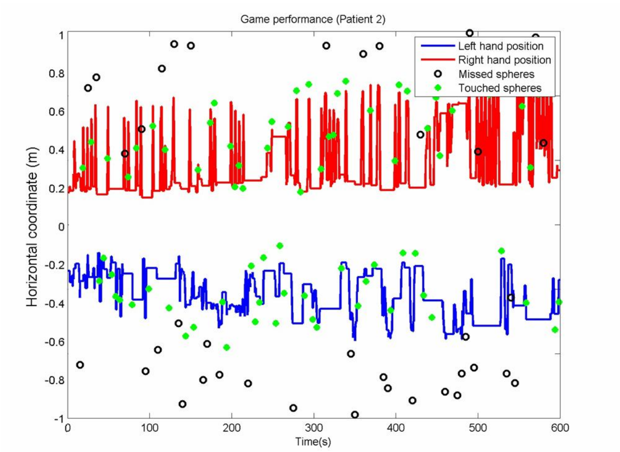

Figure 6. Example of recorded time stamped game event data for patient 2. This plot shows over time the position of both the left (blue line) and right hand (red line), and events (touched and missed spheres) during a trial. The patient, with left hemiplegia, shows a reduced reaching distance and a higher number of missed spheres with the paretic arm. Adapted from Cameirão et al. [62].

Since all data related to arm movement is stored during the performance of the game, such as joint angles and finger flexure, a number of performance indicators can be measured for each trial. These include among others precision or accuracy of the actions, speed and reaching distance.

As opposed to the calibration tasks where only few repetitions of a task are performed in order to estimate some performance values, the training task of the RGS offers approximately 300 repetitions per session. Consequently, more robust and accurate data analysis can be realized which displays properties of the performed motor actions, otherwise unlikely to be detected. In particular, the analysis of the RGS training data provides information about the distribution of the caught and missed sphere events, and the accuracy of the actions, i.e., the error distribution for both paretic and non-paretic arms. Taking again as an example the case of patient 2, we can observe that most of the spheres were missed on the farthest region of the left side (Figure 7, left top panel). In addition, if we analyze the precision in touching the spheres, the left hand is less accurate (Figure 7, right top panel), presenting a more widely spread error distribution (Figure 7, bottom panels). These results point out the importance of a high-resolution monitoring system to complement standard clinical scales, which generally lack detailed quantitative information on motor performance.

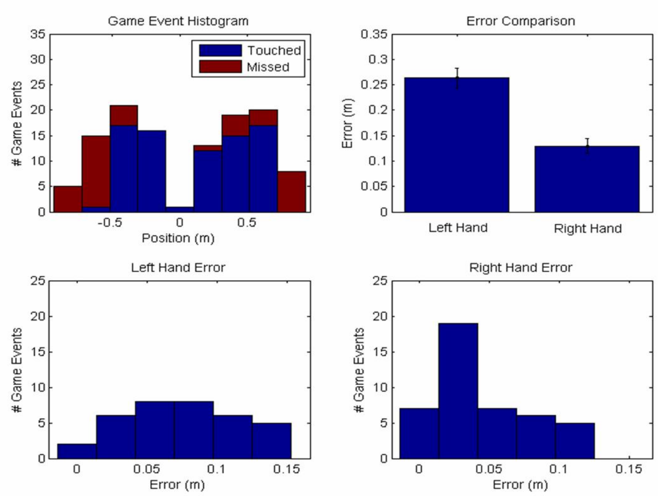

Figure 7. Example of game performance analysis with patient 2 (left hemiplegia). Top left panel: histogram of game events (caught and missed spheres and their position in the field). Top right panel: error in sphere interception for both arms. The bar denotes the median error, and the error bar the standard deviation. Bottom left panel: sphere interception error histogram of the left arm (paretic). Bottom right panel: sphere interception error histogram of the right arm (non-paretic). Adapted from Cameirão et al. [35].

2.3. Physiological Measures

An important foundation of the RGS system is that the motor actions performed in the real and virtual worlds are equivalent, and therefore the results of the training in a VR scenario can be generalized to the real world [35]. This means that subjects training with our system should react to game events as if they were real. One way to study this effect is by recording the physiological responses of subjects during the training phase of the game. Hence, assuming that both Galvanic Skin Response (GSR) and Heart Rate (HR) signals relate to the internal state of subjects, these data can be used to asses the impact of the different game events and parameters for each individual.

In a first setup, to analyze the physiological responses to single game events during the 'Hitting' task, we measured the skin conductance level (SCL) and extracted the phasic responses (GSR) [63]. The skin responses were investigated for 5 healthy subjects that performed the game. The goal was to understand how the discrete game events (touched or missed spheres) would affect the stress level. In this case, although the results were not uniform for all subjects, a prototypical response pattern was found for 3 of them. As opposed to the touched sphere events, which did not trigger an event related potential, the missed spheres did (Figure 8). Missed spheres events led to an increased GSR (arousal) during the approach of the sphere followed by a fast decay after the sphere was missed and a return to baseline. Additionally, in 2 of the 3 subjects that displayed this GSR response pattern, there was a significant difference between the GSR response for touched and missed spheres after the event occurred (p-value < 0.05, t-test).

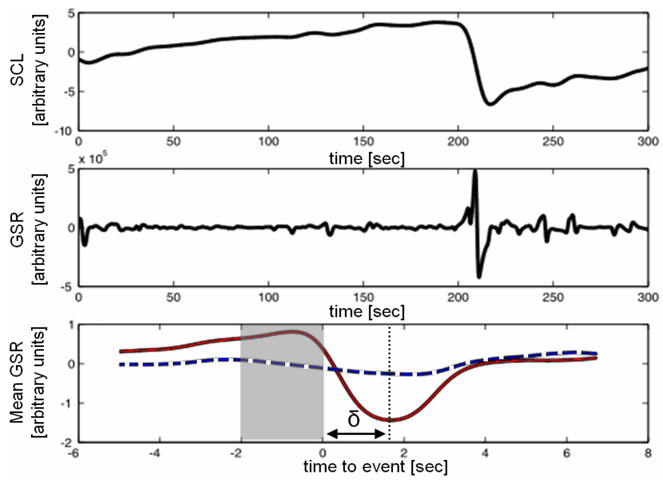

Figure 8. Electrodermal response analysis. Top panel: skin conductance level (SCL) during a trial. Middle panel: galvanic skin response (GSR) during the same trial. Bottom panel: average event centered GSR mean response for missed (solid line) and touched (dashed line) spheres. The gray area indicates when a sphere is approaching, 0 is the time of the event and δ the time between the event and the minimum of the GSR signal. Adapted from Cameirão et al. [63].

These results indicate that there is an arousal prior to a missed sphere event that could eventually be used to predict when patients are likely to fail. Therefore, it would be possible to use this biofeedback information in real time to modify game parameters to keep performance and arousal at a desirable level.

In a second study with 5 healthy subjects, we investigated the HR game event related changes and also the validity of our model of game difficulty. Interestingly, when the subjects were exposed to a random combination of game parameters, we found a correlation between the difficulty of the parameters and the HR. The difficulty model, previously developed from experimental data on the performance of chronic stroke patients with randomly changing game parameters, was now used to compute the difficulty of each trial. The difficulty level, measured from 0 (easy) to 1 (hard), had an impact on the measured HR for all subjects, relating low difficulty to lower stress levels and higher difficulty to higher level of stress (Figure 9, left panel).

In all subjects exposed to the task we could detect game event related responses in either HR or HRV. Nevertheless, although HR or HRV significant changes were found immediately before and after the event occurred, these were not consistently found for all subjects (Figure 9, right panels). In addition, no differences were found between event types (touched or missed spheres) leading both of them to comparable physiological changes.

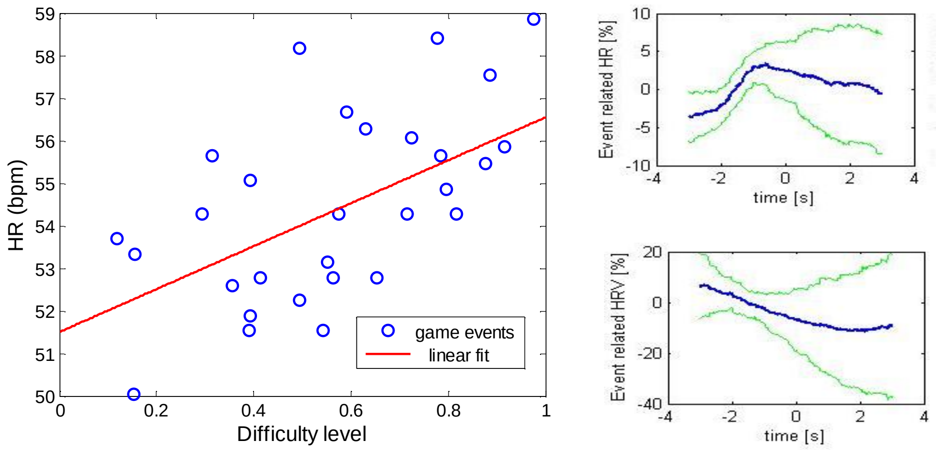

Figure 9. Heart rate event related responses. Left panel: example plot of the difficulty of the game trials vs the measured Heart Rate (HR) for a healthy subject. The difficulty level (X-X axis) is assessed by a difficulty model based on data of stroke patients. The HR (Y-Y axis) is measured as beats-per-minute (bpm). There is a monotonically increasing relationship between difficulty of trials and HR response shown by the linear regression of the data. Right panels: mean heart rate (HR) (top) and heart rate variability (bottom) responses with respect to the timing of game events (time = 0) (n=31) for a healthy subject. The event related responses (Y-Y axis) are computed as the percentage change of HR or HRV measures. The blue curve indicates the mean response and green curves +/- standard deviation.

2.4. Clinical Study

At this moment, out of 76 stroke patients admitted to the hospital during a period of 8 months, 17 fulfilled our inclusion criteria. The patients were randomly assigned to either the RGS group (n=7), the Control A group (n=4) or the Control B group (n=3). This study was approved by the ethics committee of clinical research of the Instituto Municipal de Asistencia Sanitaria (IMAS) and all the patients gave their signed informed consent.

2.4.1. Monitoring and Movement Analysis

Thanks to the calibration phases performed at the starting of every session, it is now possible to quantify the evolution of the speed of movements, reaching distance and other characteristics of the motor actions of the patients (Figure 10).

In particular, the different measures of the speed of movement can be fitted with a linear regression, in which case the slope of the fit provides us with a measure of the improvement over time. A positive slope indicates an increase of the speed of the movements whereas a flat line indicates a stable measure. In the case of patient ID.1407178, a stable movement speed is found for the non-paretic arm, around a value of 2 m/s. Interestingly, starting around 1 m/s, the paretic arm regains speed over sessions until matching the speed of the non-paretic arm (Figure 10, left panel).

A clear advantage of the RGS is that detailed information of the movements performed by the patients is recorded. This allows detecting individual movement strategies. For instance, we observe in patient ID.951736 an increased opening of the elbow angle to compensate a shoulder limitation (Figure 10, right panel).

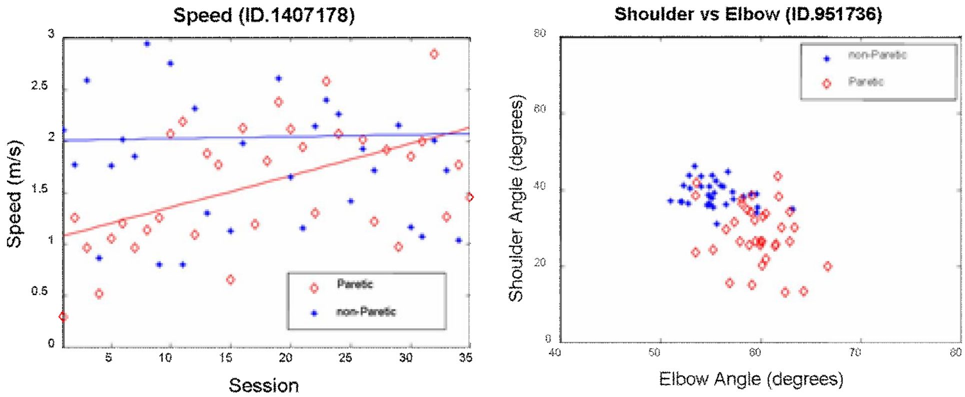

Figure 10. Monitoring of patients using the calibration tasks. Left panel: evolution of the speed of movements of the paretic and non-paretic arms over sessions for patient ID.1407178. The colored solid lines correspond to the linear regressions of the data. Right panel: phase plot of the shoulder vs elbow angles for patient ID.951736. The plot shows two distinct strategies used by the paretic and non-paretic arms to reach the same distances.

2.4.2. Clinical Measures

Since all three groups of the clinical study perform the real calibration task of the RGS at least once per week, it will be possible to compare the improvements of the different groups at two levels. First, the RGS provides quantitative data about reaching distance, movement speed, reaction times, etc. Second, clinical evaluations including 6 assessment scales (Functional Independence Measure, Barthel Index, Motricity Index, Fugl-Meyer Assessment Test, Chedoke Arm and Hand Activity Inventory, Pegboard test) are performed at four different stages of the study. In this section, we will exclusively discuss the clinical scores.

Although the group sizes are small and the intra-group variability is large, we can appreciate some tendencies in the different groups. Firstly, the RGS group shows a smaller or similar mean absolute improvement from baseline to week 5 than the control groups. This is true for all the measures except the CAHAI, for which the improvement is slightly larger for the RGS group, although no statistical significances are found [33]. Secondly, for the second half of the treatment (from week 5 to week 12) a new trend can be observed. In this case, the patients in the RGS group show a higher mean increase in all their scores compared to both control groups (see [33] for further information). However, these results should be interpreted with caution due to the heterogeneity of the baselines at admission.

As a complementary source of information, the percentage of improvement of the clinical scales with respect to baseline has been used to compensate for the differences in the baseline at admission. Out of the 6 clinical scales, we focus on the clinical scales directly related to the upper limb assessment, i.e. Motricity Index, Fugl-Meyer Assessment Test (upper extremities) and the Chedoke Arm and Hand Activity

Inventory. The CAHAI and Motricity Index scores show a sustained and slightly larger improvement for the RGS group during the training period (from baseline to week 12), whereas this is not the case for the Fugl-Meyer [33]. Although some interesting trends are observed in the clinical scores, at this point of the study the data are not conclusive and there is a need to find a better measure to compare patients with different baselines.

As an example, here we show the data of the 2 patients with the closest scores at admittance (1 RGS and 1 Control A) that completed the entire protocol. The patient in the RGS group had the following scores at admittance: motor FIM = 28, Barthel Index=39, Motricity Index = 34, Fugl-Meyer = 27 and CAHAI = 13. The patient in the Control A group had the following scores at admittance: motor FIM = 31, Barthel Index=37, Motricity Index = 34, Fugl-Meyer = 24 and CAHAI = 13. The scores of the three previously discussed clinical scales, namely the Motricity Index, the Fugl-Meyer Assessment Test for upper extremities and the Chedoke Arm and Hand Activity Inventory (CAHAI) were used to perform an analysis of the percentage of improvement over time (Figure 11).

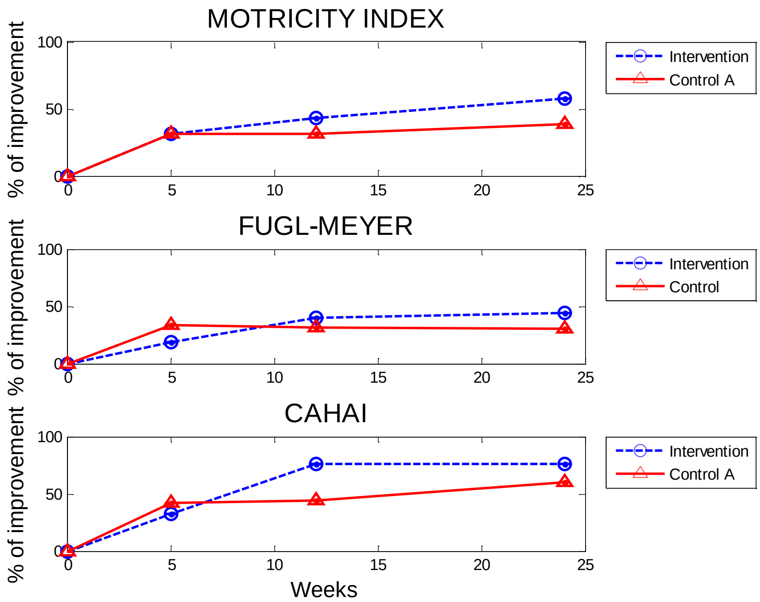

Figure 11. Percentage of improvement in standard evaluation scales obtained at different stages - week 0 (admittance), week 5, week 12 (end of treatment) and week 24 (follow-up) - for two patients with similar baseline measures. Top panel: Motricity Index for the upper extremity. Middle panel: Fugl-Meyer Assessment Test for the upper extremity. Bottom panel: Chedoke Arm and Hand Activity Inventory.

On what concerns specific properties of the movements, evaluated by the Motricity Index and the Fugl-Meyer Assessment Test, the Control A patient presented a higher or similar improvement rate at week 5, but then stabilized over the entire study period; on the other hand, the patient in the RGS group shows a smaller improvement rate at week five but the improvement is sustained over the whole intervention period (Figure 11, top and middle panels). On the evaluation of the functionality of the paretic arm

(CAHAI), the patient in the RGS group presented a trend similar to the one observed for the other measures but with accentuated differences when compared to the Control A patient (Figure 11, bottom panel). This particular measure is relevant because it directly evaluates the active use of the paretic arm in the performance of daily living activities.

3. Discussion and Conclusions

In this review of virtual reality based rehabilitation systems we have given an overview of the different approaches and focused specifically on the Rehabilitation Gaming System. We have laid out the conceptual and methodological considerations of the system. Using the results of pilot studies we have shown that the RGS is a tool for the rehabilitation of motor deficits that has a number of properties that are relevant for an efficient rehabilitative training. Firstly, unlike classical rehabilitation techniques, the RGS is grounded in an explicit neuroscientific theory about the mechanisms of recovery, activation of the motor system and cortical plasticity. Secondly, it generates task specific training scenarios designed for the rehabilitation of the upper limbs, and monitors and quantifies the improvement of the patients over time. The RGS tasks follow a model that deploys an individualized training that has been divided in three phases of increasing complexity, ranging from arm extension/flexion to a coordination task that combines arm movement with grasp and release. The parameters of the game are continuously adapted to the performance of the patient based on a model of the difficulty of the task derived from data of stroke patients, which allows for an individualized training, while ensuring that all patients are exposed to the same training rule.

In a first study of the RGS with chronic stroke patients, we analyzed the transfer of movements between real and virtual worlds [35]. We observed that our system retains qualitative and quantitative information of the patient's performance during the virtual tasks that are matched in the real world, allowing for a detailed assessment of the deficits of the patients.

In a second study, we investigated the impact of specific game events on the stress and arousal level of RGS subjects [63]. The monitoring of HR and GSR during game performance allows a more detailed control of the state of the patient during therapy, and can be used as a biofeedback system to tune the game parameters to both, the training requirements and the capabilities of the patients. The measured HR data support the difficulty model implemented in the game, since higher difficulty levels induce higher levels of stress and/or arousal.

The RGS is currently used in a randomized longitudinal study with acute stroke patients with two control conditions [33, 43]. We illustrated the overall approach and reported on preliminary results. Our data suggest that the RGS induces a sustained improvement over the training period when compared to the control groups. Nonetheless, we can not yet draw definite conclusions given the small sample size of the study at the moment (n=14, split into 3 groups). In the following months we will assess to a larger extent the impact of the RGS intervention in an inter-group comparative study with both the clinical scales and the measures delivered by our system, with a larger population of stroke patients.

Although there is little work on the use of virtual systems in the early stages of stroke, the main outcomes and cortical changes happen in the first few months after stroke [36-38]. Therefore, it is important to act during this period and there is a growing need to investigate if intervention at this stage can have an impact on the prognostic of the patients. We believe that our system includes several properties that make it a suitable tool for rehabilitation and that it captures valid working principles that generalize to many rehabilitation paradigms. Besides the automatic monitoring, and the adaptive training scenarios of graded difficulty, the system is versatile and can be easily adapted to suit different clinical situations such as lower limb rehabilitation or traumatic brain injury patients. At this moment we are exploring the additional benefits of the RGS when coupled to haptic interfaces or passive exoskeletons. To conclude, notwithstanding the therapeutic benefits of the RGS beyond conventional therapy, the RGS is a very valuable low cost tool for diagnosis and amusing training that can be largely deployed in hospitals and at home.

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