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Review Article

Robot-assisted therapy for upper limb paresis after stroke: Use of robotic algorithms in advanced practice

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Abstract.
BACKGROUND: Rehabilitation of stroke-related upper limb paresis is a major public health issue.
OBJECTIVE: Robotic systems have been developed to facilitate neurorehabilitation by providing key elements required to stimulate brain plasticity and motor recovery, namely repetitive, intensive, adaptative training with feedback. Although the positive effect of robot-assisted therapy on motor impairments has been well demonstrated, the effect on functional capacity is less certain.
METHOD: This narrative review outlines the principles of robot-assisted therapy for the rehabilitation of post-stroke upper limb paresis.
RESULTS: A paradigm is proposed to promote not only recovery of impairment but also function.
CONCLUSION: Further studies that would integrate some principles of the paradigm described in this paper are needed.

Keywords: Stroke, hemiparesis, rehabilitation, robot

1. Introduction

Upper limb paresis is the most common physical consequence of stroke (Sathian et al., 2011) and more than half of patients do not recover full upper limb function (Kong & Lee, 2013; K.B. Lee et al., 2015). The majority of recovery occurs during the first weeks after stroke (Wade et al., 1985) and the prognosis is poor if moderate to severe paresis persists three months post-stroke. Upper limb paresis considerably reduces activity and participation (Geyh et al., 2004) as well as the quality of life (Ramos-Lima et al., 2018) of those affected. The number of people affected by stroke is increasing and the social and economic impact is high, making recovery of upper limb function a major public health issue.

Rehabilitation aims at reducing neurological impairments in order to improve stroke survivors' participation in activities and quality of life. That can be achieved through the stimulation of neuronal reorganization to enhance recovery beyond the natural course of spontaneous recovery. The main factors that affect plasticity are age at the time of stroke (younger subjects progress more quickly after stroke) and the training methods used (Kleim & Jones, 2008b). These factors have been well described by Kleim and Jones (2008) – who emphasized that training must be spe-

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cific, repetitive and intensive and that patients should use their residual capacity with the aim to both improve it and to integrate it in daily living activities (Kleim & Jones, 2008b).

The benefits of specialised rehabilitation after upper limb paresis are widely recognised (Langhorne et al., 2011), even though no specific approach/treatment has yet been found to be more effective than another (Veerbeek et al., 2014).

However, robot-assisted therapy appears to promote upper limb recovery by providing the elements necessary to stimulate neuroplasticity and reduce motor impairment (Kwakkel et al., 2008b; Wu et al., 2021).

The aim of this article was not to provide a further systematic review on upper limb robotic rehabilitation after stroke but rather to discuss the principles of robot-mediated therapy as a pragmatic, evidence-based approach based on 10 years of experience with this therapy in subacute stroke patients.

2. The principles of robot-assisted therapy

2.1. *High dose of training through a hyper repetitive therapy*

In medicine, patients are administered specific doses of treatments according to certain criteria. In rehabilitation, the concept of dose remains poorly defined. In the literature, this term usually refers to the quantity of practice, and is expressed as the quantity of intended training time or total therapy time (Birkenmeier et al., 2010a; Byl et al., 2008; Lohse et al., 2014). More rarely, it is expressed as the time spent performing active movements (Host et al., 2014; Kaur et al., 2012), or the number of repetitions performed (Dorsch & Elkins, 2020; Feys et al., 1998; Lang et al., 2016). The latter two definitions are more precise since active movements are rarely performed throughout the whole therapy session.

Although it is widely accepted that a large number of active movement repetitions are required to induce neuronal changes, the specific dose of active movement has not been defined. Studies in animal models of stroke have shown that 400 to 600 repetitions of a challenging functional task must be performed per day to induce neuroplastic changes (Birkenmeier et al., 2010a; Kleim et al., 1998). A study in humans with stroke showed that over 100 daily repetitions of a finger exercise induced significant cortical reorganisation as well as functional improvement (Carey et al., 2007). However, the implementation of such quantities of practice within conventional rehabilitation sessions is a major challenge. Studies have shown that during conventional rehabilitation sessions, patients perform between 23 (Lang et al., 2009) and 32 (Kimberley et al., 2010) movement repetitions. A more recent study found a higher number (mean 86 movement repetitions per session) but with a large inter-individual variation (Vratsistas-Curto et al., 2021). These doses are far below those required for the cortical changes that lead to motor recovery (Cramer et al., 2019; Gassert & Dietz, 2018). A study of the dose-response relationship between the number of repetitions and recovery of impairment in patients with chronic stroke found no relationship when 100, 200 and 300 repetitions (per hourly session over a period of 8 weeks) were compared (Lang et al., 2016). The modest change in motor function observed in this study, independent of treatment dose, is likely due to the fact that more than 300 movements per session are necessary to induce significant cortical and clinical changes. However, the daily practice of hundreds of movements within conventional rehabilitation sessions is hardly feasible (Birkenmeier et al., 2010b; Lang et al., 2016), which explains that the number of movements performed during robot-assisted therapy sessions is far higher than the number performed during conventional therapy (Duret & Gracies, 2014).

Unlike conventional therapy, robotic devices can provide hyper-repetitive therapy at a reasonable cost (Blank et al., 2014) and without excessive fatigue reported in the literature. Furthermore, they can objectively quantify the number of movement repetitions performed, thus allowing measurement of the dose provided. Patients can perform between 280 and 1300 movements per session of robot-assisted therapy (Duret et al., 2018, 2019; Duret, Courtial, et al., 2015; Duret, Hutin, et al., 2015; Duret & Hutin, 2013; Flynn et al., 2020; Hsieh et al., 2011, 2018; Pila et al., 2017a, 2017b; Rodgers et al., 2017), on average over 600 movements per session (Duret et al., 2019; Duret, Hutin, et al., 2015; Duret & Hutin, 2013; Rodgers et al., 2019).

A pilot study compared 2 intensity-based groups (high vs low respectively 750–1000 and 375–500 movements) that performed wrist and forearm movements with a robotic device, to a control group and found a relationship between the number of movements on one hand and motor abilities and functional performance on the other hand.(Hsieh et al., 2011). The results showed that high intensity practice with a robot improved outcomes more than lower intensity practice.

2.2. *Difficulty and intensity: Non-dissociable factors*

It is now well documented and established that the number of movements performed during robot-assisted therapy sessions is far higher than the number performed during conventional therapy (Duret & Gracies, 2014). Moreover, the performance of a large number of passive movements does not lead to motor recovery (Lynch et al., 2005). Consequently, active participation and the challenging nature of the exercises are critical contributors to the effectiveness of highly intensive treatment (Dromerick et al., 2006).

A therapy is often considered intensive if it involves many repetitions. However, Page et al. (2012) defined intensity as the "amount of physical or mental work put forth by the client during a particular movement or series of movements, exercise, or activity during a defined period of time" (Page et al., 2012). The concept of intensity therefore includes several elements: repetition, effort and challenge. This explains why performing a large number of passive movements is not sufficient for motor recovery (Lynch et al., 2005). Thus, an exercise can only be considered intense if it involves effort (Connell et al., 2018), and to ensure effort, the exercise must also be challenging. However, adapting exercises to ensure they are challenging whilst also being achievable is complex in stroke rehabilitation. Furthermore, according to Kukla's theory of performance, a person's engagement in an exercise also depends on their perception of the difficulty (Kukla, 1972). The intensity of therapy is therefore not simply related to the number of repeated movements; it refers more precisely to the level of effort produced by the person executing the task (Connell et al., 2018).

In conventional therapy, therapists usually try to match the difficulty of an exercise to the patient's ability (Krebs & Hogan, 2006). To make an exercise easier, they may reduce the effects of gravity (by using suspension, forearm support, etc.) or provide manual guidance. However, "providing too much assistance may have negative consequences for (motor) learning" (Marchal-Crespo & Reinkensmeyer, 2009). It is important that the level of assistance is just sufficient to enable the patient to achieve the task, thus encouraging engagement and avoiding discouragement (Blank et al., 2014; Shirzad & Van der Loos, 2016). If the task is too difficult for the patient to achieve, this can have a negative effect on both performance and motor learning (Gendolla, 1999; Maier, Ballester, et al., 2019) and frustrate the patient; on the other hand, if it is not sufficiently challenging, this can lead to boredom (Pan et al., 2019). Moderate challenge is beneficial to learning, while a difficulty that is too low or too high can have a negative effect (Hodges et al., 2014). However, in conventional therapy, it is difficult to precisely measure the level of assistance required and provided.

Some robotic systems contain integrated adaptive algorithms specifically to ensure that the appropriate level of movement assistance is provided (Krebs et al., 2003). These assist-as-needed algorithms detect movement intention and provide only the amount of assistance required to perform the task (Emken et al., 2005; Krebs & Hogan, 2006). The precise control of the level of support and assistance, which is adjusted according to the patient's motor output, ensures that the patient remains active (Wickens et al., 2013). This is important since many studies have shown a strong relationship between providing exercises of appropriate difficulty and active participation by the patient (Grosmaire & Duret, 2017; Krishnan et al., 2013; Shirzad & Van der Loos, 2016). Furthermore, training at an appropriate level encourages engagement and motivation (Levin, 2020). Guadagnoli et al. suggested that learning is optimal when the challenge point has been reached (Guadagnoli & Lee, 2004). It has also been shown that the learning of simple tasks can be improved by increasing their difficulty (van Vliet & Wulf, 2006). Engagement and effort are automatically measured by some robots (Blank et al., 2014), which is useful for the therapist to determine when and how exercises need to be progressed.

Nonetheless, the use of assistance algorithms to optimise patient participation remains questioned, particularly for those with milder impairments. Some patients rely on the assistance and become passive, a phenomenon known as "slacking" (Washabaugh et al., 2018). However, one of our studies highlighted that assistance did not systematically lead to slacking, even when patients performed a large number of movements (Duret et al., 2018).

Assist-as-needed robot training (Emken et al., 2005; Krebs & Hogan, 2006) seems particularly useful for patients with moderate to severe paresis who have difficulty generating movement and for whom it is challenging to provide exercises at an appropriate level. In one of our studies on seventeen subacute inpatients (age 53 ± 18; 49 ± 26 days post-stroke) who had received 16 robot-assisted sessions, we have shown that the increase in the Motricity index between the first and the last session was negatively correlated with the baseline Motricity index ($r = -0.5$, $p = 0.0053$). Furthermore, the increase in the number of repeated movements was also negatively correlated with the number of movements performed at the second session ($r = -0.47$, $p = 0.0083$). In addition, we found a 10% decrease in the assistance provided by the robot (Duret, Hutin, et al., 2015). Studies conducted by our group on human-robot interactions have confirmed that robotic assistance promotes active participation and corresponds to the therapy needs of patients with moderate to severe motor impairment (Duret, Courtial, et al., 2015; Grosmaire & Duret, 2017).

2.3. *The effect of contextual interference*

Active participation can be encouraged and slacking prevented by limiting the possibility to anticipate the next movement. Some robotic systems present targets randomly (although the randomisation is organised so that each target appears the same number of times). It may be beneficial in the initial stage of stroke to practice repeated movements in a defined, blocked order; however, in later stages random practice promotes learning to a greater extent (Cauraugh & Kim, 2003). Furthermore, random learning has a longer-term effect (Smith et al., 2006). Performing tasks in a defined order promotes retention of information, while practicing in a random order promotes transfer, a phenomenon that is commonly referred to as the "contextual interference effect" (Shea & Morgan, 1979). Indeed, in everyday life, situations that are repeated in a defined order are rare. The use of contextual interference to train a task has been shown to promote transfer in stroke patients (Jo et al., 2020). Random practice forces the patient to pay more attention to the task. This type of practice thus makes training more intensive as it generates greater cognitive activity and effort than exercises provided in a defined order (Merbah & Meulemans, 2011). Engagement is thus increased and slacking is reduced.

2.4. *Other robotic algorithms and challenge-based controllers: Resistive exercises, error augmentation and constrained exercises*

Although robotic therapy uses assistive algorithms (Basteris et al., 2014) which allow it to be used with a wide range of disabilities (Colombo & Sanguineti, 2018), other work modes are available. Some robotic systems include challenge-based controllers that allow the difficulty of the exercises to be modulated, for example, by varying the forces applied to the paretic upper limb, decreasing the level of assistance, or increasing the resistance or the range of movement (Mehrholz et al., 2018). Exercises can thus be progressed along a continuum, allowing the patient to be optimally challenged throughout the course of their rehabilitation (Guadagnoli & Lee, 2004; Marchal-Crespo & Reinkensmeyer, 2009). Three broad categories of challenge-based controllers have been developed to provide either counter-resistance, movement constraints or error augmentation (Marchal-Crespo & Reinkensmeyer, 2009). Exercises involving isometric and dynamic resistance can also be practiced, depending on the patient's needs. For example, isometric exercises can be used to retrain shoulder stability in patients with severe impairment (with proximal robot modules) while dynamic resistance exercises aim to challenge patients with more movement capacity. These exercises are based on the results of studies (Morris et al., 2004; Weiss et al., 2000) that showed that strengthening the paretic upper limb improves motor function (Marchal-Crespo & Reinkensmeyer, 2009). However, dynamic resistance exercises may not be appropriate for more severely impaired patients as they require a minimal level of residual motor function (Stein et al., 2004). While assisted exercises are interesting for severe to moderate patients to promote active movements, constrained exercises can be proposed in moderate to mild patients since they allow to work on the quality of the movement. In these exercises the patient's movement is constrained by a velocity-dependent clockwise curl force field (Rezazadeh & Berniker, 2019). Error augmentation modes have been designed to challenge patients with higher levels of motor ability, based on the rationale that errors are an essential component of neuroplasticity and motor learning (Abdollahi et al., 2011; Kawato, 1990). This type of algorithm increases trajectory errors made by the patient to encourage them to increase their efforts to produce a straight movement. Error augmentation increases intrinsic feedback, which is usually disrupted after a stroke (Israely & Carmeli, 2015). Several studies have shown that error-increasing therapy increases motor control compared to standard or error-reducing therapy (Israely & Carmeli, 2015; Liu et al., 2018). The amplification of errors is also thought to promote patient attention and motivation (Abdollahi et al., 2011; Wei et al., 2005).

Although these training modalities have obvious theoretical value to reduce motor impairment, few studies have evaluated their use in clinical practice since assistive modes of robot-assisted therapy are more commonly used (Basteris et al., 2014).

2.5. *Impairment-reducing rather than function-improving therapy*

The main purpose of robot-assisted therapy is to deliver a high number of movement repetitions in a session of a similar duration to standard rehabilitation (45 min on average). A commonly reported limitation of robot-assisted therapy is that the exercises are not functional. Indeed, studies have shown poor transfer of improvements at the impairment level to activities of daily living (ADL) (Kwakkel et al., 2008a; Mehrholz et al., 2015; Veerbeek et al., 2017). However, ADL performance is not always improved by more functional training methods, as shown in a study of an 8-week, task-specific intervention (Waddell et al., 2017). Impairment-based rehabilitation has been superseded by the emergence of task-oriented therapies that are currently considered the gold standard (Krakauer & Cortés, 2018). Task-oriented therapy improves the functional performance of the upper limb (Langhorne et al., 2011; Thant et al., 2019); however in usual care, this approach may not be appropriate or possible for patients with minimal motor command unlike robot therapy that can target the more severely impaired stroke patients.

Several recent studies suggested that robotics can be integrated in clinical practice by translating impairment gains drawn from robotic training into function through combined therapy (Conroy et al., 2019; Hung et al., 2016). For example, Conroy et al. trained 45 chronic stroke patients stratified by Fugl-Meyer (FMA) impairment (mean 21 ± 1.36) to 60 minutes of robot therapy (RT; $n = 22$) or 45 minutes of RT combined with 15 minutes therapist-assisted transition-to-task training for 12 weeks and found that the replacement of part of the robotic training with nonrobotic tasks did not reduce treatment effect and may benefit stroke-affected hand use and motor task performance (Conroy et al., 2019). Their results highlight the boosting effect of the transition-to-task sessions.

The RATULS study, conducted in 770 stroke patients, comparing 3 treatment modalities (robot-assisted training, an enhanced upper limb therapy program and usual care) over a period of 12 weeks, found no difference in upper limb function at 3 months (Rodgers et al., 2019). This confirms that the practice of non-functional exercises itself does not hinder functional recovery (Conroy et al., 2019; Hsieh et al., 2014; Hung et al., 2016). However, in order to improve function, authors advocated further research to find ways to translate the improvements in upper limb impairment seen with robot-assisted training into improvements in upper limb function and ADL by combining robot-assisted training with more functionally oriented therapy strategies.

2.6. *Interaction and provision of feedback to enhance motor learning*

Intrinsic feedback is inherent to the task, generated by the movement and its consequences on the environment. Extrinsic feedback involves the use of an external artifice to increase a subject's sensitivity to sensory events that accompany performance (Magill, 1993). The intrinsic feedback systems may be compromised due to impairment of sensory pathways after a stroke. (van Vliet & Wulf, 2006). Extrinsic feedback is commonly used by therapists to give patients additional information about their performance or method of goal attainment. Extrinsic feedback is useful only if it provides additional information to the intrinsic feedback. Verbal feedback from therapists about the outcome is useless when the information is inherent to the task (van Vliet & Wulf, 2006). Feedback can be provided as knowledge of performance (KP), which gives information about the quality of the movement, and knowledge of results (KR), which gives information about the error between the response produced and the goal (magnitude of error, direction of error). Cirstea et al. (2006, 2007) compared the effects of KP and KR in two studies and showed that during repeated practice, KP resulted in greater improvements in motor function (Cirstea et al., 2006; Cirstea & Levin, 2007). Rosati et al. (2011) demonstrated that during robot-assisted movement, appropriate auditory feedback promotes engagement, performance and learning of the exercise (Rosati et al., 2011). Several authors have used sensory feedback in combination with visual feedback and all have reported beneficial effects on motor function (Broeren et al., 2006; Coote et al., 2008; Sim et al., 2015). Feedback is an important factor in motor learning because it increases active participation by helping to maintain patient motivation (Balasubramanian et al., 2012; Stefan, 2000). Robotic devices provide both visual and auditory continuously throughout the exercise and also performance feedback that includes the magnitude of directional or target errors provided at a defined frequency and summarised at the end of the exercise.

2.7. Segmental training in 2D or 3D

A major issue related to robot-assisted therapy is the transfer of improvements at the impairment level to activities of daily living and use of the arm in the real world (Mehrholz et al., 2018; Rodgers et al., 2019; Veerbeek et al., 2017). Most rehabilitation robots do not train the arm as a whole, but focus on one or two joints. Proximal robots offer targeted rehabilitation of the shoulder and elbow, while distal robots train forearm, wrist or finger movements. However, exoskeletons were developed with the intention of providing more functional therapy by training a greater number of degrees of freedom together in a larger, 3D workspace. However, studies have shown that they do not appear to provide any additional benefit in terms of functional recovery compared to impairment-based single-joint robots (Krebs, 2001; Krebs et al., 2008, 2015; Mehrholz et al., 2020; Milot et al., 2013; Veerbeek et al., 2017; Wu et al., 2021). This could be due to the fact that 2D robots are easier to use (S.H. Lee et al., 2020) and the exercises are easier to understand (Lledó et al., 2016), or could be explained by Bernstein's theory that humans begin by reducing the number of degrees of freedom when learning a new motor task (Bernstein, 1967). Krebs et al. (2015) highlighted the paradox robotic devices with a small number of degrees of freedom actually reduce impairment and increase motor control across a larger number degrees of freedom (Krebs et al., 2015).

3. A paradigm for the integration of robot-assisted therapy into rehabilitation

Based on current evidence in the literature and our 10 years of experience, we propose a plan for the optimal use of robotic devices as part of an upper limb rehabilitation program in patients with moderate to severe post-stroke upper limb paresis.

3.1. Robotic assistance: As needed but not too much or too long!

Assist-as-needed robot therapy allows patients with severe motor impairment to actively participate in rehabilitation (Duret et al., 2014). This contrasts with other therapies developed over the last 20 years, such as constraint-induced therapy, which is limited to a small group of patients (10% eligibility) (Kwakkel et al., 2015) with moderate to mild upper limb motor impairment (Brunner et al., 2011; Duret, Hutin, et al., 2015; Wolf et al., 2002). The patient's movement intention matches their execution thanks to the assistance provided by the robot (Brunner et al., 2011; Duret, Hutin, et al., 2015; Wolf et al., 2002). This form of positive reinforcement stimulates motivation and plays an important role in the early stages of motor learning (Sidarta et al., 2016). Robot-assisted therapy allows a large number of movements to be performed, and encourages active participation, despite the assistance (Grosmaire & Duret, 2017). Furthermore, the effort generated by the patient (major intensity parameter) is a key element that drives brain plasticity.

As the difficulty of the training has an important influence on its effectiveness (Pan et al., 2019), it seems obvious to us that even if our practice of robotic rehabilitation starts with the use of programs with assistance as needed, our goal is to propose exercises of appropriate difficulty, thus avoiding patients' being bored or frustrated and losing motivation.

3.2. Visual feedback (graphic interface) of results (active participation and motor performance) to increase motivation

One of the major advantages of robotic systems is the amount of information provided (i.e. feedback) on the patient's performance during the exercises as well as throughout the training process. Change-sensitive kinematic indicators (Duret et al., 2016) that are complementary to clinical measures are widely used in research, but to our knowledge, no recommendations have been developed on the use of kinematic parameters to guide rehabilitation. However, unlike feedback given by the therapist during usual care, feedback generated by robotic systems is objective and provides information that cannot be provided in conventional rehabilitation; for example they can indicate the level of active participation (number of times the robot has initiated the movement in the patient's place, time of initiation of the assistance, stiffness and power delivered by the robot) as well as performance (deviation of the trajectory from the ideal trajectory, distance to the target, movement performance time, maximum speed, average speed, smoothness). These indicators encourage the patient to improve their performance and can also be used by the therapist to determine when and how to progress the therapy.

Our approach is progressive. Initially, the therapist focuses the patient's attention on the level of active participation by indicating the number of times the robot initiated the movement for them, or the power the robot used to assist the movement. The therapist then sets specific objectives relating to active participation to challenge the patient and increase their motivation. Once the patient is reassured that they can generate movement, the therapist continues to encourage active practice while changing the focus of the objectives to the quality of the movement, using accuracy feedback (such as deviation of the trajectory from the ideal trajectory, distance to the target, etc.) provided by the robot. The aim is to implement principles of motor skill learning by proposing a pattern of trade-offs between speed and accuracy that means that the patient must first generate a movement to the target, then increase speed execution before focusing on accuracy (by decreasing speed as a physical law) (Grosmaire & Duret, 2017; Lefebvre et al., 2015).

3.3. Varying the exercises

Providing a variety of exercises within a session is important to limit boredom and disengagement. Furthermore, skill retention is improved by varied practice (Brewer et al., 2007). The exercises should involve both explicit (i.e. conscious practice) and implicit learning (i.e. the performance of motor tasks is done less consciously, more automatically). Implicit learning can be achieved through the use of games in a virtual environment (Brewer et al., 2007), in which the patient can use the motor skills already acquired in less pre-programmed, freer movements. Exercises involving implicit learning, which is generally spared after stroke (Pohl et al., 2006) seem to be just as effective as exercises based on explicit motor learning (Kal et al., 2016) but should therefore be used to diversify exercise conditions and stimulate the learning process. They have the advantage of minimising the involvement of cognitive functions and being robust over time (Steenbergen et al., 2010).

3.4. Begin with a standard target order then randomize

During the first sessions, it is useful to choose exercises where the movements are performed in a predefined order to help the patient understand the task. Once this has been achieved, it may be preferable to present exercises which involve movements in a random order, to reduce automatization, maintain the patient's attention and limit slacking. Presenting the targets in a random order also optimises the effect of contextual interference, increases the cognitive load intrinsic to the task and is therefore a means of intensifying practice (Hodges et al., 2014). However, for some patients with significant cognitive impairment it will be necessary to maintain the presentation of targets in a predefined order.

3.5. Adaptation of target distance: Shorter, challenging movements rather than longer, assisted movements

It is more beneficial for patients to practice movements of smaller amplitude, but with a greater active participation, than the larger amplitude movements that require assistance to complete. We therefore remove the assistance as soon as the patient can produce even small amplitude movements. The aim is to challenge the patient to generate effort but avoid failure. We therefore reduce the movement amplitude so that the patient practices unassisted exercises within an achievable range. As the patient progresses, we increase the range of motion. based on the principle of Fitts' law which indicates that the difficulty of the task performed is the direct relationship between the time to perform the task and the properties of the targets, i.e. their size and the distance between them (Paul M. Fitts, 1954; Zimmerli et al., 2012). In other words, increasing the distance to the target and/or decreasing the size of the targets increases the difficulty of the task.

3.6. Alternating assisted and free movement and progressing to free movement

A useful strategy to gradually progress the patient while avoiding exercises that may be too difficult or that require too much energy and would demotivate the patient, is to alternate assist-as-needed exercises with exercises that require a significant amount of effort within the same session. We usually begin with one or two assisted exercises as a warm-up, then switch to free exercises before returning to assisted exercises as the patient tires. This dual modality period can be continued until the patient has sufficient endurance and capacity to complete an entire training session without assistance.

3.7. *Different modalities*

As well as providing movement assistance, some robotic systems can generate force fields to counteract the trajectory or increase errors. While assist-as-needed modes compensate for a lack of motor ability, the aim of these modes is to stimulate adaptive plasticity, a process that complements assisted learning. Such methods are very difficult to implement in conventional therapy. After the initial phase, which involves quantitative rehabilitation, i.e. the practice of a large quantity of movements, of increasing amplitude, the aim in the next phase is to improve movement quality. Error-enhancing programmes amplify the visual presentation of lateral deviations from the ideal trajectory, thus encouraging movement accuracy by stimulating brain adaptive processes. Once this has been achieved, the patient can be progressed to modes in which force fields attempt to deviate their trajectory from the straight line. The perturbations thus force the patient to continually readapt their trajectory to the constraints produced by the machine. These exercises involve implicit learning.

The main characteristic of paresis is muscle weakness. Therefore, once the patient can perform a quality movement, it is important to increase their strength. Although robots were generally not specifically designed for strengthening, they often can provide exercises with progressive, dynamic resistance. The aim at this stage is to promote the patient's ability to perform movements against gravity, which are necessary for activities of daily living.

3.8. *How long should sessions be?*

As with conventional rehabilitation, there is no consensus on the duration of robot-assisted rehabilitation sessions. Although it is generally considered that "more is better" (Langhorne et al., 1996; Lohse et al., 2014), the optimal daily duration of an upper limb rehabilitation session has not been determined. In the literature, session durations relate to experimental protocols and vary greatly from one study to another, ranging from 20 minutes to 180 minutes per day (Yozbatiran & Francisco, 2019). In reality, the duration of rehabilitation sessions depends very much on the organisation within the specific centre. While specific sessions may be organised for robot-assisted therapy in clinical trials, in routine care it is uncommon for a specific session to be dedicated to robot-assisted therapy. Conventional therapy (physiotherapy and/or occupational therapy) sessions are often shortened to fit in robot-assisted therapy.

A retrospective study by our team that compared outcomes (Fugl-Meyer score) in patients in routine care who received 45 minutes of robotic rehabilitation with patients from a research protocol who received 30 minutes of robotic rehabilitation found no difference: patients in both groups performed over 600 movements per day with the robotic device (Pila et al., 2022). This result seems to be consistent with the work of Burgar et al. (2011), who compared 15 hours of robot-assisted rehabilitation to 30 hours of robot-assisted rehabilitation and 15 hours of additional routine care, and found no significant difference in change in Fugl-Meyer score between the groups both at post-treatment and the 6-month follow-up (Burgar et al., 2011). These results suggest that rather than defining a set duration of robot-assisted therapy, it is more relevant to set a number of movements of appropriate difficulty to achieve.

3.9. *Duration of the program: When to stop?*

It is now widely accepted that early rehabilitation leads to better recovery (Paolucci et al., 2000). However, there are no recommendations on how long robot-assisted therapy should be performed for. The durations of robot-assisted therapy used in studies is very heterogenous, ranging from 2 to 12 weeks (Mehrholz et al., 2018). A program of 36 hours of robot-assisted therapy provided over 12 weeks to patients with chronic stroke found only modest improvement in motor impairments (A.C. Lo et al., 2010), suggesting that at least 36 sessions were needed to achieve motor improvements. A study by Pila et al. (2017) found that over 3 months of robot-assisted therapy was necessary to improve motor outcomes in the most severe subacute stroke patients (Pila et al., 2017b). These results were confirmed by a recent study by Daly et al. who evaluated the needed of long dose of treatment (5 hours of daily rehabilitation including 1.5 hours of robotics, 5 days a week since 12 weeks, i.e. 300 h) for chronic stroke with moderate/severe impairment, have shown a benefit of continuing rehabilitation up to 300 hours with greater functional gains in the second part of the treatment than in the first 150 hours (Daly et al., 2019). These results refute the notion of a motor recovery plateau that would occur as early as 3 to 6 months depending on the initial level of severity of motor deficiencies (Duncan & Sue Min Lai, 1997). We suggest therefore, that robot-assisted therapy should be continued for as long as necessary (adjusting the training to keep it challenging for the patient), until clinical and kinematic (robot-measured) outcomes reach a plateau.

4. Discussion: A review of 10 years of clinical trials

Despite the continuing debate around the effectiveness of upper limb robot-assisted therapy (Chien et al., 2020; Rodgers et al., 2019), this treatment appears as an appropriate treatment dose to be administered in terms of the quantity of movements performed and the intensity of the exercises. Although many randomised studies and systematic reviews have been conducted on robot-assisted therapy (Bertani et al., 2017; Chien et al., 2020; K. Lo et al., 2017; Mehrholz et al., 2020; Zhang et al., 2017), an issue often raised is the heterogeneity of practices and poorly described interventions (Burgar et al., 2011).

Robot-assisted therapy as defined above corresponds fully to the current concepts of neurorehabilitation, based on the principles of motor learning (Maier, Rubio Ballester, et al., 2019) and has been shown to effectively improve motor recovery (Kleim & Jones, 2008a). It also improves patient motivation and participation (Morone et al., 2020). Despite the fact that robot-assisted therapy appears to be an appropriate treatment for motor recovery after stroke, after more than 20 years of use, the results are still questioned, and skepticism regarding the benefits and utility of robot-assisted therapy remains widespread among clinicians. Moreover, current guidelines for robotic rehabilitation after stroke did not provide clear clinical practice recommendations (Calabrò et al., 2021; Morone et al., 2021).

4.1. What does the literature say?

Therapists' fears that robot-assisted therapy might increase spasticity or shoulder pain seem to have been allayed. Indeed, this therapy is considered safe in subacute and chronic stroke patients, i.e. not deleterious to muscle tone and shoulder pain (Mehrholz et al., 2020). However, its effects on the reduction of spasticity remain controversial (Bertani et al., 2017; Veerbeek et al., 2017).

Overall, studies have shown that robot-assisted therapy in addition to usual care reduces upper limb motor impairment significantly more than conventional therapies, however, this improvement is minimal on functional capacity (Veerbeek et al., 2017; Wu et al., 2021). The results appear to differ according to the phase of stroke. A Cochrane review in 2015 found improvements of activities of daily living in patients with acute and subacute stroke but not in the chronic phase (Mehrholz et al., 2015) while three recent systematic reviews found that robot-assisted therapy was more effective than standard care in the chronic phase (Bertani et al., 2017; Wu et al., 2021; Zhang et al., 2017).

The application of additional care, i.e. conventional therapy plus supplementary therapy such as robotic therapy, is not always easy to achieve due to budget constraints, and we believe the clinical reality of robotic therapy is rather a partial substitution of conventional therapy time.

The partial substitution of usual care by robotic therapy in the acute (40 minutes out of 120 minutes conventional therapy per day were substituted by robot therapy) (Masiero et al., 2014) and subacute (conventional therapy was substituted by robot therapy for 25% of the total weekly rehabilitation time) (Dehem et al., 2019) phases also seems interesting as these combined programmes show comparable results.

The functional benefits of robot-assisted therapy are still controversial. The 2018 Cochrane review appeared to have closed the debate since it reported a high level of evidence that this therapy improved the ability to perform ADLs: however, the results of the RATULS study published just after the Cochrane review re-opened the debate (Mehrholz et al., 2018). This large multicentre study of 770 stroke patients with severe upper limb paresis in the subacute and chronic phase found no difference in upper limb functional abilities (assessed by the Action Research Action Test (Lyle, 1981)) at 3 months between a programme using robot-assisted therapy compared to a programme of intensive manual therapy of the upper limb and standard care (Rodgers et al., 2019). The improvements observed in upper limb motor function (impairment, assessed by the Fugl-Meyer assessment scale (Fugl-Meyer et al., 1975)) in patients who received robot-assisted therapy were not transferred to activities of daily living. However, the main objective of robot-assisted therapy is not the improvement of functional capacities but the use of motor learning principles to reduce impairment at the joints trained. Furthermore, the robotic device used in the RAUTLS study did not include distal rehabilitation or grip training (Hung et al., 2016). The authors therefore concluded that robotic therapy must be coupled with functional exercises in order to ensure a functional benefit (Rodgers et al., 2019).

Few studies have attempted to determine the patient groups who most benefit from robot-assisted therapy. However, it seems that it may be particularly effective in patients with more severe impairment. This was suggested in earlier studies (Conroy et al., 2011; Finley et al., 2005; MacClellan et al., 2005) and more recently in a retrospective study by our team (Duret, Hutin, et al., 2015). A recent meta-analysis also showed that the functional benefits of the therapy were more significant in patients with moderate to severe motor deficits (Wu et al., 2021).

Finally, a large variety of robotic devices has become available, further complicating the issue of effectiveness. Furthermore, not only are designs different (e.g. exoskeletons versus end-effectors, distal versus proximal robots), but also the methods of control vary, thus confounding the effects. A comparison of an end-effector robot and an exoskeleton in patients with chronic, moderate-to-severe stroke found that outcomes relating to activity and participation improved more in the group who trained with the end-effector (S.H. Lee et al., 2020). A systematic review also showed that only end-effectors reduced impairment more than conventional therapy (Wu et al., 2021).

4.2. Combination is the key

As suggested by Bernhardt et al. (2019), it is time to accelerate the development of effective rehabilitation practices by designing evidence-based protocols, identifying target populations, providing precise descriptions of the content of interventions so that protocols can be reproduced using appropriate standardised clinical scales and objective movement analyses (Bernhardt & Mehrholz, 2019).

Rehabilitation robots should be part of the battery of tools available to clinicians to intensify the treatment of patients with the most severe motor deficiencies, as a synergistic complement to therapies based on the functional integration of the paretic upper limb in manual activities. This is the sense of the studies that showed positive results of combined treatments (Conroy et al., 2019; Hung et al., 2016). Brokaw et al. in a pilot cross-over design study compared the effects of equal doses of robotic and conventional therapy in chronic stroke patients with moderate to severe impairments (Brokaw et al., 2014). Patients were randomized to 12 hours of robotic or conventional therapy and then crossed over to the other therapy type after a 1-month washout period. They found that robot therapy improved motor coordination and range of movement, and that the results were enhanced when followed by conventional therapy to apply the improvements in a free environment. These findings suggest that robotic therapy may be a starter to prime motor recovery before functional integration. Conroy et al. confirmed this outcome more recently in 45 chronic stroke patients (Conroy et al., 2019).

4.3. How to implement robot-assisted therapy for upper limb rehabilitation

Although there is no consensus on the content of an optimal programme using a robotic device (Burgar et al., 2011; Gassert & Dietz, 2018), it seems logical to imagine a challenging programme depending on the patient's motor deficits. This programme of increasing difficulty implemented during a 30 minutes session could be as follows:

- Practice of 500 large-amplitude movements with assistance-as-needed with a standardised (predictable) order of target presentation
- Isometric resistance exercises to improve shoulder stability
- Varied exercises (targeting both explicit and implicit learning)
- Combination of assisted and unassisted short-amplitude exercises
- Exercises with assistance-as-needed with targets presented randomly
- Unassisted exercise with random targets and a progressive increase in amplitude
- Exercises increasing errors to constrain at better movement quality
- Force fields exercises to promote motor control
- Dynamic resistance exercises

4.4. Future of robotic rehabilitation?

The supporters of robotic therapy are trying to optimize the use of these devices to get the best out of them with a combination of robot-mediated training focused on disabilities in adjunct to more functional conventional therapies in order to transfer the benefits of one to the others which is our point of view.

Another way is to create different tools integrating the two treatment modalities, impairment reduction and ability enhancement, which seems to be the direction taken by the engineers.

The variety of devices on the market suggests future developments in robotics for improving functional capabilities in activities of daily living. Some research teams have added haptic feedback to robots in order to integrate more sensory input to approximate the sensations perceived during functional interactions in the real world (Aiple & Schiele, 2013; Elangovan et al., 2019; Mazzoleni et al., 2018). Others have integrated connected objects (Díez et al., 2016; Mizanoor Rahman, 2019). Some are developing versions that can be used at home so that rehabilitation can be continued in telecare or in autonomy at home (Alamdari & Krovi, 2015; Housley et al., 2018; Sivan et al., 2014). Other teams are seeking to add artificial intelligence to the robots in order to constantly evaluate the patient's participation and propose a rehabilitation programme accordingly (Fazekas & Tavaszi, 2019). Finally, immersive virtual reality is another solution under development. All these concepts need clinical studies to see their impact on the recovery of patients after stroke, but it seems that robotics still has a bright future ahead.

5. Conclusion

Rehabilitation using robotic devices is still a promising field of exploration in 2021; indeed, despite the sometimes disappointing results of well-conducted clinical studies, its optimal implementation is still ahead of us because the evidence-based use of all the potentialities of these toolboxes has not yet been really realised. Further studies that would integrate some principles of the paradigm described in this paper are needed.

Conflict of interest

The authors have no conflict of interest to declare.

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