Edinburgh Research Explorer

Robotic devices and brain-machine interfaces for hand rehabilitation post-stroke

REVIEW ARTICLE

ROBOTIC DEVICES AND BRAIN-MACHINE INTERFACES FOR HAND REHABILITATION POST-STROKE

Alistair C. McCONNELL, MSc[1,2], Renan C. MOIOLI, PhD[3], Fabricio L. BRASIL, PhD[3], Marta VALLEJO, MSc[1], David W. CORNE[1], Patricia A. VARGAS, PhD[1] and Adam A. STOKES, PhD[2]

From the [1]Robotics Lab., School of Mathematical and Computer Sciences, Heriot-Watt University, [2]Stokes Research Group, Scottish Microelectronics Centre, Edinburgh University, The King's Buildings, Edinburgh, UK and [3]Edmond and Lily Safra International Institute of Neuroscience, Santos Dumont Institute, Macaiba, Brazil

Objective: To review the state of the art of robotic-aided hand physiotherapy for post-stroke rehabilitation, including the use of brain-machine interfaces. Each patient has a unique clinical history and, in response to personalized treatment needs, research into individualized and at-home treatment options has expanded rapidly in recent years. This has resulted in the development of many devices and design strategies for use in stroke rehabilitation.

Methods: The development progression of robotic-aided hand physiotherapy devices and brain-machine interface systems is outlined, focussing on those with mechanisms and control strategies designed to improve recovery outcomes of the hand post-stroke. A total of 110 commercial and non-commercial hand and wrist devices, spanning the 2 major core designs: end-effector and exoskeleton are reviewed.

Results: The growing body of evidence on the efficacy and relevance of incorporating brain-machine interfaces in stroke rehabilitation is summarized. The challenges involved in integrating robotic rehabilitation into the healthcare system are discussed.

Conclusion: This review provides novel insights into the use of robotics in physiotherapy practice, and may help system designers to develop new devices.

Stroke is a global issue affecting people of all ethnicities, genders and ages (1, 2); approximately 20 million people per year worldwide experience a cerebrovascular accident (3), of which strokes are one of the primary causes (4, 5). Typically, one year on from a stroke 65% of these patients remain severely handicapped and dependent on assistance in daily life (6). A patient may be left with mild to acute disabilities, depending on the type and severity of the stroke. Levels of restoration of hand mobility and motor skills are often very low following conventional therapies for stroke (7).

In recent years, several new forms of rehabilitation using robot-aided therapy have been developed, and have been shown to improve upper limb motor function (8).

This paper reviews the current state of the art of robotic devices and brain-machine interface (BMI) techniques developed for post-stroke hand rehabilitation. The following 4 themes are discussed: development of these robotic systems; current challenges; future potential; and inherent ethical issues.

POTENTIAL CONSEQUENCES OF STROKE

Patients typically begin rehabilitation immediately after a stroke, with the first phase taking place in hospital under the supervision of a physiotherapist (9). This is usually followed by the provision of a set of physiotherapy exercises, for the patient to perform unaided and unsupervised after discharge from hospital. The reason for the use of unsupervised rehabilitation is the lack of resources available to health services worldwide, such as a shortage of physiotherapists and limited availability of mobile or affordable equipment (10, 11).

Hand rehabilitation after stroke is considered to be a lower priority than recovery of the upper arm, which itself is secondary to restoration of the motion of the trunk and lower body, such as walking through gait relearning. Thus, when rehabilitation of the hand begins, it is often after the acute stage (the period during which treatment has the greatest potential for recovery (12–14)). Due to this missed window of opportunity, only minor additional measurable improvement occurs after the 6 months following stroke onset (15–17), leading to less-than-satisfactory results (18). A robotic-based rehabilitation framework might have the potential to improve the treatment process, by guiding the rehabilitation exercises and storing and providing access to data for physiotherapists to analyse.

Recently, some new recovery strategies, such as constraint-induced movement therapy (CIMT), and robot-assisted therapy, have been clinically tested for stroke rehabilitation and shown to be effective. However, their application is restricted to stroke patients with residual movement capabilities, who typically account for 50–70% of cases (19). Where these systems cannot be used; for example, for patients with chronic stroke and no residual hand movement, there is no accepted efficient rehabilitation strategy available (20).

CONVENTIONAL PHYSIOTHERAPY

There have been many in-depth reviews, meta-analyses, and comparisons of the ideas, theories and practice of different physiotherapy schools. For example, Kalra et al. (21), Kwakkel et al. (22) and Lincoln et al. (23) reviewed the effects of training intensity, timing in relation to the stroke, and the precise motions used.

The typical programme of stroke physiotherapy exercises for the hand was researched. Details of how these exercises can be applied to develop effective rehabilitation devices are described below.

There are 3 key exercises given to patients for rehabilitation of full motion of the wrist and hand (24):

- *Opening the hand* from a closed to a fully open position, followed by relaxing the hand. This is typically the first exercise used, since most stroke patients initially have their hand locked into a "claw" shape. To gauge the severity of this disability, the patient typically attempts to perform the exercises unaided, after which the physiotherapist manipulates the fingers into the correct position to fully open the hand. The patient will slowly progress to unaided motion.
- *Grasping motion*: aiming to rehabilitate holding an object in the hand, as in everyday life. Again, the patient will slowly progress to unaided motion. This movement adds difficulty by having the patient attempt to hold an object, requiring different finger positions depending on the item used (e.g. cylindrical grasp: involving opening the hand as far as possible before closing it slowly around a cylindrical object, such as a tin; or precision (pinch) grasp: bringing the thumb and forefinger together in a pinching motion (Fig. 1)).
- *Wrist movement:* flexion and extension of the hand (Fig. 2). In a flexion motion, the patient assumes a neutral or flat wrist position, then tilts their hand downwards as far as possible. Extension starts with the patient's hand in a neutral or flat wrist position, then the patient tilts their hand upwards as far as possible. This combination of movements helps the patient rehabilitate the "claw-like" shape of their wrist and hand after stroke. Due to the layout of the muscles in the human arm, if the extensor or flexor muscles become overextended, the motion of the fingers and wrist becomes compromised, resulting in a high probability of limiting the patient's range of motion.

There are 4 other wrist movements that patients may be advised to carry out for rehabilitation: abduction, adduction, pronation and supination. These movements, however, are of a far lower priority than flexion and extension. Abduction and adduction describe the motion of moving the wrist from side to side in alignment
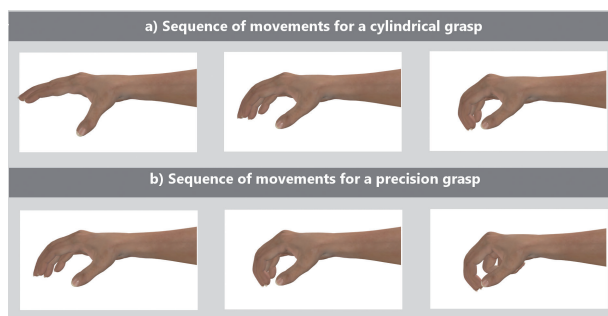

Fig. 1. The sequence of movements required to perform cylindrical grasp and precision grasp. T*op row*: open-hand position, moving to grasping a cylindrical object. *Second row*: open-hand position, moving to a precision grasp or a "pinch" position.

with the arm, and pronation and supination describe the motion of rolling the wrist so that the hand turns from palm up to palm down.

ROBOTIC DEVICES FOR HAND REHABILITATION POST-STROKE

Existing robotic devices for hand and wrist rehabilitation can be divided into 2 categories based on the following criteria:

- technology readiness level (TRL) of the device;
- type of mechanism (end-effector or exoskeleton system) used to achieve the desired movement. An example of an end-effector system is the haptic knob (25) from the National University of Singapore and Imperial College London. Examples of an exoskeleton system is the PMHand from Heriot-Watt University (26). Fig. 3 illustrates the differences between end-effector and exoskeleton systems.

End-effector systems

End-effector systems, in the context of rehabilitative robotics, are devices that interact with the patient through a single point, which is either attached to the patient's hand (27) or gripped by the hand (25). This
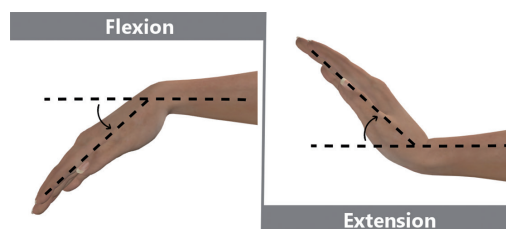

Fig. 2. Example of the exercises a patient should perform to regain full range of motion and use of their wrist and hand are (*i*) flexion, where the patient moves from a neutral palm-down position to bringing the palm closer to the underside of the arm and (*ii*) extension, where the hand is raised, to bring the back of the hand closer to the upper side of the arm.
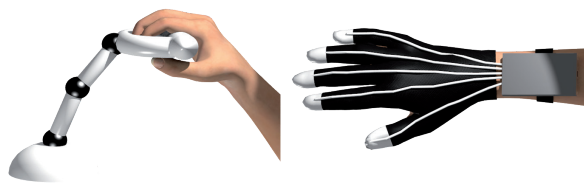
Fig. 3. End-effector set-up in a unilateral configuration (*left*). A generic full-hand exoskeleton (*right*).

single-point interaction allows the patient to perform their given exercises within the robot's predefined XYZ Cartesian space, which can be represented graphically on a monitor, displaying their progress in a realistic manner (28). End-effector systems ensure that the patient is restricted to the correct range of motions, by controlling the paths along which their joints can move. These systems can also include sections that support the patient's arm, if needed. End-effector systems may be incorporated into bilateral therapy, through the use of a second system on the non-paretic arm. This enables the recording of motion data from the non-impaired "master" arm to be translated into movement of the paretic "slave" arm. Such a data collection process was used in the system implemented by Kawasaki et al. (29).

Exoskeleton systems

In contrast, exoskeleton systems are devices that are fully mounted on the patient, such as the system developed by Ates et al. (30), enabling more realistic and engaging treatment. These body-worn devices, however, apply extra weight to the patient unless they are aided by some form of cable mount.

ATTRIBUTES OF REHABILITATION SYSTEMS

Within these categories, another key element is the training modality of the system, which can be assistive, passive, active or active-assistive:

- In an assistive system the patient performs the exercise, but the robotic system provides assistance during the whole routine.
- An active system is not actuated, but can perform measurements. The patient is constrained to the appropriate range of motion.
- Passive systems are interactive and help the hand or wrist to achieve the correct range of motion through the use of actuators, which apply a force to aid motion.
- Active-assistive systems are hybrid-style systems, which include a mode allowing them to be utilized in a similar manner to an active device. This mode offers no resistance to the patient and only monitors

the movement, but can assist the patient in completing their task if required. Further training modalities are suggested by Basteris et al. (31).

A critical design goal in creating these devices is minimization of the sense of technological intrusion experienced while using the system. The objective is to mimic as closely as possible the manner in which a physiotherapist would interact with the patient during rehabilitation. In addition, the system should allow a greater sense of continuity and a smooth transition between interaction with the physiotherapist and use of the device.

Device aesthetics and user comfort (both physical and psychological) are important; patients must feel comfortable with the device in order to continue its use. Previous surveys on the use of artificial hands found that up to 50% of amputees did not use their prosthetic hands regularly. The main reasons for discontinuing use were poor functionality, cosmetic appearance and controllability (32).

When assisting in performing a movement, the device should provide the patient with a safe range of motion at all times, suited to their individual measurements. The devices will be used by a wide range of patients (10) and must be able to cope with a wide variety of anthropomorphic parameters (33).

The system should also provide physiotherapists with the data required to track the patients' progress. Ideally, this information should be accessible both as raw data, retrieved directly from the device, and as post-processed data, displayed for ease of analysis. This monitoring could be conducted during interaction between the patient and the physiotherapist, which may occur once per week, and would allow the physiotherapist to explain the progress directly to the patient. Alternatively, if in-person visits are not feasible, the device could present the option of conducting sessions remotely. This might be done with either the physiotherapist controlling the device via teleoperation, in order to study the patient using the device in real-time, or through monitoring the data gathered during the exercises, if this information was uploaded to a cloud-based system.

Interaction can also be aided by using the device data to demonstrate to the patients that they are making progress through feedback graphing, as well as the potential use of interactive games to motivate the patients' continued progress (34).

LOWER ARM ROBOTIC DEVICES

This section describes a number of devices designed for stroke rehabilitation, compares their key features, and divides the devices into 2 groups: commercial devices

currently available for purchase; and research-based devices that are either at the prototype or clinical trial stage.

The focus of the current paper is the hand and wrist, and therefore upper arm stroke rehabilitation is not discussed. This can be found in Loureiro et al.'s review article (35).

A literature search was performed in PubMed, ScienceDirect, Google Scholar and Web of Science, using the following key words and phrases: robotic hand rehabilitation, robotic wrist rehabilitation, lower arm robotic rehabilitation, robotic stroke rehabilitation, BMI in stroke rehabilitation, BMI in rehabilitation, (brain computer interface (BCI) in stroke rehabilitation, arm based exoskeletons, arm-based end-effectors, global stroke statistics, and stroke rehabilitation.

Commercial hand and wrist devices

There are many commercial rehabilitation devices; the most prevalent of which are listed in Table SI[1]. These devices have a wide range of cost and complexity. For example, Fig. 4 (*left*) shows the Power-Web (36); a non-responsive piece of rubber used to guide stretches, which costs £10 (GBP), and the Kinetec Maestra (37) (*right*), an advanced mounted exoskeleton that provides a constant force to create motion in the fingers and feedback, which has a unit cost of approximately £4,000.

Non-commercial hand and wrist devices

The non-commercial devices, divided into 2 categories according to device type (end-effector or exoskeleton). are shown in Tables SII and SIII.

End-effector devices

The first end-effector device developed for hand and wrist rehabilitation was based on the haptic sensor

---

[1]http://www.medicaljournals.se/jrm/content/?doi=10.2340/16501977-2229
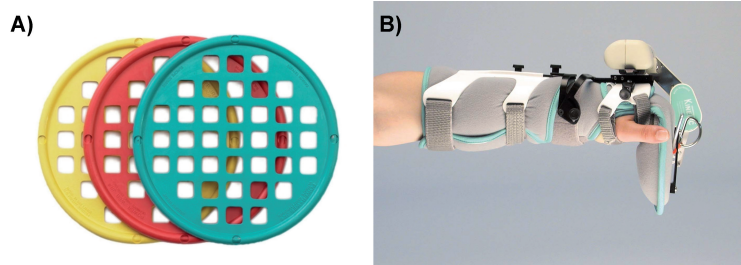

Fig. 4. (A) Power-Web: consisting of a simple circular rubber sheet containing multiple small spaces. The Power-Web allows the patient to insert their fingers and then move the fingers in different motions with the rubber providing a form of resistance training. (B) Kinetec Maestra: worn mounted to the wrist and the tips of the fingers, the Kinetic Maestra can open and close the fingers in a single motion. Through raising the arm on which the device is worn, the user can achieve a full opening and closing motion.

device known as the Space Interface Device for Artificial Reality (SPIDAR). This device was conceived in 1989 at the Tokyo Institute of Technology (147), where all subsequent SPIDAR iterations were also developed (148).

The first SPIDAR was a single-point interaction system in which one finger was attached to the device and the patient could interact with a Virtial Reality (VR) system. There were many versions of the SPIDAR device (e.g. SPIDAR-II (149), which allowed a pinch motion to more accurately reflect reality). This model was followed by the Both-Hand SPIDAR, which allowed the use of both hands, then the Big SPIDAR (150), a full-body interactive system, and SPIDAR-G, which used a ball mounted in the centre of a link system to allow the patient to grasp objects in a more realistic manner. The current iteration is SPIDAR-8 (52), a 2-handed multi-finger interactive device designed to incorporate all of the advantages of the previous devices, which is currently undergoing clinical trials.

The Rutgers Master II, created in 2002 by Bouzit et al. (55), is an end-effector device that is attached to the fingers through a palm-side individual grip and uses a piston combination to reflect the force a patient could apply in a VR game.

HI-FI Hand, created by Mali & Munih (59), is the first end-effector device capable of both aiding the patient in the movement, being able to provide up to 10 N force, and collecting feedback data from the force generated by the patient. The HI-FI Hand, however, can only manipulate a single finger and is a very elaborate system compared with the SPIDAR and Rutgers Master II systems.

The HIRO (Haptic Interface Robot), created by Kawasaki et al. (29) in 2003, used a 2-finger and thumb configuration to allow an object to be felt through a VR-based environment with haptic feedback sent to the patient's fingertips. Next came the HIRO II (57), a full-hand 15 DOF system created in the image of the human hand, that was capable both of interacting with a VR environment, with a passive 6 DOF control device on the non-piratic arm, which would control the active arm. HIRO II+ (61), built in 2007, was created to overcome problems with the HERO II, such as the inability to perform pinch motions, but it was still based on the same model of the human hand to interact with a modified method of motion. The final system was the HIRO III (73), created in 2011, based on the previous systems, retaining its number of degrees of freedom (DOF) and hand shape as well as master/slave system, but with the inclusion of a

new travel mechanism and a reduction in wires to create a minimal friction system with near-zero backlash.

The HapticKnob, developed in 2007 by Lambercy et al. (25), uses an adjustable grip that can be used as a stand-alone grip for any number of fingers or to allow everyday items to be clamped into the device for more realistic rehabilitation. It provides force feedback by measuring both the strength of the patient's grip and the motion of the wrist. In 2011 the ReHapticKnob (76) was created to overcome previous limitations with the HapticKnob, such as low output force and only limited DOF measurements. To overcome these issues the ReHapticKnob used 2, 6 DOF force/torque sensors, allowing for greater sensory cover, and a different linkage design to correct for the force limitation.

HandCARE "Cable Actuated Rehabilitation" built by Dovat et al. (62) in 2008 is a system that uses a single motor to provide direct feedback of the force exerted by the patient, who is connected to the device through the fingertips. HandCARE is portable, as it is lightweight and easy to set up. The device can also exert a force on the patient's fingers to allow for a resistance similar to what they would feel in reality.

GENTLE/s, developed by Loureiro et al. (56), is a whole-arm motion system, which is a combination of an exoskeleton and an end-effector. Although its mounting could be considered an exoskeleton due to it encasing the entire hand, the system could also be classed as an end-effector due to its grasping mechanism. In 2009, the Grasp assist unit was developed by Loureiro & Harwin (27) as a module for the Gentle/G, in which the patient uses a full-hand monitoring system that shows their grasping motion and strength on a VR system.

Master Finger-2, developed by Ueki et al. (95) in 2011, is a haptic end-effector that uses the finger and thumb to simulate a pinching motion. It can also use other fingers and provide force feedback for VR use. Master Finger-2 is similar to the SPIDAR-II, Rutgers Master II and the HapticKnob regarding the type of rehabilitation exercise motion that would be performed by the patient.

Several of these devices have been used to conduct small-scale trials on both non-impaired and stroke patients; for example, the HapticKnob (25) was tested using 3 stroke patients and 12 non-impaired volunteers and the GENTLE/s, included in 1 study conducted by Coote et al. (151), was used by 20 stroke patients with various motor deficits.

All of the end-effector devices discussed here are listed in Table SII.

Exoskeleton devices

The Hand-Wrist Assisting Robotic Device (HWARD) was one of the first stroke rehabilitation exoskeletons to be developed. The device, created in 2005 by Takahashi et al. (86), incorporated the wrist and full hand in a 3 DOF arrangement, allowing movement of the wrist in flexion and extension, as well as a grasp motion for the fingers. Due to its exposed palm design, for additional realism patients could also feel the object they were grasping. The HWARD was designed to fulfil 2 goals: to translate the force the patient generated, and to apply a force to help the patient's motion.

The Actuated Finger Exoskeleton (AFX) (103), fabricated in 2010, is a single-finger rehabilitation system created as a reach-to-pinch system with 2 motors: 1 motor provides force for extension and a second motor provides force for flexion of each finger. Full actuation is provided for each joint in the finger.

The first hybrid-exoskeleton, constructed in Gifu University by Kawsaki et al. (89), part of the NEDO project, used a 2-finger mounted exoskeleton that fitted in an end-effector style, allowing support for a pinching motion. Their next generation device (90), a semi-exoskeleton, encased both the hand and the wrist in an end-effector-style unit, allowing for full flexion and extension of the fingers, while aiding in wrist stability. Each individual joint of the finger was controlled by a single motor; with a passive joint to ensure complete alignment. In addition, the wrist arrangement used a single motor to provide motion. This system not only provided the power to move the hand for exercise, but was also capable of recording the motion for use in a VR environment.

The HANDEXOS, designed by Chiri et al. (96), was a hand-mounted exoskeleton designed to open and close the fingers, with an open palm to allow for interaction with everyday objects. This system used an arrangement of wire tendons running through a specifically-designed kinematic set-up. This mechanism ensured that the fingers could not move in the wrong alignment.

Brokaw et al. (115) created the HandSOME systems in 2011, a group of exoskeletons designed to train the patient in 1 particular aspect of hand rehabilitation: the pinch motion. An elastic cord was used to aid extension of the hand. This method, however, could lead to issues if a patient with weak flexion abilities was using the device.

The IHRG exoskeleton, developed in 2013 by Popescu et al. (122), used a plastic moulded glove with a mechanical structure mounted on the back of the hand to control the motion of each finger individually. The IHRG system is still in development.

An initial soft-exoskeleton-based system, the Pneu Glove, was designed in 2009 by Connelly et al. (97). This device used a combination of servos and a pneumatic pump arrangement to inflate a bladder in each finger of the glove, pushing the finger into extension.

This device could be used with or without a VR game and incorporated a headset to allow for a more interactive rehabilitation experience.

Soft robotic devices advanced again in 2013, when the Walsh group at Harvard University developed a soft robot glove that allowed for grasping of an object using inflatable cells mounted on the backs of the fingers (127). This device was capable of grasping an object in a realistic manner and, due to its soft robot construction, reduced the chance of injury.

The PMHand, developed by McConnell et al. (26), uses a 3D-printed low-profile exoskeleton and a wire-tendon-motor linked system to allow both flexion and extension motions of the fingers. Data from all the exercises are collected to show the patient's progress.

A new device, the Hand Exoskeleton System (HES), was created in 2015 by Conti et al. (144). HES is a 3D-printed, inexpensive, portable exoskeleton system designed to run as a cable-driven single-phalanx motion system. This device allows for successful grasping of different objects and is currently being used in tests with patients.

SOPHIA (145), created at Heriot-Watt University in 2016, uses a combination of soft robotic actuators to physically aid rehabilitation by providing extension motion, incorporating a BMI interface to increase neural recovery.

Helping Hand, created by Zhao et al. (146) at Cornell University, is the most recent example of the soft robotic progression of exoskeletons, in which an EMG controller is used as the trigger for motion of the fingers. The Helping Hand also uses a novel fibre optic solution to counteract inherent errors in several flexible sensors.

Further details of the devices mentioned in this section are given in Table SIII.

SUMMARY OF DEVICE PROGRESS

Most currently available commercial systems are of the end-effector type, which are the more mature and stable type of device. However, this review found a gradual decrease in the number of end-effector systems being developed. This might be because these systems cannot aid in full movement of the fingers or wrist, since they have reached maturity in their construction and are primarily only available at fixed locations. In addition, while end-effector systems can simulate the approximate force/resistance that an object would offer, they cannot provide the texture or tactile interface of a real object, as the patient grips the end-effector and not the object in question.

End-effector systems, however, could be regarded as a more robust technology due to their fixed nature.

Thus, they can provide accurate feedback and apply resistance to the patient in the same alignment as they are experiencing in a VR simulation.

Exoskeleton systems are currently being developed at more than twice the rate of end-effector systems. These new exoskeleton systems counteract some of the flaws found in end-effector systems, by aiding the motion of the fingers and wrist. Exoskeleton systems also provide accurate feedback to a VR system, but they remain bulky, intimidating and not very robust.

There have also been attempts to develop hybrid end-effector/exoskeleton-based systems, such as the Gifu NEDO (90). These hybrids overcome the problem of not being able to provide force to move the fingers and wrist. However, this approach has the disadvantage of requiring a large complex system design.

Even with these issues, there has been an increase in the number of exoskeleton devices now reaching small-scale clinical trials, with either individual or complementary modules to be used in combination with other upper limb rehabilitation aids to gain a better view of robotic rehabilitation overall.

Recently, a minimum of 3 forms of orthosis have been developed every year. As shown previously, all have remarkably different approaches to solving the problems that occur in the different stages of stroke rehabilitation.

BRAIN-MACHINE INTERFACES

BMI systems are a novel area of technology with great potential in medical robotics. BMIs have been proposed for motor neurorehabilitation, motor replacement and assistive technologies (152). These systems use physiological signals originating in the brain to activate or deactivate external devices or computers.

BMI systems integrate the recorded brain signals with controllable devices in order to re-establish or expand sensorimotor limitations, as stated by Pfurtscheller & Neuper (153). They may rely on passively generated brain signals (e.g. staring at a blinking light to modulate the visual cortex frequency band) or actively generated brain signals, (e.g. imagining moving the own hand; motor imagery (MI)).

Non-invasive BMIs relate to systems that gather brain signals without surgical procedures. The experimental set-up ranges from bulky, expensive options, such as functional magnetic resonance imaging (fMRI) or magnetoencephalography (MEG), to lightweight and relatively cheap approaches, including electroencephalography (EEG) and, recently, near-infrared spectroscopy (NIRS). Due its availability and ease of use, EEG is widely used in clinical stroke rehabilitation; thus, these systems are the focus of this review.

An EEG can record rhythm activity, such as the mu-rhythm, also called the sensori-motor rhythm (SMR) (154, 155) (4–200 Hz) and its harmonics (8–30 Hz), which show a clear functional specificity, disappearing during planned, actual, or imagined movements and event-related potentials (ERPs), and occurring in response to a specific sensory, cognitive or motor event. Primary examples are the P300-based (156, 157), steady-state visual evoked potential (SSVEP) (158), slow cortical potentials (SCP) (159) and hybrid systems (160, 161).

Despite the fact that all these techniques could be used to control devices, only the application of SMRs (involving motor imagery and neuroplasticity) has been developed as a rehabilitation strategy to date. Thus, this review only addresses this specific type of BMI.

The use of BMIs in stroke rehabilitation is divided into 2 main approaches: a monitoring mechanism, with recorded brain signals serving as feedback for concentration levels of the physiotherapy practice; and a control framework in which an artificial actuator is driven at will.

A significant number of patients present with hand motor impairment post-stroke. In addition, loss of concentration limits the efficacy of conventional physiotherapy. Mental practice of voluntary movement (e.g. MI, in which patients are instructed to imagine moving their own limbs, but without performing a real movement) has been envisaged to alleviate this loss of focus (162). This positive effect may be due to the promotion of neural plasticity and engagement of relevant sensorimotor regions of the brain (163, 164). Nevertheless, further studies are needed to clarify the effects and mechanisms of MI in stroke rehabilitation.

EEG-based BMI is attractive because it combines MI with active orthosis control. More specifically, voluntary movement or motor intention of the arm, hand and wrist activates the primary sensorimotor area in the brain, which is characterized by a desynchronization of the 8–30 Hz brain rhythms over the hemisphere contralateral to the limb in use (165). This neural signature can be detected in the EEG signals and processed to provide control commands for an artificial actuator. EEG-based BMI aids the patient, either by bypassing a physical impairment in the ability to control the hand, or by highlighting engagement with the task. Fig. 5 illustrates a possible configuration for the signal flow between the BMI, patient and repetive hypoxic preconditioning.

Birbaumer et al. (166, 167) suggested BMI technology as a possible solution for treatment of stroke patients who require simultaneous rehabilitation of the impaired limb and brain functions. The authors showed that using a BMI system would strengthen the patient's sensorimotor loop by re-establishing the lost connectivity between ipsilesional (i.e. located in the area of the brain damaged by stroke) cortical activity related to the execution of finger movements, and proprioceptive (haptic) feedback. In turn, feedback would foster neuroplasticity, the ability of the brain to form and reorganize synaptic connections, especially in response to injury, thus facilitating motor recovery (166, 168, 169).

Two issues challenge the advancement of BMI in post-stroke rehabilitation robotics. Firstly, not every patient can consistently modulate their mu (8–13 Hz) and beta (12–30 Hz) rhythms in response to MI tasks, thus preventing the extraction of reliable control signals (170). Secondly, the small signal-to-noise ratio, combined with the poor spatial resolution inherent to EEG systems, results in low bit rates (Fig. 6), which in turn prohibit sophisticated control strategies for the orthosis. Nevertheless, recent studies point out that the use of neuromodulation techniques, such as transcranial direct current stimulation, which applies a small current exciting or inhibiting brain activities, may improve performance in MI (171).

Although there is increasing clinical evidence showing the benefits of BMI-related tools in stroke neurorehabilitation, more and larger clinical studies are needed to fully establish the efficacy of these systems, as demonstrated by Kansaku et al. (172).

DISCUSSION

The increasing use of both robotic-aided techniques and BMI systems is reviewed in this paper, through examples from key clinical trials involving these devices. To clarify how the conclusions of these studies were assessed the most common scores used to measure stroke incidence are described here.

Evaluating the efficacy of robotic devices in hand rehabilitation

Several systems of measurement are currently in use to record the state and progress of the stroke patient's reha-
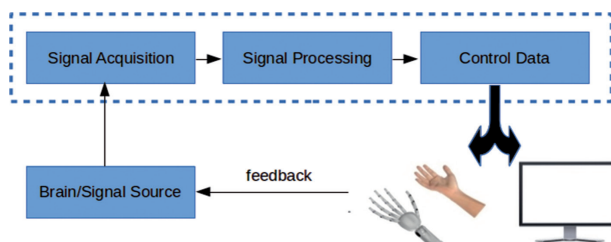
Fig. 5. Brain-machine interface framework. Electrophysiological signals are extracted and processed to produce control signals for external actuators, which in turn provide visual and somatosensory feedback to the user.
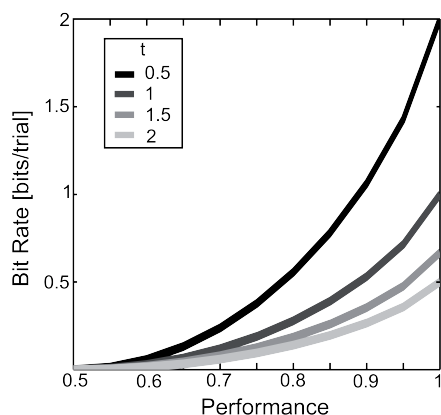
Fig. 6. Bit rate, defined as: bit rate = log 2N – P log 2P + (1–P) log2 [(1–P)/(N–1)]*1/t, where N = number of classes, P = task performance, and t = time (in s) needed to reach peak performance in a trial. In the figure N = 2. Note, that if a patient is to control a more complex device (which requires more bits/trial) whilst maintaining trial duration, it implies on significantly higher performance in the task (accuracy).

bilitation, according to the International Classification of Functioning Disability and Health (ICF) domains, such as the Upper Extremity Fugl-Meyer Assessment (FMA-UE) proposed by Fugl-Meyer et al. (173), the Motor Activity Log-14 (MAL) defined by Uswatte et al. (174), the Manual Ability Measure-36 created by Chen & Bode (175), the Jebsen Hand Function Test (JHFT) introduced by Spaulding et al. (176), the Grip Strength by Schmidt & Toews (177), the Action Research Arm Test (ARAT) created by Lyle (178), the Ashworth Scale by Ashworth (179), the Modified Ashworth Scale defined by Bohannon & Smith (180), and the Motricity Index (MI) by Demeurisse et al. (181) A full in-depth review of the different ways to measure the outcome of stroke rehabilitation, both for the hand and the rest of the body, was carried out by Salter et al. (182).

Multiple clinical trials using robotic-aided rehabilitation have been carried out; among them, the most extensive trial was conducted in 2010 by Lo et al. (183) on upper limb rehabilitation. This experiment was performed using the In-motion robot (MIT-Manus with horizontal, vertical, wrist and hand modules) and involved 127 patients. The study provided evidence for the benefits of robotic-aided rehabilitation after a stroke. In summary, the researchers found that using the device over 36 1-h sessions of robotic therapy was equally as beneficial as 36 1-h sessions of high-intensity traditional therapy regarding improvement measured over both 12- and 36-week periods.

The commercially-available Amadeo system was used in a hand-specific trial (184), involving 12 patients who performed exercises for 18 h in total. This trial showed comparable improvements in all of the measurements used, compared with the standard physiotherapy treatment a patient would undertake. It was also noted that this improvement lasted beyond 6 months after stroke.

The Haptic Master (185), a full arm exoskeleton, was used by Timmermans et al. (186) in a single-blind randomized controlled trial involving 22 patients over an 8-week period, with the exercises being performed 4 times per week, twice a day for 30 min. Trial results showed a significant improvement in the ARAT using the robot system and a noticeable, but similar improvement on the MAL for both robot and standard rehabilitation. The researchers noted that the effects of the robotic therapy were sustained after the trial was completed, while the benefits from conventional therapy were not. The Haptic Master is not directly a hand rehabilitation system, but, due to its common usage in upper limb rehabilitation and that it is grasped by the hand, it has been included in the clinical tests.

The PneuGlove was used in a 6-week trial with 7 stroke patients; each performing the exercise in 18 training sessions over the trial period (97). A significant improvement was shown in the patients' FMA scores, which was maintained over a 1-month period after the sessions had ended.

There have been multiple other studies of robotic-aided rehabilitation that show either comparable or, in some cases, greater progress in patients' recovery as measured against a traditional approach. The sample sizes of these trials are not large enough to draw statistically significant conclusions, but the majority of them show a common pattern, that the benefits of robot therapy outlast the standard treatment. Due to the preliminary nature of these studies, not all of the clinical trials used the same score system or the full list of measurements described earlier.

BMI systems were also included within some clinical studies as a rehabilitation technique for stroke recovery. Several examples can be highlighted from this perspective.

Prasad et al. (187), submitted 5 post-stroke participants to a 6-week BMI programme, in which neurofeedback was given proportionally to the MI-measured activity. They concluded that the more subjects could modulate their mu and beta rhythm synchronization, the greater the performance in a goal-directed task. Prasad's work emphasizes the importance of incorporating BMI strategies into post-stroke rehabilitation protocols despite the heterogeneous MI capabilities of the subjects.

Initial studies of stroke rehabilitation using BMI revealed that patients learnt to control the rehabilitation device accurately over a few weeks of training, but such a short trial period meant that they did not improve significantly regarding motor function (188). However, further studies combining BMI training with goal-directed behavioural physiotherapy over a longer period showed significant improvements in motor and cognitive capacities of severely affected chronic stroke

survivors (189). Based on these findings, Ramos-Murguialday et al. (190) conducted a larger controlled double-blinded randomized clinical trial with 32 chronic stroke survivors who had no residual finger movement. This study showed that 20 sessions of ipsilesional BMI training, combined with goal-directed behavioural therapy, led to motor improvements in the experimental group superior to those in the control group, who were trained under random BMI feedback, receiving the same goal-directed behavioural therapy. Using the FMA score, the experiments showed that the group who could control a BMI-based orthosis improved their motor control more than the ones submitted to random orthosis movements. Furthermore, subjects presented cortical activity reorganization linked to BMI training. These results further corroborate that, robotics and BMI combined with physiotherapy is a suitable solution to enhance motor recovery for severely affected stroke patients.

A recent clinical study involving 26 chronic stroke survivors with less severe paralysis compared conventional robot-assisted therapy with BMI-controlled robotic training and found similar results (165). Other studies with smaller samples further corroborate this trend (191, 192).

Finally, Pichiorri et al. (193) conducted a related study with 28 subacute stroke patients. They found a significantly higher probability of achieving a clinically relevant increase in the FMA score in subjects submitted to BMI training than in those involved solely in MI training.

Taken together, these trials provide evidence of both the efficacy of robotic rehabilitation independent of BMI and the benefits of incorporating BMI techniques in stroke rehabilitation. With further development of this theory in mind, in addition to the number of new studies with a greater number of patients, this reinforces the evidence that adapting the current BMI strategies to work with commercial orthoses and other robotic devices has a strong potential for progression of this type of therapy.

Inherent ethical issues

The trend towards developing systems that are capable of gathering a great deal of patient data raises many questions. A critical issue is the potential use of this data by research groups, companies and physiotherapists, and the level of anonymity that would need to be applied to the data for each group to be able to use it ethically (194, 195).

Safety considerations for patients using a device that evolves unsupervised would be far-ranging if the device manipulated the patient's motion in an incorrect manner, inhibited the rehabilitation process, or injured the patient. These ethical issues are discussed in more detail by Feil-Seifer & Matari (196), who explore these and other matters, their ramifications and potential solutions.

Factors restricting widespread uptake of robotic devices for hand rehabilitation

The current review shows that the increase in regular use of orthotic devices is related not only to the growth in their functionality, but also to their portability, location of use (clinical or domestic), simplicity of use, level of safety data or framework to evaluate the system, aesthetics factors, and overall system cost.

Lack of consistent framework of metrics

Unlike the framework of accepted metrics for bipedal locomotion proposed by Mombaur et al. (197) that has been established between clinicians and research groups regarding lower limb rehabilitation, there is currently an absence of a similar agreement for the upper limb counterpart. A framework for classifying the training modalities in robot-aided therapy for the upper limb has been suggested by Basteris et al. (31).

Sivan et al. (198) evaluated multiple studies and trials for the different metrics used in each, judging which were used more often and include suitable measurable properties for use in robot-assisted exercise criteria finding that FMA and ARAT are compatible. All of the scoring methods mentioned, e.g. MAL, measure the progress and recovery of the patient's movement. However, they do not assess the device itself. For this task there are 2 different factors that quantify the reliability of an instrument in medicine and sport: the intra-class correlation coefficient and the standard error of measurement. These techniques have been examined further by Maggioni et al. (199).

Even with the application of these techniques, new methods for measuring the adequacy of robotic rehabilitation devices are required in order to make a complete comparison.

In summary, the fragmented nature of the results from the multiple trials using different metrics leads to complications in their comparisons of effectiveness. This fact can discourage medical bodies from purchasing robotic rehabilitation equipment, as it would be an unproven investment.

Control system and human-robot interaction

Control of these devices is an important issue. While the use of integrated exercise apps or a function for remote control by a physiotherapist can be made user-friendly, the end goal would arguably be to remove the intermediate interface layer entirely. In this scenario,

the ultimate aim for non-intrusive assistive devices would be to be able to respond to the user's thoughts of, for example, "open hand" by doing just that.

Therefore, the development and provision of rehabilitative robotics integrating BMI, particularly those which can function even with existing damage to the patient's peripheral nervous system, represent a promising avenue of research. If devices can be controlled intuitively and without requiring extensive training to gain reliable control (20), BMI systems promise to enhance assistive technology for stroke patients, and even for wider application in other forms of neurological damage (152).

Thus, the development and provision of assistive devices that are independent of the integrity of the peripheral nervous system represent a promising and appealing prospect.

Cost of purchase and service

Two of the biggest problems regarding robotic rehabilitation devices are their predominantly high price and a lack of large-scale clinical evidence. This leads to healthcare providers being unwilling or unable to purchase a still largely-untested device, as it would be safer to use their budgets for conventional treatments with a physiotherapist and medication. Due to this lack of uptake, there is a shortage of large-scale evaluations of these robotic devices, which contributes to the cyclical problem of staging clinical trials.

The increasing use of 3D printing to rapidly prototype new and individually customizable devices is a possible solution to this problem. Soft robotic technologies eliminate complex mechanical linkages and, in combination with 3D printing, have the potential to reduce the cost of servicing and replacement (200).

The increase in cost-effective and viable BMIs that are commercially available has the potential to reduce the cost of robotic rehabilitation.

Portability and aesthetics

The aesthetic appearance of these devices is a further issue. If a machine appears intimidating, it may affect the patient's progress or desire to use the device. One way to mitigate this problem is to include patients and clinicians in the design process (201, 202). Through an iterative process of consultations, researchers could develop devices that proved practical and, at the same time, visually reassuring to patients.

The traditional hard robotic approach, in which movements are driven entirely by motors and the direction of motion is controlled by rigid mechanical frames, can appear intimidating and cause concern among patients. Instead, the use of more recent soft

robotics technologies can be embraced to create a system that provides the correct motion, while using soft silicone-based materials to allow for a lighter and safer device. Several systems with these characteristics exist at present, such as the Harvard Soft Robotic Hand (127) and A Helping Hand (146).

The portability of robotic rehabilitation systems is a 2-fold issue; it may be related to the exoskeleton or to the end-effector itself, which could either be used only in a laboratory due to requiring supervision or due to it being of a fixed nature. This is correlated with the fact that the majority of BMI devices are wired and only tested in a laboratory environment, where portability is not an issue. Systems that are wireless and more portable are currently emerging onto the market.

The SOPHIA system (145) proposes a way to increase the portability of a system by using the wireless EMOTIV EPOC+ (203) and a soft robotic-based system, which is envisioned to be used unsupervised and in a domestic setting. This illustrates the potential for future work in the synergy of BMI and soft robotics.

CONCLUSION

Despite the wide range in both size and focus of the trials that have been conducted in robot-aided rehabilitation, there is an increasing body of evidence that such rehabilitation can be highly beneficial to stroke patients. From the trends seen in current research, it appears that a combination of robotic and traditional treatment would produce the best results.

At present, a constant failing in the rehabilitation cycle is that the assigned exercises have to be performed unsupervised at the patient's home, with little monitoring or correction. With the robotic systems discussed in this paper, the potential for unsupervised rehabilitation is now developing. More devices are being designed specifically for independent use at home, with the aim of helping patients perform their exercises more often and in the correct manner. As has been shown in the overall area of stroke rehabilitation research, the increased intensity and frequency of rehabilitation exercises should result in a better prognosis for regaining use of the limb in question.

There is also the opportunity to incorporate a greater number of sensors into future systems, allowing for a more in-depth analysis of patients' progress. The new data could be used by more intelligent devices to aid patients' recovery by adjusting the internal parameters of the system, or by incorporating the data into interactive games. The data gathered would also allow physiotherapists to examine and compare progress between patients, allowing for a greater knowledge of the patterns and challenges each patient faces through their recovery.

Current advances in this field provide great potential for wider development and distribution of these types of devices.

ACKNOWLEDGEMENTS

REFERENCES
(for complete reference list see electronic version)

3. World Health Organization. WHO World report on disability. 2011.
4. Ward NS, Cohen LG. Mechanisms underlying recovery of motor function after stroke. Arch Neurol 2004; 61: 1844–1848.
6. Wolfe CD. The impact of stroke. Br Med Bull 2000; 56: 275–286.
7. Schaechter JD. Motor rehabilitation and brain plasticity after hemiparetic stroke. Prog Neurobiol 2004; 73: 61–72.
8. Prange GB, Jannink MJA, Groothuis-Oudshoorn CGM, Hermens HJ, IJzerman MJ. Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke. J Rehabil Res Dev 2006; 43: 171.
11. Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, et al. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke 2005; 36: e100–e143.
12. Jørgensen HS, Nakayama H, Raaschou HO, Vive-Larsen J, Støier M, Olsen TS. Outcome and time course of recovery in stroke. Part II: time course of recovery. The Copenhagen Stroke Study. Arch Phys Med Rehabil 1995; 76: 406–412.
15. Bruno-Petrina A. Motor recovery in stroke: recovery considerations, theories of recovery, mechanisms of recovery. 2014. Available from: http: //emedicine.medscape.com/article/324386-overview.
19. Kwakkel G, Kollen BJ, van der Grond J, Prevo AJH. Probability of regaining dexterity in the flaccid upper limb: impact of severity of paresis and time since onset in acute stroke. Stroke 2003; 34: 2181–6218.
20. Ramos-Murguialday A, Schürholz M, Caggiano V, Wildgruber M, Caria A, Hammer EM, et al. Proprioceptive feedback and brain computer interface (BCI) based neuroprostheses. Hendricks M, editor. PLoS One 2012; 7: e47048.
21. Kalra L, Dale P, Crome P. Improving stroke rehabilitation. A controlled study. Stroke 1993; 24: 1462–1467.
24. Woodson A. Occupational therapy for physical dysfunction. CA T, editor. Baltimore: Lippincott, Wilkins & Williams &; 1995. p. 607–704.
26. McConnell A, Kong X, Vargas PA. A novel robotic assistive device for stroke-rehabilitation. In: The 23rd IEEE International Symposium on Robot and Human Interactive Communication. IEEE; 2014, p. 917–923.
27. Loureiro RCV V, Harwin WS. Reach & grasp therapy: design and control of a 9-DOF robotic neuro-rehabilitation system. In: IEEE 10th International Conference on Rehabilitation Robotics. IEEE; 2007, p. 757–763.
29. Kawasaki H, Takai J, Tanaka Y, Mrad C, Mouri T. Control of multi-fingered haptic interface opposite to human hand. In: Proceedings 2003 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS 2003) (Cat No03CH37453). IEEE; 2003, p. 2707–2712.
31. Basteris A, Nijenhuis SM, Stienen AHA, Buurke JH, Prange GB, Amirabdollahian F. Training modalities in robot-mediated upper limb rehabilitation in stroke: a framework for classification based on a systematic review. J Neuroeng Rehabil 2014; 11: 111.
32. Atkins DJ, Heard DCY, Donovan WH. Epidemiologic overview of individuals with upper-limb loss and their reported research priorities. JPO J Prosthetics Orthot 1996; 8: 2–11.
36. Power-Web International. [cited 2014 Jun 16]. Available from: http: //www.pwrwebintl.com/.
37. Kinetec Maestra Hand & Wrist CPM. [cited 2014 Jun 16]. Available from: http: //theratechequip.com/products/kinetec-maestra-hand-wrist-cpm/.
38. Tyromotion. [cited 2014 Jun 16]. Available from: http: //tyromotion.com/en/.
51. Rehab-Robotic - Rehabilitation. [cited 2015 Jul 15]. Available from: http: //www.rehab-robotics.com/intro.html.
52. Walairacht S, Yamada K, Hasegawa S, Koike Y, Sato M. 4 + 4 Fingers manipulating virtual objects in mixed-reality environment. Presence Teleoperators Virtual Environ 2002; 11: 134–143.
60. Masia L, Krebs HI, Cappa P, Hogan N. Whole-Arm rehabilitation following stroke: hand module. In: The First IEEE/RAS-EMBS International Conference on Biomedical Robotics and Biomechatronics, 2006 BioRob 2006. IEEE; 2006, p. 1085–1089.
68. Mohamaddan S, Komeda T. Wire-driven mechanism for finger rehabilitation device. In: IEEE International Conference on Mechatronics and Automation. IEEE; 2010, p. 1015–1018.
73. Yoshikawa T, Endo T, Maeno T, Kawasaki H. Multi-fingered bimanual haptic interface with three-dimensional force presentation. IFAC Proc Vol 2009; 42: 651–656.
80. Ab Rahim AH, Ab Patar MNAB, Amin ATM, Mahmud J. The development of finger rehabilitation device for stroke patients. Appl Mech Mater 2013; 393.
84. Lee N, Lee YH, Chung J, Heo H, Yang H, Lee KS, et al. Shape-changing robot for stroke rehabilitation. In: Conference on designing interactive systems - DIS '14. New York, New York, USA: ACM Press; 2014, p. 325–334.
89. Kawasaki H, Kimura H, Ito S, Nishimoto Y, Hayashi H, Sakaeda. Hand rehabilitation support system based on self-motion control, with a clinical case report. In: World Automation Congress. IEEE; 2006, p. 1–6.
90. Kawasaki H, Ito S, Ishigure Y, Nishimoto Y, Aoki T, Mouri T, et al. Development of a hand motion assist robot for rehabilitation therapy by patient self-motion control. In: IEEE 10th international conference on rehabilitation robotics. IEEE; 2007, p. 234–240.
98. Ochoa JM, Yicheng Jia, Narasimhan D, Kamper DG. Development of a portable actuated orthotic glove to facilitate gross extension of the digits for therapeutic training after stroke. In: Annual international conference of the IEEE Engineering in Medicine and Biology Society. IEEE; 2009, p. 6918–6921.
99. Kim Y-m, Jung S-y MI. Design of a wearable upper-limb rehabilitation robot using parallel mechanism. In: ICROS-SICE international joint conference. 2009, p. 785–789.
102. Worsnopp TT, Peshkin MA, Colgate JE, Kamper DG. An actuated finger exoskeleton for hand rehabilitation following stroke. In: IEEE 10th international conference on rehabilitation robotics. IEEE; 2007, p. 896–901.
111. Bi Q, Yang CJ. Design of a hand exoskeleton rehabilitation device. Adv Mater Res 2011; 328–330: 1778–1783.
124. Lambercy O, Schroder D, Zwicker S, Gassert R. Design of a thumb exoskeleton for hand rehabilitation. In: 7th international convention on rehabilitation engineering and assistive technology. 2013, p. 41: 1–41: 4.
127. Polygerinos P, Lyne S, Zheng Wang, Nicolini LF, Mosadegh B, Whitesides GM, et al. Towards a soft pneumatic glove for hand rehabilitation. In: IEEE/RSJ International Conference on Intelligent Robots and Systems. IEEE; 2013, p. 1512–1517.

129. Song K-T, Chai Y-Y. Compliance control of wearable robotic fingers for rehabilitation applications. In: CACS International Automatic Control Conference (CACS). IEEE; 2013, p. 306–311.

134. Zhang F, Hua L, Fu Y, Chen H, Wang S. Design and development of a hand exoskeleton for rehabilitation of hand injuries. Mech Mach Theory 2014; 73: 103–116.

144. Conti R, Allotta B, Meli E, Ridolfi A. Development, design and validation of an assistive device for hand disabilities based on an innovative mechanism. Robotica 2015; p. 1–15.

145. Vargas PA, Brasil FL, McConnell AC, Vallejo M, Corne DW, Stokes AA, et al. Combining soft robotics and brain-machine interfaces for stroke rehabilitation. In: Converging Clinical and Engineering Research on Neurorehabilitation II. 2017, p. 1257–1262.

146. Zhao H, Jalving J, Huang R, Knepper R, Ruina A, Shepherd R. A helping hand: soft orthosis with integrated optical strain sensors and EMG control. IEEE Robot Autom Mag 2016; 23: 55–64.

148. Sato M. Development of string-based force display: SPIDAR. In: 8th international conference on virtual systems and multimedia. 2002.

152. de Almeida Ribeiro PR, Lima Brasil F, Witkowski M, Shiman F, Cipriani C, Vitiello N, et al. Controlling assistive machines in paralysis using brain waves and other biosignals. Adv Human-Computer Interact 2013; 2013: 1–9.

153. Pfurtscheller G, Neuper C. Motor imagery activates primary sensorimotor area in humans. Neurosci Lett 1997; 239: 65–68.

154. He B, Baxter B, Edelman BJ, Cline CC, Ye WW. Noninvasive brain-computer interfaces based on sensorimotor rhythms. Proc IEEE 2015; p. 1–19.

157. Postelnicu C-C, Talaba D. P300-based brain-neuronal computer interaction for spelling applications. IEEE Trans Biomed Eng 2013; 60: 534–543.

158. Kimura Y, Tanaka T, Higashi H, Morikawa N. SSVEP-Based brain-computer interfaces using fsk-modulated visual stimuli. IEEE Trans Biomed Eng 2013; 60: 2831–2838.

160. Cao L, Li J, Ji H, Jiang C. A hybrid brain computer interface system based on the neurophysiological protocol and brain-actuated switch for wheelchair control. J Neurosci Methods 2014; 229: 33–43.

162. Malouin F, Richards CL. Mental practice for relearning locomotor skills. Phys Ther 2010; 90: 240–251.

163. K Shiraliyeva R. Towards Effective neurorehabilitation for stroke patients. Int J Phys Med Rehabil 2013; 2.

165. Ang KK, Chua KSG, Phua KS, Wang C, Chin ZY, Kuah CWK, et al. A randomized controlled trial of EEG-Based motor imagery brain-computer interface robotic rehabilitation for stroke. Clin EEG Neurosci 2015; 46: 310–320.

166. Birbaumer N, Cohen LG. Brain-computer interfaces: communication and restoration of movement in paralysis. J Physiol 2007; 579: 621–636.

168. Dimyan MA, Cohen LG. Neuroplasticity in the context of motor rehabilitation after stroke. Nat Rev Neurol 2011; 7: 76–85.

171. Kansaku K, Cohen LG, Birbaumer N. Clinical systems neuroscience. Kansaku K, Cohen LG, Birbaumer N, editors. Tokyo: Springer Japan; 2015.

172. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scand J Rehabil Med 1975; 7: 13–31.

173. Uswatte G, Taub E, Morris D, Vignolo M, McCulloch K. Reliability and validity of the upper-extremity motor activity log-14 for measuring real-world arm use. Stroke 2005; 36: 2493–2496.

174. Chen CC, Bode RK. Psychometric Validation of the Manual Ability Measure-36 (MAM-36) in patients with neurologic and musculoskeletal disorders. Arch Phys Med Rehabil 2010; 91: 414–420.

176. Schmidt RT, Toews J V. Grip strength as measured by the Jamar dynamometer. Arch Phys Med Rehabil 1970; 51:

321–57.

177. Lyle RC. A performance test for assessment of upper limb function in physical rehabilitation treatment and research. Int J Rehabil Res 1981; 4.

178. Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner 1964; 192: 540–542.

179. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 1987; 67: 206–207.

180. Demeurisse G, Demol O, Robaye E. Motor evaluation in vascular hemiplegia. Eur Neurol 1980; 19: 382–389.

181. Salter K, Campbell N, Richardson M, Methta S, Jutai J, Zettler L, et al. Outcome measures in stroke rehabilitation. In: Evidence-based review of stroke rehabilitation. 2013, p. 1–144.

182. Lo AC, Guarino PD, Richards LG, Haselkorn JK, Wittenberg GF, Federman DG, et al. Robot-assisted therapy for long-term upper-limb impairment after stroke. N Engl J Med 2010; 362: 1772–1773.

183. Stein J, Bishop L, Gillen G, Helbok R. A pilot study of robotic-assisted exercise for hand weakness after stroke. In: IEEE International Conference on Rehabilitation Robotics. IEEE; 2011, p. 1–4.

184. van der Linde RQ, Lammertse P. HapticMaster – a generic force controlled robot for human interaction. Ind Robot An Int J 2003; 30: 515–524.

185. Timmermans AA, Lemmens RJ, Monfrance M, Geers RP, Bakx W, Smeets RJ, et al. Effects of task-oriented robot training on arm function, activity, and quality of life in chronic stroke patients: a randomized controlled trial. J Neuroeng Rehabil 2014; 11: 45.

187. Buch E, Weber C, Cohen LG, Braun C, Dimyan MA, Ard T, et al. Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke. Stroke 2008; 39: 910–917.

189. Ramos-Murguialday A, Broetz D, Rea M, Läer L, Yilmaz Ö, Brasil FL, et al. Brain-machine interface in chronic stroke rehabilitation: a controlled study. Ann Neurol 2013; 74: 100–108.

192. Pichiorri F, Morone G, Petti M, Toppi J, Pisotta I, Molinari M, et al. Brain-computer interface boosts motor imagery practice during stroke recovery. Ann Neurol 2015; 77: 851–865.

193. The Scottish Government. Data management board: a data vision for Scotland. 2014.

194. The Scottish Government. Charter for safe havens in Scotland: handling unconsented data from National Health Service patient records to support research and statistics. 2015.

195. Feil-Seifer BD, Matari MJ. Ethical issues related to technology. Robot Autom Mag 2011; 18: 24–31.

196. Mombaur K, Tsagarakis N, Moreno JC, Pons JL. Benchmarking Bipedal Locomotion. IEEE Robot Autom Mag. 2015; p. 103–115.

197. Sivan M, O'Connor R, Makower S, Levesley M, Bhakta B. Systematic review of outcome measures used in the evaluation of robot-assisted upper limb exercise in stroke. J Rehabil Med 2011; 43: 181–189.

199. Shepherd RF, Ilievski F, Choi W, Morin S, Stokes A, Mazzeo AD, et al. Multigait soft robot. Natl Acad Sci 2011; 108: 20400–20403.

200. Holt R, Makower S, Jackson A, Culmer P, Levesley M, Richardson R, et al. User involvement in developing Rehabilitation Robotic devices: an essential requirement. In: IEEE 10th International Conference on Rehabilitation Robotics. IEEE; 2007, p. 196–204.

201. Blabe CH, Gilja V, Chestek CA, Shenoy K V, Anderson KD, Henderson JM. Assessment of brain–machine interfaces from the perspective of people with paralysis. J Neural Eng 2015; 12: 43002.

202. EMOTIV Epoc – 14 Channel Wireless EEG Headset. [cited 2017 Jan 5]. Available from: https: //www.emotiv.com/ epoc/.