

Mónica S. Cameirão and Sergi Bermúdez i Badia

14 An Integrative Framework for Tailoring Virtual Reality Based Motor Rehabilitation After Stroke

Abstract: Stroke is a leading cause of life-lasting motor impairments, undermining the quality of life of stroke survivors and their families, and representing a major challenge for a world population that is ageing at a dramatic rate. Important technological developments and neuroscientific discoveries have contributed to a better understanding of stroke recovery. Virtual Reality (VR) arises as a powerful tool because it allows merging contributions from engineering, human computer interaction, rehabilitation medicine and neuroscience to propose novel and more effective paradigms for motor rehabilitation. However, despite evidence of the benefits of these novel training paradigms, most of them still rely on the choice of particular technological solutions tailored to specific subsets of patients. Here we present an integrative framework that utilizes concepts of human computer confluence to 1) enable VR neurorehabilitation through interface technologies, making VR rehabilitation paradigms accessible to wide populations of patients, and 2) create VR training environments that allow the personalization of training to address the individual needs of stroke patients. The use of these features is demonstrated in pilot studies using VR training environments in different configurations: as an online low-cost version, with a myoelectric robotic orthosis, and in a neurofeedback paradigm. Finally, we argue about the need of coupling VR approaches and neurocomputational modelling to further study stroke and its recovery process, aiding on the design of optimal rehabilitation programs tailored to the requirements of each user.

Keywords: Stroke Rehabilitation, Virtual Reality, Accessibility, Personalization, Computational Neuroscience

14.1 Introduction

Stroke remains one of the main causes of adult disability, with about one third of survivors experiencing permanent motor impairments that severely affect their quality of life (Feigin et al., 2008). This represents a challenge for modern societies, which have to handle the resulting social and economical burden that already accounts for 2–4% of total healthcare costs worldwide (Donnan et al., 2008). In the last years, important neuroscientific findings have contributed to the understanding of functional recovery after stroke, and it is nowadays widely accepted that recovery relies to a large extent on neuronal plasticity mechanisms, such as synapse strengthening and activity-dependent rewiring that can lead to the formation of new neural connections and/or altered pathways to regain function (Dimyan et al., 2011; Murphy et al., 2009).

Motor rehabilitation focused on physical and occupational therapy is still considered a critical driver for restoration, but the challenge remains identifying the optimal way to mobilize plasticity (Bowden et al., 2013; Dimyan et al., 2011).

Information and communication technologies are leading to new breakthroughs in this area, with Virtual Reality (VR) systems receiving special attention (Fluet et al., 2013; Laver et al., 2012). VR is a powerful tool because it enables personalizing artificial environments to particular users and manipulating feedback in such a way that users with disabilities can interact with the virtual environment in a way that would not be possible in the real world (Bohil et al., 2011). Because of its properties, VR technology has been incorporated in several systems aimed for stroke rehabilitation. Particularly, it has been widely used in conjunction with devices for robotic assistance for providing support to patients with limited motor function (Frisoli et al., 2012, Tyryshkin et al., 2014), devices that provide haptic feedback to increase the validity of the virtual interaction (Turolla et al., 2013b, Cameirao et al., 2012, Boos et al., 2011), and also in combination with EEG to study brain activation during virtual training (Steinisch et al., 2013, Bermúdez i Badia et al., 2013). A more recent trend focuses on using virtual reality based serious games that use sophisticated tracking and/or commercial games and movement controllers to increase challenge, enjoyment and adherence to training (Shin et al., 2014, Cameirao et al., 2010, Cho et al., 2012). Rehabilitation paradigms that combine VR with well-defined clinical and neuroscientific guidelines have been shown to moderately improve motor function in stroke patients when compared to traditional physical and occupational therapy (Cameirao et al., 2011, Lohse et al., 2014, Turolla et al., 2013a). While the potential of these technologies for supporting recovery is large, the amount of evidence on the benefit of such paradigms is still limited, and consequently a consensus has not yet been reached concerning the best way of personalizing rehabilitation protocols in terms of system type, method and dose (Laver et al., 2012). This is largely because patients display mismatched outcomes depending on the neural areas and networks affected by stroke (Carey et al., 2005; Stinear et al., 2012). Further, most VR based rehabilitation paradigms usually focus on a specific subset of patients, mainly those with a mild to intermediate impairment level, who allow exploring more inexpensive solutions.

In this chapter, we present strategies that rely on the use of multi-interface and customizable VR solutions for addressing the interindividual variability of stroke survivors and providing training protocols tailored to the specific requirements of each individual.

14.2 Human Computer Confluence (HCC) in neurorehabilitation

The scientific and technological advancements in the rehabilitation area have reached a point in which the mere application of technology leads to unsatisfactory solutions. The use of VR and associated technologies in rehabilitation post-stroke

was initially popularized by its surface properties, such as the affinity with gaming elements, capacity of objectively assessing performance, monitoring over time by clinicians, active involvement of the patient, or ease of transferring the technology to home environments (Iosa et al., 2012, Laver et al., 2012). Although these are very useful and necessary features, they describe features of the implementation of VR based neurorehabilitation but not necessarily operational principles that are able to boost rehabilitation's efficacy. However, taking also into consideration neuroscientific principles of brain functioning it is possible to utilize VR in a more effective way to tackle specific mechanisms that support recovery after stroke. We are therefore not dealing anymore with the application of technology to rehabilitation but instead working towards its confluence with the patient's specificities.

The pressing need to find novel and more effective solutions require us to work at the confluence of computer science, human computer interaction, engineering, rehabilitation medicine and neuroscience. It is by exploiting the synergies among those disciplines that a deeper understanding about the brain and the underlying processes of stroke recovery may arise, and consequently, also novel rehabilitation approaches. In this respect, two core aspects of HCC are particularly well suited to enhance the motor rehabilitation process by enabling a more targeted intervention at the level of the brain: 1) the use of (physical and/or mental) invisible interfaces; and 2) the augmentation of the patient's abilities, not only through training but also through technology.

- Invisible interfaces: The capacity of patients to perform meaningful goal oriented motor actions depends on the existence and extent of residual movement after stroke. This is an important limiting factor because motor rehabilitation requires the active involvement of error correction and planning processes (Beets *et al.*, 2012). Because interfaces carry the responsibility of mediating between the patient's intentions and the motor training tasks, interfaces have to support the correct physical and/or mental execution of actions to ensure that the motor training experience engages those planning and error correction processes. Hence, the role of interfaces for post-stroke motor rehabilitation is of major importance and goes beyond a mere selection of actions to be performed in VR. Interfaces need to be invisible (physically or mentally) in the mediation between the intents of patients and their perceived actions. This is, however, very challenging because of the heterogeneity of motor deficits we find in stroke patients, which result in a yet greater diversity of training paradigms. A VR training paradigm that is adapted to the deficits of a particular patient may require a very specific use of interface technology. Patients' interactions with VR training tools can be based on body kinematics (movement and electromyography), but also on autonomic nervous system responses (such as galvanic skin response, respiration, and heart rate among other) or even brain activity (such as electroencephalography, near-infrared spectroscopy or functional magnetic resonance imaging), extending motor rehabilitation paradigms beyond physical execution. As a result, there is

the need to work towards a unified and coherent framework for interfaces for motor rehabilitation that is able to accommodate a large variety of motor deficits and map motor intent to VR training paradigms in a transparent way.

- Augmenting patient’s abilities: Similar to what happens with the interfaces, VR training paradigms need to go beyond the mere computerization or “gamification” of motor training, which has already been shown effective to contribute to recovery (Takeuchi and Izumi, 2013). It has already been shown that the use of controlled multimodal (visual, auditory and/or tactile) cues for reward and error correction is important for motor learning (Levin, 2010). Thus, VR motor training tools need to be designed, together with its interfaces, to maximally exploit the remaining neural mechanisms of stroke survivors in order to mobilize brain plasticity (Tunik *et al.*, 2013). By means of the possibility of altering the feedback provided in VR training, we propose to use VR to create an alternative reality to allow for a more direct intervention at the level of the central nervous system. VR allows us to augment the motor abilities of the patient in order to be able to restore compromised sensorimotor contingencies, closing the sense-act loop in a very controlled manner. Consequently, VR will enable patients to generate meaningful goal oriented motor actions despite their physical limitations. Hence, personalizing the parameters of motor training to each patient as well as maximizing the recruitment of the Mirror Neurons (MN) system – responsible for action recognition (Rizzolatti *et al.*, 2009) – and the engagement of motor adaptation, error feedback and sensorimotor integration networks (Shadmehr *et al.*, 2010) (Figure 14.1).

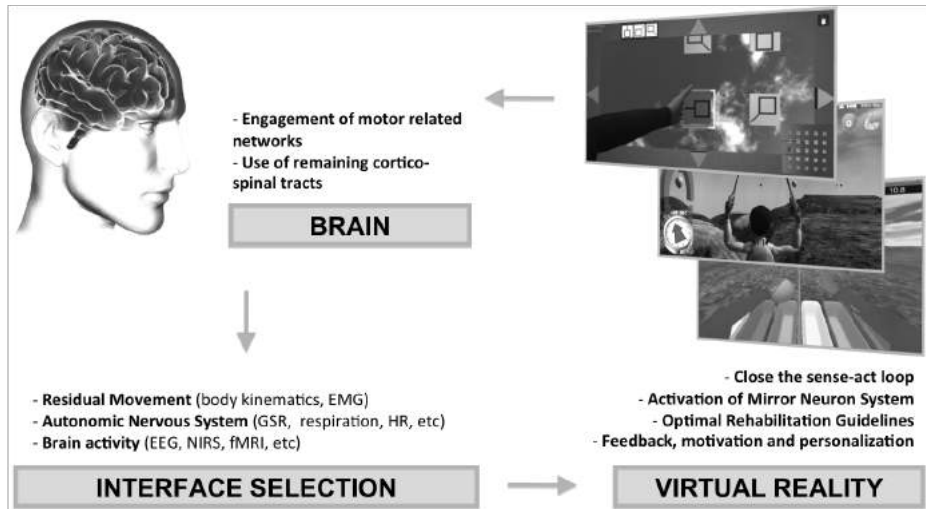


Figure 14.1: Framework for tailoring VR based motor rehabilitation after stroke. The goal is to utilize HCC concepts to achieve a maximal engagement of motor control brain related networks, to mobilize cortical plasticity for maximizing the use of remaining cortico-spinal tracts, and to generate meaningful functional movement. There is therefore a confluence of technology with the patient in which interface technology captures the available voluntary and involuntary control signals, and VR closes the act-sense loop to generate meaningful actions. This approach is designed to recruit motor related networks, to support optimal rehabilitation guidelines and to provide appropriate feedback, motivation and personalization in training

In the following sections we will introduce RehabNet, a technological framework that has been implemented to support the proposed neurorehabilitation approach. We will show in several pilot experiments how the RehabNet framework supports the confluence of technology and patient, allowing interfaces and VR to work in a symbiotic relation with the patient. In previous research we showed that the interface technology of a VR based intervention can have an impact and modulates motor improvements as well as the retention of gains in follow up measures (Cameirao et al., 2012). In RehabNet, interfaces are used to enable patient's access to novel training paradigms unavailable when motor control is seriously compromised, at the same time that VR offers a more direct intervention at the central nervous system level that is not possible by traditional therapy. Thus, interfaces are both enablers and determinant factors of VR based rehabilitation. Nevertheless, there is still limited knowledge available on how to best utilize interfaces and VR to mobilize the remaining motor related networks after stroke. For this reason, in the last section of this chapter we discuss the need of studying the effect of these approaches with brain imaging as well as combining it with a complementary computational modelling effort. A combined effort, bringing together neurocomputational modelling and clinical research, can

give rise to very specific testable model-driven hypothesis on how to improve current neurorehabilitation practices, and enable us to further elucidate the brain mechanisms of recovery after stroke.

14.3 The RehabNet Framework

RehabNet's primary goal is to enable patient's access to novel training paradigms unavailable when motor control is seriously compromised. The existing variability in motor deficits in stroke patients, ranging from mild impairment to no movement, require a broad spectrum of training paradigms based on sensibly different principles, such as for instance training of active movement, robotic assisted movement or neurofeedback (see (Takeuchi et al., 2013) for a review). Thus, technological solutions need to be flexible enough to accommodate numerous interfaces and training paradigms. However, access to therapy does depend exclusively on the availability or use of appropriate interfaces. There are many other factors that influence the access of patients to VR based therapies, among them location, versatility and cost. VR technologies installed at health centres have a great potential of reaching many users but they also require shared usage, transportation from the patient's place, and support by trained professionals. Additionally, the cost of these systems is still prohibitive for the large majority of patients. Either of these factors may result in impossibility of access or in a lack of compliance with the desired frequency of use of VR therapy. Hence, there is the need to develop technological solutions that enable patient's access to VR therapy, but that also consider the economical and social aspects. That is, they should be designed for home usage, be scalable and compatible with low cost mass consumption devices.

To face the above problems we have developed RehabNet, a low cost and accessible system architecture for VR based rehabilitation that provides VR based training directly from the web, supporting several interface technologies and enabling more accessible training paradigms (Figure 14.2) (Vourvopoulos et al., 2013). VR training content is accessible via any standard web browser and is compatible with all major operating systems and android based smart TVs. The control panel, a client application that runs on the home computer, acts as a bridge between the hardware and the online VR training content. The control panel supports multiple low cost and medical grade interface technologies, ranging from a mouse to Brain Computer Interfaces (BCIs). In addition, it translates and maps the information provided by the different interfaces (currently openVibe compatible (Renard et al.) and EPOC (Emotiv Systems, Australia) BCIs), myo-electric robotic orthosis (mpower 1000, Myomo Inc, USA), MS kinect tracking, webcam tracking (Bermúdez i Badia, 2004–2013), android phones as pointing devices, and any VRPN (Taylor Ii et al., 2001) and OSC (Wright, 2005) compatible hardware) onto meaningful control commands for the VR training tasks. While keeping the VR training tasks consistent and interface independent, the control

panel enables adapting the VR training paradigms to a broader range of patients and disabilities, ranging from an active movement based upper limb training to a neurofeedback paradigm based on Sensory Motor Rhythms (SMR) detection using BCIs (Pfurtscheller et al., 1997).

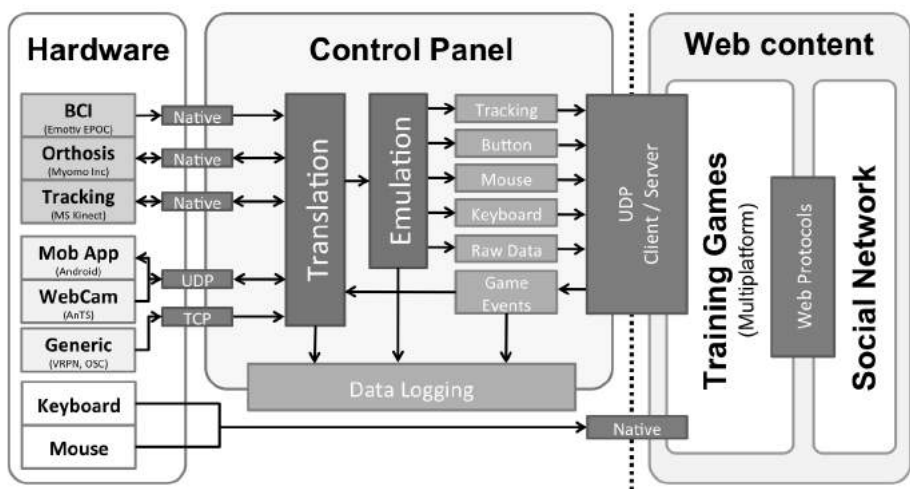


Figure 14.2: The RehabNet system architecture. It consists of three main building blocks: Hardware for device support, Control Panel for data translation and emulation, and Web content for accessing the rehabilitation content. All blocks are interconnected in a client-server (open) architecture. Adapted from (Vourvopoulos et al., 2013)

14.4 Enabling VR Neurorehabilitation Through its Interfaces

14.4.1 Low Cost at Home VR Neurorehabilitation

The Neurorehabilitation Training Toolkit (NTT) is a rehabilitation system implemented with the RehabNet architecture (Bermúdez i Badia & Cameirao, 2012). This rehabilitation system was designed with the primary focus of enabling upper limb VR training anywhere at the lowest possible cost. Therefore, it is a free and worldwide accessible tool for at home rehabilitation with minimal technical requirements¹⁸. The VR training system is operated using only two computer mice and is accessible through a web browser. Because the NTT is designed for home use, it has a strong emphasis on intelligent and automated personalization of training (see section 14.5

¹⁸ Available at <http://neurorehabilitation.m-iti.org/NTT>

for details on personalization). It trains bimanual coordinated movements on a tabletop in a simulated glider control task, allowing support of the paretic arm by the non paretic arm (Figure 14.3a). Despite the simplicity and limitations of the use of two computer mice as interface technology, we have shown that this configuration allows extracting relevant movement kinematic data such as movement smoothness, range of motion and arm coordination, and can successfully adapt the training to each user accordingly (Figure 14.3b).

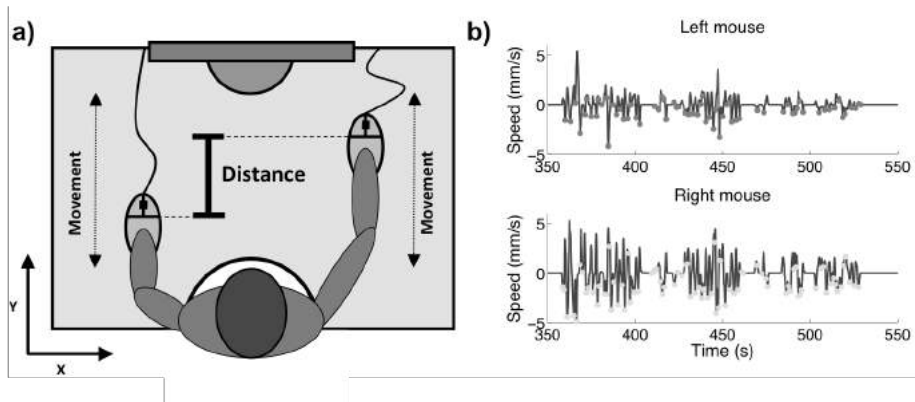


Figure 14.3: The Neurorehabilitation Training Toolkit (NTT). a) The NTT trains bimanual coordination and requires the use of a personal computer and 2 computer mice. b) Mice data provide accurate information on movement speed and acceleration that is used to adapt the rehabilitation training parameters. Adapted from (Bermúdez i Badía & Cameirao, 2012)

14.4.2 Enabling VR Neurorehabilitation Through Assistive Robotic Interfaces

Despite the clear benefits that a system such as the NTT provides, they come at a cost. In its simplest configuration, the NTT can only be used by patients that have sufficient control of active movements and can grasp a computer mouse. Although the adaptation of the physical aspects of interfaces for patients suffering spasticity or flaccidity is feasible, the training does not hold for patients without or with minimal active movement capabilities. For those patients we propose the use of adaptive assistive interfaces for the restoration of active movement. Previous myo-electric driven robotic interventions have been shown to lead to improved motor function and reduced spasticity of the upper extremities (Hu et al., 2009). Consequently, we augmented the NTT with a portable myo-electric limb orthosis equipped with 2 electromyography (EMG) channels and 1 actuated joint (mpower, Myomo Inc., USA) to restore active movement. The orthosis can detect residual muscle activity and provide an adaptive robotic assistance to facilitate movement. The mpower assists in the completion of arm movement based on the detection of biceps and/or triceps EMG activity.

In this new configuration, the NTT integrates the myo-electric robotic system, a camera based hand position tracking and a VR training task for granting access to active movement training to patients with minimal or no active movement capabilities but with residual EMG activation (Figure 14.4a). In order to assess how the provided assistance affects movement quality, task performance and training outcome we evaluated the system in a pilot study with stroke survivors with very low level of control of their paretic arm but still able to generate voluntary EMG activation (Bermúdez i Badia, Lewis et al., 2012). Results showed that the level of myo-electric assistance provided a linear increase of biceps flexion/extension (Figure 14.4b). An analysis of biceps movement assisted by the robotic orthosis revealed a positive but low correlation coefficient with that of the end effector (Pearson's $r = .37$), indicating that most of the arm movement was supported by the glenohumeral joint (shoulder) (Figure 14.4c). When compared to the movement of the non paretic arm, we observed that with myo-electric assistance we could restore active movement up to about 60% of the non paretic arm capabilities (Figure 14.4d). Thus, this robotic interface enables a match between motor intent and performed action transparent to the patient, what is consistent with the recruitment of both the motor control networks and the MN system. In addition, this system allows objectively assessing and monitoring the active contribution of the elbow joint to overall arm movement, and detecting and quantifying the presence of compensatory strategies.

14.4.3 Closing the Act-Sense Loop Through Brain Computer Interfaces

In some cases active movement therapies are not possible even with the aid of assistive interfaces. Without the existence of a physical action, the patient's capability to recruit the brain mechanisms necessary for re-learning – such as motor planning, motor adaptation, or sensorimotor integration – may be disrupted. In these cases there is the need to provide an alternative channel to associate motor intent and perceived action. One solution is to use BCIs in electroencephalography (EEG) based neurofeedback paradigms to promote cortical plasticity (Bundy et al., 2012; Grosse-Wentrup et al., 2011). Mental imagery or simulation training has been shown to be able to engage neuronal systems consistent with those activated during motor training (Miller et al., 2010). VR is very well suited for providing multisensory feedback on mentally simulated motor actions, allowing closing the act-sense loop even in absence of physical movement. We have shown in a study with healthy participants that (1) mental simulation and (2) combined mental simulation and physical motor training are more effective at engaging cortical motor related networks than motor actions alone (Figure 14.5). This effect is most visible in β and γ EEG frequency bands, generally associated to SMRs, active concentration, busyness, alertness, and cross-modal processing and binding (see (Bermúdez i Badia et al., 2013) for details). Consequently, the potential of VR based neurofeedback paradigms based on SMRs

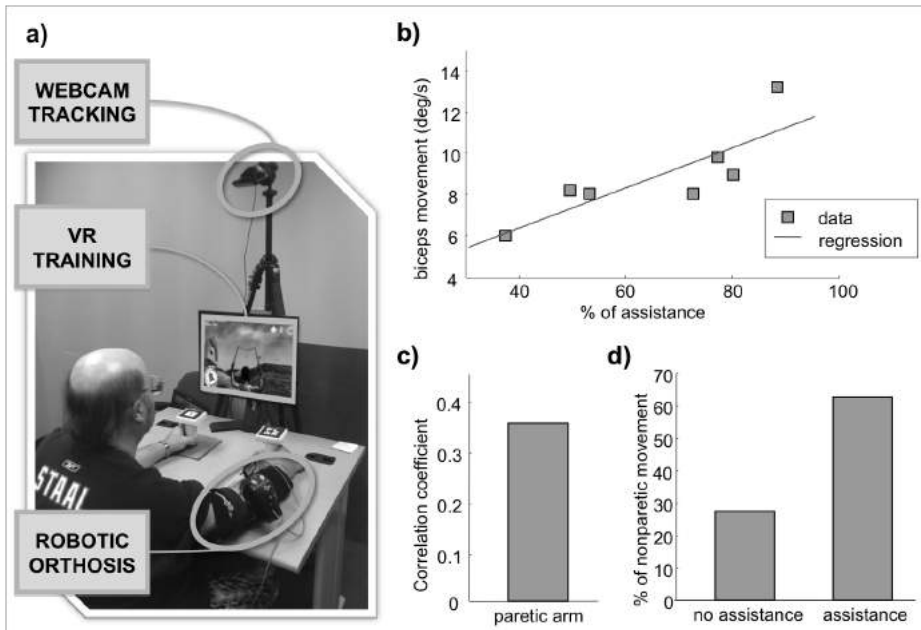


Figure 14.4: NTT with a myo-electric robotic system. a) Components of the system (robotic orthosis, tracking setup, and training game task) while being used by a stroke patient. b) Effect of the level of assistance of the limb orthosis on the amount of biceps movement. c) Quantification of the correlation of biceps movement and overall arm movement. d) Restoration of paretic arm movement as % of non-paretic arm in presence and absence of robotic assistance. Adapted from (Bermúdez i Badia, Lewis et al., 2012)

generated by motor imagery is enormous considering that they can enable access to VR based therapies to most stroke patients, regardless of their level of motor impairment.

14.5 Creating Virtual Reality Environments For Neurorehabilitation

Two critical aspects have to be considered when creating virtual rehabilitation environments for neurorehabilitation: 1) how to adjust automatically the task, assessing patient's skills and matching them with task difficulty; and 2) how to keep the user engaged by controlling the levels of stress and challenge. An efficient way of combining task personalization with challenge within VR rehabilitation scenarios is creating training tasks presented in the form of games. Serious games for stroke rehabilitation have received increased attention during the last few years mainly because of their potential to increase engagement with the rehabilitation task and keep patients working during longer periods of time (Deutsch et al., 2011; Peters et al., 2013). Compliance with training is in fact one critical aspect, particularly when considering the deployment of home based solutions for enduring rehabilitation. The main obstacle

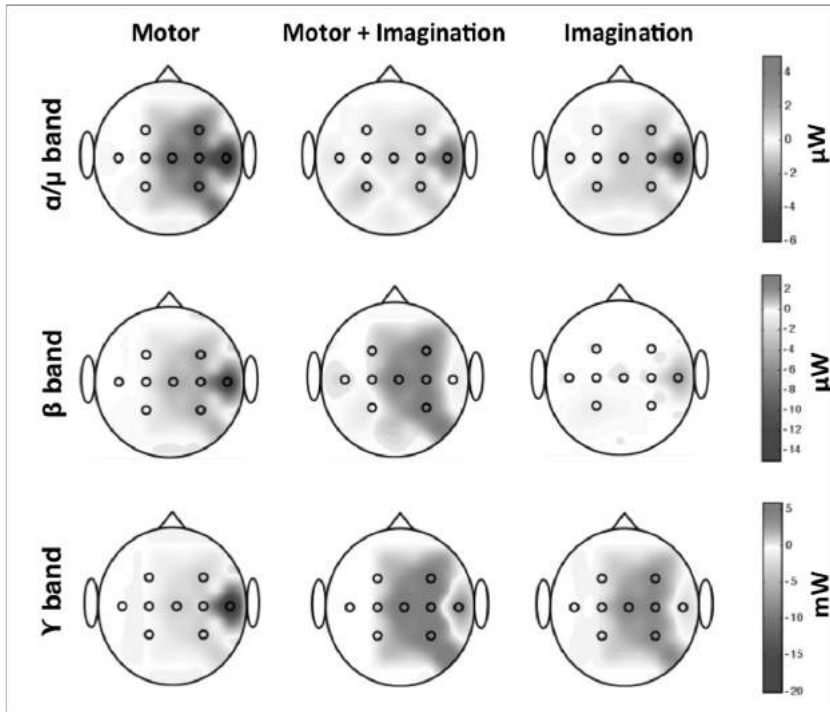


Figure 14.5: Analysis of brain activity for different motor training conditions: motor only, motor and mental imagination, and mental imagination only. Blue indicates de-synchronization of neural responses and red enhanced synchronization of neural responses as compared to baseline. EEG mapping realized with electrodes at F3, C3, P3, T3, F4, C4, P4, T4 and Cz of the international 10–20 system. Adapted from (Bermúdez i Badia et al., 2013)

is to get patients to use these solutions in a systematic way (Jurkiewicz et al., 2011). Here, games have the potential to motivate users and increase adherence to training. From the rehabilitation point of view there are however some aspects that have to be considered when developing serious VR games that aim at promoting recovery following stroke. First, games should be specifically designed for the stroke population and incorporate therapy approaches. Hence, games should target the training of specific movements (for example, reaching and grasping) with realistic short- and long-term goals. Most commercial off-the-shelf games are not appropriate because they lack the specificity of the movements to be executed, and because the tasks are often too demanding. Second, games should be related to functional movements, preferably related to activities of daily living, within a meaningful context (Hochstenbach-Waelen et al., 2012). For example, if the goal is to learn how to reach and grasp and object, performing the movement sequence without an object to be grasped is meaningless and may not contribute to motor learning (Arya et al., 2011; Wu et al., 2000).

Finally, ideally games should be varied and aesthetically pleasant to sustain interest and long-term use.

One of the main advantages of VR rehabilitation when compared to traditional treatment is that it allows implementing artificial environments for task-specific training that determine in real-time the most appropriate task parameters for each user based on his/her specific requirements. This enables bringing to patients tailored rehabilitation tasks fully adjusted to their individual capabilities and with goals that patients are able to accomplish within the range of their motor limitations. Goal oriented task-specific training is common practice in stroke rehabilitation and there is a large body of evidence that suggests its relevance for promoting cortical reorganization, hence recovery after stroke (Buma et al., 2013; Takeuchi et al., 2013). VR has potential to reinforce this effect by allowing users to interact and accomplish goals in a way that would not be possible in the real world, effectively augmenting their capabilities through VR. However, this requires identifying the capabilities of patients and tailoring training exercises depending on their specific motor deficits. In most cases, this is done by having experienced therapists allocating tasks and adjusting the parameters (Duff et al., 2013; Turolla et al., 2013a). While we believe that the involvement of rehabilitation practitioners is crucial for the development of novel VR approaches, we also think that these systems should be somehow autonomous in allocating personalized rehabilitation exercises. We have two main reasons for defending this view. First, it allows having unified frameworks for personalization, i.e., the same set of rules is applied to all users, which will ease assessing the impact of VR based rehabilitation approaches as a function of the profile of stroke patients. Second, one of the main advantages of low-cost VR rehabilitation systems is that patients have the possibility of using them at home after hospital discharge. Hence, these systems should be independent in the decision process and require only minimum intervention of the therapist.

Adjusting the task to the user requires assessing his/her current performance and setting the difficulty level with the task parameters accordingly. Matching appropriate difficulty levels in multi-parameter virtual tasks requires the development of patient based performance models. These models need to be trained with sufficient performance data to provide a thorough assessment of the specific contribution of each VR feature to the overall task difficulty. Hence, these models provide an objective way of tuning task parameters to specific difficulty levels. One specific example of the implementation of this methodology is the Rehabilitation Gaming System (Cameirao et al., 2010). The detailed psychometrics of a sphere catching game were assessed by exposing stroke patients to random combinations of the game parameters, and this information was used to build an adaptation module for adjusting the game difficulty to users. Moreover, it is yet more valuable when these models are able to capture not only task difficulty but also clinically relevant performance metrics (for example, interjoint coordination, velocity of movement, movement smoothness or range of

movement) and provide a more clinically relevant adaptation (Figure 14.6) (Bermúdez i Badia & Cameirao, 2012).

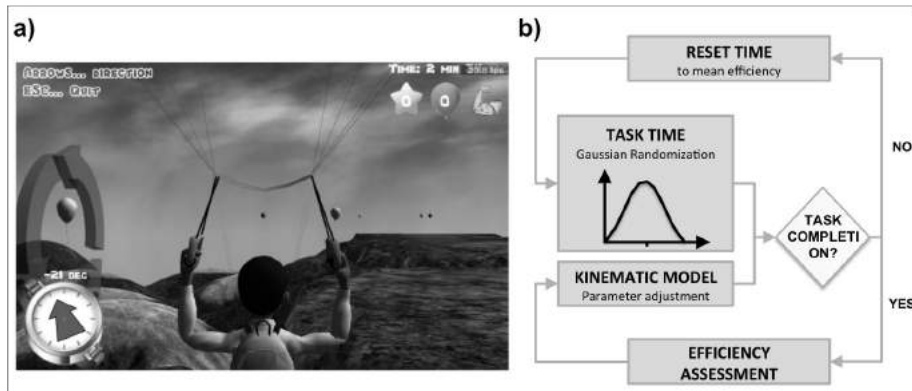


Figure 14.6: Personalization in the Neurorehabilitation Training Toolkit (NTT). a) The user controls the movements of an avatar that flies a glider to collect a number of objects in a VR environment. The target direction is achieved by balancing left and right arm movements. b) The training task is adjusted to the performance of the user through an algorithm that captures the efficiency of actions and adapts the parameters of the task accordingly. Adapted from (Bermúdez i Badia & Cameirao, 2012)

Another critical aspect in personalization is engagement. It has been acknowledged that optimum levels of performance and engagement are obtained at intermediate levels of stress, i.e., when the task is neither too easy nor too hard (Csikszentmihalyi 2002). This means that a degree of failure is necessary for keeping the user challenged and interested. In the context of rehabilitation, strategies based on incremental task complexity have been shown to correlate with cortical reorganization after stroke (Page et al., 2009; You et al., 2005). One way to sustain challenge is by increasing gradually the difficulty of the task while keeping the user in a level that he/she can perform, thus avoiding high levels of stress and frustration. For example, one possible rule can be: for a specific difficulty level, if the user performs without errors the difficulty level is increased; if the failure rate is higher than the success rate, the difficulty is decreased; otherwise, the difficulty level stays the same. In the case of the NTT the user has to collect items in a virtual environment within a limited time window, the time-to-collect of new items being derived from the time used when collecting previous items (Figure 14.6) (Bermúdez i Badia & Cameirao, 2012). Based on the efficiency of motor performance in a race against time task, the personalization algorithm provides an adaptive training that is neither too easy nor too hard to avoid boredom and frustration. This means that the more efficient the user the more demanding and challenging the task. An interesting feature of the NTT's race against time model is that it enables to control stress levels (time-to-perform) independently from motor skills (kinematic training parameters) (Figure 14.6b). In previous studies, we have shown that VR tasks that personalize training and adjust difficulty based on

failure rates have a positive impact in both acute and chronic stroke patients (Cameirao et al., 2012; Cameirao et al., 2011). Although further evidence is needed to assess and understand the particular benefits of personalized VR gaming in stroke rehabilitation, we believe that these tools have all the ingredients to become common practice in rehabilitation in the near future.

14.6 Looking Forward: Tailoring Rehabilitation Through Neuro-Computational Modelling

With the aging of the population and the unsustainable cost of current rehabilitation, new solutions must come from novel scientific approaches that bring further insights on how to improve the effectiveness of rehabilitation. Although the field of stroke rehabilitation has advanced enormously during the last years and VR is a very promising tool for stroke recovery, we are likely to be reaching the boundaries of what can be achieved without a solid and integrated theoretical framework on stroke and its recovery. Rehabilitation approaches need to take into account how neuroanatomical determinants, such as lesion size and location, affect motor execution; how the corresponding brain mechanisms underlie recovery; and need to be able to provide optimal rehabilitation strategies for each individual case. Unfortunately we are still far from such a holistic understanding of stroke, and as consequence we cannot take full advantage of the technological advantages brought by VR training tools.

We believe that one way to address this challenge systematically is by using a neurocomputational modelling approach that considers the neural areas and circuits involved in movement planning and execution; replicates the effect of focal brain lesions in specific brain areas; and simulates recovery mechanisms. By simulating lesions to the model and integrating plasticity mechanisms following stroke, such an approach could be used to simulate stroke and study the effect of different rehabilitation approaches. Here VR is the key piece because the coupling of a computational model of motor control and a virtual body allows closing the act-sense control loop and having a cohesive framework to systematically study healthy and impaired motor control. There has been some work on computational modelling for stroke (Goodall et al., 1997; Han et al., 2008; Reinkensmeyer et al., 2012) but to our knowledge there is no work that couples a neurocomputational model with a VR rehabilitation environment. If the VR environments used for simulations of the neurocomputational models were consistent with those used for motor rehabilitation training, the generalization of results would be straightforward. In fact, the use of a common VR environment for both model simulation and patient training enables direct transfer of results from the clinical praxis to the computational modelling approach, enabling model training to fit available performance, kinematic and clinical patient data.

Although being a very ambitious and laborious research goal, this is a path that will increase our knowledge on stroke, its recovery and will enable us to design personalized VR rehabilitation programs that take into account the neuroanatomical constrains of each patient to maximize functional recovery, bringing personalization of VR training to the next level. This modelling effort enables investigating how recovery patterns are modulated by lesion location and training routines, in a unique manner not yet explored. The potential impact of such an approach is multifold. At the scientific level, it would provide a comprehensive and integrative platform for neuroscientists, engineers and clinicians to further understand the mechanisms underlying stroke recovery and the impact of different rehabilitation strategies. For rehabilitation medicine, it would represent an important step towards model based tailoring of rehabilitation protocols for maximizing recovery. Finally, in the long-term such a strategy would contribute to further increase the quality of life of stroke survivors; improve the management of healthcare services and resources; and reduce the overall socio-economic burden of stroke.

Acknowledgements: This work is supported by the European Commission through the RehabNet project – Neuroscience Based Interactive Systems for Motor Rehabilitation – EC (303891 RehabNet FP7-PEOPLE-2011-CIG) and the Fundação para a Ciência e Tecnologia (Portuguese Foundation for Science and Technology) through CMU-Pt/0004/2007, SFRH/BPD/84313/2012, and Projeto Estratégico – LA 9 – 2013–2014.

References

- Arya, K. N., Pandian, S., Verma, R., et al. (2011). Movement therapy induced neural reorganization and motor recovery in stroke: a review. *J Bodyw Mov Ther*, 15(4), 528–537.
- Beets, I. A., Mace, M., Meesen, R. L., et al. (2012). Active versus passive training of a complex bimanual task: is prescriptive proprioceptive information sufficient for inducing motor learning? *PLoS One*, 7(5), e37687.
- Bermúdez i Badia, S. (2004–2013). Analysis and Tracking System [version 2]. Retrieved 28/10/2013, from <http://sergibermudez.blogspot.com>
- Bermúdez i Badia, S., & Cameirao, M. S. (2012). The Neurorehabilitation Training Toolkit (NTT): A Novel Worldwide Accessible Motor Training Approach for At-Home Rehabilitation after Stroke. *Stroke Res Treat*, 2012, 802157.
- Bermudez i Badia, S., Garcia Morgade, A., Samaha, H., et al. (2013). Using a hybrid brain computer interface and virtual reality system to monitor and promote cortical reorganization through motor activity and motor imagery training. *IEEE Trans Neural Syst Rehabil Eng*, 21(2), 174–181.
- Bermúdez i Badia, S., Lewis, E., & Bleakley, S. (2012, September). *Combining virtual reality and a myo-electric limb orthosis to restore active movement after stroke: a pilot study*. Paper presented at the 9th Intl Conf. Disability, Virtual Reality & Associated Technologies, Laval, France.
- Bohil, C. J., Alicea, B., & Biocca, F. A. (2011). Virtual reality in neuroscience research and therapy. *Nat Rev Neurosci*, 12(12), 752–762.

- Boos, A., Qiu, Q., Fluet, G. G., & Adamovich, S. V. (2011). Haptically facilitated bimanual training combined with augmented visual feedback in moderate to severe hemiplegia. *Conf Proc IEEE Eng Med Biol Soc*, 2011, 3111–3114.
- Bowden, M. G., Woodbury, M. L., & Duncan, P. W. (2013). Promoting neuroplasticity and recovery after stroke: future directions for rehabilitation clinical trials. *Curr Opin Neurol*, 26(1), 37–42.
- Buma, F., Kwakkel, G., & Ramsey, N. (2013). Understanding upper limb recovery after stroke. *Restor Neurol Neurosci*. 31(6):707–722.
- Bundy, D. T., Wronkiewicz, M., Sharma, M., et al. (2012). Using ipsilateral motor signals in the unaffected cerebral hemisphere as a signal platform for brain-computer interfaces in hemiplegic stroke survivors. *Journal of neural engineering*, 9(3), 036011.
- Cameirao, M. S., Badia, S. B., Duarte, E., et al. (2012). The combined impact of virtual reality neurorehabilitation and its interfaces on upper extremity functional recovery in patients with chronic stroke. *Stroke*, 43(10), 2720–2728.
- Cameirao, M. S., Badia, S. B., Oller, E. D., et al. (2010). Neurorehabilitation using the virtual reality based Rehabilitation Gaming System: methodology, design, psychometrics, usability and validation. *J Neuroeng Rehabil*, 7, 48.
- Cameirao, M. S., Bermudez, I. B. S., Duarte, E., et al. (2011). Virtual reality based rehabilitation speeds up functional recovery of the upper extremities after stroke: a randomized controlled pilot study in the acute phase of stroke using the rehabilitation gaming system. *Restor Neurol Neurosci*, 29(5), 287–298.
- Carey, L. M., Abbott, D. F., Egan, G. F., et al. (2005). Motor impairment and recovery in the upper limb after stroke: behavioral and neuroanatomical correlates. *Stroke*, 36(3), 625–629.
- Cho, K. H., Lee, K. J., & Song, C. H. (2012). Virtual-reality balance training with a video-game system improves dynamic balance in chronic stroke patients. *Tohoku J Exp Med*, 228(1), 69–74.
- Csikszentmihalyi, M. (2002). *Flow: The Classic Work on How to Achieve Happiness*. London: Rider & Co
- Deutsch, J. E., Brettler, A., Smith, C., et al. (2011). Nintendo wii sports and wii fit game analysis, validation, and application to stroke rehabilitation. *Top Stroke Rehabil*, 18(6), 701–719.
- Dimyan, M. A., & Cohen, L. G. (2011). Neuroplasticity in the context of motor rehabilitation after stroke. *Nat Rev Neurol*, 7(2), 76–85.
- Donnan, G. A., Fisher, M., Macleod, M., et al. (2008). Stroke. *Lancet*, 371(9624), 1612–1623.
- Duff, M., Chen, Y., Cheng, L., et al. (2013). Adaptive mixed reality rehabilitation improves quality of reaching movements more than traditional reaching therapy following stroke. *Neurorehabil Neural Repair*, 27(4), 306–315.
- Feigin, V. L., Barker-Collo, S., McNaughton, H., et al. (2008). Long-term neuropsychological and functional outcomes in stroke survivors: current evidence and perspectives for new research. *Int J Stroke*, 3(1), 33–40.
- Fluet, G., & Deutsch, J. (2013). Virtual Reality for Sensorimotor Rehabilitation Post-Stroke: The Promise and Current State of the Field. *Current Physical Medicine and Rehabilitation Reports*, 1(1), 9–20.
- Frisoli, A., Procopio, C., Chisari, C., Creatini, I., Bonfiglio, L., Bergamasco, M., Rossi, B., & Carboncini, M. C. (2012). Positive effects of robotic exoskeleton training of upper limb reaching movements after stroke. *J Neuroeng Rehabil*, 9, 36.
- Goodall, S., Reggia, J. A., Chen, Y., et al. (1997). A computational model of acute focal cortical lesions. *Stroke*, 28(1), 101–109.
- Grosse-Wentrup, M., Mattia, D., & Oweiss, K. (2011). Using brain-computer interfaces to induce neural plasticity and restore function. *Journal of neural engineering*, 8(2), 025004.
- Han, C. E., Arbib, M. A., & Schweighofer, N. (2008). Stroke rehabilitation reaches a threshold. *PLoS Comput Biol*, 4(8), e1000133.

- Hochstenbach-Waelen, A., & Seelen, H. A. (2012). Embracing change: practical and theoretical considerations for successful implementation of technology assisting upper limb training in stroke. *J Neuroeng Rehabil*, *9*, 52.
- Hu, X. L., Tong, K.-y., Song, R., et al. (2009). A comparison between electromyography-driven robot and passive motion device on wrist rehabilitation for chronic stroke. *Neurorehabilitation and Neural Repair*, *23*(8), 837–846.
- Iosa, M., Morone, G., Fusco, A., Bragoni, M., Coiro, P., Multari, M., Venturiero, V., De Angelis, D., Pratesi, L., & Paolucci, S. (2012). Seven capital devices for the future of stroke rehabilitation. *Stroke Res Treat*, *2012*, 187965.
- Jurkiewicz, M. T., Marzolini, S., & Oh, P. (2011). Adherence to a home-based exercise program for individuals after stroke. *Top Stroke Rehabil*, *18*(3), 277–284.
- Laver, K., George, S., Thomas, S., et al. (2012). Cochrane review: virtual reality for stroke rehabilitation. *Eur J Phys Rehabil Med*, *48*(3), 523–530.
- Levin, M. F., Heidi Sveistrup, and Sandeep K. Subramanian. (2010). Feedback and virtual environments for motor learning and rehabilitation. *Schedae* *1*, 19–36.
- Lohse, K. R., Hilderman, C. G., Cheung, K. L., Tatla, S., & Van der Loos, H. F. (2014). Virtual reality therapy for adults post-stroke: a systematic review and meta-analysis exploring virtual environments and commercial games in therapy. *PLoS One*, *9*(3), e93318.
- Miller, K. J., Schalk, G., Fetz, E. E., et al. (2010). Cortical activity during motor execution, motor imagery, and imagery-based online feedback. *Proceedings of the National Academy of Sciences*, *107*(9), 4430–4435.
- Murphy, T. H., & Corbett, D. (2009). Plasticity during stroke recovery: from synapse to behaviour. *Nat Rev Neurosci*, *10*(12), 861–872.
- Page, S. J., Szaflarski, J. P., Eliassen, J. C., et al. (2009). Cortical plasticity following motor skill learning during mental practice in stroke. *Neurorehabil Neural Repair*, *23*(4), 382–388.
- Peters, D. M., McPherson, A. K., Fletcher, B., et al. (2013). Counting repetitions: an observational study of video game play in people with chronic poststroke hemiparesis. *J Neurol Phys Ther*, *37*(3), 105–111.
- Pfurtscheller, G., & Neuper, C. (1997). Motor imagery activates primary sensorimotor area in humans. *Neuroscience letters*, *239*(2), 65–68.
- Reinkensmeyer, D. J., Guigon, E., & Maier, M. A. (2012). A computational model of use-dependent motor recovery following a stroke: optimizing corticospinal activations via reinforcement learning can explain residual capacity and other strength recovery dynamics. *Neural Netw*, *29–30*, 60–69.
- Renard, Y., Lotte, F., Gibert, G., et al. OpenViBE: an open-source software platform to design, test, and use brain-computer interfaces in real and virtual environments. *Presence: teleoperators and virtual environments*, *19*(1), 35–53.
- Rizzolatti, G., Fabbri-Destro, M., & Cattaneo, L. (2009). Mirror neurons and their clinical relevance. *Nat Clin Pract Neurol*, *5*(1), 24–34.
- Shadmehr, R., Smith, M. A., & Krakauer, J. W. (2010). Error correction, sensory prediction, and adaptation in motor control. *Annu Rev Neurosci*, *33*, 89–108.
- Shin, J. H., Ryu, H., & Jang, S. H. (2014). A task-specific interactive game-based virtual reality rehabilitation system for patients with stroke: a usability test and two clinical experiments. *J Neuroeng Rehabil*, *11*, 32.
- Steinisch, M., Tana, M. G., & Comani, S. (2013). A post-stroke rehabilitation system integrating robotics, VR and high-resolution EEG imaging. *IEEE Trans Neural Syst Rehabil Eng*, *21*(5), 849–859.
- Stinear, C. M., Barber, P. A., Petoe, M., et al. (2012). The PREP algorithm predicts potential for upper limb recovery after stroke. *Brain*, *135*(Pt 8), 2527–2535.

- Takeuchi, N., & Izumi, S. (2013). Rehabilitation with poststroke motor recovery: a review with a focus on neural plasticity. *Stroke Res Treat*, 2013, 128641.
- Taylor II, R. M., Hudson, T. C., Seeger, A., et al. (2001). *VRPN: a device-independent, network-transparent VR peripheral system*. Paper presented at the Proceedings of the ACM symposium on Virtual reality software and technology.
- Tunik, E., Saleh, S., & Adamovich, S. V. (2013). Visuomotor discordance during visually-guided hand movement in virtual reality modulates sensorimotor cortical activity in healthy and hemiparetic subjects. *IEEE Trans Neural Syst Rehabil Eng*, 21(2), 198–207.
- Turolla, A., Dam, M., Ventura, L., et al. (2013a). Virtual reality for the rehabilitation of the upper limb motor function after stroke: a prospective controlled trial. *J Neuroeng Rehabil*, 10, 85.
- Turolla, A., Daud Albasini, O. A., Oboe, R., Agostini, M., Tonin, P., Paolucci, S., Sandrini, G., Venneri, A., & Piron, L. (2013b). Haptic-based neurorehabilitation in poststroke patients: a feasibility prospective multicentre trial for robotics hand rehabilitation. *Comput Math Methods Med*, 2013, 895492.
- Tyryshkin, K., Coderre, A. M., Glasgow, J. I., Herter, T. M., Bagg, S. D., Dukelow, S. P., & Scott, S. H. (2014). A robotic object hitting task to quantify sensorimotor impairments in participants with stroke. *J Neuroeng Rehabil*, 11(1), 47.
- Vourvopoulos, A., Faria, A. L., Cameirão, M. S., et al. (2013, October 9–12). *RehabNet: A Distributed Architecture for Motor and Cognitive Neuro-Rehabilitation. Understanding the Human Brain through Virtual Environment Interaction*. Paper presented at the 2013 IEEE 15th International Conference on e-Health Networking, Applications and Services (Healthcom), Lisbon.
- Wright, M. (2005). Open Sound Control: an enabling technology for musical networking. *Organised Sound*, 10(03), 193–200.
- Wu, C., Trombly, C. A., Lin, K., et al. (2000). A kinematic study of contextual effects on reaching performance in persons with and without stroke: influences of object availability. *Arch Phys Med Rehabil*, 81(1), 95–101.
- You, S. H., Jang, S. H., Kim, Y. H., et al. (2005). Virtual reality-induced cortical reorganization and associated locomotor recovery in chronic stroke: an experimenter-blind randomized study. *Stroke*, 36(6), 1166–1171.