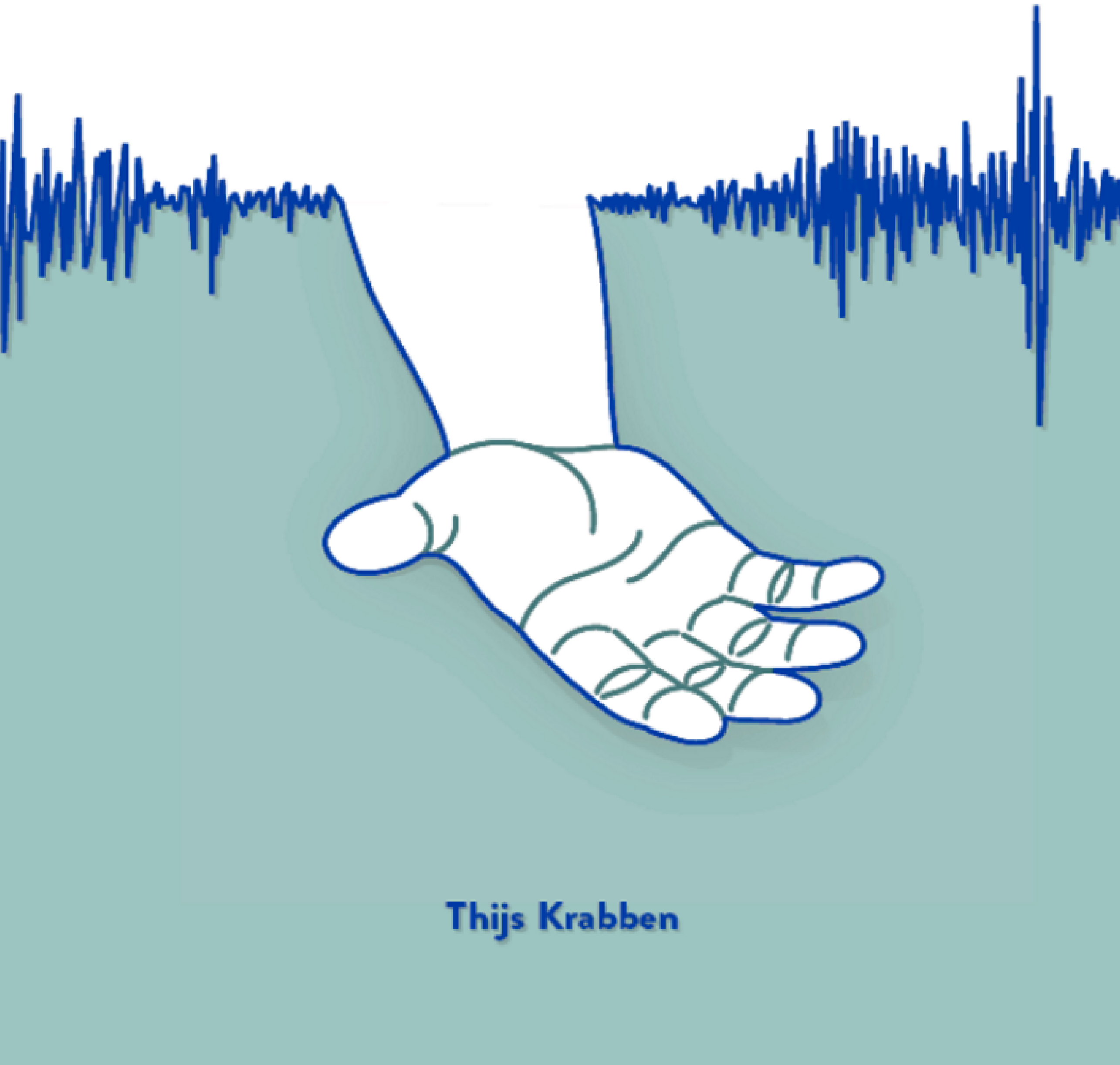
A REACHING HAND

Towards an Active Therapeutic Device for the upper extremity following stroke



Thijs Krabben

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TOWARDS AN ACTIVE THERAPEUTIC DEVICE FOR THE UPPER EXTREMITY FOLLOWING STROKE

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TOWARDS AN ACTIVE THERAPEUTIC DEVICE FOR THE UPPER EXTREMITY FOLLOWING STROKE

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Chapter 1

Introduction

The World Health Organization (WHO) defines a Cerebrovascular Accident (CVA) or stroke as ”rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin” [1, 2]. Strokes can be ischemic (85 %) due to occlusion of a blood vessel, or hemorrhagic (15 %) due to rupture of a blood vessel [3]. About two thirds of the heamorrhagic strokes occur in the intracerebral area and one third in the subarachnoid area of the brain [3]. Stroke, either ischemic or hemorrhagic, often leads to damaged corticospinal nerve pathways, and integration of motor and sensory information is disturbed.

Stroke is one of the leading causes of permanent disability in Europe [4] and North America [5]. In 2000, stroke incidence rates in the Netherlands were 182 per 100 000 men and 116 per 100 000 women [6]. It is expected that stroke incidence will increase with an ageing society and that the burden on healthcare services will increase substantially the next years [7].

1.1 Hemiparetic arm function

Around 45 % of the stroke patients have an a-functional hand at 6 months post stroke. Around 40 % of the stroke patients have to cope with mildly to severely affected arm- and hand function [8] and complete functional dexterity is only found in approximately 15 % of stroke survivors 6 months post stroke [9]. Motor problems of the upper extremity following stroke include muscle weakness [10, 11], spasms, disturbed muscle timing [12] and a reduced ability to selectively activate muscles. After stroke, muscles are often contracted in a synergistic way. With respect to arm and hand function, two synergistic patterns are often observed. These patterns were first described by Twitchell [13] and Brunnstrom [14], based on clinical observations. The flexion synergy consists of abduction, external rotation and retraction of the shoulder, supination of the forearm and flexion of the elbow, wrist and fingers. The extension synergy consists of adduction, endorotation and protraction of the shoulder, pronation of the forearm and extension of the elbow, wrist and fingers. In the majority of stroke patients, the flexion synergy is predominant [15].

More recently, these synergistic patterns were objectively quantified during isometric contractions [16, 17, 18]. Isometric shoulder abduction torques were accompanied by simultaneous elbow flexion torques. This involuntary coupling is also expressed as abnormal muscle co-activation [19] during isometric contraction. When stroke patients perform reaching movements, the required shoulder abduction torque to hold the arm against gravity induces involuntary elbow flexion torques which limits elbow extension and consequently reduces the work space of the hemiparetic arm [20, 21]. As a result, skilled use of the arm and hand and the performance of fine tuned movements are often impaired, especially during activities of daily living [22] where the weight of the object that is being manipulated results in even higher shoulder abduction torques and coupled elbow flexion.

After stroke, rehabilitation is started preferably as soon as possible after stroke, when the patient reaches a stable medical condition. The aim of rehabilitation training is to re-learn (partly) lost functions and/or learn compensational strategies in order to achieve the highest possible degree of physical and psychological performance. A multidisciplinary team of physicians, physical therapists, occupational therapists, speech therapists, recreational therapists and vocational therapists help the stroke patient to increase the level of functional independence. Training intensity, task specific training, active contribution of the patient, exercise variability, ability to make errors, and feedback on performance have been identified as key principles of rehabilitation training.

Training intensity, or training duration, is positively correlated with functional outcome. Several reviews conclude that increased dose of exercise therapy results in better functional outcome [23, 24, 25, 26, 27, 28]. A systematic review [29] specifically targeting the dose-response relationship between therapy dose and motor improvement supports the hypothesis that a higher dose of exercise therapy improves upper limb muscle function. However, early after stroke (i.e. $\leq$ 10 weeks), this dose-response relationship may be less pronounced [30, 31]. Preferably, this increase in therapy time goes along with an increase in task-specific training [32, 33].

Task specific training is defined as '*practicing context-specific motor tasks and receive some form of feedback*' [34]. In post stroke upper extremity rehabilitation, the value of task-specific training is seen in the amount of improvement that is seen in a trained task compared to an untrained task. After a period of training, improvements in the trained task are bigger compared to improvements in the untrained task, as demonstrated in a study by Schaefer et al. [35]. They trained a group of eleven stroke patients in a feeding task, and studied improvements in the trained movement task (feeding) and untrained movement tasks (sorting and dressing). The improvements were highest in the trained feeding task, but were also present in the untrained movement tasks. In rehabilitation, task specific training focuses on functional, goal-directed movement tasks rather than on impairment such as increasing muscle strength. The best way to relearn a movement task, is to train specifically that movement task [36].

Another important aspect during relearning of movements after stroke is an active contribution of the stroke patient while performing the movements. During passively and actively elicited movements, almost identical brain regions are active, which, in both cases, lead to reorganization in the primary motor cortex [37]. However, gain in motor performance and cortical reorganization is higher after a short period of active training compared with the same period of passive training [38]. Compared to passive training, active training also leads to a more effective encoding of a motor memory in the primary motor cortex, indicated by an increased corticomotorneural excitability [39]. These findings indicate that active initiation of movement during rehabilitation training is related to increased improvement in motor control compared with passively elicited movements.

Exercise variability is believed to improve retention of training effects[40]. Shea et al. found that random acquisition practice led to increased retention performance, compared to blocked acquisition practice [41]. In other words, random practice usually leads to more effective learning than blocked practice [42]. Preferably, training complexity is increased over time. In this case, stroke patients are always challenged within tolerable limits of movement ability.

A fifth important aspect of motor relearning is feedback on motor performance [43, 44]. Allowing patients to make mistakes while training a movement task, and providing them with feedback or possible solutions to solve the mistakes, are beneficial for motor learning activities. In a systematic review, Timmermans et al. [45] identified 15 task oriented training components and studied the possible influence of each component on the effect size of the training. It was concluded that the total number of included training components was not significantly correlated to the effect size of the training, but that 'feedback' and 'distributed practice' (i.e. practice schedule including rests between blocks of practice) were identified in studies with larger effect sizes.

1.2 Robot aided rehabilitation

The desired, repetitive nature of rehabilitation training led to development of rehabilitation robots. Robots deliver highly repetitive therapeutic tasks with minimal supervision of a therapist and these additional sessions of rehabilitation therapy improve motor recovery of the hemiparetic shoulder and elbow of patients with stroke [46]. Robots are often equipped with a variety of sensors that allow for precise measurement of movement data such as position, velocity, acceleration and torque. Based on these inputs, robots can provide high movement controllability which make them very suitable to help (physical) therapists with the challenges facing neurorehabilitation [47]. During training, the amount of support delivered by the rehabilitation robot can be monitored and adjusted precisely. This enables several training modalities for stroke patients, such as dynamic training (variable amount of support) and assist-as-needed control algorithms. Robot aided upper extremity rehabilitation training is believed to be as effective as manual rehabilitation training when provided in the same dose and intensity, but is probably more cost efficient [48].

Besides therapeutic purposes, rehabilitation robotics are also useful for diagnostics. The values of the integrated sensors can be used to specifically measure various aspects of human motion on the ICF impairment level. The use of objectively measured or calculated outcome measures can help to increase the understanding of post stroke rehabilitation and enables comparison of studies performed at different research groups. Position sensors can be used to measure range of motion. Time derivatives of the positional data can be used to calculate movement speed, acceleration and jerk. Based on these data, quantitative outcome measures such as movement smoothness, the number of peaks in the velocity profile, travelled path etc. can be derived. Force sensors that are integrated in several robotic systems can be used to measure the ability of the subject to generated force in several joints of the upper extremity.

1.3 Electrical stimulation

Besides robot aided rehabilitation training of the arm, electrical stimulation (ES) is used to support arm and/or hand function. A meta-analysis by Glanz et al. showed a positive effect of electrical stimulation on muscle strength, in both lower and upper extremity after stroke [49]. After electrical stimulation [50] and EMG-triggered electrical stimulation [51, 52], the ability to voluntarily generate wrist and finger extension increases, especially when patients have some residual function at the wrist and fingers [50, 53, 54]. Another systematic review of randomized clinical trials by Stein et al. [55] reported improvements in spasticity and range of motion in patients after stroke after electrical stimulation. Recently, a randomized controlled study by Gharib et al. [56] showed increased improvement of hand motor skills of stroke patients who received electrical stimulation of hand muscles in addition to repetitive task practice therapy, compared to the control group who received only the repetitive task practice therapy.

1.4 Active Therapeutic Device

The rehabilitation robotics that were commercially available at the beginning of the project, had several shortcomings. The majority of the robots was designed to train the arm, but not the hand. Around 2010, awareness was raised that training of both the arm and the hand is needed to induce functional gains in the upper extremity [57, 58]. The ease of use and usability of many robots was inadequate. Some rehabilitation robots were derived from industrial robots which was clearly visible. Many of the exoskeleton based robots had alignment issues which led to time-consuming procedures to align the axes of rotation of the robot with the axes of rotation of the patient, or discomfort for the patient when not done properly. The experiments that are described in this thesis were performed in parallel to the development of an *Active Therapeutical Device (ATD)* which aims to offer stroke patients task-specific, intensive and motivating rehabilitation training, in which the patient is actively involved.

The ATD is intended to be used in a domestic environment (i.e. training at home) to ease the burden on health care and provide a motivating training environment for stroke patients. Several key elements of neuro-rehabilitation are implemented in the design of the ATD. The robot is able to (partly) support the arm in such a way that it compensates for the weight of the arm. This feature is called gravity compensation and studies by Prange et al. showed that application of gravity compensation lead to an instantaneous increase of the range of motion of the paretic arm [59]. This increased range of motion is predominantly caused by an increased ability to extend the elbow [59]. A multichannel electrical stimulator is used to support opening and/or closing of the hand. Stimulation parameters such as amplitude (i.e. current) and timing can be adjusted on individual channels.

1.5 Objective and research questions

The aim of this thesis is to contribute to the development of a therapeutic rehabilitation robot used in post stroke upper extremity rehabilitation training. The intended use of the robot is to train both arm and hand function by actively supporting the arm against gravity and support hand function by means of multichannel functional electrical stimulation. More specifically, this thesis aims to answer the following research questions:

1. What are the differences and commonalities in timing of muscle activation and kinematics during reaching for and grasping of objects, between healthy elderly and stroke patients?

2. Can gravity compensation training affect the influence of abnormal synergies on unsupported arm movements in chronic stroke patients?

3. Is it possible to induce an instantaneous functional increase in arm and hand function by providing arm support and functional electrical stimulation?

4. Is it possible to autonomously detect bursts of sEMG activity to create Muscle Onset Offset Profiles of muscles involved in reaching and grasping objects?

5. Which outcome measures derived from rehabilitation robotics can be used to objectively quantify upper extremity function in stroke patients?

1.6 Outline of the thesis

The study described in Chapter 2 is related to the last research question. Objective outcome measures derived from circle metrics were used to quantify arm function. Also synergistic movement patterns based on simultaneous changes in joint angles are quantified. Correlations between circle metrics and the clinically used Fugl-Meyer Assessment were calculated to study the relation between these circle metrics and stroke severity. Chapter 3 and 4 relate to the second research question which addresses the effect of gravity compensation training on hemiparetic arm function. Before and after training, arm function of the stroke patients was assessed with the outcome measures described in the previous chapter, the clinically used FM assessment and with surface electromyography recorded from eight muscles of the hemiparetic shoulder and arm. The fourth research question is addressed in chapter 5 which describes how a combination of algorithms can be used to autonomously created muscle onset and offset profiles. This method is applied to data obtained from healthy elderly and stroke patients to provide an answer to the first research question in chapter 6. Finally, chapter 7 describes an experiment how functional electrical stimulation can be used to support hand function after stroke. In chapter 8, the main findings and conclusions of this thesis were discussed, along with suggestions for clinical implications and future research.

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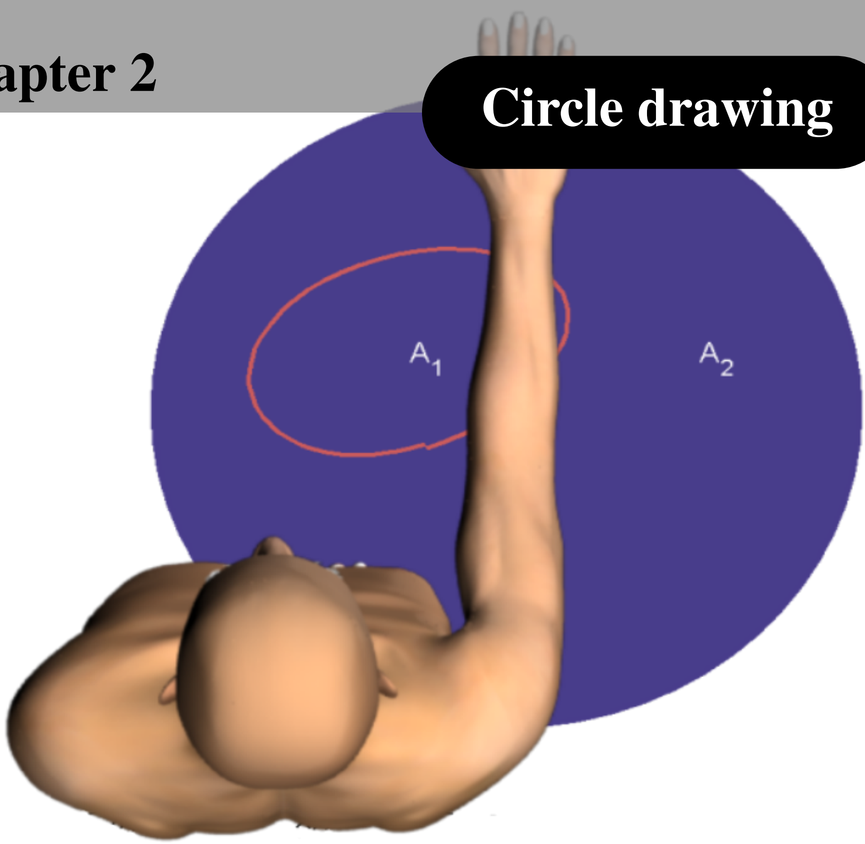
Chapter 2

Circle drawing



Circle drawing as evaluative movement task in stroke rehabilitation: an explorative study.

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Abstract

Background

The majority of stroke survivors have to cope with deficits in arm function, which is often measured with subjective clinical scales. The objective of this study is to examine whether circle drawing metrics are suitable objective outcome measures for measuring upper extremity function of stroke survivors.

Methods

Stroke survivors (n = 16) and healthy subjects (n = 20) drew circles, as big and as round as possible, above a table top. Joint angles and positions were measured. Circle area and roundness were calculated, and synergistic movement patterns were identified based on simultaneous changes of the elevation angle and elbow angle.

Results

Stroke survivors had statistically significant lower values for circle area, roundness and joint excursions, compared to healthy subjects. Stroke survivors moved significantly more within synergistic movement patterns, compared to healthy subjects. Strong correlations between the proximal upper extremity part of the Fugl-Meyer scale and circle area, roundness, joint excursions and the use of synergistic movement patterns were found.

Conclusions

The present study showed statistically significant differences in circle area, roundness and the use of synergistic movement patterns between healthy subjects and stroke survivors. These circle metrics are strongly correlated to stroke severity, as indicated by the proximal upper extremity part of the FM score. In clinical practice, circle area and roundness can give useful objective information regarding arm function of stroke survivors. In a research setting, outcome measures addressing the occurrence of synergistic movement patterns can help to increase understanding of mechanisms involved in restoration of post stroke upper extremity function.

2.1 Background

STROKE is described as ”an extremely complex breakdown of many neural systems, leading to motor as well as perceptual, cognitive and behavioral problems” [1]. Motor problems of the upper extremity following stroke include muscle weakness, spasms, disturbed muscle timing and a reduced ability to selectively activate muscles. Many stroke survivors move in abnormal synergistic movement patterns that already have been described decades ago [2, 3]. More recent studies of Beer [4, 5, 6] and Dewald [7, 8, 9] showed strong coupling of the shoulder and elbow joint in stroke survivors in both isometric and dynamic conditions.

Six months after stroke, motor problems are still present in the majority of stroke survivors [10], limiting their ability to perform activities of daily living (ADL). Post stroke rehabilitation training aims to regain (partly) lost functions by stimulation of restoration or promoting compensational strategies, in order to increase the level of independence. During rehabilitation training movements are practiced preferably with high intensity, in a task-oriented way, with an active contribution of the stroke survivor in a motivating environment where feedback on performance and error is provided [11].

Robotics

A promising way to integrate these key elements of motor relearning into post stroke rehabilitation training is the use of robotic systems. Systematic reviews indicated a positive effect on arm function after robot-aided arm rehabilitation training [12, 13]. Six months after training, the effect of robotic training is at least as large as the effect of conventional training [14].

Besides training, robotic rehabilitation systems can be valuable tools for evaluation purposes. Quantities of body functions concerning movement performance [15] can be measured objectively with integrated sensors of many robot systems. Objective measurement of motor performance in stroke survivors is important to study the effectiveness of different rehabilitation training programmes, in order to identify the most beneficial approaches. The use of objective outcome measures, strongly related to affected body functions and structures, can help to understand the mechanisms that are involved in restoration of arm function in order to maximize the effect of future approaches. Despite the increasing use of robotic systems in clinical and research settings, it is still questioned which of the wide variety of available robotic outcome measures are relevant to study arm movement ability following stroke.

Outcome measures

Currently, therapy effectiveness is generally assessed with clinical scales. However, some clinical scales show a lack of reproducibility, in addition to subjectivity when scoring the test. One way to obtain objective and specific information concerning arm function at the body function level is to measure kinematics of the arm, as can be done by many upper extremity robotic systems. Recently, relations between active range of motion (aROM) and clinical scales as the Fugl-Meyer (FM) scale, the Chedoke McMaster Stroke Assessment score and the Stroke Impact Scale were studied [16]. Strong correlations were found between the FM scale and an aROM task, performed in the horizontal plane with the upper arm elevated to 90 degrees. A movement task highly similar to the aROM task used in [16] is circle drawing.

Circle task

Successful circle drawing requires coordination of both the shoulder and elbow joint which makes it a potentially useful movement task to study multi-joint coordination. Dipietro et al. [17] showed that the effect of a robotic training intervention could be quantified by several outcome measures obtained during circular hand movements that were performed at table height. Because of the multi-joint nature of the movement task, circle drawing is a suitable task to study body functions [18] such as ranges of joint motion and coupling between the shoulder and elbow joint. In addition, circle area gives a quantitative description of the size of the region where someone can place his/her hand to grasp and manipulate objects. Such an outcome measure at the activity level gives functional information, in this case regarding the work space of the arm.

Objective

The aim of this study is to examine whether circle drawing metrics are suitable outcome measures for objective assessment of upper extremity function of stroke survivors. A new method to objectively quantify the occurrence of synergistic movement patterns is introduced. Outcome measures will be compared between healthy subjects and stroke survivors to study the discriminative power between these groups. Within stroke survivors, correlations between outcome measures including the FM are addressed to study mutual dependencies.

2.2 Methods

Subjects

Chronic stroke survivors were recruited at rehabilitation centre ’Het Roessingh’ in Enschede, the Netherlands. Inclusion criteria were a right-sided hemiparesis because of a single unilateral stroke in the left hemisphere and the ability to move the shoulder and elbow joints partly against gravity. Healthy elderly (45-80 years) were recruited at the research department and from the local community. Exclusion criteria for both groups were shoulder pain and the inability to understand the instructions given. All subjects provided written informed consent. The study was approved by the local medical ethics committee.

Procedures

During a measurement session, subjects were seated on a chair with the arm fastened to an instrumented exoskeleton called Dampace [19]. This exoskeleton was only used for measurements and did not support the arm. Stroke subjects were asked to draw 5 and healthy subjects were asked to draw 15 consecutive circles during a continuous movement in both the clockwise (CW) and counter clockwise (CCW) direction. Circle drawing started with the hand close to the body, just above a tabletop of 75 cm height. The upper arm was aligned with the trunk and the angle between the upper arm and forearm was approximately 90 degrees. Templates of circles of different radii were shown on the tabletop to motivate subjects to draw the circles as big and as round as possible. To minimize the effect of compensatory trunk movements on the shape and size of the circles, the trunk of each subject was strapped with a four point safety belt. Movements were performed at a self selected speed, without touching the table. The order of direction of the circle drawing task (CW or CCW) was randomized across subjects.

Measurements

Kinematic data were recorded with sensors integrated in the robotic exoskeleton [19]. Potentiometers on three rotational axes allowed measurements of upper arm elevation, transversal rotation, and axial rotation. A rotational optical encoder was used to measure elbow flexion and extension. Shoulder translations were measured with linear optical encoders. Signals from the potentiometers were converted from analog to digital (AD) by a 16 bits AD-converter (PCI 6034, National Instruments, Austin, Texas). The optical quadrature encoders were sampled by a 32 bits counter card (PCI6602, National Instruments, Austin, Texas). Digital values were sampled with a rate of 1 kHz, online low-pass filtered with a first order Butterworth filter with a cut-off frequency of 40 Hz and stored on a computer with a sample frequency of at least 20 Hz.

Arm segment lengths were measured to translate measured joint angles into joint positions. Upper arm length was measured between the acromion and the lateral epicondyle of the humerus. The length of the forearm was defined as the distance between the lateral epicondyle of the humerus and the third metacarpophalangeal joint. Thoracohumeral joint angles were measured according to the recommendations of the International Society of Biomechanics [20]. The orientation of the upper arm was represented by three angles, see Figure 2.1. The plane of elevation (EP) was defined as the angle between the humerus and a virtual line through the shoulders. The elevation angle (EA) represented the angle between the thorax and the humerus, in the plane of elevation. Axial rotation (AR) was expressed as the rotation around a virtual line from the glenohumeral joint to the elbow joint. The elbow flexion angle (EF) was defined as the angle between the forearm and the humerus. Joint excursions were calculated as the range between minimal and maximal joint angles during circle drawing.

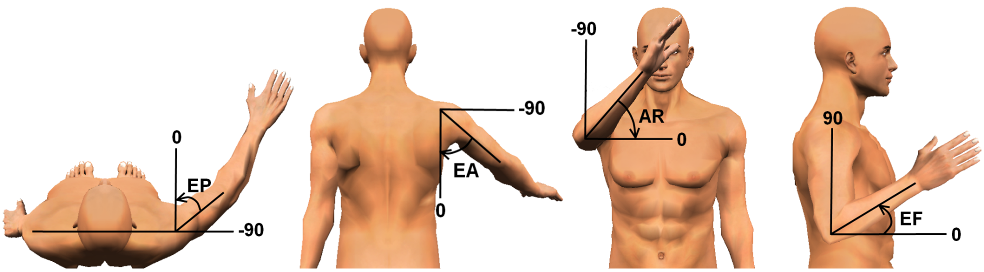

Figure 2.1: Visual representation of the joint angles of the upper arm. Arrows indicate positive rotations. EP = Elevation Plane, EA = Elevation Angle, AR = Axial rotation, EF = Elbow Flexion.

Level of impairment of the hemiparetic arm of stroke survivors at the time of the experiment was assessed with the upper extremity part (max 66 points) of the FM scale [21]. Because the focus of the present study is on proximal arm function, a subset of the upper extremity part of the FM scale consisting of items A_{II}, A_{III} and A_{IV} (max 30 points) was addressed separately (FMp).

Data analysis

All measured signals were off-line filtered with a first order zero phase shift low-pass Butterworth filter with a cut-off frequency of 5 Hz. Joint positions were calculated by means of the measured shoulder displacement and successive multiplication of the measured joint angles and the transformation matrices defined for each arm segment. Joint positions were expressed relative to the shoulder position to minimize the contribution of trunk movements to the size and shape of the drawn circles. Individual circles were extracted from the data between two minima of the Euclidean distance in the horizontal plane between the hand path and the shoulder position, which was represented in the origin. After visual inspection of the data for correctness and completeness, the three largest circles in both the CW and CCW direction were averaged and used for further analysis.

Circle drawing metrics

The area of the enclosed hand path reflects the active range of motion of both healthy subjects and stroke survivors, see Figure 2.2 for typical examples. Normalized circle area (normA) is expressed as ratio between the area of the enclosed hand path and the maximal circle area that is biomechanically possible to compensate for the effect of arm length on maximal circle area, see Figure 2.3. Circle area is considered maximal when the diameter of the circle equals the arm length of the subject.

Circle morphology was evaluated by calculation of the roundness as described in Oliveira et al. [22] and previously used to evaluate training induced changes in synergistic movement patterns during circle drawing of stroke survivors [23, 17]. In this method, roundness is calculated as the quotient of the minor and major axes (see Figure 2.2) of the ellipse which is fitted onto the hand path by means of a principal component analysis. The calculated roundness lies between 0 and 1 and a perfectly round circle yields a roundness of 1.

To explicitly study the potential impact of synergistic movement patterns on circle drawing, movements within and out of the flexion and extension synergies were identified based on simultaneous changes in shoulder abduction/adduction (EA) and elbow flexion/extension (EF) angles. When the angular velocity of both shoulder

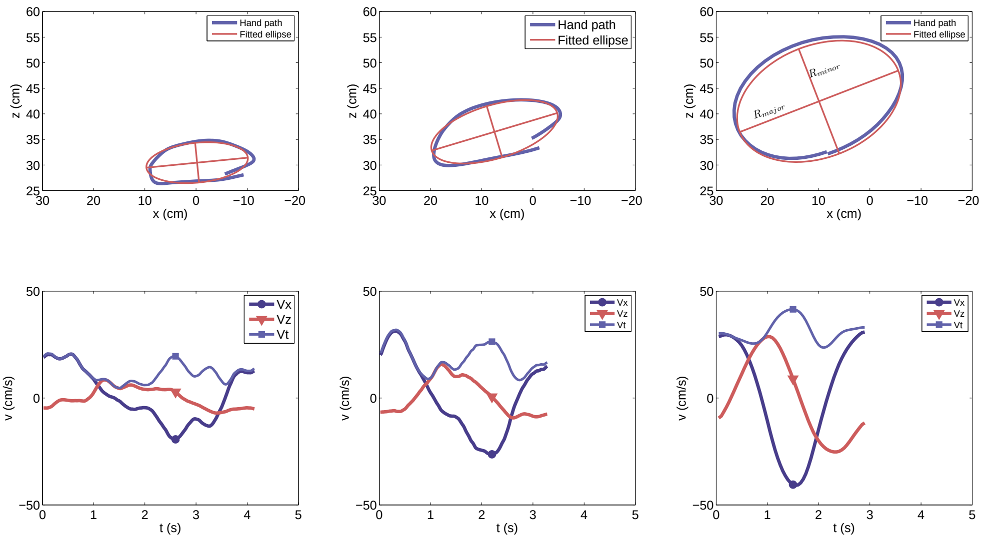

Figure 2.2: Typical examples of hand paths (top) and corresponding speed profiles (bottom). Data from stroke survivors with FM = 9 (left), FM = 45 (middle) and a healthy subject (right). FM = Fugl-Meyer, Vx = speed in x-direction, Vz = speed in z-direction, Vt = tangential speed, Rmajor = major axis fitted ellipse, Rminor = minor axis fitted ellipse.

abduction and elbow flexion exceeded 2% of their maximal values, movement was regarded as movement within the flexion synergy (InFlex). Movement within the extension synergy (InExt) was characterized by concurrent shoulder adduction and elbow extension, both exceeding the threshold value of 2% of the maximal angular velocity. In a similar way movement out of the flexion synergy (OutFlex) was characterized by simultaneous shoulder abduction and elbow extension, while movement out of the extension synergy (OutExt) comprised shoulder adduction and elbow flexion. If the angular velocity of one joint was below the threshold this was regarded as a single-joint movement (SJMov). InFlex and InExt represented movement within a synergistic pattern (InSyn). The ability to move out of a synergistic pattern (OutSyn) was calculated as the sum of OutFlex and OutExt.

Statistical analysis

For statistical analysis, all data were tested for normality with the Kolmogorov-Smirnov test. Initial analysis revealed a small but statistically significant difference in age between both groups, see Table 2.1. For that reason, all outcome measures were

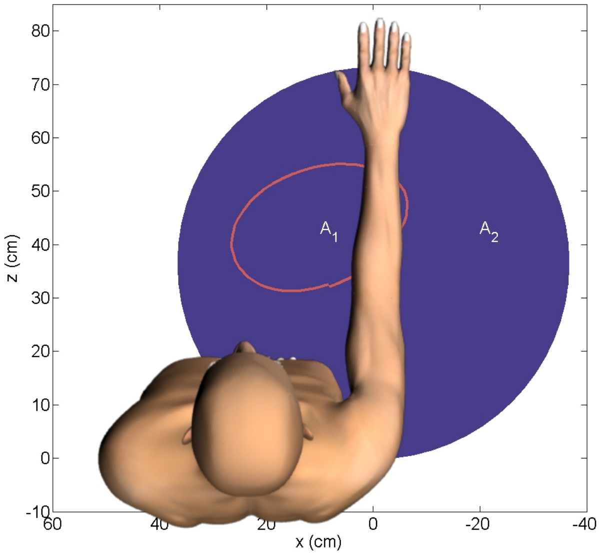

Figure 2.3: Graphical representation of the calculation of the normalized work area (normA). The area (A1) enclosed by the hand path is divided by the area (A2) of a circle with a diameter equal to the length of the arm, measured between the acromion and the third metacarpophalangeal joint.

tested for their ability to discriminate between healthy subjects and stroke survivors by means of analysis of covariance (ANCOVA) with fixed factor 'group' and covariate 'age'. Within-subject relations between outcome measures were identified and tested with Pearson's correlation coefficients. Correlations were considered weak when $\rho < 0.30$, moderate when $0.30 \leq \rho \leq 0.50$ and strong when $\rho > 0.50$ [24]. The significance level for all statistical tests was defined as $\alpha = 0.05$.

2.3 Results

Subjects

A total of 36 subjects, 20 healthy subjects and 16 stroke survivors, participated in this study. Characteristics of the subjects are summarized in Table 2.1. All stroke survivors had right-sided hemiparesis, which affected the dominant arm in all but one subject. All healthy subjects performed movements with the dominant arm. Stroke survivors were on average 4.8 years older than healthy subjects, $p = 0.032$. The effect of age on

Table 2.1: Subject demographic and clinical characteristics.

	Healthy	*Stroke*
n	20	16
Age (yrs)	53.9 ± 5.3	58.7 ± 7.4
Gender	10 M / 10 F	8 M / 8 F
Dominance	20 R / 0 L	15 R / 1 L
Time post stroke (yrs)	-	3.3 ± 2.6
Fugl-Meyer (max 66)	-	33.4 ± 17.6 (7 - 60)
Fugl-Meyer proximal (max 30)	-	15.8 ± 8.5 (1 - 29)

Abbreviations:
M = male, F = female, R = right side, L = left side

all outcome measures did not differ significantly between stroke survivors and healthy elderly, as indicated by non-significant interaction terms (group*age), $p > 0.12$.

Circle metrics

Outcome measures were normally distributed in both healthy subjects ($p \geq 0.337$) and stroke survivors ($p \geq 0.365$) as indicated by the Kolmogorov-Smirnov test for normality. Group mean normA in healthy subjects was $34.6 \pm 6.7\%$, which is significantly ($p < 0.001$) larger than the mean normA in stroke survivors, which was $12.8 \pm 12.3\%$ (see Figure 2.2 for typical examples). On average, roundness was significantly higher ($p < 0.001$) in the healthy group (0.66 ± 0.07) compared to the stroke survivor group (0.39 ± 0.17). Healthy subjects had significantly ($p < 0.001$) higher self selected movement speeds compared to stroke survivors (respectively 45.5 ± 8.6 and 16.2 ± 8.0 cm/s) and significantly ($p < 0.001$) shorter movement times to draw one circle (respectively 3.2 ± 0.9 and 7.8 ± 5.1 s).

Joint excursions

All measured joint excursions during circle drawing were significantly smaller ($p < 0.001$) in stroke survivors compared to the healthy subjects, see Figure 2.4. Healthy subjects varied EP on average 89.4 ± 9.5 degrees, against 58.7 ± 25.3 degrees for stroke survivors. The mean excursion of EA in healthy subjects was 16.1 ± 3.8 degrees, and 8.1 ± 5.9 degrees in stroke survivors. Mean variations in AR for healthy subjects and stroke survivors were respectively 42.9 ± 9.8 and 25.6 ± 14.3 degrees.

EF was on average 91.9 ± 6.9 degrees in healthy subjects and 34.9 ± 25.5 degrees in stroke survivors.

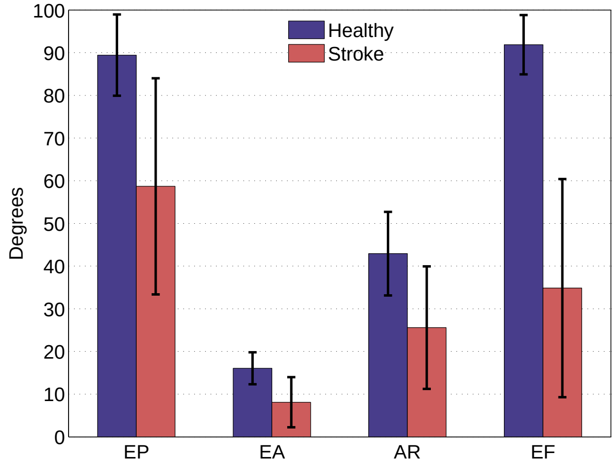

Figure 2.4: Group mean joint excursions during circle drawing of healthy subjects and stroke survivors. Error bars indicate one standard deviation. EP = Elevation Plane, EA = Elevation Angle, AR = Axial Rotation, EF = Elbow Flexion.

Synergistic movement patterns

The occurrence of synergistic movement patterns during circle drawing in both healthy subjects and stroke survivors are graphically displayed in Figure 2.5. Healthy subjects moved on average $11.5 \pm 4.6\%$ of the movement time within synergistic patterns, which was significantly ($p = 0.005$) less than stroke survivors, who moved during $22.2 \pm 15.6\%$ of the movement time within synergistic patterns. In the healthy group, OutSyn was on average $82.2 \pm 4.7\%$ which was significantly ($p < 0.001$) higher than in the stroke survivor group with mean OutSyn of $66.7 \pm 16.6\%$. Finally, SJMov was on average $6.3 \pm 0.9\%$ in healthy subjects, and $11.1 \pm 6.6\%$ in stroke survivors, which is a statistically significant difference, $p = 0.011$.

Relations between outcome measures

Pearson's correlation coefficients between the used outcome measures of stroke survivors are displayed in Table 2.2. The outcome measures used to describe the size and shape of the drawn circles are strongly related to the proximal part of the upper

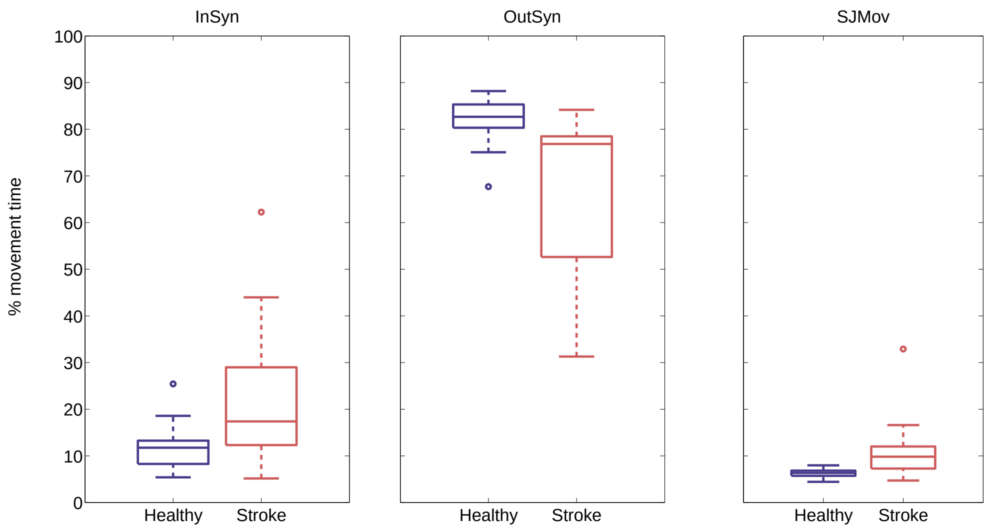

Figure 2.5: Occurrence of synergistic movement patterns during circle drawing. Boxplots of movement within (InSyn) or out of (OutSyn) synergistic movement patterns and single-joint movements (SJMov) of healthy subjects and stroke survivors.

extremity portion of the FM scale ($\rho = 0.86$ and $\rho = 0.79$, respectively). Strong positive correlations can also be seen between the joint excursions and the size and shape of the circle ($\rho \geq 0.76$).

Movement within synergistic patterns is negatively correlated with FMp ($\rho = -0.76$), FM ($\rho = -0.72$), and the size and shape of the circles, $\rho < -0.56$, see Table 2.2 and Figure 2.6. InSyn is also negatively correlated with joint excursions ($\rho < -0.48$), indicating that subjects generally have smaller joint excursions when movement takes place within synergistic patterns. The ability to move out of synergistic movement patterns as indicated by OutSyn is positively correlated with the FMp ($\rho = 0.84$), FM ($\rho = 0.84$) and the size and shape of the circles ($\rho > 0.62$). Movement out of synergistic patterns is also positively correlated with joint excursions ($\rho > 0.52$).

2.4 Discussion

In this study a standardized motor task and corresponding metrics were examined for discriminative power between healthy subjects and stroke survivors. Significant differences in normalized circle area, circle roundness, and the occurrence of synergistic

Table 2.2: Pearson's correlation coefficients between outcome measures.

	FM	*FMp*	*normA*	*rness*	*InSyn*	*OutSyn*	*SJMov*	*EP*	*EA*	*AR*	*EF*
FM	1.00	0.97	0.79	0.75	−0.72	0.84	−0.41	0.63	0.58	0.63	0.83
FMp	0.97	1.00	0.86	0.79	−0.76	0.84	−0.33	0.77	0.68	0.72	0.90
normA	0.79	0.86	1.00	0.78	−0.56	0.62	−0.24	0.87	0.90	0.84	0.95
rness	0.75	0.79	0.78	1.00	−0.65	0.78	−0.44	0.76	0.79	0.87	0.91
InSyn	−0.72	−0.76	−0.56	−0.65	1.00	−0.92	−0.06	−0.61	−0.48	−0.49	−0.64
OutSyn	0.84	0.84	0.62	0.78	−0.92	1.00	−0.35	0.57	0.52	0.59	0.73
SJMov	−0.41	−0.33	−0.24	−0.44	−0.06	−0.35	1.00	0.01	−0.18	−0.33	−0.31
EP	0.63	0.77	0.87	0.76	−0.61	0.57	0.01	1.00	0.81	0.90	0.86
EA	0.58	0.68	0.90	0.79	−0.48	0.52	−0.18	0.81	1.00	0.85	0.87
AR	0.63	0.72	0.84	0.87	−0.49	0.59	−0.33	0.90	0.85	1.00	0.87
EF	0.83	0.90	0.95	0.91	−0.64	0.73	−0.31	0.86	0.87	0.87	1.00

Abbreviations:
FM = Fugl-Meyer, FMp = proximal part FM, normA = normalized circle area, rness = roundness
InSyn = movement within synergistic pattern, Outsyn = movement out of synergistic pattern
SJMov = single joint movement, EP = elevation plane, EA = elevation angle, AR = axial rotation, EF = elbow flexion/extension

movement patterns between healthy and stroke survivors were found, indicating the ability of these outcome measures to discriminate between these two groups. Also strong within-subject relations were found between several outcome measures in a sample of mildly to severely affected chronic stroke survivors.

Work area

Reduced aROM during various movement tasks is commonly observed in stroke survivors, for example during planar pointing movements [25]. The present study indicates that joint excursions of the hemiparetic shoulder and elbow are diminished, resulting in a reduced work area of the hand. This finding is supported by studies of Sukal and Ellis [16, 26] who showed a reduced work area of the paretic arm compared to the unaffected arm, during an aROM task with the upper arm elevated to 90 degrees (comparable to EA = -90 degrees in the present study).

Roundness

Roundness of circles drawn by stroke survivors was previously studied by Dipietro and colleagues [23, 17]. The method of determining roundness of a circle [22] was equal in the present study and the studies by Dipietro et al. During baseline measurements Dipietro et al. [17] found a mean roundness of 0.51 in a sample of 117 chronic stroke survivors with a mean FM score of 20.5. Mean roundness of the circles drawn by the chronic stroke survivors (mean FM 33.4 points) in the present

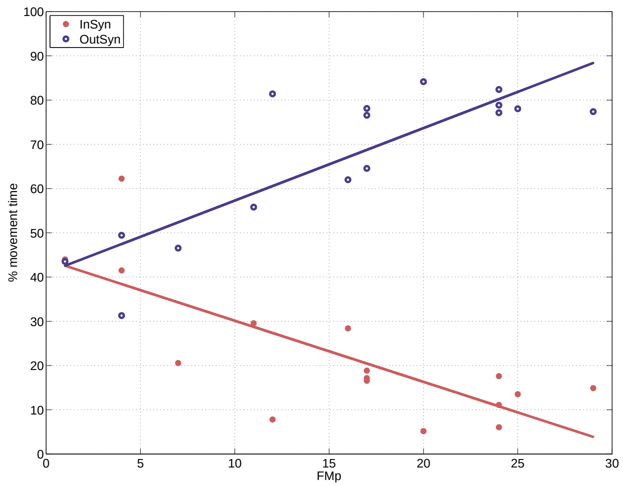

Figure 2.6: Relation between the proximal part of the upper extremity part of the FM scale (FMp) and the occurrence of synergistic movement patterns. InSyn = movement within synergistic pattern, OutSyn = movement out of synergistic pattern.

study was 0.39, indicating that circles were more elliptical (i.e. less round). This was unexpected since a positive correlation coefficient ($\rho = 0.76$) between the FM score and roundness was found. A possible explanation for this discrepancy was already hypothesized in Dipietro et al., they measured subjects while the arm was supported against gravity. Application of gravity compensation reduces the activation level of shoulder abductors needed to hold the arm against gravity, and as a result the amount of coupled involuntary elbow flexion is decreased, leading to an increased ability to extend the elbow [6, 27]. In the case of circle drawing, increase in aROM due to gravity compensation can lead to smaller differences in lengths of the major and minor axes of the fitted ellipse, resulting in higher values for roundness.

Work area and FM

In the present study, a strong correlation between aROM, as represented by the normalized circle area, and the FM scale was found. Similar results were found in a study performed by Ellis et al. [16]. In that study, aROM of stroke survivors during different limb loadings was measured. Movement was performed in the horizontal plane, with the upper arm elevated to 90 degrees. Correlation between aROM and FM varied with limb loading, and was 0.69 in the unsupported condition. In the present study, correlation between FM and normalized circle area was higher with a correlation coefficient of 0.79. The difference in correlation coefficients can be caused by differences in the performed movement task. During the study by Ellis et al. subjects were asked to make a movement as big as possible without instructions concerning the shape of the movement. Participants of the present study were asked to make circular movements as big and as round as possible. Also some differences in applied normalization procedures to minimize the effect of arm length on work area may contribute to differences in correlation between FM and aROM. Nevertheless, both studies showed strong relations between FM and aROM, indicating that circle area is a suitable outcome measure to objectively study activities of the upper extremity following stroke.

Roundness and FM

Compared to the present study, Dipietro et al. [17] found similar, but less pronounced correlations between roundness and the FM scale ($\rho = 0.55$ against $\rho = 0.75$) and between roundness and the proximal upper extremity part of the FM scale ($\rho = 0.61$ against $\rho = 0.79$) during baseline and evaluation measurements. Because subjects in the study of Dipietro et al. drew circles in a gravity compensated environment, joint coupling during circle drawing is likely to be less pronounced compared to the unsupported arm movements that were made during the FM assessment, resulting in a less strong correlation between the FM score and circle roundness.

Joint coupling and FM

Again, concerning the correlation between the FM and joint coupling, a comparison between Dipietro et al. [17] and the present study reveals a stronger correlation in the latter one, which is likely related to the use of gravity compensation in Dipietro et al. Also, Dipietro et al. studied joint coupling by comparison of shoulder horizontal ab-/adduction (i.e. plane of elevation in the present study) and elbow flexion/extension angles whereas in the present study simultaneous changes in elevation angle and elbow angle represented joint coupling. A lower correlation between the proximal part of the FM scale and joint coupling as calculated by Dipietro et al. could also indicate that coupling between plane of elevation and elbow angle is less strong than coupling between elevation angle and elbow angle. This is supported by a smaller amount of secondary torque of elbow flexion measured during an isometric maximal voluntary contraction (MVC) of shoulder flexion (i.e. shoulder horizontal adduction) compared to an MVC of shoulder abduction [28]. Despite small differences in motor task, methods and analyses, both studies indicate that circle drawing is a suitable movement task to study coupling between two joints.

Multi-joint movement

Compared to a rather strong focus on single-joint movements of the FM assessment, outcome measures concerning multi-joint movements are more suitable to study motor control during movements that resemble ADL tasks. Circle drawing is a multi-joint movement task that requires selective and coordinated movement of both the shoulder and elbow joint. At the activity level, normalized circle area gives a quantitative description of the size of the area where the stroke survivor can place his hand to grasp and manipulate objects. In addition, the measured joint excursions, the calculated roundness, and the occurrence of synergistic movement patterns quantify arm movement at the body function level. Drawing tasks are often used to study motor control of the arm during multi-joint movements, for example to study control of interaction torques between the shoulder and elbow joints [29, 30].

As demonstrated in the present study and several other studies, circle size and roundness are strongly related to the widely used FM scale. This suggests that measurement of circle size and shape can give similar information about the level of impairment of stroke survivors. However, circle metrics are measured objectively and are insusceptible to subjective judgment by the examiner.

Objective outcome measures

Quantitative outcome measures strongly related to pathological impairments can help to create a better understanding of neurological changes induced by post stroke rehabilitation therapy. Knowledge of size and shape of circular movements after stroke is extended in the present study by measurement of circle metrics in healthy subjects. The ability to compare changes of circle metrics induced by post stroke interventions with values obtained from a healthy population can provide insight in whether neural recovery takes place or whether stroke survivors use compensatory strategies. The degree to which both processes occur may influence future post stroke rehabilitation programmes [31].

A better understanding of mechanisms involved in post stroke rehabilitation is needed to maximize the effect of future approaches to improve upper extremity functionality. The use of standardized quantitative outcome measures allows a uniform comparison of different interventions to study their efficacy and identify which interventions are the most beneficial for stroke survivors.

Clinical implications

Measurement of the use of synergistic patterns as described in this paper requires an advanced measurement system that is capable of measuring joint angles. These outcome measures can be useful to study underlying mechanisms of restoration of arm function after stroke in a research setting. Circle size and roundness can be measured not only with advanced measurement systems, but with any measurement device that is capable of measuring hand position. Besides advanced robotic systems, one can think of simple and affordable hand tracking devices, for instance based on a camera. Such equipment is suitable to deploy in clinical practice which allows simple but objective measurement of meaningful measures of arm function.

2.5 Conclusions

The aim of this study was to examine whether circle drawing metrics are suitable outcome measures for stroke rehabilitation. The present study indicates that it is possible to make a distinction in circle area, roundness and the use of synergistic movement patterns between healthy subjects and stroke survivors with a wide range of stroke severity. These circle metrics are also strongly correlated to stroke severity, as indicated by the proximal upper extremity part of the FM score.

Outcome measures such as circle area and roundness can be a valuable addition to currently used outcome measures, because they can be measured objectively with any measurement device that is capable of measuring hand position. Such simple and affordable equipment is suitable to be deployed in clinical settings.

Identification of abnormal synergistic movement patterns requires more advanced equipment that is capable of measuring joint angles of the shoulder and elbow. Research into changes in the use of abnormal movement patterns is useful for a better understanding of mechanisms that are involved in restoration of post stroke arm function. Data obtained from healthy elderly can help to interpret changes in circle drawing metrics of stroke survivors, for instance to study effectiveness of post stroke interventions aiming at restoration of arm function.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TK performed the design of the study, acquisition and analysis of data and drafting of the manuscript. BIM made substantial contributions to acquisition of the data and drafting of the manuscript. AH, JSR and JHB were involved in interpretation of results and critical revision of the manuscript for important intellectual content. JHB was also involved in conception and design of the study. GBP was involved in design of the study, acquisition and interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content. All authors have read and approved the final manuscript.

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Chapter 3

Freebal training

Influence of gravity compensation training on synergistic movement patterns of the upper extremity after stroke, a pilot study.

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Abstract

Background

The majority of stroke patients have to cope with impaired arm function. Gravity compensation of the arm instantaneously affects abnormal synergistic movement patterns. The goal of the present study is to examine whether gravity compensated training improves unsupported arm function.

Methods

Seven chronic stroke patients received 18 half-hour sessions of gravity compensated reach training, in a period of six weeks. During training a motivating computer game was played. Before and after training arm function was assessed with the Fugl-Meyer assessment and a standardized, unsupported circle drawing task. Synergistic movement patterns were identified based on concurrent changes in shoulder elevation and elbow flexion/extension angles.

Results

Median increase of Fugl-Meyer scores was 3 points after training. The training led to significantly increased work area of the hemiparetic arm, as indicated by the normalized circle area. Roundness of the drawn circles and the occurrence of synergistic movement patterns remained similar after the training.

Conclusions

A decreased strength of involuntary coupling might contribute to the increased arm function after training. More research is needed to study working mechanisms involved in post stroke rehabilitation training. The used training setup is simple and affordable and is therefore suitable to use in clinical settings.

3.1 Background

STROKE is one of the main causes of disability in Europe [1] and North America [2]. Due to hemorrhagic or ischemic damage to brain tissue, motor planning and the integration of sensorimotor information are degraded. In many cases, this results in an altered generation of muscle activity, which may present as weakness, co-contraction and disturbed timing [3, 4]. Coordination between muscles can also be impaired, leading to less selective movements. In clinical practice, stereotypical movement patterns because of abnormal muscle synergies are often observed [5, 6]. Movements are restrained within either a flexion synergy (shoulder abduction, shoulder external rotation, elbow flexion and forearm supination) or an extension synergy (shoulder adduction, shoulder internal rotation, elbow extension and forearm pronation), or a combination of components of both synergies [7]. In the majority of stroke patients, these limitations account for a reduced ability to use the arm. During rehabilitation training, restoration of (partly) lost functions is stimulated and compensational strategies are promoted in order to increase the functional abilities of the affected arm and increase the level of independence. At most 20 % of all patients have complete arm function 6 months post stroke [8].

Synergies

In stroke patients, abnormal coupling between shoulder and elbow movements was observed during isometric contractions: high torques of shoulder abduction are related to simultaneous elbow flexion torques [9, 10]. Indications for coupling of these components were also observed in muscle activity during isometric contractions [11]. In the case of reaching movements, a certain amount of shoulder abduction is needed to lift the arm, provoking simultaneous elbow flexion torques and limiting elbow extension [12, 13].

Gravity compensation

A way to instantaneously reduce the influence of these abnormal, post stroke synergistic patterns (i.e. abnormal coupling) is to counterbalance the weight of the arm. As recent research has shown, arm support decreases the required shoulder abduction torques during two-dimensional reaching movements at shoulder height, subsequently causing a decrease in coupled elbow flexion, leading to an increase in the range of elbow extension [12, 13]. Using the gravity compensation device *Freebal* [14], similar results were found in a study examining maximal reaching distance during supported and unsupported three-dimensional reaching movements of stroke patients [15]. Regarding muscle activity, research in healthy persons showed that the application of gravity compensation facilitates movements by instantaneously reducing the amount of muscle activity needed for a reaching movement, particularly in muscles counteracting gravity [16]. Similar results were observed in a sample of chronic stroke patients with mild hemiparesis [17].

The facilitating influence of gravity compensation can be used to improve unsupported arm movements in stroke patients. Since gravity compensation has shown to instantaneously reduce the influence of abnormal synergies in cross-sectional studies, one can hypothesize that a long(er) term application has the potential to reduce the degree in which abnormal synergies affect unsupported arm movements of stroke patients. Several studies have shown that reach training using arm support can result in improved movement ability of the unsupported hemiparetic arm. After arm training using a passive exoskeleton to support the arm, motor status of the arm improved [18, 19]. This improvement was accompanied by an increased maximal reaching distance [18]. A training period with sling suspension also induced a modest improvement in motor status of the arm [20]. Although maximum reaching distance increased, little is known about the underlying mechanisms causing these beneficial results. It is still unclear whether a reduction of the impact of abnormal coupling is involved in those improvements of arm function.

Previous studies showed that abnormal coupling influences circle drawing performance. Due to synergistic movement constraints, elliptical instead of round shapes are produced by stroke patients during supported [21] and unsupported [22] circle drawing. After a period of robot-aided point-to-point arm movement training in a gravity-compensated environment, elliptical shapes drawn by a sample of 117 stroke subjects changed towards circular movements. Changes in supported circle drawing were due to reduced impact of abnormal coupling and a consequently more selective, or more isolated, control of shoulder and elbow movements [21].

3.2 Methods

Subjects

Subjects were recruited at rehabilitation centre 'Het Roessingh' (RCR) in Enschede, the Netherlands. Inclusion criteria were: 1) a history of a single unilateral stroke in the left hemisphere, resulting in a right-sided hemiparesis, 2) the onset of the stroke was more than six months (chronic phase) before the start of the intervention period, 3) ability to move the shoulder and elbow joint against gravity but unable to hold the joints against a combination of moderate resistance and gravity, and 4) adequate cognitive function to understand the experiments, follow instructions, and give feedback to the researchers. Subjects were excluded from this study if: 1) a fixed contracture deformity in the affected upper limb was present, 2) pain was a limiting factor for the subject's active range of motion, or 3) if they participated in other training experiments. All subjects provided written informed consent. The study was approved by the local medical ethics committee.

Gravity compensation training

Subjects received three half-hour gravity compensation training sessions per week for a period of six weeks, making a total of 18 sessions. To study the effect of gravity compensated rehabilitation training two baseline and one evaluation measurement were performed. Baseline measurements were performed two weeks prior to the start of the intervention period, spaced one week apart. Within one week after the last training session, subjects performed the evaluation measurement.

During a training session subjects practiced three-dimensional (3D), goal-directed arm movements in a gravity compensated, virtual reality (VR) augmented environment (see Figure 3.1). The weight of the subject's arm was (partially) counterbalanced by a gravity compensation system device named Freebal [14], providing a constant amount of support during natural 3D movements. The Freebal consists of two overhead slings connected to ideal spring mechanisms by wires. One sling supports the subject's arm at the elbow joint and one sling at the wrist. The Freebal allows easy and quick adjustment of the level of gravity compensation by altering the force which is applied to the slings by the spring mechanisms. If arm function improved, indicated by increasing scores of the FurballHunt game throughout the training, the supervising physical therapist decreased the level of gravity compensation to ensure a challenging and motivating training environment.

Figure 3.1: Training setup with FurballHunt and Freebal.

Virtual reality was delivered by a game named FurballHunt [23], in which the user has to chase away little birds, called Furballs [23]. During the game, Furballs fly from a birdhouse to a tree branch where they sit down, while the user holds the affected hand on a start button. The starting position of the user is with the upper arm along the trunk and the elbow bent approximately 90 degrees, with the hand on the start button at table height. The bird can be chased away by lifting the hand from the start button and moving the hand towards the bird, i.e. reaching forward at table height, and touch it. Motion capturing software detects arm movement by substraction of two consecutive images obtained from a commercially available webcam (Logitech Quickcam Messenger, Logitech Inc., Fremont, CA, USA) that is located above and aiming towards the screen that displays FurballHunt. Points are awarded to the user if a Furball is chased away within a certain time frame. The game was shown on a horizontally placed flat screen, which is mounted on an in height adjustable frame, see Figure 3.1. All training sessions were supervised by the same physical therapist, who decided when the difficulty level had to be increased, based on clinical experience. The level of gravity compensation was decreased with steps of approximately 10% when maximal scores of the FurballHunt game were approached. Throughout the training, reaching distance (i.e. location of the tree branches), training intensity (i.e. the number of Furballs) and the level of randomization of target sequence were increased, to maintain a challenging training environment for each user. The level of gravity compensation, the number of performed reaching movements and the level of target randomization were stored in a logbook by the trained physical therapist.

Procedures

All measurements were performed by one researcher, who was not involved in the training sessions. During evaluation measurements subjects performed an unsupported, i.e. without gravity compensation, circle drawing task at table height. Before movement execution, upper and forearm lengths were measured. Upper arm length was measured between the ventral tip of the acromion and the lateral epicondyle of the humerus. Forearm length was measured between the lateral epicondyle of the humerus and the third metacarpophalangeal joint. After measurement of the arm lengths, a non-actuated instrumented exoskeleton (Dampace [24]) to measure joint angles was attached to the upper and forearm and the wrist was immobilized with a splint. To minimize trunk and shoulder movement, subjects were strapped with a four point safety belt. Subjects were asked to perform a circular motion in the transversal plane, just above a tabletop, in a clockwise (CW) and counter-clockwise (CCW) direction. The order of direction has been randomized throughout the measurements. Subjects were instructed to draw five circles in each direction, as big and as round as possible. For the latter purpose template circles of different radii were shown on a tabletop. Movements were performed at a self selected speed while verbal encouragement was provided to the subjects throughout the experiment.

Measurements

During evaluation measurements, the upper extremity part of the Fugl-Meyer (FM) was assessed to clinically evaluate arm function. Joint angles of the shoulder and elbow were recorded with the instrumented exoskeleton [24]. Built-in potentiometers on three rotational axis of the shoulder joint allow measurements of upper arm elevation, transversal rotation, and axial rotation. Elbow flexion and extension were measured with a rotational optical encoder. Translations of the shoulder were measured with linear optical encoders. Signals from the potentiometers were converted from analog to digital (AD) values by a 16 bits AD-converter (PCI 6034, National Instruments, Austin, Texas). The rotational and linear optical quadrature encoders were sampled by a 32 bits counter card (PCI6602, National Instruments, Austin, Texas). Digital values were sampled with a sample frequency of 1 kHz, on-line low-pass filtered with a first order Butterworth filter with a cut-off frequency of 40 Hz and stored on a computer with a sample frequency of 50 Hz.

Data analysis

Because the focus of the present study is on proximal arm function, a subset of the upper extremity part of the FM scale consisting of items A_{II}, A_{III} and A_{IV} (max. 30 points) that reflect the ability to move the shoulder, elbow and forearm within and out of pathological synergies was addressed separately (FMp). Positions of the shoulder, elbow, and hand were calculated from the measured joint angles and arm lengths. To exclude contributions of shoulder and trunk movements to the size of the circles drawn by the subjects, the position of the hand relative to the position of the shoulder was calculated.

Active work area of the arm was represented by the area of the circles that was calculated as the area enclosed by the projection of the hand trajectory onto the table surface. The three largest circles in both directions (CW and CCW) were selected for further analysis. To compensate for differences in arm length among subjects, circle area is normalized (normA) to arm length by dividing circle area by the maximal circle area that is biomechanically possible. Circle area is considered maximal when the diameter of the circle equals the arm length of the subject.

A method [25] to calculate circle roundness was used to quantify circle morphology. In this method, circle roundness is defined as the quotient of the minor and major axes of a fitted ellipse, see Figure 3.2 for a graphical representation. This method was previously used to quantify preferred movement directions and circle roundness to evaluate gravity compensated reach training in a sample of chronic stroke survivors [21, 26].

Thoracohumeral joint angles were calculated from the measured joint angles according to the recommendations of the International Society of Biomechanics [27]. Orientation of the upper arm was represented by the plane of elevation (EP), elevation angle (EA) and axial rotation (AR), see Figure 3.3. Joint angles were offline filtered with a zero-phase shift, 2nd order Butterworth low-pass filter with a cut-off frequency of 10 Hz. Joint excursions were calculated as the range of each measured joint angle needed to draw one circle. To study the potential effect of gravity compensation training on elbow flexion and extension (EF) in more detail, maximal and minimal values of EF were calculated, besides the excursion.

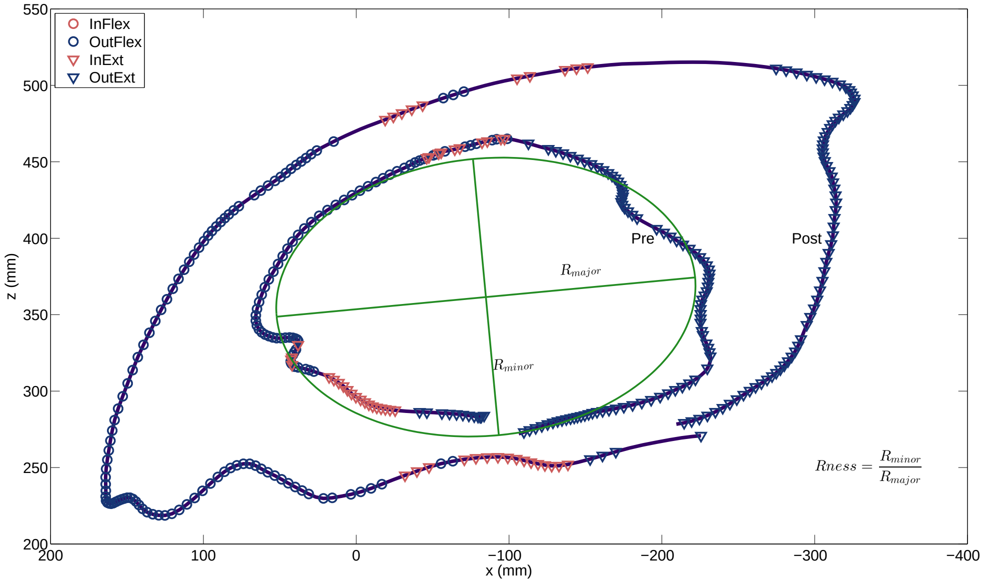

Figure 3.2: Typical example of circles drawn before (Pre) and after (Post) training. Roundness (Rness) is calculated as the quotient of the length of the minor axis (Rminor) and the major axis (Rmajor) of the fitted ellipse (green).

To study the potential role of abnormal synergies during circle drawing tasks, circles were divided into four combinations of shoulder abduction/adduction and elbow flexion/extension. Shoulder abduction/adduction was defined as decrease/increase of the elevation angle in the plane of elevation, as recommended by the International Society of Biomechanics [27], also see Figure 3.3. Flexion and extension synergies were identified, based on simultaneous changes in EA and EF according to the method described in [22]. Movement within the flexion synergy (InFlex) is defined as simultaneous shoulder abduction (EA $\downarrow$) and elbow flexion (EF $\uparrow$). Other synergistic patterns were defined in a similar way: movement within the extension synergy (InExt) is characterized by simultaneous shoulder adduction (EA $\uparrow$) and elbow extension (EF $\downarrow$); concurrent shoulder abduction (EA $\downarrow$) and elbow extension (EF $\downarrow$) represents movement out of the flexion synergy (OutFlex); shoulder adduction (EA $\uparrow$) and elbow flexion (EF $\uparrow$) indicate the ability to move out of the extension synergy (OutExt). All combinations were calculated as percentages of movement time. The remaining part indicates to which extent subjects performed single joint movements (SJMov). InFlex and InExt represented movement within a synergistic pattern (InSyn). The ability to

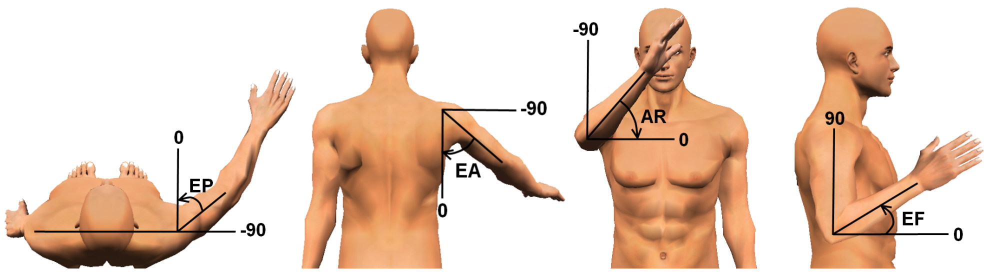

Figure 3.3: Visual representation of the joint angles of the upper arm. Arrows indicate positive rotations. EP = Elevation Plane, EA = Elevation Angle, AR = Axial rotation, EF = Elbow Flexion.

move out of a synergistic pattern (OutSyn) was calculated as the sum of OutFlex and OutExt. See Figure 3.2 for typical examples of circles drawn before and after training, and the occurrences of synergistic movement patterns.

Statistical analysis

Consistency of the data obtained during both baseline measurements was evaluated by calculation of the intraclass correlation coefficient (ICC) according a two-way mixed model. Outcome measures obtained during both baseline measurements were statistically tested by means of a Wilcoxon signed rank test to reveal a possible learning effect between both measurements. These initial analyses revealed some variation (ICC $\geq$ 0.43) in motor performance, but differences were not statistically significant (p $\geq$ 0.09) and no clear trend was visible. Since an equal number of datapoints is needed for pairwise comparison of outcome measures before and after training, data of both baseline measurements were averaged per subject and compared with the data obtained during the evaluation measurement. Data in the results section are reported as median and interquartile (25^{th} - 75^{th} percentile) range (IQR). Because of the small sample size, training effects were non-parametrically tested for significance by means of a related samples Wilcoxon signed ranks test. Spearman's correlation coefficients between outcome measures were calculated. Effects were considered statistically significant for $p < 0.05$.

3.3 Results

Subjects

A convenient sample of 59 patients who have received treatment at RCR were screened. From this group 22 were contacted. A total of 12 patients did not meet the inclusion criteria because of a fully recovered arm ($n = 3$), an a-functional arm ($n = 1$) or refused to participate because of time constraints ($n = 7$) and too high travelling costs ($n = 1$). Initially ten subjects participated in this study. One subject (S3) withdrew after two weeks of training because of a too high physical burden, mainly caused by the distance he had to cover travelling from his home to the rehabilitation centre. One subject (S6) had a cerebellar infarction while the other subjects experienced a first-ever ischemic stroke in the medial cerebral arteric region. One subject (S10) was not able to complete the evaluation tasks because of physical limitations. Data from these subjects were excluded from further analysis for reasons of incompleteness (S3 and S10) and heterogenity (S6). Demographic data at baseline of the remaining seven subjects are displayed in Table 3.1.

Table 3.1: Subject demographic and clinical characteristics at baseline.

Subject	*Gender*	*Dominance*	*Months PS*	*pre FM*	*pre FMp*
1	M	Right	58	12.0	6.0
2	F	Right	13	45.5	22.0
4	F	Right	27	10.0	4.0
5	F	Right	24	44.5	18.0
7	F	Right	39	45.5	17.5
8	F	Right	39	7.0	1.5
9	M	Right	8	25.5	13.5
Group	-	-	27 (15.8-39.0)	25.5 (10.5-42.3)	13.5 (4.5-17.9)

Abbreviations:
M = male, F = female, PS = post stroke, FM = Fugl-Meyer

Gravity compensation training

The level of gravity compensation and the training intensity throughout the training are graphically displayed in Figure 3.4. Two severely affected subjects (S8 and S9) were overcompensated at the beginning of the training. The level of gravity compensation decreased throughout the training in all subjects. The number of reaching movements per session increased in all subjects throughout the training.

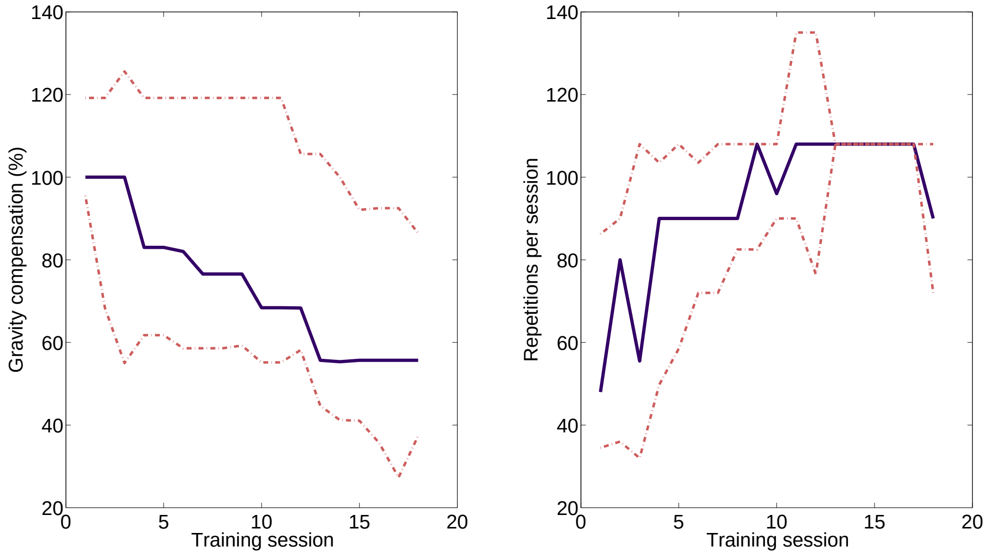

Figure 3.4: Level of gravity compensation in % of the arm weight (left) and training intensity (right) throughout the training. Blue solid lines are median values. Red dashed lines indicate 25^{th} and 75^{th} percentile.

Clinical evaluation

FMp scores before and after the training are graphically displayed in Figure 3.5. On group level a statistically significant ($p = 0.017$) median increase of 3.5 points on the FMp scale is noticed after six weeks of training. Four subjects showed an increase of more than 10 percent of the maximal value, i.e. 3 points, which is considered clinically relevant [28].

Circle metrics

After training all subjects were able to increase their normalized circle area, see Figure 3.6. Median normalized circle area increased from 3.3 (IQR: 1.5 – 4.9) % before training to 4.1 (IQR 2.1 – 6.7) % after training, which is statistically significant, $p = 0.018$.

Circle roundness did not change significantly, $p = 1.0$. After training, three

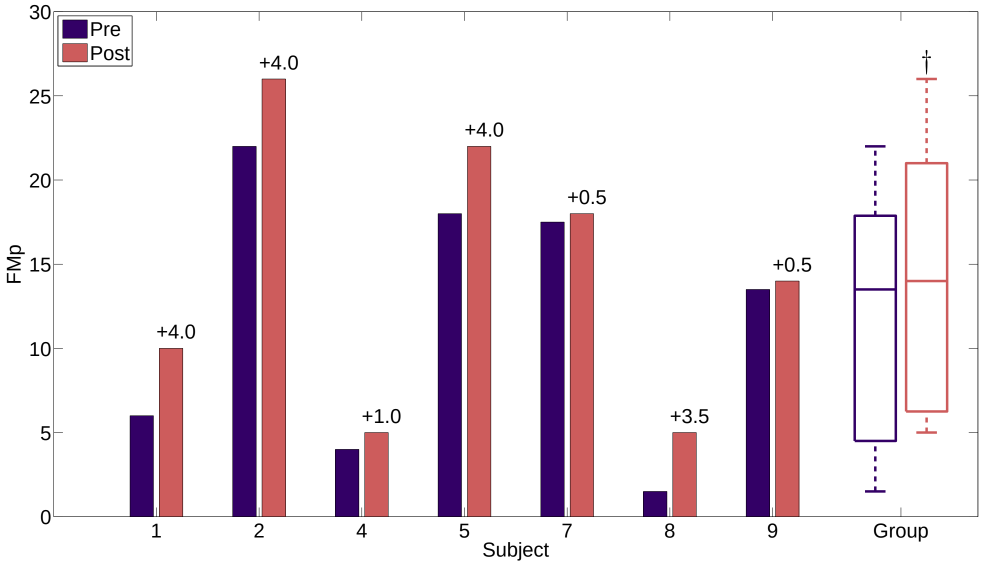

Figure 3.5: Scores of the proximal part of the upper extremity part of the Fugl-Meyer assessment (FMp) per subject and group before (Pre) and after (Post) training. Changes in FMp are displayed above the bars. †Indicates a statistically significant change.

subjects showed minor increases in circle roundness, whereas minor decreases in circle roundness were observed in four subjects. Median circle roundness was 0.30 (IQR: 0.22 – 0.43) during baseline measurements and 0.32 (IQR: 0.23 – 0.42) during the evaluation measurement. Changes in circle roundness are graphically displayed in Figure 3.7.

Joint excursions

Joint excursions of EA, EP, AR and EF before (pre) and after (post) training are graphically displayed in Figure 3.8. After training five subjects increased the range of EP and two subjects (S5 and S9) had similar excursions during baseline and evaluation measurements. On group level, median increase in EP was 7.5 (IQR: 3.1 – 13.9)° which was a statistically significant ($p = 0.043$) change.

Excursions in EA were bigger in six subjects after training compared to baseline values. One subjects (S8) had similar values of EA during baseline and evaluation measurements. On group level a small but statistically significant ($p = 0.028$) increase of EA excursion from 4.4 (IQR: 3.6 – 7.3)° to 5.9 (IQR: 4.1 – 10.1)° was noticed.

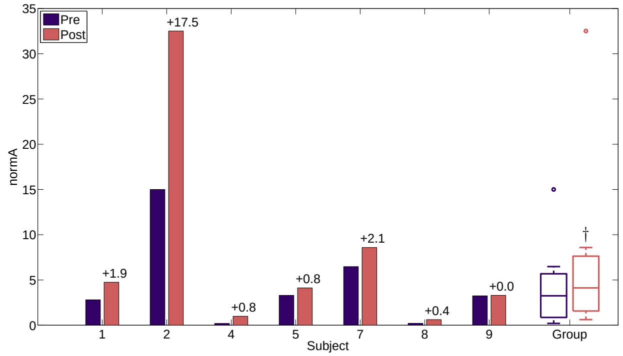

Figure 3.6: Normalized circle area (normA) per subject and group mean before (Pre) and after (Post) training. Changes in normA are displayed above the bars. †Indicates a statistically significant change.

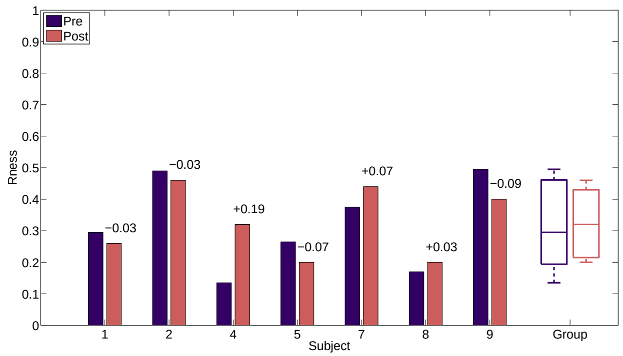

Figure 3.7: Roundness (Rness) of the circles drawn before (Pre) and after (Post) training.

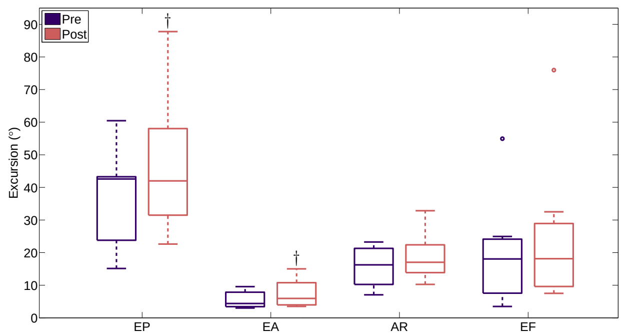

Figure 3.8: Joint excursions during circle drawing before (Pre) and after (Post) training. EP = Elevation Plane, EA = Elevation Angle, AR = Axial Rotation, EF = Elbow Flexion/extension. †Indicates a statistically significant change.

Small decreases in AR excursions were observed in three subjects (S1, S5 and S9) whereas the remaining four subjects increased their AR excursions after training. Group median AR excursion increased from 16.2 (IQR: 11.9 – 20.5)° before training to 17.0 (IQR: 13.9 – 22.2)° after training. This increase was not statistically significant, $p = 0.237$. Six subjects increased EF excursion after training, whereas one subject showed a small decrease. Median EF excursion increased from 18.0 (IQR: 8.8 – 23.3)° before training to 18.1 (IQR: 10.6 – 25.4)° after training. This increase was not statistically significant, $p = 0.091$. Maximal elbow extension (i.e. minimal EF, see Figure 3.3) increased in 5 out of 7 patients. The median change was -1.7 (IQR: -6.6 – -0.5)° which was not statistically significant, $p = 0.128$. Maximal elbow flexion increased in 5 out of 7 patients with a non significant ($p = 0.398$) median change of 1.1 (IQR: -0.6 – 0.2)°.

3

Synergistic movement patterns

The occurrence of synergistic movement patterns during circle drawing before and after training is graphically displayed in Figure 3.9. During baseline measurements median InSyn was 35.0 (IQR: 11.3 – 45.9) % of the movement time. Median OutSyn was 56.4 (IQR: 39.1 – 81.9) % of the movement time. During the remaining 8.7 (IQR: 7.9 – 12.3) % of the movement time at most one joint moved. During evaluation measurements group median InSyn was 27.9 (IQR: 18.8 – 41.9) %, OutSyn 59.0 (IQR: 43.8 – 67.1) % and SJMov was 13.1 (IQR: 11.3 – 14.8) %. Changes in InSyn, OutSyn and SJMov were not statistically significant ($p > 0.310$).

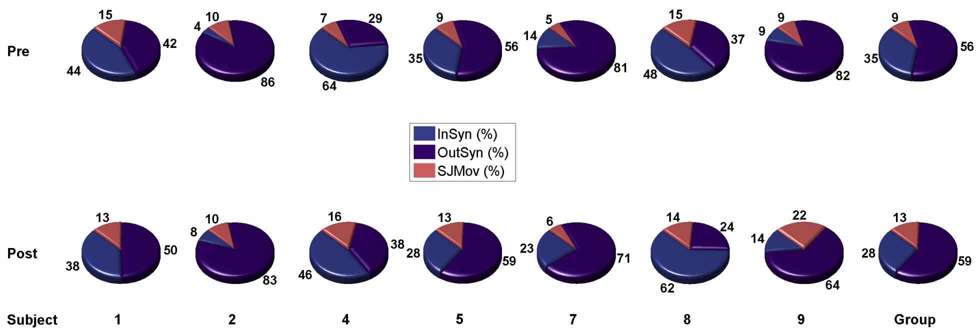

Figure 3.9: Occurence of synergistic movement patterns before (Pre) and after (Post) training.

Correlation between training parameters and outcome measures

The strongest correlations were between the decrease in gravity compensation and change in FM ($\rho = -0.54, p = 0.22$) and change in normA ($\rho = -0.61, p = 0.22$). Training parameters such as the decrease of the level of gravity compensation and increase of training intensity were not significantly correlated to outcome measures ($p \geq 0.10$). Between other outcome measures the only statistically significant correlation has been found between changes in EF and normA ($\rho = 0.82, p = 0.023$).

3.4 Discussion

In this study changes in unsupported arm movements, induced by gravity compensation training, and the impact of abnormal coupling on arm movements in chronic stroke patients were studied by means of a circle drawing task [22]. After 6 weeks of moderately intense gravity compensated reach training, a sample of 7 chronic stroke patients showed improved arm function, as indicated by a median increase of 3 points on the FM scale. Subjects also significantly increased the active work area of the hand as indicated by the normalized circle area, whereas circle roundness remained almost constant. Statistically significant changes were observed in excursions of EP and EA, accompanied by increasing trends in excursions of AR and EF. The occurrence of synergistic movement patterns was similar before and after training.

The effect of abnormal coupling between shoulder and elbow movements on circle roundness was previously studied by Dipietro et al. [21]. Roundness of the circles drawn in the present study before training (mean $\pm$ SD 0.32 $\pm$ 0.14) was lower compared to the roundness of circles (mean 0.51) drawn in the study by Dipietro et al., despite a less severe patient group in the present study, as indicated by a higher FM score (FM = 27.1 and 20.5 respectively). This discrepancy is most likely related to the level of arm support during evaluation measurements. Dipietro et al. evaluated circle drawing while the subject's arm was supported against gravity, while in the present study unsupported circle drawing was evaluated. Application of gravity compensation has been shown to reduce the influence of abnormal coupling between the shoulder and elbow [15, 29] which is likely to result in rounder circles.

After robot-assisted, gravity compensated point-to-point reach training Dipietro et al. found an average increase in roundness of 0.10 [21, 26]. The increase in roundness was the result of increasing minor axis of the fitted ellipse, while the major axis remained constant. In the present study, roundness remained similar before and after training, while the normalized circle area increased, i.e. both minor and major axes increased. A possible explanation for this discrepancy is a difference in training method. In both studies the arm was supported against gravity. However, in Dipietro et al. subjects who were not able to reach a target were assisted by the robot to complete the movement task, as well. Although recent reviews [30, 31] that addressed technology supported arm training could not discern whether or not certain training modalities are more effective than others, it may be that differences in training modalities influenced roundness of the circles. A second explanation is related to the nature of the movement task that was assessed during evaluation measurements. In the study by Dipietro et al. subjects were asked to draw a copy of a template circle with a fixed radius of 14 cm. In the present study, subjects were asked to draw circles as big and as round as possible, during both evaluation measurements before and after the training period. As confirmed by the circle metrics, the focus of most subjects in the present study was in increasing circle area at the expense of increasing roundness.

Horizontal circle drawing can be seen as a continuous reaching task in the medio / lateral and forward / backward direction. Previous studies showed that gravity compensation training led to increased range of motion of the impaired arm as represented by increased maximal unsupported reach distance [13, 18, 19]. Ellis et al. [32] observed increased work area at various limb loadings after point-to-point reach training during which the level of arm support decreased progressively. Increased range of motion during unsupported arm movements was also found in the present study, as indicated by an increased normalized circle area after training.

Dipietro et al. [21] observed that the elliptical shapes drawn by stroke patients became rounder throughout the robot-assisted training period because the minor axis of the ellipse increased while the major axis of the ellipse remained almost constant. It was concluded that existing coupling between the shoulder and elbow joint remained after robot-aided reach training, but that the strength of the coupling decreased, which led to more selective control of the shoulder and elbow joint, as indicated by a lower correlation between shoulder horizontal ab-/adduction and elbow flexion/extension.

Although roundness and the occurrence of synergistic movement patterns were comparable before and after training in the present study, the changes in work area present some indications that a reduced impact of abnormal coupling may play a role in improved arm function. The improved ability to move the shoulder, in combination with a slight increase in elbow flexion and extension resulted in an increased circle area. However, when elbow extension is increased, i.e. the hand is moved away from the torso, higher muscle activations in the shoulder and elbow joint are needed to hold the arm against gravity, and stabilize the joints [33]. Consequently, these higher abduction torques will induce an increased amount of involuntary elbow flexion [9, 10, 13]. In other words, it is possible that stroke patients increased their work area because of a decreased impact of abnormal coupling between shoulder and elbow, but that the higher shoulder abduction torques needed to perform the movement task, again provoke an abnormal coupling at the elbow, resulting in similar amounts of movement within/out of synergistic patterns and consequently a proportional increase in both the major and minor axes of the fitted ellipse before and after training. A possibility to increase insight into the mechanisms involved in improving post stroke arm function, is to combine the circle drawing task used in the present study, in which patients maximize circle area, with a circle tracking task in which the size of the circles remains constant. With this second circle drawing task, the effect of synergistic movement patterns on circle shape can be studied, without the effects of increases in shoulder abduction torques that are needed to draw bigger circles. Differences in occurrence of synergistic movement patterns are likely to result in changes of circle area and roundness [21, 22].

Besides involuntary coupling between the shoulder and elbow joint, many stroke patients also have to deal with muscle weakness [34] and/or strength imbalances across joints [35]. It is possible that patients strengthen their muscles during training, improve their temporal muscle activation or muscle coordination in general. To illustrate this, in the same sample of stroke patients, increased activity of agonist muscles during a maximal forward reaching task was observed after training [36]. This increased agonist muscle activity can be a result of increased ability to selectively activate agonist muscles, or improved control of agonist muscles. More research regarding changes in muscle activation patterns or changes in maximal voluntary torques (MVT) is needed to study the working mechanisms involved in changes of arm function after gravity compensated reach training.

Limitations and recommendations

The present findings show that reach training with a low-cost arm support system and a low-tech computer game is able to improve hemiparetic arm function in a sample of chronic stroke patients. The reported increases in FM scores are comparable with interventions using more advanced training systems [30]. Nevertheless, results of the present study should be interpreted carefully, because of the small sample size of the study and the absence of a control group. Because of the small number of participants, it was not possible to subdivide the subjects into subgroups with different levels of stroke severity, to study potential differences in effects of gravity compensated reach training on hemiparetic arm function.

Since all subjects who participated were in the chronic phase after stroke, it may me be that subjects learned to avoid using the impaired arm [37]. It is not known whether improvement in hemiparetic arm function is due to improved neuromuscular control induced by the training, or by overcoming possible learned nonuse of the impaired arm. Inclusion of a control group in future research can yield information to what extent both processes occur.

Further research with larger and more homogeneous samples of stroke patients is needed to increase insight in the physiological mechanisms involved in the training induced changes in arm function, for example by studying training induced changes in muscle activation patterns.

Clinical implications

The present study indicates that a moderately intense training program consisting of gravity-compensated point-to-point reach training within a VR augmented training environment can lead to increased work area of the hemiparetic arm in a sample of mildly to severely affected chronic stroke patients. Results concerning the underlying mechanisms causing these changes point towards a less pronounced influence of synergistic movement patterns, although more research is needed for further elucidation. The used training setup is simple and affordable and is therefore suitable to be deployed in clinical settings.

3.5 Conclusions

Gravity compensated goal-directed reach training led to increased work area of the hemiparetic arm in a sample of 7 chronic stroke patients, as indicated by significantly increased normalized circle area. Circle roundness and the occurrence of synergistic movement patterns remained similar after the training period despite increased joint excursions of the shoulder and the elbow joints. A decreased strength of involuntary coupling between shoulder and elbow movements might play a role in increased arm function after gravity compensated reach training, but more research, specifically addressing muscle activation patterns, is needed to further elucidate the mechanisms involved in post stroke rehabilitation training. Inclusion of a circle tracking task besides the used maximal circle drawing task is helpful to study synergistic movement patterns in future research. Although training intensity was relatively low, improvement in arm function was achieved with the use of simple and affordable equipment that is suitable to deploy in clinical settings.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TK performed the design of the study, acquisition and analysis of data and drafting of the manuscript. BM assisted during acquisition of the data. AS developed and built the gravity compensation system. JR, JB and MJ were involved in interpretation of results and critical revision of the manuscript for important intellectual content. JB was also involved in conception and design of the study. GP was involved in design of the study, acquisition and interpretation of data, drafting of the manuscript and critical revision of the manuscript for important intellectual content. All authors have read and approved the final manuscript.

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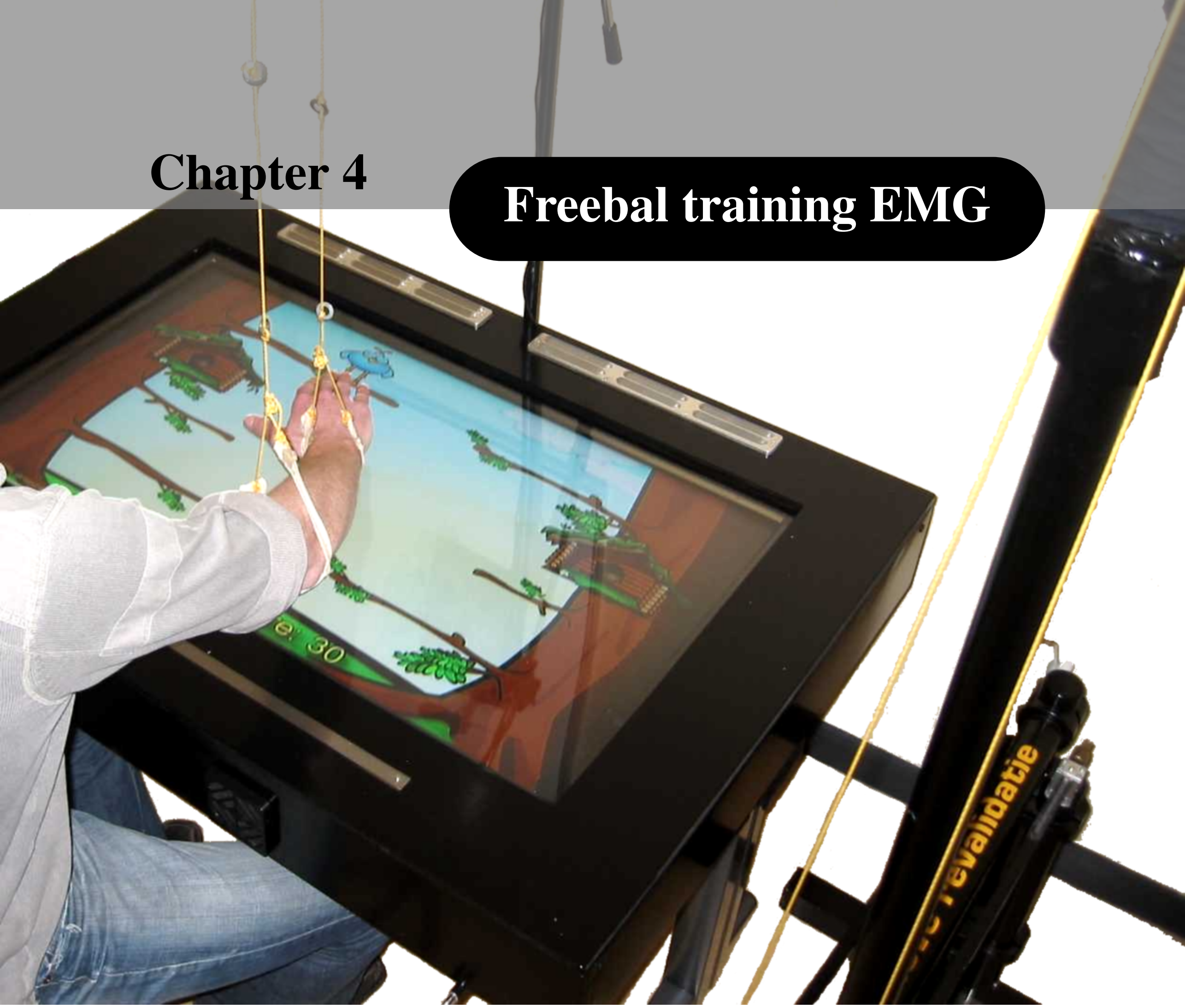
Chapter 4

Freebal training EMG



Changes in muscle activation after reach training with gravity compensation in chronic stroke patients.

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Abstract

Objectives

The objective of this study is to examine the effect of gravity compensation training on reaching and underlying changes in muscle activation.

Methods

In this clinical trial, eight chronic stroke patients with limited arm function received 18 sessions (30 min) of gravity-compensated reach training (during 6 weeks) in combination with a rehabilitation game. Before and after training, unsupported reach (assessing maximal distance, joint angles and muscle activity of eight shoulder and elbow muscles) and the Fugl-Meyer assessment were compared.

Results

After training, the maximal reach distance improved significantly by 3.5 % of arm length, together with increased elbow extension (+9.28 °) and increased elbow extensor activity (+ 68 %). In some patients, a reduced cocontraction of biceps and anterior deltoid was also involved, although this was not significant on group level.

Conclusions

Improvements in unsupported reach after gravity compensation training in chronic stroke patients with mild to severe hemiparesis were mainly accompanied by increased activation of prime movers at the elbow, although in some patients, improved selective joint control may also have been involved. Gravity compensation seems to be a suitable way to provide active, task-specific treatment, without the need for high-tech devices. Further research on a larger scale, including control groups and combinations of arm support with functional hand training, is essential to enhance the potential of arm support to complement poststroke arm rehabilitation.

4.1 Introduction

At least 90 % of stroke survivors have to cope with limitations in arm function, often compromising activities of daily life [1]. After a stroke, the ability to activate and contract muscles appropriately for a motor task is often impaired [2, 3]. An involuntary, abnormal coupling of predominantly shoulder abduction and elbow flexion exists as well [4], limiting the selectivity of movements.

To stimulate the restoration of hemiparetic arm function, a training program should incorporate motivating, taskspecific exercises involving active initiation and execution of functional tasks at a high intensity [5, 6, 7]. A promising intervention to provide these key aspects is the application of robotic devices [8, 9]. However, it is not clear which aspects of such robot-aided approaches are major contributors to improved arm function [8]. A basic aspect incorporated into the design of most robotic devices is arm support [10].

When the arm is supported during two-dimensional planar reach, the amount of shoulder abduction needed to lift the arm is decreased by arm support, simultaneously reducing involuntary elbow flexion torques, enabling larger elbow extension than during unsupported reach [11]. In terms of more functional three-dimensional reaching movements using the Freebal device for arm support [12], we found an increase in the range of motion (ROM) with gravity compensation as well [13, 14].

When gravity compensation is applied as a training intervention during a longer period of time, arm movement ability without any support increases [15, 16], suggesting the potential benefit of application of gravity compensation as an intervention in stroke rehabilitation. It is expected that a reduced expression of involuntary intermuscle coupling between shoulder abductors and elbow flexors plays a role, but the specific mechanisms involved in these improvements have not be determined so far.

Therefore, the aim of the present explorative study is to examine the effect of gravity compensation training on reaching and underlying changes in muscle activation.

4.2 Methods

Patients

Ten stroke patients were recruited from a local rehabilitation centre who fulfilled the following inclusion criteria: (a) a single unilateral stroke in the left hemisphere; (b) more than 6 months since stroke; (c) limited shoulder and elbow movement ability; (d) movements not limited by pain or other orthopaedic or neuromuscular deformities; and (e) ability to follow instructions. All patients provided written informed consent. The study was approved by the local medical ethics committee.

Gravity compensation training

Patients received 18 sessions of 30-min gravity compensation training over a period of 6 weeks (three sessions per week). A trained physical therapist supervised all sessions. The training consisted of goal-directed reaching movements with gravity compensation in a virtual gaming environment (see Figure 4.1). The weight of the patient's arm was counterbalanced by the Freebal device, designed to provide adjustable gravity compensation during threedimensional movements through ideal spring mechanisms [12].

Figure 4.1: Gravity compensation device *Freebal* and virtual gaming environment *FurballHunt*.

In the virtual gaming environment, FurballHunt, patients had to chase away birds from a tree branch by reaching for them with their hand; the faster the birds were chased, the more points were awarded [17]. The game was displayed on a horizontally placed television screen, above which arm movements were detected using a webcam and identified by motion-capturing software. One therapist was involved in the training of all participants, who was instructed to encourage and provide feedback in the same way as in regular treatments. Starting from 100 % compensation of arm weight, the physical therapist decreased the level of gravity compensation stepwise by approximately 10 % each time the maximal scores on the FurballHunt game were approached consistently throughout one game session.

Evaluation

Changes in arm movement performance were evaluated before (on two occasions within 2 weeks) and after training (within 1 week) by researchers blinded to the progress of training. Initial analysis of the data obtained during the two pretraining evaluations showed no clear trend in the baseline outcome. Therefore, pretraining data of the two sessions were averaged per patient.

Changes in movement performance and muscle activation were evaluated during an unsupported maximal reaching movement to a target placed beyond arm's length in front of the acromion of the hemiparetic arm at elbow height (in the sagittal plane). To minimize trunk and shoulder movements, the patient was strapped to the chair with a fourpoint safety belt. The starting position of patients during the reaching task was with the upper arm aligned with the trunk and the forearm pointing straight forward. Each patient was instructed to perform five reaching movements as far forward as possible at a comfortable speed.

In addition, the upper extremity part of the Fugl-Meyer assessment (a maximal score of 66 points indicates fully selective movements) was evaluated before and after training to represent the general motor status of the hemiparetic arm [18].

Measurements

During the maximal reach task, bipolar surface electromyography (EMG) was recorded from eight muscles, according to Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles (SENIAM) guidelines [19]. EMG signals of biceps (BIC), long and lateral head of triceps (TILO and TILA), anterior deltoid (AD), posterior deltoid (PD), the upper part of pectoralis major (PEC), lattissimus dorsi (LD) and the upper trapezius (TRA) were recorded at a sample frequency of 2048 Hz, band-pass filtered (second-order zero phase shift Butterworth, cut-off frequencies 10 – 400 Hz) and converted into smooth rectified electromyography (SRE) signals (using a low-pass second-order zero phase shift Butterworth filter at 25 Hz for smoothing).

Joint angles of the arm were defined according to the recommendations of the International Society of Biomechanics [20], and recorded using an instrumented, passive exoskeleton device, Dampace [21]. Angular sensors measured transversal rotation [shoulder plane of elevation (SP): angle of humerus with a virtual line through shoulders; the humerus pointing straight forward represents 0 ° and pointing laterally -90 °], upper arm elevation [shoulder angle of elevation (SE): angle between the humerus and the trunk in the plane of elevation; the humerus aligned with the trunk represents 0 °] and elbow flexion and extension (E; the upper arm fully extended represents 180 °). Joint angles were sampled at 1000 Hz, low-pass filtered (first order Butterworth filter, cut-off frequency 40 Hz) and stored on a computer with a sample frequency of 50 Hz.

From these data, joint and hand positions were calculated, using segment lengths of the upper arm (between the acromion and the lateral epicondyle of the humerus) and the forearm (between the lateral epicondyle of the humerus and the third metacarpophalangeal joint).

Data analysis

The position of the hand was calculated relative to the position of the shoulder to exclude any shoulder and trunk movements from the reaching movements. The maximal distance between the acromion and the third metacarpophalangeal joint represents the maximal reach distance and the distance travelled by the hand from the start to the end of reach represents the range of reach (cm), also expressed as percentage of arm length. Movement velocity of the hand (cm/s) was also calculated. Minimal and maximal joint angles at the start and the end of reach were used to determine ROMs of the shoulder and elbow (°) during reach.

EMG and kinematic data were displayed synchronously and of the five repetitions, data from the three furthest reaches were averaged. The duration of the reaching movement was determined by identifying minimal (start of reach) and maximal (end of reach) elbow joint angles and expressed as 100 %, to account for intrasubject and intersubject variations. A typical example is shown in Figure 4.2. After an initial qualitative inspection of muscle activation patterns, the level of muscle activity was quantified by calculating the mean SRE value during the averaged reaching movement for each muscle. Cocontraction ratios (CC) were calculated to examine individual intermuscle coupling between BIC and TILA, BIC and TILO, PD and AD, and BIC and AD:

$$CC = \frac{\overline{SRE}_{antagonist}}{\overline{SRE}_{agonist}} \tag{4.1}$$

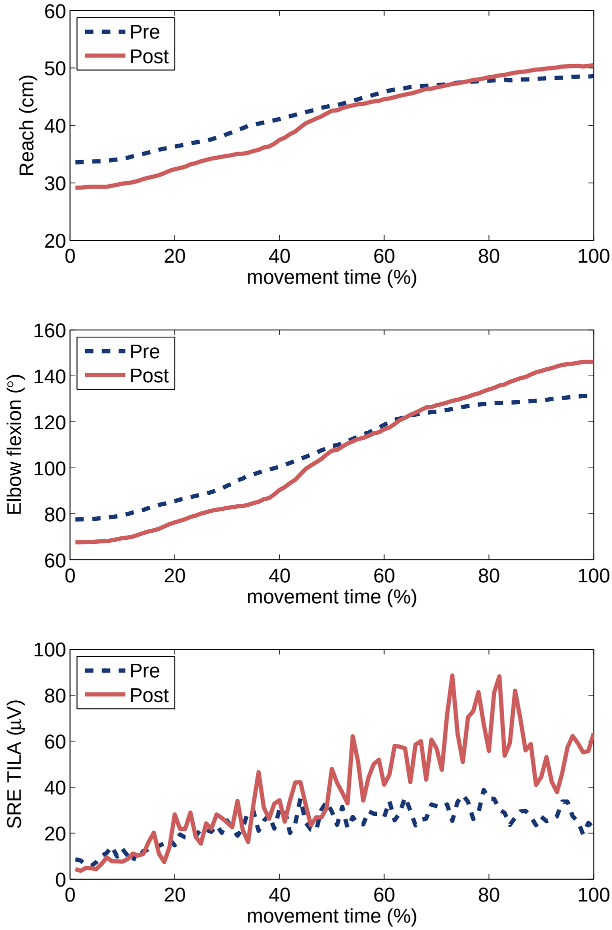

Figure 4.2: Typical example (S2) of reach distance, elbow extension and muscle activity of TILA before (dotted lines) and after (solid lines) gravity compensation training. SRE, smooth rectified electromyography; TILA, lateral head of triceps.

Table 4.1: Subject characteristics and changes in Fugl-Meyer (FM) scores after training.

S	*Sex*	*Age (yr)*	*Months PS*	*Stroke type*	*AS*	*DS*	*pre FM**	*post FM*	*Δ FM*
1	M	53	58	ischemic MCA	R	R	12.0	20	+ 8.0
2	F	72	13	ischemic MCA	R	R	45.5	53	+ 7.5
4	F	55	27	ischemic MCA	R	R	10.0	11	+ 1.0
5	F	53	24	ischemic MCA	R	R	44.5	51	+ 6.5
6	M	62	30	ischemic cerebellar	R	R	61.0	64	+ 3.0
7	F	64	39	ischemic MCA	R	R	44.5	47	+ 1.5
8	F	69	39	ischemic MCA	R	R	7.0	10	+ 3.0
9	M	55	8	ischemic MCA	R	R	25.5	21	− 4.5

* average value of the first two baseline measurements

Abbreviations:
S = subject, M = male, F = female, yr = years, PS = post stroke, FM = Fugl-Meyer
MCA = medial cerebral artery region, AS = affected side, DS = dominant side

Statistical analysis

Differences between the pretraining and the post training measurements were tested for significance using a pairedsamples t-test for Fugl-Meyer and movement performance parameters. Changes in SRE and cocontraction ratio were determined using the nonparametric Wilcoxon signed ranks test, as muscle activation data were not normally distributed. For all tests, the significance level was 0.05.

4.3 Results

Ten chronic stroke patients were included in the present study; one patient did not complete the training period because of time constraints (S3). Another patient had to be excluded from analyses because of inability to perform the reach task correctly (S10). Of the remaining eight chronic stroke patients (Table 4.1), two stroke patients (S1 and S2) continued to receive additional general physical therapy in the community. The initial severity of stroke ranged from 7 to 61 points on the Fugl-Meyer score.

The amount of gravity compensation was decreased over the 6 weeks of training in all patients, although this varied between patients from -10 % (in S4) to -100 % (in S2), depending on the initial severity of the stroke and the degree of progress.

After 6 weeks of gravity compensation training (see Table 4.1), the average increase in the Fugl-Meyer score was 3.3 (SD 4.1) points, approaching significance

($p = 0.061$). In three patients (involving mild, moderate and severe hemiparesis), the increase in Fugl-Meyer was substantial (≥ 6.5 points).

Self-selected movement speed was largely unchanged after gravity compensation training ($p = 0.828$), with an average movement speed of 5 cm/s. The average maximal reach distance (see Table 4.2) increased significantly by 2.4 cm (SD 2.9) ($p = 0.049$), corresponding with 3.5 % of arm length. The total range of reach increased by 3.1 cm (SD 4.0) ($p = 0.065$).

Table 4.2: Reach distance before and after training.

	*Max reach (%)**			*ROM reach (%)**		
Subject	*pre*	*post*	Δ	*pre*	*post*	Δ
1	54.5	55.6	+ 1.1	30.6	35.9	+ 5.3
2	80.2	83.8	+ 3.6	79.2	91.2	+ 12.0
4	44.0	40.1	– 3.9	32.8	31.0	– 1.8
5	83.8	85.3	+ 1.5	68.1	65.8	– 2.3
6	91.6	93.6	+ 2.0	97.9	101.9	+ 4.0
7	69.3	77.6	+ 8.3	53.4	66.9	+ 13.5
8	47.0	55.6	+ 8.6	32.9	42.6	+ 9.7
9	72.1	79.3	+ 7.2	51.5	50.4	– 1.1
Mean ± SD (%)	67.8 ± 17.6	71.4 ± 18.6	+ 3.5 ± 4.3	55.8 ± 24.4	60.7 ± 25.7	+ 4.9 ± 6.3
Mean ± SD (cm)	45.6 ± 12.8	48.0 ± 13.6	+ 2.4 ± 2.8	37.3 ± 16.1	40.4 ± 16.4	+ 3.1 ± 4.1

* Reach distance is represented as percentage of arm length, except for mean values displayed in cm in the bottom row

Abbreviations:

ROM = range of motion, SD = standard deviation

In terms of accompanying changes in joint angles (see Figure 4.3), a significant increase in E ROM of 9.21 (SD 3.6) was found ($p = 0.037$). In addition, the upper arm was held in a more forward-directed position, represented by a larger SP of 8.71 (SD 7.8) ($p = 0.016$).

Changes in the SRE values after training (see Figure 4.4) were most pronounced in agonists. TILA activity increased significantly by 21.6 µV (SD 26.3), corresponding to an increase of 68 % in the pretraining SRE values ($p = 0.050$). TILO activity increased by 9.1 µV (SD 12.8) or 35 % ($p = 0.069$). Increases in AD activity were less pronounced with 9.6 µV (SD 19.7) or 20 % ($p = 0.161$).

All cocontraction ratio combinations decreased after training, but none of these changes reached significance ($p \geq 0.123$). Remarkably, the changes in $CC_{BIC/AD}$ varied largely between patients, with a substantial reduction (between -0.27 and -1.38) in four patients (of whom two had severe, one had moderate and one had mild

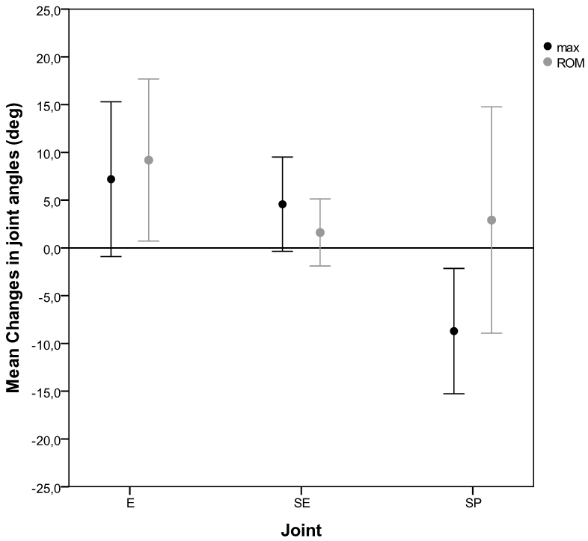

Figure 4.3: Changes in maximal and range of joint excursions after training (± 95 % confidence interval). E, elbow flexion and extension; Max, maximal; ROM, range of motion. Joints: SE, shoulder angle of elevation; SP, shoulder plane of elevation.

hemiparesis), an increase in two patients and no substantial change in two other stroke patients.

4.4 Discussion

In the present study, improvements in unsupported reaching movements after gravity compensation training were accompanied by an increased range of elbow extension. These findings are in agreement with the results of studies applying other types of arm support, in which unsupported reaching distance increased (by 3.2 and 2.8 cm, respectively) after training with a passive exoskeleton instrumented with elastic bands (T-WREX), suggesting an improved selectivity in shoulder and elbow movements [15, 16].

This is expected to be related to a reduced abnormal coupling between shoulder elevation and elbow flexion [11]. However, our findings on changes in muscle activity suggest that another mechanism is involved. Improvements in reach performance after gravity compensation training were accompanied by more pronounced muscle activity of the prime movers, without significant changes in the cocontraction ratio of muscles

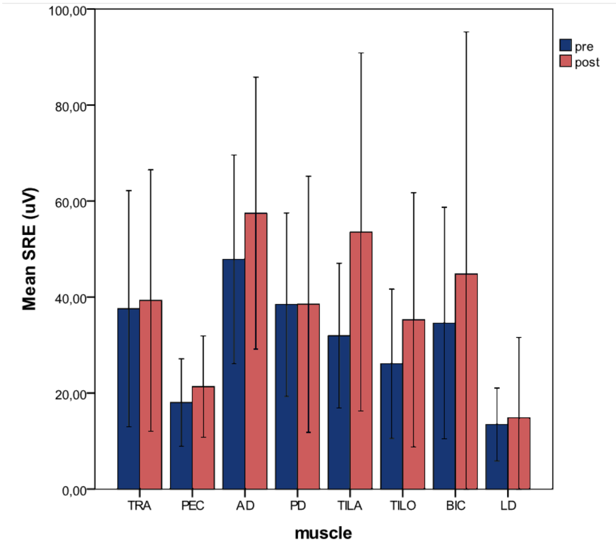

Figure 4.4: SRE values (± SD) per muscle before (light bars) and after (dark bars) training. AD, anterior deltoid; BIC, biceps; LD, lattissimus dorsi; PD, posterior deltoid; PEC, pectoralis major; SRE, smooth rectified electromyography; TILA, lateral head of triceps; TILO, long head of triceps; TRA, upper trapezius.

acting at either single or multiple joints. Especially BIC and AD are expected to act together in abnormal synergies after stroke [22]. Remarkably, on an individual level, coactivation of BIC and AD did show substantial reductions in some patients, but this varied widely across patients.

These findings suggest that improved reaching after gravity compensation training was mainly related to an improved ability to activate prime movers, although a reduced abnormal coupling may also be involved in some patients. These findings do not fully support expectations from previous research proposing a reduction of abnormal coupling between the shoulder and the elbow as a main underlying mechanism of the impact of arm support [11]. This discrepancy may be related to the functional, submaximal nature of the movement task applied in the present study, to comply with arm use in daily life. The reaching movement in the present study did not require as much shoulder elevation torques as in the studies by Beer et al. [4, 11]. As involuntary coupling at the elbow increases with increasing shoulder elevation torques [23], less shoulder elevation during reaching may have resulted in a reduced contribution of involuntary coupling to reaching performance in the group of stroke patients in the present study.

Both limited selective joint control [24] and increased agonist activation [25] have been identified separately as a major contributor to functional reach impairments after stroke. In a study investigating arm movements that were very similar to the functional movements in the present study, improved reach performance during the first months of recovery from stroke was not related to reduced cocontraction ratio, but predominantly to improved agonist coordination and contraction [25]. This underlines the indication from the present study that improved voluntary control of elbow extension can play an important role in improved reach performance, besides improved selectivity of movement in some patients.

A study comparing sling suspension training with robotaided therapy using the Gentle/S system showed no advantage of the use of robotics over arm support [26]. Moreover, the pooled amount of improvement after robot-aided therapy [8] is in the same order as the increase in the Fugl-Meyer score after arm support training in this and other studies [15, 16]. This suggests that the application of arm support alone may provide a simple and relatively inexpensive way to complement poststroke arm rehabilitation, especially in comparison with robot-aided therapy.

Despite this potential of gravity compensation, the improvements in motor status are relatively small, which questions whether transfer to functional abilities will take place. This is a problem observed for many exercise therapy approaches in stroke rehabilitation [27], including robot-aided therapy [8, 9]. A way to enhance this is to incorporate hand training [28], by integrating arm support for the proximal arm with functional hand training, to stimulate functional abilities as much as possible.

Because of the explorative nature of the present study, involving a limited number of stroke patients, the findings should be interpreted carefully. First, it is not possible to attribute the increased agonist activation during functional reach solely to the application of gravity compensation, as a potential effect of an increase in the overall training intensity cannot be discerned. Stroke patients in the chronic phase may have learned to avoid the use of their affected arm, which is reversed to a certain extent during gravity compensation training. In addition, two of the three patients with the largest Fugl-Meyer increases continued to receive additional physical therapy in the community throughout the study, which may have biased the results of those patients to some extent, even though their therapy schedule remained as usual throughout the study period. Furthermore, a potential impact of the gaming environment cannot be discerned from the gravity compensation in the present study. These issues should be taken into account in future research by including control groups receiving training in equal intensity.

In conclusion, this study provided an insight into two mechanisms involved in the impact of armsupport training after stroke: increased elbow extensor activation and reduced abnormal coupling between shoulder elevators and elbow flexors in some cases. Gravity compensation seems to be a suitable way to provide active and taskspecific treatment of the arm. Especially in combination with a gaming environment, it enables more independent training by a patient him/herself, allowing alleviation of the amount of one-to-one supervision by a therapist. These considerations should be further researched in terms of the potential of gravity compensation training for more functional and independent training after stroke, especially when the hand can be incorporated into such a low-tech application of rehabilitation technology.

Acknowledgements

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Conflicts of interest

There are no conflicts of interest.

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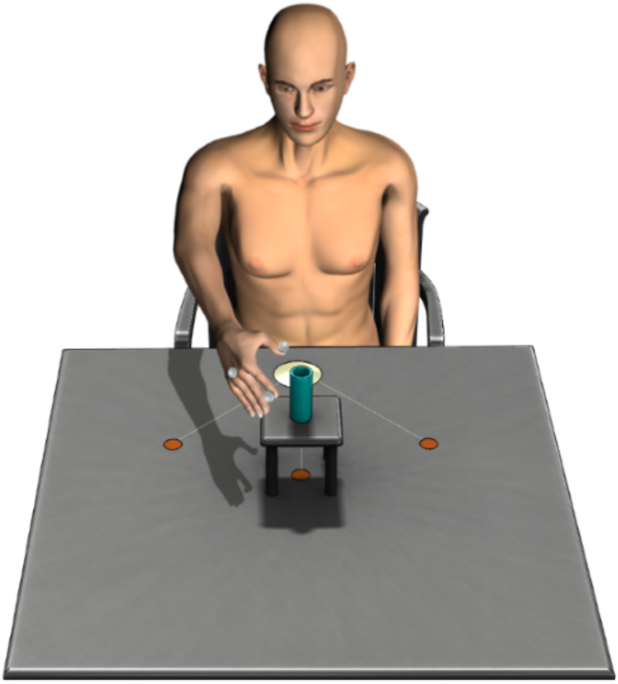
Chapter 5

EMG burst detection



Application of the Teager Kaiser Energy Operator in an autonomous burst detector to create onset and offset profiles of forearm muscles during reach-to-grasp movements.

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Abstract

Objectives

The primary aim of this study is to investigate the potential benefit of the Teager Kaiser Energy Operator (TKEO) as data pre-processor, in an autonomous burst detection method to classify electromyographic signals of the (fore)arm and hand. For this purpose, optimal settings of the burst detector, leading to minimal detection errors, need to be known. Additionally, the burst detector is applied to real muscle activity recorded in healthy adults performing reach-to-grasp movements.

Methods

The burst detector was based on the Approximated Generalized Likelihood Ratio (AGLR). Simulations with synthesized electromyographic (EMG) traces with known onset and offset times, yielded optimal settings for AGLR parameters *window width* and *threshold value* that minimized detection errors. Next, comparative simulations were done with and without TKEO data pre-processing. Correct working of the burst detector was verified by applying it to real surface EMG signals obtained from arm and hand muscles involved in a sub-maximal reach-to-grasp task, performed by healthy adults.

Results

Minimal detection errors were found with a window width of 100 ms and a detection threshold of 15. Inclusion of the TKEO contributed significantly to a reduction of detection errors. Application of the autonomous burst detector to real data was feasible.

Conclusions

The burst detector was able to classify muscle activation and create Muscle Onset Offset Profiles (MOOPs) autonomously from real EMG data, which allows objective comparison of MOOPs obtained from movement tasks performed in different conditions or from different populations. The TKEO contributed to improved performance and robustness of the burst detector.

5.1 Introduction

Surface electromyography (sEMG) is widely used to study physiological processes involved in movement execution [1]. Electromyographic signals are related to force production [2] and muscle fatigue [3] and are often used to study muscle activation patterns (MAPs) after neurological disorders such as spinal cord injury [4] and stroke [5]. Timing of muscle activation can help in understanding motor deficits after neurological injury, and planning therapeutic interventions such as (multichannel) electrical stimulation to support arm and hand function [6, 7].

Muscle onset and offset times are often studied by means of visual inspection [8]. However, this method is prone to intuitive, heuristic and subjective judgment of the researcher or clinician and has poor reproducibility. In the past decades, computer assisted methods [8, 9] have been developed to objectively quantify muscle onset and offset times, such as a simple threshold algorithm [8], a double threshold algorithm [10], Teager-Kaiser Energy Operator (TKEO) [11] and the Approximated Generalized Likelihood Ratio (AGLR) [12].

The AGLR algorithm [12] detects changes in signal variance. In the case of sEMG onset and offset detection, two hypotheses (H_0 and H_1), describing the statistical properties of two probability density functions, represent the state of the muscle. The null hypothesis H_0 corresponds to a muscle in a relaxed state; H1 corresponds to a muscle in contracted state. In the detection and estimation phases of the AGLR algorithm, a fixed window of length L is shifted along the input signal. When the log-likelihood ratio test, comparing the probability density functions of H_0 and H_1, exceeds a threshold h, a change in signal variance is detected and the H_1 hypothesis is accepted that the muscle is contracted. The exact change time t_0 of signal variance is estimated by a maximum likelihood ratio. The output of the AGLR algorithm is influenced by the threshold h and window length L. These parameters need to be chosen a priori [9, 12] and determine the sensitivity, false positive and false negative detection ratios of the algorithm. To increase robustness and decrease sensitivity to artifacts, the signal can benefit from pre-processing before it is analyzed by the AGLR algorithm. A promising pre-processor is the nonlinear Teager-Kaiser Energy Operator [13].

The TKEO calculates the energy of a signal, based on its amplitude and frequency content. It was first used in speech signal analysis [14], and more recently in EMG analysis [11]. The discrete TKEO is defined as:

$$\Psi[x(n)] = x^2(n) - x(n-1)x(n+1) \tag{5.1}$$

in which $x(n)$ is the amplitude on discrete time n and $x(n-1)$ and $x(n+1)$ are the preceding and succeeding samples, respectively. Li and Aruin [11] explored the possibility to detect muscle onset times by applying the TKEO to simulated and human EMG signals, and thresholding the TKEO signals. Onset detection errors were smaller after applying the TKEO, compared to only thresholding the raw EMG signals [15]. Solnik et al. [16] observed that EMG onset detection improved after applying TKEO in three different methods (visual inspection, single threshold and AGLR) and that improvement was independent of the signal-to-noise-ratio (SNR) [17]. Solnik et al. used modified sEMG signals, obtained from lower extremity muscles such as the quadriceps and vastus lateralis during maximal voluntary contractions. A burst detector consisting of AGLR and TKEO has not been previously tested on (rather slowly varying) sEMG signals that were obtained from upper extremity muscles during a sub-maximal movement task, which corresponds better with the functional nature of most upper extremity movements while performing daily activities.

Objectives

The primary aim of this study is to investigate the added value of applying TKEO data pre-processing to an AGLR-based method for burst detection in surface EMG of the hand and forearm, during submaximal movements. As a first step, optimal parameters of the burst detector, leading to minimal detection errors, are identified by applying it to simulated EMG traces with known onset and offset times. Next, comparative simulations are performed with and without TKEO pre-processing. It is hypothesized that inclusion of the TKEO as pre-processor will reduce onset and offset errors. Additionally, the burst detector is applied to real muscle activity recorded from the arm and hand in a group of healthy adults who performed reach-to-grasp movements, to verify correct functioning of the burst detector by creating Muscle Onset and Offset Profiles (MOOPs) of the sub-maximal reach-to-grasp movements.

5.2 Methods

Simulations for burst detection settings

The autonomous burst detector consisted of three major steps, see Figure 5.1. In the first step, data is pre-processed by the TKEO [13] to increase the SNR of the sEMG signal. Comparison between onset and offset errors with and without the TKEO decided whether this step needs to be included in the burst detector.

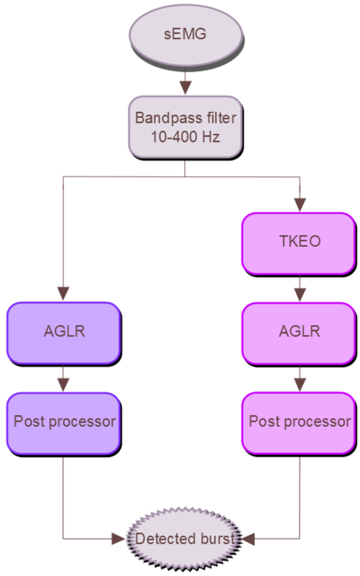

Figure 5.1: The three major steps involved in sEMG burst detection without (left) and with (right) TKEO data pre-processing

Gravity compensation training

Second, the AGLR [12] algorithm was used to estimate changes in the variance of the (pre-processed) sEMG signal. As part of this procedure, optimal values for window length L and threshold h were determined based on simulations. Third, a rule-based postprocessor classified the detected changes in signal variance in muscle onset and offset times, in term of *muscle contracted* or *muscle relaxed* based on a priori defined thresholds Th_{on} (15 µV) and Th_{off} (10 µV).

TKEO pre-processing

To be able to compare onset and offset errors with and without data pre-processing with the TKEO, the thresholds Th_{on} and Th_{off} need to be known in the TKEO domain. For this purpose 1000 traces of sEMG with amplitudes varying from 1 to 25 µV RMS, in steps of 1 µV, were generated (25000 traces in total). EMG was simulated as band pass filtered brown noise [18]. Each trace was band-pass filtered with a 2$^{\text{nd}}$ order, zero-phase-shift Butterworth band-pass filter with cut-off frequencies of 20 and 400 Hz in Matlab (R2011b, the Mathworks, Natick, MA) and converted into the TKEO domain. A second order polynomial was fitted through the data points in the least squared error sense and evaluated at 10 and 15 µV to obtain thresholds Th_{on} and Th_{off} in the TKEO domain.

AGLR settings

Simulations were used to optimize performance and robustness of the burst detector. Several parameters of the burst detector such as window lengths (L, Δ) and threshold values (h, Th_{on}, Th_{off}) of the burst detector need to be set, either heuristically, based on simulations or based on a priori knowledge. To find optimal settings for the AGLR parameters L (length of detection window) and h (detection threshold) , sEMG signals with known onset and offsets were synthesized. A burst of muscle activity was simulated as a ramp up from 0 to 25 µV RMS at $1.0 < t < 1.2s$, a block of constant activity with an RMS value of 25 µV at $1.2 < t < 3.8s$ and a ramp down from 25 to 0 µV at $3.8 < t < 4.0s$, see also the upper panel of Figure 5.2. Gaussian white noise with RMS values between $A_n = 1$ and $A_n = 10\ \mu V$ was added to create EMG signals with a SNR between 8.0 and 28 dB.

Onset and offset errors were calculated for synthesized EMG signals with different SNR and different values for L and h. For each combination of SNR, L and h, 50 EMG traces were analyzed. Onset and offset errors ε were defined as the difference between the exact and the detected onset and offset times: $\varepsilon = t_{exact} - t_{estimated}$, see also Figure 5.2. The detection window length L of the AGLR algorithm should be bigger than the shortest event to be detected. Muscle contractions with duration shorter than the electromechanical delay were discarded, because they will not result in noticeable movement of the limb. Since the electromechanical delay for muscle contractions of arm muscles is around 80 ms [19], window length L should preferably exceed 80 ms. Window length L was varied between 30 and 500 ms in steps of 10 ms.

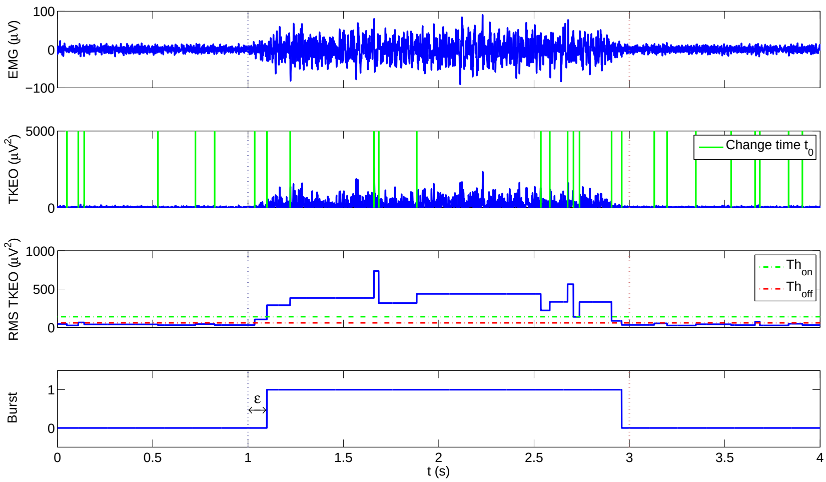

Figure 5.2: Example of a synthesized EMG trace (upper panel) before transformation into the TKEO domain (second panel). The RMS values between two alarm times (t_0) are thresholded (third panel) which yielded the final detected burst (fourth panel) with onset detection error ε

Threshold h was varied between 5 and 150 in steps of 5. To find optimal parameter settings, onset and offset errors were averaged over the 50 repetitions and the 10 noise levels A_n. Optimal parameter settings were defined as minimal detection errors for each combination of threshold h and window length L. Parameter Δ which is used to determine the exact change time t_0 from the estimated change time is chosen to be the same length as L [12].

Post processor

After the two steps of the AGLR algorithm, changes in signal energy have been identified. A knowledge based postprocessor is needed to decide whether a detected change time t_0 is a true muscle onset or offset. Root mean squared (RMS) values of the TKEO signal between two consecutive change times were calculated. If the RMS of the TKEO signal between two change times exceeds a threshold Th_{on} the muscle is regarded as being contracted. When the RMS of the TKEO signal is below a threshold Th_{off} the muscle is regarded being relaxed. Finally, bursts of muscle activity with duration shorter than 100 ms are removed. Similarly, periods of muscle relaxation with duration shorter than 125 ms are removed [20]. When the TKEO data pre-processing

Table 5.1: Subject demographic data

Subjects(n)	18
Age (yrs)	60.4 ± 8.4
Gender	11 M / 7 F
Arm dominance	18 R / 0 L

Abbreviations:
M = Male, F = Female, R = Right side, L = Left side

was omitted, a highly similar postprocessor was used. The muscle is regarded as being contracted when the RMS of the (10 - 400 Hz bandpass filtered) EMG between two consecutive change times exceeds threshold Th_{on} and being relaxed when the RMS value is below Th_{off}.

The automated burst detector consisting of the TKEO and AGLR algorithms and the postprocessor described above was applied to EMG signals recorded during the reach-to-grasp task performed by healthy adults, in order to create MOOPs.

Subjects

Twenty subjects were recruited from the local community. Inclusion criteria were an age over 40 years, no history of neurological disorders and no limitations in upper extremity range of motion due to pain or other disorders. Data of two subjects were excluded because of wrong execution of the movement task and technical failure during the measurement. Demographic data of the remaining 18 subjects are summarized in Table 5.1. All subjects provided written informed consent. The study was approved by the local medical ethics committee (NTR2638).

Reaching movements

Subjects performed reaching movements while seated on a chair with a sitting height of 50 cm in front of a custom designed table with a height of 75 cm. Before movements started, the subjects hand was placed on a white instrumented button containing 5 micro switches that represented the starting position, see Figure 5.3. The signal of the starting button indicated that subjects released the button and started movement. Subjects reached for a cylindrical object with a diameter of 4.0 cm, a height of 9.8 cm and a weight of 0.14 kg. The object was placed on the tabletop, 35 cm in front of the starting button, see Figure 5.3. Subjects were asked to transfer the cylindrical object towards the starting position at a self-selected speed, which required a forward reaching and grasping movement, followed by a reverse movement towards the trunk. The object was returned to the target location by the researcher. Movement duration of each individual reaching movement was time-normalized, defined as the time between release of the start button (0%) and the time when maximal reaching distance, based on the position of MCP3 (100%), occurred. EMG signals were analyzed between -100 and 200 % of the movement duration. Application of the burst detector to an EMG signal yielded a binary signal which was zero when the muscle was relaxed and one when the muscle was contracted.

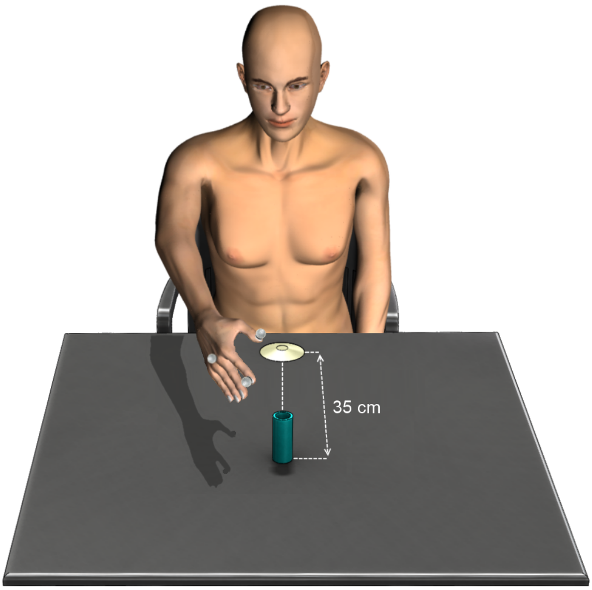

Figure 5.3: Setup for the reach-to-grasp task where subjects reached for and grasped a blue cylindrical object

Kinematics

To be able to quantify the reach-to-grasp movements, 3D kinematics of the arm and hand were recorded with a 6-camera VICON motion analysis system (VICON MX + 6 MX13, VICON, Oxford Metrics, UK). Reflective, 9 mm spherical markers were placed on the tip of the thumb and index finger and on the third metacarpophalangeal (MCP3) joint to measure movement of the hand and the amount of hand opening (i.e., 3D Euclidean distance between the markers on the tip of the thumb and index finger), see Figure 5.3. Positions of the markers were recorded with a frame rate of 100 Hz. Positional data of the markers were offline filtered with a first order, zero-phase-shift Butterworth filter with a cut-off frequency of 10 Hz, in Matlab (R2011b, the Mathworks, Natick, MA).

Electromyography

Bipolar surface electromyography (EMG) was recorded with rectangular 16 x 19 mm Ag/AgCl electrodes (Ambu, type BRS-50-K/12, Ambu BV, Schiphol Airport, the Netherlands). The inter electrode distance was 20 mm. Six muscles in the forearm and 1 thenar muscle were recorded: the abductor pollicis brevis (APB), abductor pollicis longus / extensor pollicis brevis (EPB), extensor digitorum communis (EDC), extensor carpi ulnaris (ECU), extensor carpi radialis (ECR), flexor carpi ulnaris (FCU) and flexor carpi radialis (FCR). Before application of the surface electrodes, the skin was shaved and prepared [21] with an abrasive gel (Nuprep, Weaver and Company, Aurora, CO). EMG signals were differentially amplified by a K-Lab amplifier (K-Lab, Haarlem, the Netherlands) with a gain of 18750, input impedance > 10 GΩ, common mode rejection ratio > 110 dB and input voltage noise < 2 µV. EMG signals were digitized by a 16 bits analog-to-digital converter with a sample rate of 2 kHz. To reduce noise and movement artifacts, EMG signals were online filtered with a 3rd order Butterworth high-pass filter with a cut-off frequency of 20 Hz and offline filtered with a 2nd order, zero-phase-shift Butterworth band-pass filter with cut-off frequencies of 20 and 400 Hz in Matlab (R2011b, the Mathworks, Natick, MA).

Subjects performed 10 repetitions of the movement task. The resulting binary output from the autonomous burst detector was averaged to obtain a group-mean MOOP. The resulting MOOP indicated in how many cases the muscle was contracted during the reaching movement. To calculate differences in timing of muscle activation, the MOOP of each muscle was compared to the MOOP of the EDC, which was regarded as the prime mover during these reach-to-grasp tasks. For this purpose the time derivative of each MOOP was cross correlated with the time derivative of the MOOP of EDC. This cross correlation yielded a phase lead or lag, compared to the activation of EDC.

Statistics

For the simulations, onset and offset errors were compared by means of a repeated measures analysis of variance (ANOVA) with within-subjects factors $TKEO$ (2 levels) and between-subjects factor noise amplitude A_n (10 levels). With Šidák adjustment for multiple post-hoc comparisons, effects were considered statistically significant for $p < 0.05$. Statistical tests were performed with IBM SPSS Statistics version 19 (International Business Machines Corp, New York, NY).

5.3 Results

Simulations

The RMS values of the synthesized EMG traces and their corresponding RMS values in the TKEO domain are displayed in Figure 5.4. EMG with an RMS value below 10 μV($62.3\mu V^2$ in the TKEO domain) was regarded as noise. The muscle was regarded as being active when RMS EMG exceeds 15 μV($138.7\mu V^2$ in TKEO domain). An example of a synthesized EMG trace and the output of the burst detector is displayed in Figure 5.2.

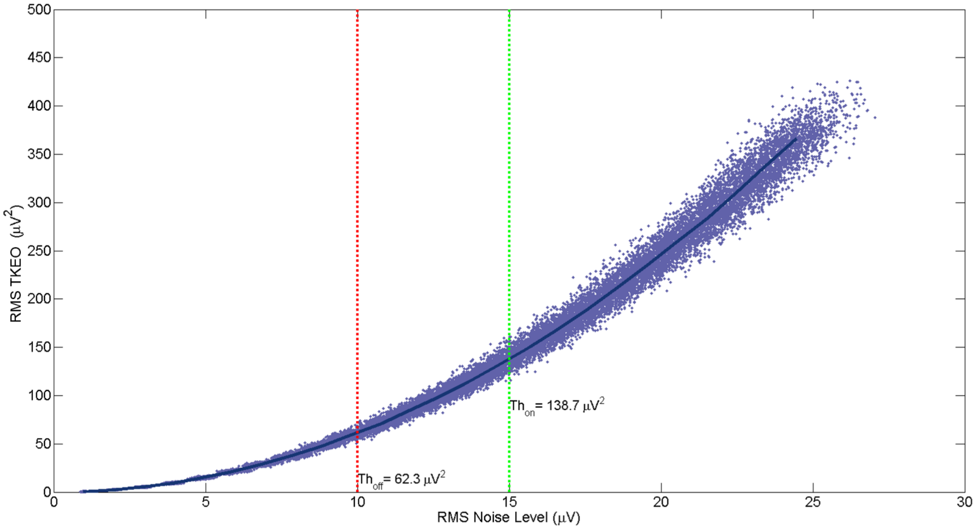

Figure 5.4: Relation between the RMS value of synthesized EMG traces and the corresponding RMS values in the TKEO domain. The green and red lines represent threshold values for muscle onset (Th_{on}) and offset (Th_{off}) respectively

Onset and offset errors

Both onset and offset errors increased with increasing noise amplitudes, see Figure 5.5. Onset errors differed significantly ($p < 0.001$) after inclusion of the TKEO algorithm. Changes in onset errors were also dependent of noise level ($TKEO * A_n$, $p < 0.001$), leading to smaller onset errors after applying TKEO for $3 \leq A_n \leq 10\mu V$ and slightly bigger onset errors after applying TKEO for A_n = 1 and 2 µV.

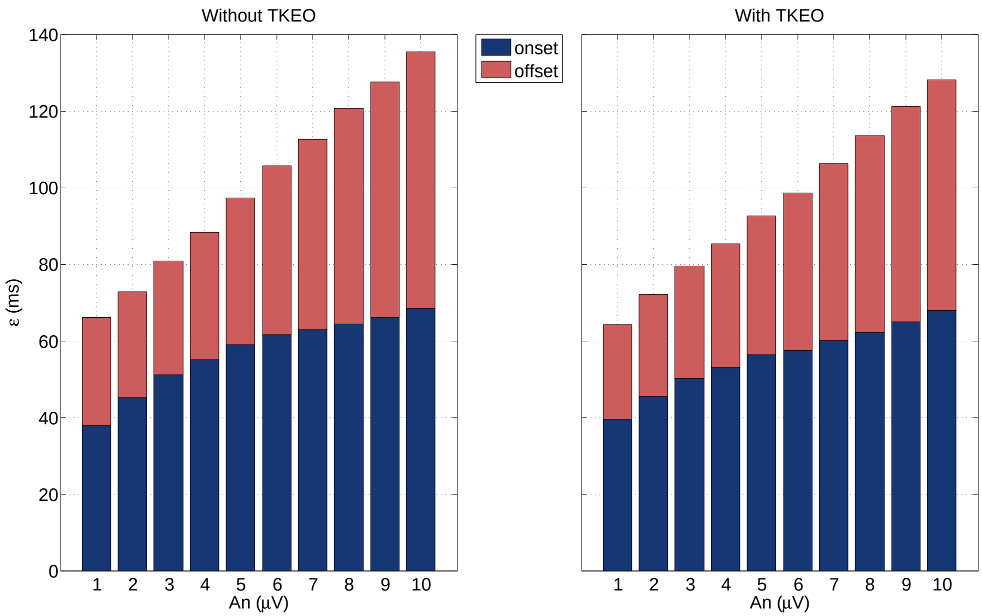

Figure 5.5: Onset and offset errors in ms without Teager-Kaiser data pre-processing (left) and with Teager-Kaiser data pre-processing (right)

Mean onset and offset detection errors in ms for each combination of threshold h and window length L are shown in Figure 5.6 and Figure 5.7, respectively. Combinations of h and L where the detection ratio differed from 100 %, either because more than 1 burst of EMG was detected (type I error) or no burst at all was detected (type II error), are indicated by white color, see Figure 5.7.

The minimal value of the total detection error, i.e. the sum of onset and offset errors, was achieved with a threshold h of 15 and a window length L of 100 ms. These values are highlighted in Figure 5.6 and Figure 5.7 by purple asterisks. These values were used when the burst detector was applied to real EMG activity.

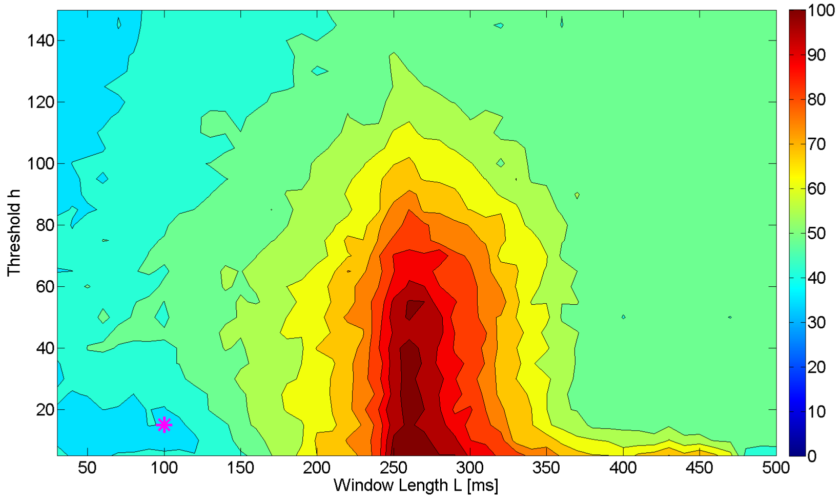

Figure 5.6: Mean onset detection errors in ms depending on threshold h and window length L

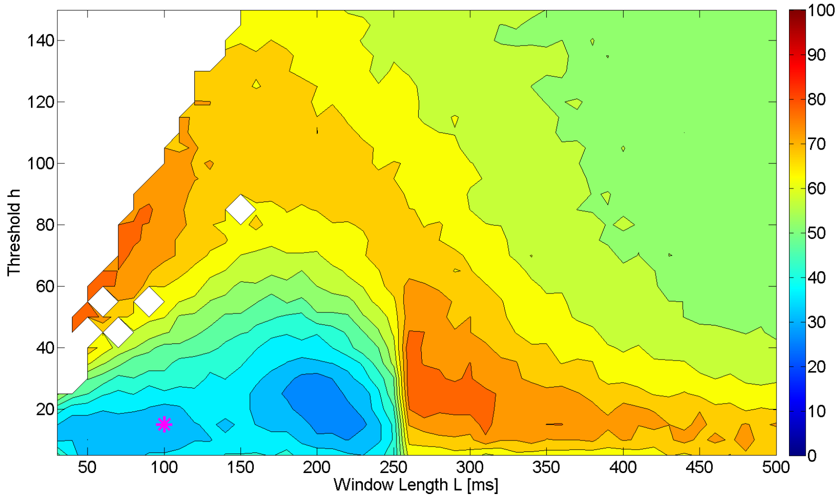

Figure 5.7: Mean offset detection errors in ms depending on threshold h and window length L

Reaching movements

Maximal hand opening during reaching movements was on average 12.8 cm. Maximal hand opening occurred when the distance between the MCP3 and the target was on average 11.1 cm which corresponds to 68.4 % of the reaching phase, see also Figure 5.8.

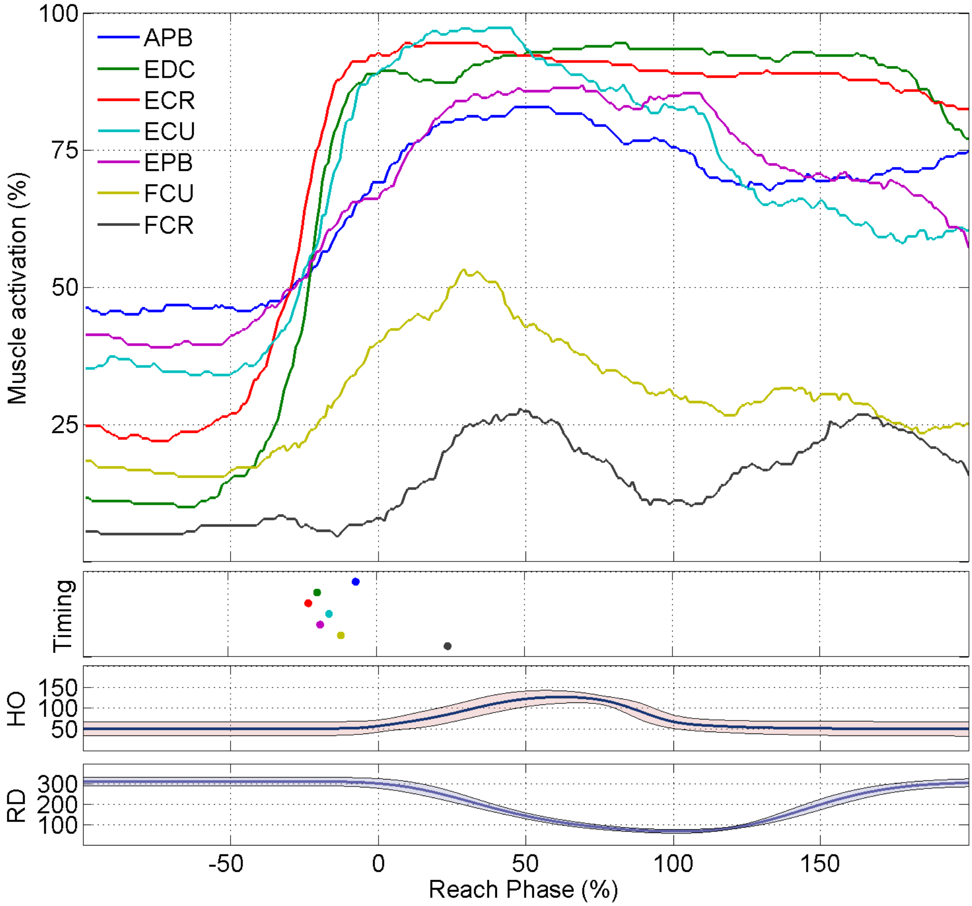

Figure 5.8: Group mean Muscle On- and Offset Profile (MOOP) and timing with respect to EDR onset (top and second panel) as well as hand opening (HO in mm) and reaching distance (RD in mm) in the bottom two panels (mean +/- 1 standard deviation)

Figure 5.8 displays the MOOP of the reaching task. Based on timing and amplitude of the MOOP, muscle activation during the reach-to-grasp task can be divided into three groups. The first group containing EDC, ECR, and ECU, has the most pronounced muscle activation characterized by almost no muscle activation before movement onset, high activation during movement and a high slope just before movement onset (Reach Phase = 0 %). Muscle activation of ECR and ECU was almost simultaneous with EDC (lag = -3 % and 4 % respectively).

The second group contains the thumb extensor and abductor muscles APB and EPB. Before movement onset, these muscles are activated in around 50 % of the cases. Maximum increase of the MOOP of these muscles occurred almost simultaneously with EDC, with lags of 13 % and 1 % of the movement time respectively. The third group is formed by the flexors FCU and FCR. Muscle activation of these muscles remained below 55 % during the entire movement. Low values around 15 % and 10 % are observed before movement onset. With respect to EDC, muscle activation of FCU and FCR is delayed with 8 % and 44 % of the movement time.

5.4 Discussion

The present study shows that inclusion of the TKEO in an AGLR-based burst detector, leads to decreased muscle onset and offset detection errors in simulated EMG traces. The burst detector consists of the TKEO [13] to enhance signal quality, the AGLR [12] algorithm to detect changes in signal variance and a cascaded knowledge based postprocessor that classifies the detected change times as muscle onset and offsets. AGLR parameters were optimized for minimal onset and offset detection errors by applying the burst detector to simulated EMG traces with known onset and offset times. The resulting burst detector is able to autonomously create MOOPs of 7 muscles of the forearm and hand involved in reaching for and grasping of objects in a sample of 18 healthy adults.

A study applying TKEO to EMG recordings of the vastus lateralis muscle in 17 healthy subjects showed that adding TKEO to onset detection with a threshold based algorithm [17] resulted in smaller onset errors regardless of the SNR of the EMG. In a subsequent study [16], similar results were observed when EMG bursts were identified by visual inspection and by means of the AGLR algorithm. This is in line with the present simulation results, in terms of reduction of detection errors. In the present study, onset errors were smaller after application of the TKEO when the background noise level exceeded 2 μV (SNR $<$ 18.4 dB), and slightly bigger when noise levels were below 2 μV. The magnitude of onset errors was comparable to those reported by

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Solnik et al., ranging from 40-66 ms [17, 16]. Remarkably, Solnik used EMG signals constructed from EMG recordings during rest and during near-maximal contractions, i.e. the ramp-up EMG signal during initiation of muscle activation was removed from the data. However, the slow ramp-up signal (125 μV s^{-1}) included in the EMG recordings in the present study corresponds better with real-life functional movements at a sub-maximal level. Adding the finding that TKEO is mainly beneficial when noise in EMG exceeds 2 μV as found in the present study, which is very likely to occur in such context, TKEO presents a useful tool as data preconditioning to reduce onset and offset errors in autonomous burst detection.

An additional advantage of the TKEO, particularly for application with smaller muscles, regards its tendency to increase the SNR in EMG signals, since both signal amplitude and frequency content increase during muscle contraction. Due to its non-linear behavior it is particularly sensitive to high frequency content, which primarily originates from superficial muscles directly below the sEMG electrodes. Higher frequency EMG signals that originate from neighbouring muscles are attenuated by the surrounding tissue acting like a low pass filter [21, 1]. In other words, only low-frequency cross talk signals arrive at the electrode, for which TKEO is less sensitive. Therefore, the use of TKEO leads to spatial filtering that suppresses cross talk [22] which is likely to occur in EMG measured at the forearm where small muscles lie close to each other. Furthermore, TKEO requires only three samples to estimate the signal energy at each sample time, resulting in low computational demands, which even enables semi real time applications such as EMG driven (training) devices. Even though absolute improvements in onset detection were rather small, these advantages warrant application of TKEO as data preconditioning for autonomous burst detection during real life, sub-maximal arm-hand movements.

To confirm correct functioning of the burst detector in realistic conditions, the burst detector was applied to real sEMG signals that were obtained from a sub-maximal reach-to-grasp task performed by healthy adults. During this task, maximal hand opening occurred between 60 and 70 % of the reaching phase, which is in accordance with previous studies addressing kinematics of reaching for and grasping of a cylindrical object [23, 24, 25]. Furthermore, Sangole et al. [24] observed that hand shaping started simultaneously with the arm transport or reaching phase. Similar results were seen in this study, both in kinematic and EMG data. The autonomously extracted MOOP showed that hand opening started with finger extension, shortly followed by thumb abduction/extension and by contraction of the wrist flexors, approximately halfway through the reaching phase.

Application of the burst detector in other groups of muscles is possible, but might require adjustment of thresholds Th_{on} and Th_{off}. The application of the autonomous burst detector will be explored further in future work, where firstly kinematics and MOOPs will be compared between both healthy adults and stroke patients. Subsequently, this information can be used to develop control algorithms for an EMG driven electrical stimulator that can be used to support hand opening and closing in conjunction with a robotic arm training device.

5.5 Conclusions

The present study demonstrated a beneficial effect of the TKEO as data pre-processor in an autonomous burst detector that can be used to create onset and offset profiles from surface EMG. Simulations yielded parameter settings with minimal onset and offset errors, combining AGLR based burst detection with TKEO for data preconditioning. Using an additional knowledge-based postprocessor, the burst detector was able to autonomously create MOOPs from muscles in the forearm and hand that are in accordance with muscle activation profiles described in literature. The burst detector can be used to objectively compare MOOPs that are obtained from different movement tasks or different groups of subjects, such as healthy adults and people with neurological disorders. Burst detectors that can operate autonomously and in real time, can be used to control biomedical (training) devices such as for example, EMG controlled prostheses.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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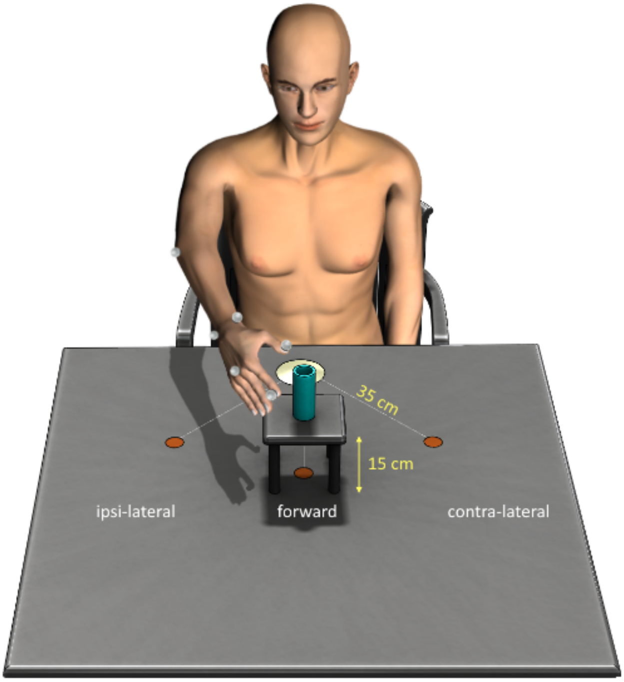
Chapter 6

Healthy vs. stroke



Timing of forearm muscles during reach-to-grasp movements with and without arm support in healthy subjects and stroke patients.

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Submitted to: PLOS ONE

Abstract

Introduction

Many stroke patients have to cope with deficits in arm and hand function. This study aims to identify differences in movement execution and timing of muscle activation between healthy elderly and stroke patients during unsupported and supported reach-to-grasp tasks. Such differences in muscle activation can be used as input to control robotics and/or electrical stimulators to support hand opening and closing during post-stroke rehabilitation.

Materials and Methods

Eighteen healthy elderly and fifteen stroke patients performed functional reach-to-grasp-movements, with and without arm support. Muscle activity of 7 forearm muscles was measured. Kinematic outcome measures such as path length ratio, timing of hand opening and wrist excursions were compared between conditions and groups. Muscle onset and offset profiles were generated autonomously and descriptively compared between healthy and stroke patients and between the supported and unsupported conditions.

Results

Stroke patients have a more curved path towards the target object than healthy subjects and movements are processed more serially. Compared to healthy helderly, stroke patients have a delayed activation of Abductor Pollicis Brevis and Extensor Pollicis Longus, and an early activation of the Flexor Carpi Radialis. In both stroke patients and healthy elderly, the path length ratio, timing of hand opening and wrist excursions are dependent of movement direction, but not of support condition.

Discussion

Stroke patients seem to compensate for a delayed hand opening with respect to healthy elderly, by making a more circumferential movement towards the target object to prevent colliding into the target object.

Conclusion

Temporal differences in muscle activation between healthy elderly and stroke patients can serve as input to control assistive and/or therapeutic robotic systems or electrical stimulators to support arm- and hand movements. The used algorithms may also be useful in real-time applications that require sEMG as control input, such as assist-as-needed control algorithms. Preferably, such control algorithms will be highly task-specific and will adapt to movement direction.

6.1 Introduction

Many stroke patients have to cope with deficits in arm- and hand function. Upper extremity paresis can seriously affect independence [1] after stroke. Compared to healthy elderly, stroke patients show reduced movement velocities, reduced coordination of the arm [2], hand and between joints and digits of the hand [3]. Rehabilitation training aims to improve arm and hand function and increase the level of independence.

Among many emerging technological approaches, hybrid therapeutic devices are being developed to deliver task-oriented, repetitive training to stroke patients [4, 5], combining robotics [6, 7] and electrical stimulation (ES) [8] to provide proximal and distal [9, 10] arm and hand training.

Several hybrid systems use EMG as input to control active therapeutic and/or assistive devices such as robotics and electrical stimulators [11, 12]. To develop such EMG-based control algorithms (for example assist-as-needed), muscle activation patterns (MAPs) of muscles involved in opening/closing of the hand of both healthy elderly and stroke patients need to be quantified. Commonalities and differences in MAPs between stroke patients and healthy elderly, such as muscle weakness, cocontraction [13] and delayed muscle activation [14] can serve as input for ES or other supporting modalities. Autonomous generation of muscle on- and offset profiles (MOOPs) is useful to objectively quantify delays and differences in duration of activation between different muscles [15]. Currently, little is known about differences between healthy elderly and stroke patients in timing of activation of muscles acting on the distal arm during submaximal, functional tasks.

Gravity compensation (GC) or arm support is often incorporated in both conventional and robot-aided upper extremity rehabilitation training [16, 7, 17]. It is known that this directly increases the work area of the arm and reduces effects of involuntary synergistic movement patterns [16, 18] during maximal and submaximal reaching tasks. Most of those studies focused on the proximal arm, and although it is indicated that such synergistic movement patterns also include the wrist and the hand [19], little is known how gravity compensation affects timing of the muscles of the distal arm.

Objectives

This study was undertaken to better understand motor control of the arm and hand of stroke patients with respect to healthy elderly, during both unsupported and supported functional reach-to grasp movements. The aim of the study is to identify differences in movement execution and timing of muscle activation between healthy elderly and stroke patients during unsupported and supported reach-to-grasp tasks. Ultimately, this information is believed to provide input for an active (hybrid) therapeutic or assistive device such as an electrical stimulator or robotic system, to support hand opening/closing during sub-maximal reach-to-grasp movements.

6.2 Materials and Methods

Subjects

Healthy subjects were recruited from the local community. Inclusion criteria were an age over 40 years and no history of neurological disorders. Chronic stroke patients were recruited at Roessingh Center for Rehabilitation in Enschede, the Netherlands. Inclusion criteria were: 1. A history of a single unilateral stroke in the medial cerebral artery (MCA) region resulting in single-sided hemiparesis; 2. The onset of the stroke was more than six weeks ago; 3. The ability to voluntarily generate excursions of at least 20 degrees in the plane of elevation (horizontal ab-/adduction) and elevation angle (ab-/adduction, ante-/retroflexion) of the shoulder joint; 4. The ability to voluntarily generate an excursion of 20 degrees of elbow flexion/extension; 5. The ability to voluntarily extend the wrist 10 degrees from neutral flexion/extension; 6. Adequate cognitive and communicative function to understand the experiments, follow instructions, and give feedback to the researchers. Exclusion criteria for both groups were a fixed contracture deformity in the (affected) upper limb and pain as a limiting factor for the subjects active range of motion. All subjects provided written informed consent. The study was approved by the local medical ethics committee (registered at the Dutch Trial Registry under number NTR2638).

Study setup

In this cross-sectional study, subjects were invited in the movement analysis lab of Roessingh Research and Development for a single measurement session. During this session, subjects performed reach-to-grasp movements, while seated on a chair (sitting height 50 cm) in front of a tabletop (height 75 cm). Healthy elderly made the movements with their dominant arm, stroke patients with their affected arm. Each movement started with the hand on a round instrumented button with a diameter of 90 mm that contained micro switches to detect the start of a reaching movement. The subject was asked to reach for, grasp and retrieve a cylindrical object with a diameter of 40 mm, a height of 98 mm and a weight of 0.14 kg. The object was placed at a distance of 35 cm from the starting position. Movements were performed in the forward movement direction or at an angle of 45 degrees in the ipsi-lateral or contra-lateral movement direction, see Figure 6.1.

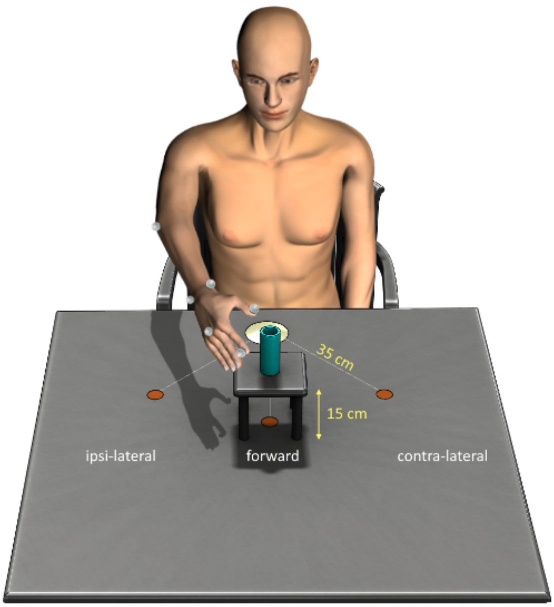

Figure 6.1: Measurement setup

Movements were performed at tabletop height (i.e. low condition), and repeated at a height of 15 cm above the tabletop (i.e. high condition). For the latter condition, a small platform with a height of 15 cm was placed on the tabletop, see also Figure 6.1. Subjects made 10 reaching movements in each condition. The order of movements was randomized across subjects. Movements were performed at a self-selected speed. Movement duration of each individual reaching movement was defined as the time between release of the start button (0%) and the time when movement direction of the hand reversed (100%). The first of 10 movement repetitions was omitted because this movement differed from the subsequent movements, due to a different starting orientation (supinated instead of pronated) of the hand. The remaining 9 movements were selected for further analysis.

The trunk of the subject was restrained by a four-point harness, which allowed full scapular motion, but prevented compensatory trunk movements while performing the reaching task. Movements were performed with and without arm support. A device called Freebal [20] was used to passively counteract the effect of gravity on the arm, i.e. the arm was fully supported. The order of movements, with or without arm support, was block randomized across subjects.

Kinematics

Kinematics of the arm and hand were recorded with a 6 camera VICON motion analysis system (VICON MX + 6 MX13, VICON, Oxford Metrics, UK). Reflective 9 mm spherical markers were placed on the tip of the thumb and index finger, on the third metacarpophalangeal (MCP3) joint, radial styloid process (PRSR), ulnar styloid process (PRSU), and the lateral epicondyle of the humerus (EPLA) to record movements of the arm and hand. Marker data were recorded with a sample rate of 100 Hz. Positional data were offline filtered with a first order zero-phase-shift Butterworth low pass filter with a cut-off frequency of 10 Hz, in Matlab (R2011b, the Mathworks, Natick, MA).

Hand opening was defined as the 3D Euclidean distance between the markers on the tip of the index finger and thumb. Reaching distance was defined as the 2D Euclidian distance in the horizontal plane between the MCP3 marker and the center of the movement target with known position. The path length ratio PLR was calculated similar to Kamper et al. [21] and was defined as the actual travelled path of MCP3 in the horizontal plane, divided by the shortest possible path in the horizontal plane, between the starting button and target position times 100%.

Timing of hand opening (THO) was calculated similar to Kordelaar et al. [22] and is defined as the moment of peak hand opening (PHO) relative to the moment of peak reaching velocity (PRV):

$$THO = \frac{t_{PHO}}{t_{PRV}} \cdot 100\% \tag{6.1}$$

In the present study, PHO is defined as the moment when hand opening exceeds 95%

6

of max hand opening, since hand opening reaches a plateau at the end of the reaching phase.

The wrist angle (WA) was defined as the angle between the normal vector of the hand plane defined by MCP3, PRSU and PRSR and the normal vector of the arm plane, which was defined by PRSU, PRSR and EPLA. In the neutral position between wrist flexion and extension, WA = 0. Wrist flexion results in positive angles for WA and extension results in negative values.

Electromyography

Before surface electromyography (sEMG) electrodes were applied to the forearm, the skin was shaved and prepared with an abrasive gel (Nuprep, Weaver and Company, Aurora, CO) to reduce impedance. Bipolar sEMG was recorded with rectangular 16 x 19 mm Ag/AgCl electrodes (Ambu, type BRS-50-K/12, Ambu BV, Schiphol Airport, the Netherlands). The inter electrode distance was 20 mm. The SENIAM guidelines for electrode placement were followed [23]. sEMG of seven muscles was recorded: the abductor pollicis brevis (APB), abductor pollicis longus / extensor pollicis brevis (EPB), extensor digitorum communis (EDC), extensor carpi ulnaris (ECU), extensor carpi radialis (ECR), flexor carpi ulnaris (FCU) and flexor carpi radialis (FCR).

A K-Lab amplifier (K-Lab, Haarlem, the Netherlands) amplified the signals differentially with a gain of 18750, common mode rejection ratio > 100 dB, input impedance > 10 GΩ and input voltage noise < 2 μV. The sEMG signals were filtered online with a 3^{rd} order Butterworth highpass filter with a cut-off frequency of 20 Hz, to reduce noise and movement artifacts. Subsequently, sEMG was filtered offline with a 2^{nd} order Butterworth zero-phase-shift bandpass filter with cut-off frequencies of 10 and 400 Hz in Matlab (R2011b, the Mathworks, Natick, MA).

The signal to noise ratio of sEMG signals was improved by applying the Teager Kaiser Energy Operator (TKEO) [24, 25]. Changes in signal variance of the sEMG signal were autonomously detected by means of the Approximated Generalized Likelihood Ratio (AGLR) [26]. A knowledge based post processor identified muscle onset and offset by thresholding the smooth rectified TKEO signal between two alarm times, i.e. changes in signal variance [15]. Timing of muscle activation was calculated by cross correlating the time derivative of MOOPs. This cross correlation yielded a phase lead or lag, relative to the muscle activation of the EDC, which was considered as the prime mover with the most pronounced muscle activation during the reach-to-grasp tasks.

Table 6.1: Subject demographic data

	Healthy	**Stroke**
n	18	15
Age (yrs)	60.4 ± 8.4	62.5 ± 10.2
Gender	11 M / 7 F	9 M / 6F
Arm dominance	18 R / 0 L	15 R / 0 L
Affected arm	-	8 L / 7 R
Fugl Meyer (max 66)	-	55.1 ± 8.0 [40-64]
ARAT (max 57)	-	53.2 ± 9.0 [24-57]
Time post stroke (yrs)	-	3.32 ± 2.6

Abbreviations:
M = Male, F = Female, R = Right side, L = Left side

Statistics

Data were visually checked for normality by visual inspection of histograms. Differences between groups were tested by means of Students T-tests for unrelated samples. Differences in THO, PLR and WA between conditions were tested by means of Students T-tests for related samples. P values were corrected for multiple testing by means of the Holm-Bonferroni method. Effects were considered statistically significant for (adjusted) $p < 0.05$. Statistical tests were performed with IBM SPSS Statistics version 19 (International Business Machines Corp, New York, NY).

6.3 Results

Twenty healthy subjects and twenty stroke patients were included in this study. Data of two healthy subjects and five stroke patients were excluded because of wrong execution of the movement task or technical failure during the measurement. Demographic data of the remaining 18 and 15 subjects respectively, are summarized in Table 6.1.

The mean age of the subjects did not statistically differ between both groups ($p = 0.502$). The average movement time (reach and grasp) was significantly longer ($p < 0.001$) in stroke patients (1.24 ± 0.07 s) compared to healthy subjects (0.92 ± 0.11 s). On average, maximal hand opening occurred at 52.6 ± 8.3 % of the reaching phase in the healthy elderly group and at 55.1 ± 10.1 % in the group of stroke patients ($p = 0.007$).

Timing of hand opening

In all possible conditions (movement direction, height and gravity compensation), THO was larger ($p < 0.001$) in stroke patients (212.8 ± 128.4) than in healthy subjects (178.7 ± 80.1), see Figure 6.2. THO was smaller for the elevated, i.e. high, movements (171.4 ± 86.5) compared to the movements performed at table height, i.e. low (217.0 ± 118.5), in both healthy subjects and stroke patients ($p < 0.001$).

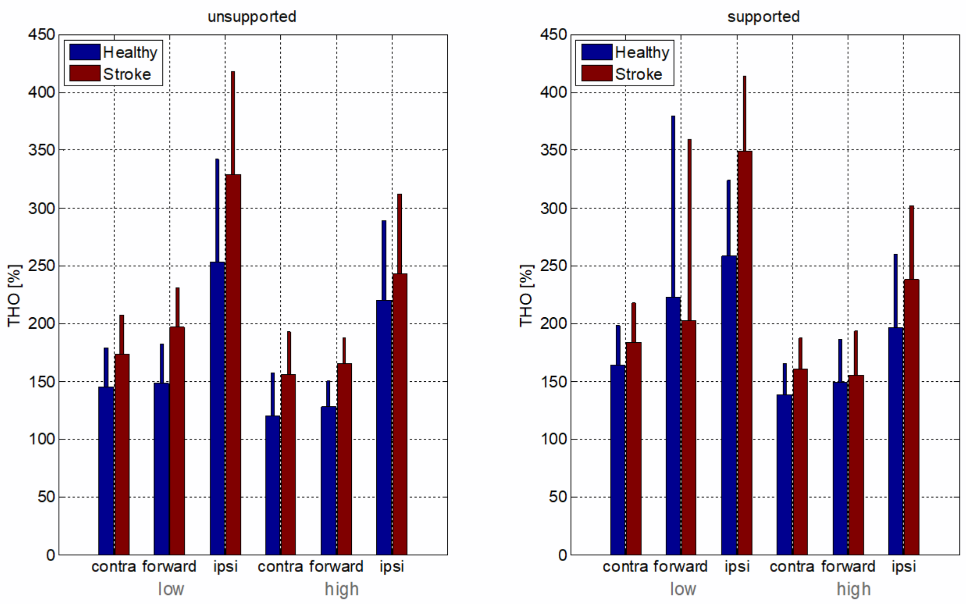

Figure 6.2: timing of hand opening of stroke patients and healthy elderly during unsupported and supported reach-to-grasp movements.

Also, movement direction influences THO. Movements in the contra-lateral direction had smaller THO (153.8 ± 51.1; $p = 0.01$) compared to the forward movement direction (170.3 ± 79.0; $p = 0.01$). Furthermore, movements in the ipsilateral movement direction (258.4 136.9) had larger THO compared to the forward direction (170.3 ± 79.0; $p < 0.001$) and to the contralateral movement (153.8 ± 51.1; $p < 0.001$).

Values for THO were slightly increased in the supported condition (200.4 ± 106.3) compared to the unsupported condition (188.0 ± 105.8), although the effect of arm support on THO was not significant ($p = 0.244$). The influence of either movement direction ($p > 0.246$) and target height ($p > 0.118$) on THO did not differ between groups.

Wrist excursion

Wrist excursion during the grasping phase did not differ ($p = 0.859$) between healthy elderly (15.2 ° ± 7.2 °) and stroke patients (15.4 ° ± 7.6 °). Movement to elevated targets required more ($p = 0.026$) more wrist excursion (16.1 ° ± 7.4 °) than movement on tabletop height (14.7 ° ± 5.8 °). Wrist excursion differed with direction ($p < 0.001$), see Figure 6.3. Wrist excursion increased from 11.5 ° ± 5.0 ° in the contralateral movement direction to 14.7 ° ± 5.8 ° in the forward movement direction to 19.6 ° ± 7.8 ° in the ipsilateral movement direction. Gravity compensation did not affect wrist excursion ($p = 0.918$).

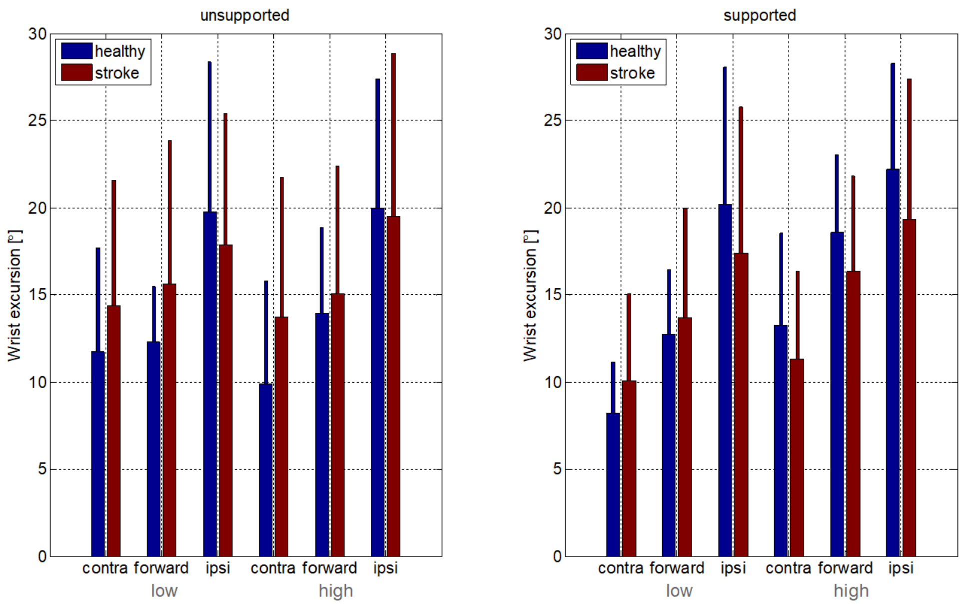

Figure 6.3: wrist excursions of stroke patients and healthy elderly during unsupported and supported reach-to-grasp movements.

In both groups, wrist excursions increased from the contralateral towards the ipsilateral direction. This direction dependent increase in wrist excursion is larger in the healthy group than in the stroke group ($p = 0.011$).

Path Length Ratio

Stroke patients have on average a PLR of 1.28 ± 0.24, which is larger ($p < 0.001$) than healthy subjects (1.18 ± 0.17). The PLR increases from 1.08 ± 0.08 in the

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contralateral movement direction, to 1.19 ± 0.17 in forward direction, to 1.41 ± 0.21, $p < 0.001$, see Figure 6.4. PLR is not affected by movement height ($p = 0.934$) or gravity compensation ($p = 0.330$).

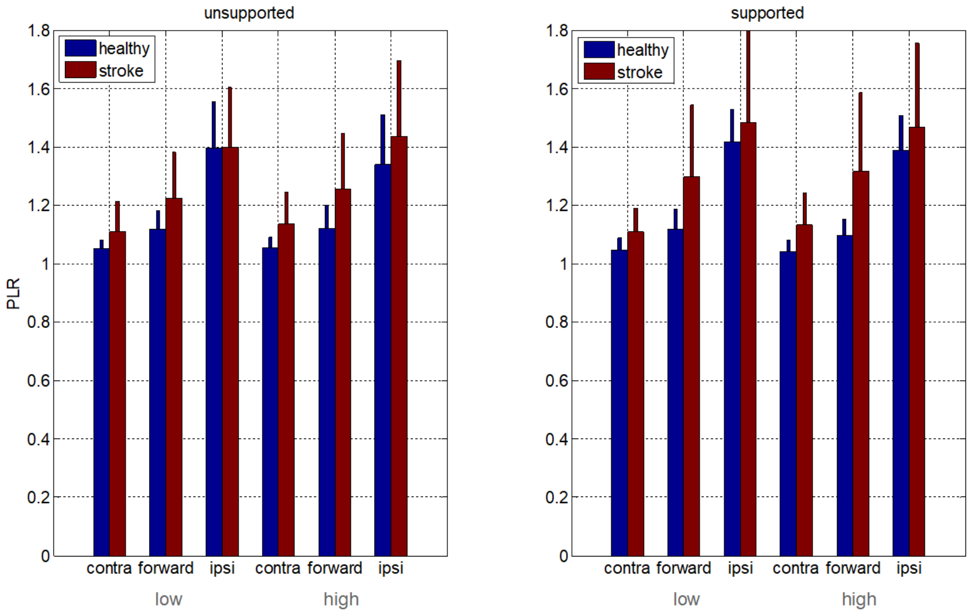

Figure 6.4: Path length ratio (PLR) in stroke patients and healthy elderly during unsupported and supported reach-to-grasp movements.

MOOP

The MOOPs of healthy elderly and stroke subjects are shown in Figure 6.5. The lines in the upper panel represent the percentage of occurrences in which a muscle was contracted at a certain phase of the reaching movement. In both healthy subjects and stroke patients, muscle activation is initiated before movement initiation (i.e. reach phase < 0 %).

Compared to healthy subjects, activation of APB and EPB is delayed in stroke patients with respectively 18 and 26 %. Contrary, activation of the FCR is 26 % earlier in stroke patients compared to healthy subjects, see Table 6.2. Only minor differences in timing were observed in EDC, ECR, ECU and FCU. On average, the FCU and FCR are more often activated in stroke patients than in healthy elderly. MOOPs were not affected by application of arm support.

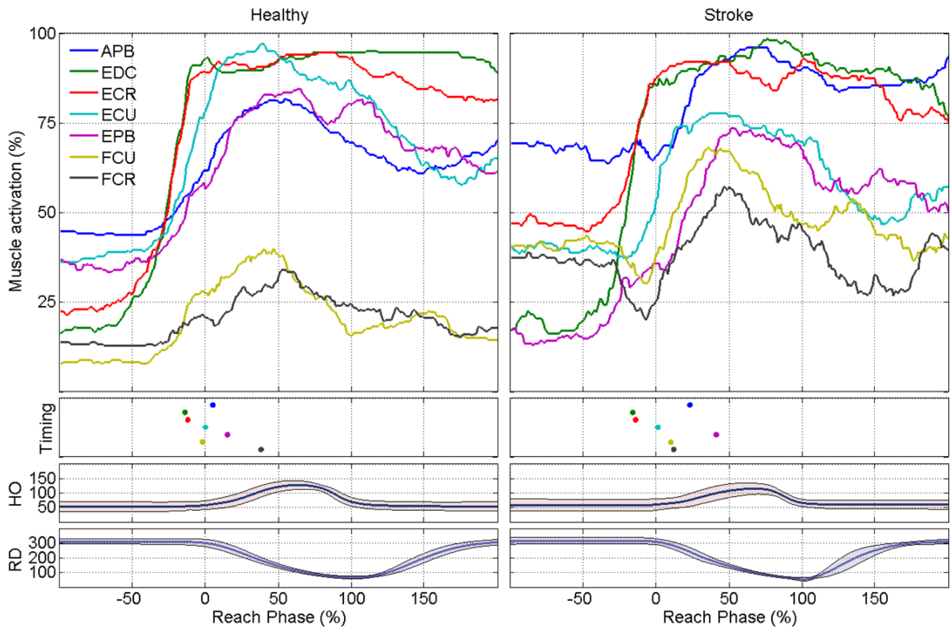

Figure 6.5: Muscle Onset and Offset profiles of healthy elderly and stroke patients during forward reaching movements. The third row shows the lead/lag times relative to EDC. Handopening (HO) in mm and reaching distance (RD) in mm are shown in the third and fourth row.

6.4 Discussion

The present study identified differences in motor control involved in reaching and grasping between healthy elderly and stroke patients. Compared to healthy elderly, stroke patients have longer movement time, higher path length ratio (PLR) and have a more serial control of the arm and hand, as indicated by higher values of THO. Even though FCR activation is earlier in stroke patients, no significant differences in wrist excursion were found between both groups. Application of gravity compensation did not affect arm movements as indicated by wrist excursion and PLR, nor did it affect timing parameters such as THO and MOOPs.

The present study showed that maximal hand opening occurs at 52.6 and 55.1 % of the reaching phase, in healthy elderly and stroke patients respectively. These values are slightly lower than a study by van Vliet et al. [27] who reported that maximal hand opening occurs between 62 - 68 % of the reaching phase, in healthy subjects and stroke patients. This difference is most likely caused by the fact that in the study

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Table 6.2: MOOPs of healthy elderly and stroke patients

	Healthy [%]	**Stroke [%]**	**Difference [%]**
APB	5	23	18
EDC	-14	-16	-2
ECR	-12	-14	-2
ECU	0	1	1
EPB	15	41	26
FCU	-2	10	12
FCR	38	12	-26

by Van Vliet et al. [27] objects with a diameter of 60 and 70 mm were used. These require bigger hand opening, which is being achieved later during the reaching phase, compared to the object used in the present study, which had a diameter of 40 mm.

To our knowledge, the effect of movement direction in the horizontal plane, reflecting variations in object position as encountered during functional tasks in daily life, on THO, PLR and wrist excursion has not been reported before. This study shows that from the contra-lateral movement direction to the ipsi-lateral movement direction, THO, PLR and wrist excursion increased, in both stroke patients and healthy subjects. This can be explained by the fact that in the contra-lateral movement direction, it is possible to start with hand opening just after the start of the reaching phase, i.e. almost parallel execution of both movements. The wrist is already in a convenient orientation, so only small excursions of the wrist are needed to grasp the object. In the ipsi-lateral movement direction, the hand remained closed (including delayed thumb abduction/opposition) for a bigger part of the movement, likely to reduce the risk of colliding into the cylinder during the reaching phase. Contrary to the other movement directions, stroke patients have smaller wrist excursions than healthy elderly in the ipsilateral movement direction. The smaller wrist excursions are compensated for, by a more outflanking / circumferential movement, as indicated by the higher path length ratio. A possible explanation for this observation is that stroke patients have a reduced ability to modulate multi-muscle coordination across functional tasks [28]. This inability to modulate muscle coordination is likely to contribute to functional deficits of stroke survivors and induce compensational movements to fulfil the requested movement task.

Path Length Ratio was previously studied by Kamper et al. [21]. They showed that stroke patients had 32 % bigger PLR than healthy subjects and that healthy subjects had an average PLR of 1.08 [21], which is comparable to the PLR in the forward and contralateral movement direction of the present study. Mildly impaired stroke patients had an average PLR of 1.23 [21], which is also comparable to the PLR of stroke patients in the forward and contralateral movement direction in the present study.

Delayed activation of thumb extensors in stroke patients has been previously reported in literature. Stroke patients demonstrated a reduced ability to extend the thumb and fingers which affects grasp performance [29]. These delays can be present during both grip initiation and grip termination [30].

Application of arm support did not affect the amount of wrist excursion during the reach-to-grasp movements in both healthy elderly and stroke patients. Although smaller joint excursions during unsupported movements for stroke patients have been reported previously in literature [31, 32, 33], the stroke patients in this study had only mildly impaired arm and hand function as indicated by the relatively high Fugl-Meyer and ARAT scores. Since such abnormal coupling is shown to be more pronounced in subjects with higher levels of functional impairment [34, 35], this may explain the lack of influence of gravity compensation in the present study.

Study limitations

The present study has some limitations. First, subjects needed quite good arm and hand function to perform the requested movement tasks. For this reason, only mildly affected stroke patients were included in this study. Comparable research in moderately and severely affected stroke patients is needed to study whether or not the present findings generalize to more severely affected stroke patients, who may benefit even more from an assistive or therapeutic device.

In the present study wrist excursions were calculated based on the position of 4 VICON markers. However, the position of the 4 markers in neutral wrist flexion/extension position was not measured separately. Since high variation between subjects in absolute wrist angles is expected, only wrist excursions are calculated. As a result, changes in wrist excursions cannot be addressed directly to changes in the ability to flex or extend the wrist.

Practical implications

The current study shows that muscle activation can be detected using sEMG before starting of the actual movement in stroke patients and healthy elderly. This makes sEMG useful as a control signal, for controlling rehabilitation robots or electrical stimulators [36] in the case of involvement of the distal arm in sub-maximal functional tasks. The sEMG values, together with the autonomous burst detection described in detail in a previous article [15], can be used to autonomously detect the intention of the hemiparetic user, when running (semi-) real-time. Such input can be used to create various control algorithms for assistive or therapeutic rehabilitation devices, such as an assist-as-needed control algorithm based on muscles on/off times, which ensures an active contribution of the patient. The latter is believed to have a positive effect in (re)learning motor tasks [37] and led most consistently to improvements in arm function in robot mediated rehabilitation training [38].

The findings from the present study can be used in future work to combine autonomous intention detection with multichannel electrical stimulation. One can think of a system that is able to stimulate and measure sEMG of 3 muscle groups; thumb abductors, wrist/finger extensors and wrist/finger flexors. The sEMG of the wrist/finger extensors can be used as a trigger during submaximal reach-to-grasp tasks. Shortly after the trigger, one channel of the electrical stimulator can help to support thumb abduction. The second channel can induce wrist and finger extension to counteract the early activation of wrist flexors that is present in many stroke patients.

6.5 Conclusions

The present study identified differences in kinematics during execution of submaximal reach-to-grasp tasks between healthy and stroke subjects. Compared to healthy subjects, stroke subjects had a more curved path towards the targeted object, as indicated by increased PLR. Secondly, stroke subjects processed arm and hand movements more serially than healthy subjects, as indicated by increased THO values. In both healthy elderly and stroke patients, PLR, THO and wrist excursion are dependent on movement direction. In the current movement task, stroke patients and healthy subjects showed similar wrist excursions. Concerning muscle activation, the MOOPs of the stroke patients showed a delayed activation of APB and EPB and an early activation of FCR. These temporal differences in muscle activation can for instance be used as input to control (multichannel) electrical stimulators or (soft) robotics to support hand opening and closing during post stroke rehabilitation.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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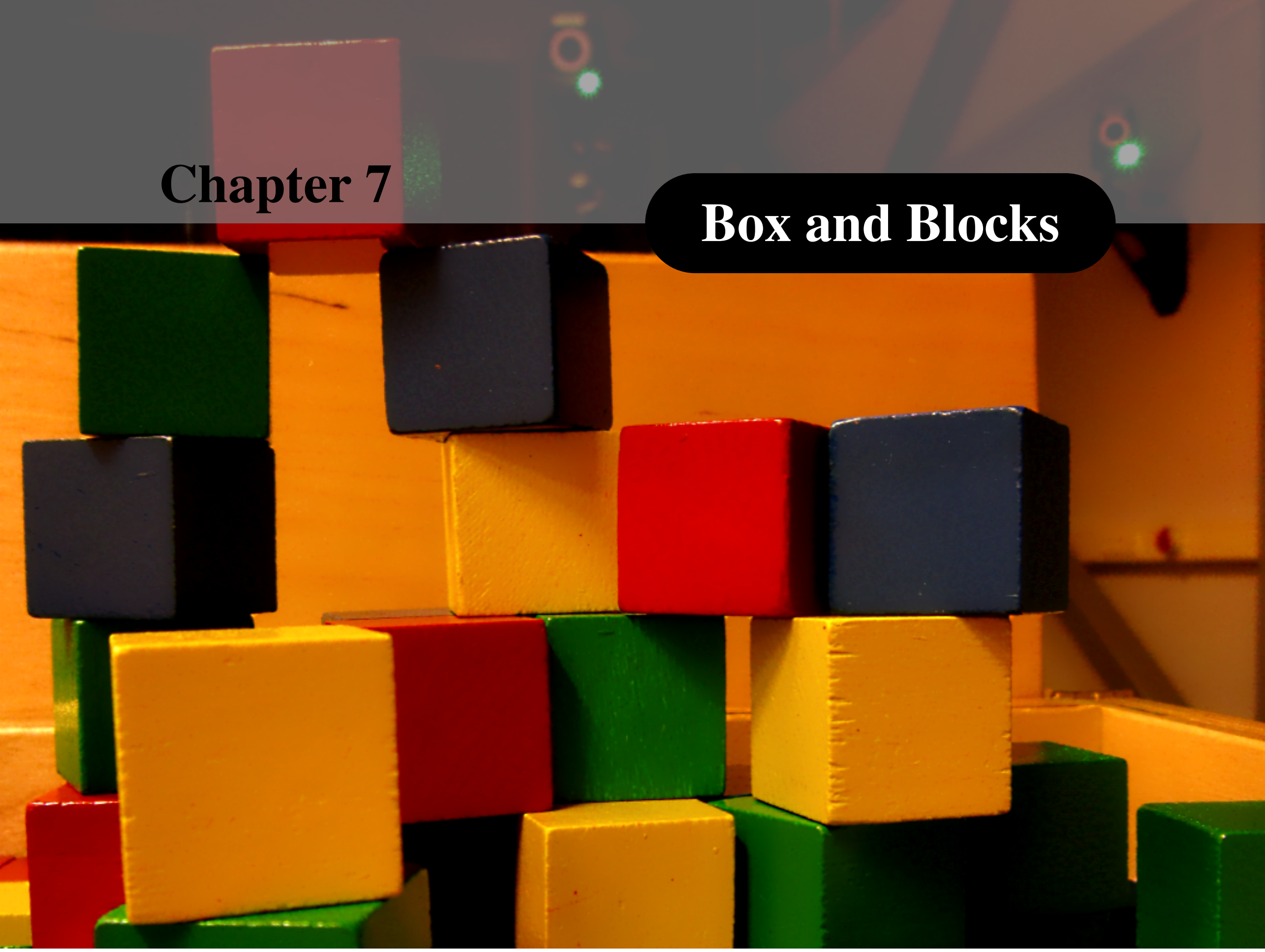
Chapter 7

Box and Blocks



A feasibility study of the effect of multichannel electrical stimulation and gravity compensation on hand function in stroke patients: a pilot study.

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Abstract

Introduction

Many stroke patients have to cope with impaired arm and hand function. As a feasibility study, gravity compensation (GC) and multichannel electrical stimulation (ES) were applied to the forearm of eight stroke patients to study potential effects on dexterity.

Methods

ES was triggered by positional data of the subject's hand relative to the objects that had to be grasped. Dexterity was evaluated by means of the Box and Blocks Test (BBT). The BBT was performed with four combinations of support; with and without GC and with and without ES.

Results

In all patients, it was possible to induce sufficient hand opening for grasping a block of the BBT by means of ES. There was no significant increase in dexterity as measured with the BBT.

Discussion and conclusion

GC and/or ES did not improve instantaneous dexterity in a small sample of stroke patients although sufficient hand opening was reached in all patients. More research in a larger sample of stroke patients with more specific and more sophisticated control algorithms is needed to explore beneficial effects of GC and ES on hand function in post stroke rehabilitation.

7.1 Introduction

STROKE is one of the leading causes of permanent disability in Europe [1] and North America [2]. Around 40 % of the stroke patients have to cope with severely affected arm- and hand function [3] and dexterity is only found in 38 % of stroke survivors 6 months post stroke [4]. Motor problems of the upper extremity following stroke include muscle weakness, spasms, disturbed muscle timing and a reduced ability to selectively activate muscles.

Post stroke rehabilitation training aims to regain (partly) lost functions by stimulating restoration of function or promoting compensational strategies, in order to increase the level of independence during activities of daily living (ADL). Currently, highly intensive, repetitive, task specific training in a motivating environment with (augmented) feedback on movement error and performance, is regarded as the most effective way to promote motor restoration after stroke [5, 6].

The last decades, several robotic training systems have been developed and applied in post stroke upper extremity rehabilitation. Systematic reviews indicated a positive effect on proximal (i.e. shoulder and elbow) arm function [7, 8, 9] and recently also on distal (i.e. wrist and hand) arm function [10, 11] after robot-aided arm rehabilitation training.

One training modality that is commonly integrated in robotics is arm support, or gravity compensation (GC). Arm support decreases the effort by the stroke patient to hold the arm against gravity, which enables the patient to perform more repetitions of the movement that is being relearned. Research has shown that stroke patients can instantaneously increase the ability to extend the elbow due to a reduced effect of involuntary coupling between shoulder abduction/elevation and elbow flexion, when the arm is supported against gravity [12, 13]. This reduced effect of coupled movements leads to an increase of maximal forward reaching [14] and work area of the affected arm [15]. Training with progressively decreasing levels of arm support leads to increased reaching distance [16, 17] and increased work area [18, 19] without any support. In this study [17], the increased maximal forward reaching distance was accompanied by increased activity of the elbow extensors and a decreased involuntary coupling between shoulder and elbow movements in some patients.

Recent research showed that besides movements of the elbow, also movements of the wrist are coupled to shoulder abduction forces [20]. When shoulder abduction forces increase during lifting and reaching tasks, coupled flexion forces of the wrist and/or fingers were measured, together with increasing activation of the flexor digitorum superficialis. This involuntary coupled flexion impedes releasing of grasped objects. Seo et al. [21] reported decreased grip initiation and termination times in the hemiparetic hand, compared to the non-paretic and control hands. Application of gravity compensation leads to decreased delays in grip initiation and termination [21].

Besides (robotic) gravity compensation of the arm, electrical stimulation (ES) is often used to support arm and hand function. A meta-analysis of Glanz et al. indicated a positive effect of ES on muscle strength in both lower and upper extremity after stroke [22]. The ability to voluntarily generate wrist and finger extension increases after ES [23] and electromyography (EMG) triggered ES [24, 25], especially when patients have some residual function at the wrist and fingers [23, 26, 27].

When both arm and hand training are combined, goal directed and meaningful movements such as reach-to-grasp tasks can be practiced. Exercise programs in which goal directed tasks are intensively trained are beneficial for stroke patients [28].

For this purpose, a new hybrid Active Therapeutic Device (ATD) is being built, see Figure 7.1. The ATD will consist of a robotic manipulator with the main purpose to support the arm. Besides counteracting gravitational forces on the arm, the ATD can also provide small assisting or resisting forces by tilting the supporting force vector. A manually adjustable spring delivers a constant primary supporting force. Electric motors apply secondary variations to the magnitude and direction of the primary (supporting) force. Due to these variations in magnitude and direction of force, several training modalities are possible, such as actively assisted training, actively resisted training, and haptic simulation.

To facilitate hand opening, the ATD is equipped with a custom built multichannel electrical stimulator. This stimulator is capable of stimulating three channels independently. The stimulator can be used both with 12-pad array electrodes and with conventional single electrodes. The stimulator is equipped with a communications port so it can be controlled by an external device. For this purpose, as part of the present study, control algorithms have been developed that enable support of functional tasks and object manipulation. In the present study, a control strategy together with a rule-based system that uses positional data of the hand, relative to objects that subjects have to grasp, to trigger stimulation at the right moment during a functional task, is applied and assessed.

As a feasibility study, GC and multichannel surface ES are applied to the (fore)arm

Figure 7.1: Prototype of the Active Therapeutic Device (ATD).

in a small sample of stroke patients. Instantaneous effects on hand opening due to GC and/or ES are examined and the algorithms that control the electrical stimulator are evaluated. The objective is to study the instantaneous effect of multichannel ES and GC on dexterity, which is evaluated in the activity domain [29] of the International Classification of Functioning, disability and health (ICF). It is expected that application of GC [20, 21] and multichannel ES [30] will facilitate hand opening and consequently improve dexterity. The present study was performed as part of the design phase of the ATD.

7.2 Methods

Subjects

Subjects were recruited from rehabilitation centre 'Het Roessingh' in Enschede, the Netherlands. Subjects had to meet the following inclusion criteria: a history of a single unilateral stroke resulting in single-sided hemiparesis, the onset of the stroke was more than six weeks ago, the ability to voluntarily generate excursions of at least 20 degrees in the plane of elevation (horizontal ab-/adduction) and elevation angle (ab-/adduction, ante-/retroflexion) of the shoulder joint, the ability to voluntarily generate an excursion of at least 20 degrees of elbow flexion/extension, the ability to voluntarily extend the wrist at least 10 degrees from neutral flexion/extension, adequate cognitive function to understand the experiments, follow instructions, and give feedback to the researchers. Subjects were excluded if a fixed contracture deformity in the affected upper limb was present, or pain was a limiting factor for the subject's active range of motion.

Procedures

Before the experiment, patient characteristics were gathered and arm and hand function were clinically tested by means of the upper extremity part of the Fugl-Meyer (FM) assessment [31] and the Action Research Arm Test (ARAT) [32]. Because of the strong focus on hand opening and closing in this study, the individual scores on FM items 'mass flexion' (Flex) and 'mass extension' (Ext) of the fingers are reported in the results section. A score of 0 means 'no movement', a score of 1 means 'some, but not full active movement' and a score of 2 means 'full active movement'. After clinical testing, the electrodes used for electrical stimulation were applied to the forearm. The Box and Blocks Test (BBT) [33] was performed with four different combinations of support, i.e. with and without GC and with and without ES. The order of combinations was randomized across subjects to minimize possible learning effects and effects of fatigue. Each condition was preceded by a trial period of 15 seconds [33] and followed by a rest period of 2 minutes. During the BBT the subject had to move as many as possible wooden blocks (2.5 x 2.5 x 2.5 cm) from one compartment into another within a time frame of one minute.

Gravity compensation

The BBT was performed with 0 and 100 % gravity compensation, which means that the arm was either not supported or that the weight of that subject's arm was fully counterbalanced. Since the ATD was not fully ready to be used at the time of the experiments, an alternative GC device 'Freebal' [34] was used to support the arm. The Freebal consists of two adjustable ideal spring mechanisms that were attached to the wrist and elbow of the subject via overhead slings.

Electrical stimulation

A 50 x 50 mm square reference (ref) electrode (ti2013, tic Medizintechnik GmbH & Co. KG, Dorsten, Germany) was attached to the dorsal side of the wrist. A similar surface electrode was used to stimulate the m. extensor digitorum (EDI). A 32 mm round surface electrode (ti2011, tic Medizintechnik GmbH & Co. KG, Dorsten, Germany) was used to stimulate the m. abductor pollicis brevis (APB). The electrodes were placed on the muscle belly and connected to a custom built three channel electrical stimulator (tic Medizintechnik GmbH & Co. KG, Dorsten, Germany), that delivered trains of biphasic rectangular pulses with a pulse width of 200 µs and a frequency of 50 Hz.

After application of the electrodes, the amplitudes of both channels were increased in steps of 1 mA, starting at 0 mA to get a proper hand opening. Increasing the amplitude stopped when a natural, proper hand opening was achieved, or when the stimulation led to discomfort for the subject.

Control of the electrical stimulator

The electrical stimulator was connected to a computer and controlled via an RS-232 communication protocol by custom written software in Matlab (R2011b, Natick, MA). For this purpose, 3 reflective optical markers (H1 – H3) were attached to the proximal interphalangeal joints of digits 2 and 4 and to the metacarpophalangeal joint of digit 3 of the subject's hand, see Figure 7.2. The mean of the positions of H1 – H3 represented the hand position. Three spherical 14 mm VICON markers (M1 – M3) were attached to the BBT, see Figure 7.2. The markers were automatically labeled in real-time by VICON Nexus (version 1.8.2). The positions of the VICON markers were acquired in real-time in Matlab via the VICON DataStream SDK version 1.2 by the laptop that controlled ES. Based on the positions of the markers attached to the hand and BBT, commands were sent to the electrical stimulator to support hand opening. When the hand was above the compartment containing the blocks (source) the EDI and APB were stimulated to support opening of the hand. When the z-position (height) of the hand came below a threshold of 15 cm, measured from the bottom of the BBT, stimulation stopped to enable the subject to grasp a block. The stimulation remained off until the subject moves the hand across the divider, above the empty part of the BBT (target). At this point the muscles were stimulated to release the block. The subject moved the hand towards the source part, while the stimulation was still enabled. When the z-position of the hand came below the threshold, the stimulation was stopped again so the subject was able to grasp the next block.

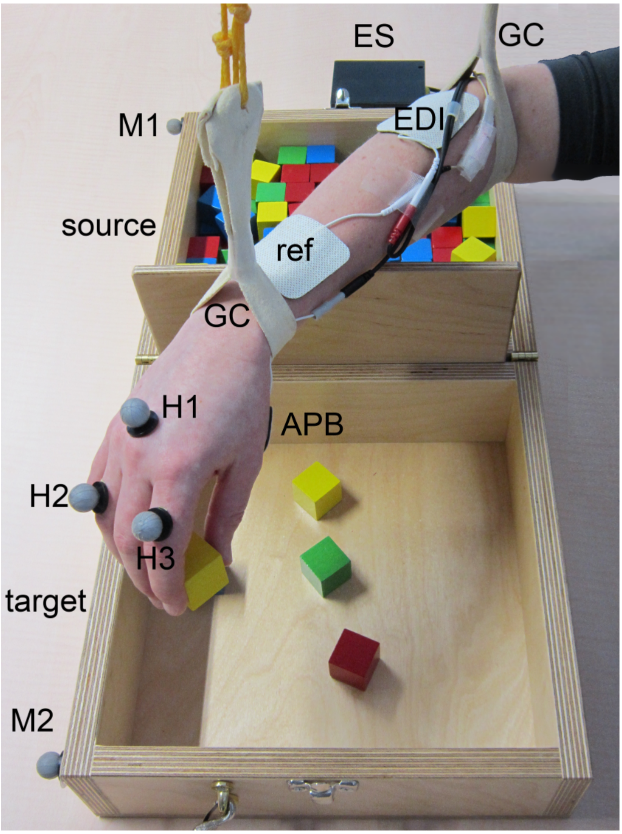

Figure 7.2: Locations of the VICON markers and surface electrodes used for electrical stimulation (marker M3 is not visible in the picture).

Statistics

Because of the explorative character of the study, effects of multichannel electrical stimulation on hand opening are reported descriptively. The primary outcome measure was the number of blocks that had been moved within one minute during the BBT. Individual data are reported in the results section. Data representing group averages are reported as median and interquartile ($25^{th} - 75^{th}$ percentile) range (IQR). To statistically test the effect of GC and ES a related samples Friedman's two-way ANOVA for ranks was applied to the data. Differences were non-parametrically tested

Table 7.1: Subject demographic and clinical data

N	8
Dominance before stroke	7 male / 1 female
Impaired arm	8 right / 0 left
Age (years)	64.4 (IQR: 48.5 – 65.8)
Months post stroke	12.0 (IQR: 6.0 – 28.5)
FM (max. 66)	22.0 (IQR: 19.0 – 28.5)
ARAT (max. 57)	12.0 (IQR: 6.5 – 17.0)

Abbreviations:
IQR = interquartile range
FM = Fugl-Meyer, ARAT = Action Research Arm Test

for statistical significance due to the small sample size. Effects were considered statistically significant for $p < 0.05$.

7.3 Results

Eight sub-acute and chronic stroke patients were included in the study. Demographic data and the clinical FM and ARAT scores of the subjects are presented in Table 7.1. Five subjects had severe hemiparesis (FM < 25) and three had moderate hemiparesis ($25 \leq$ FM < 45). Two subjects (S2 and S6) were (almost) not able to close the hand due to weakness/paresis of the finger and wrist flexors which affects closing of the hand.

The other subjects were able to partly (S5 and S7) or fully (S1, S3, S4, S8) flex the fingers. Two subjects were not able to volitionally open the hand due to weakness of the finger extensors (S2) or increased muscle tone in the finger flexors (S8), see also Table 7.2. The other six subjects were able to partly extend the fingers but none of them had a full range of motion.

With two-channel ES it was possible to achieve a hand opening big enough to grasp a wooden block with a vertex length of 2.5 cm in all subjects. The EDI was stimulated with a median amplitude of 32.5 mA (IQR: 25.0 – 40.0 mA). The APB was stimulated with a median amplitude of 14 mA (IQR: 5 – 17.5 mA). Application of GC did not lead to a visible increase of maximal hand opening. Some subjects (S2 and S8) had difficulty to detect whether or not their hand contained a block, probably due to reduced hand sensibility. Occasionally, S2 moved his hand towards the empty compartment to release a block, while he had not succeeded in grasping a block.

The individual scores of the FM, ARAT and the BBT are presented in Table 7.2.

Table 7.2: Individual scores on the FM, ARAT and BBT

					GC Off		*GC on*	
Subject	*FM*	*Flex*	*Ext*	*ARAT*	*ES off*	*ES on*	*ES off*	*ES on*
1	27	2	1	16	14	12	16	12
2	22	1	0	11	5	4	1	5
3	32	2	1	33	10	10	9	8
4	20	2	1	7	2	3	2	7
5	16	1	1	6	5	5	6	5
6	30	1	1	13	9	15	12	11
7	22	1	1	18	9	5	10	5
8	18	0	0	3	0	0	0	0

Abbreviations:
FM = Fugl-Meyer, Flex = mass flexion of the fingers, Ext = mass extension of the fingers
ARAT = Action Research Arm Test, GC = gravity compensation, ES = electrical stimulation

The median number of blocks transported within one minute on group level was 7 (IQR: 3.5 – 9.5) without ES and without GC. With only ES, the median number of blocks was 5 (IQR: 3.5 – 11). When the arm was supported against gravity (GC), the median number of blocks was 7.5 (IQR: 1.5 – 11). When the arm was supported against gravity (GC) and hand opening was supported by ES, the median number of blocks was 6 (IQR: 5 – 9.5). The number of blocks transported within one minute in each condition is graphically displayed in Figure 7.3. On group level, the number of transported blocks did not differ statistically significant across conditions, $p = 0.853$.

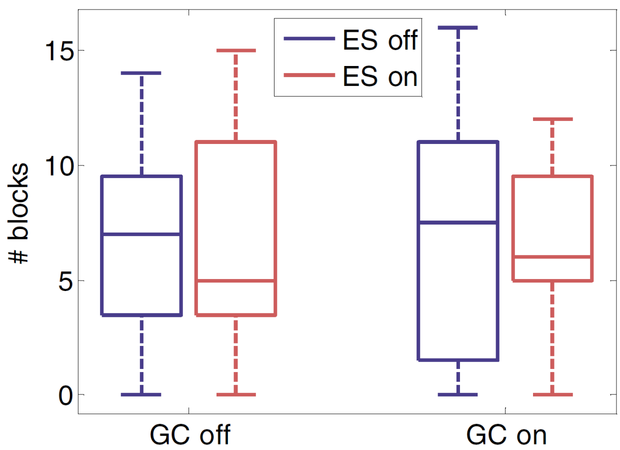

Figure 7.3: Box and Blocks Test scores in each of the four conditions

7.4 Discussion

As a feasibility study, GC and multichannel ES were applied to the (fore)arm of eight moderately to severely affected stroke patients. In all subjects it was possible to induce sufficient hand opening to grasp a wooden block of the BBT by means of two channel surface ES on the EDI and APB. The instantaneous effect of GC and multichannel ES on dexterity was evaluated by means of the Box and Blocks Test. Contrary to our expectations, application of multichannel ES, GC and the combination of both did not result in an instantaneous improvement in dexterity on group level.

The effect of arm support on involuntary wrist and finger flexion as found in Miller et al. [20] did not generalize to instantaneous gains in dexterity as measured with the BBT in the present study. A possible reason is that the amount of shoulder abduction torque needed to perform the BBT is less compared to the movements that subjects had to perform in the experiment carried out by Miller [20]. In that study subjects had to perform lift and reach tasks while maintaining different shoulder abduction forces, resulting in coupled, involuntary wrist and finger flexion forces. During the BBT subjects move their hand relatively close to the body, which implies that shoulder abduction/anteflexion torques are probably less compared to shoulder abduction/anteflexion forces that subjects had to generate in the experiment of Miller [20].

Whether or not application of GC led to increased hand opening, as could be expected from the previous research [20], or decreased time to terminate grip as found in [21], could not be discerned in the present study because hand opening and temporal aspects of hand opening were not measured explicitly. However, if application of GC led to quicker hand opening, it did not lead to an increase in BBT scores, which could imply that this process only has modest impact on dexterity as measured with the BBT.

This statement is strengthened by the observation that the most challenging aspect of the BBT for this patient group was to grasp a single block. Due to poor arm and hand coordination during the experiment, many blocks were moved around by the patient within the BBT compartment when trying to grasp a single block. This resulted in a very dense and compact layer of blocks, making it very difficult to grasp a single block. The stimulator was controlled in such a way that after releasing a block above the target compartment, ES continued until the hand was below the 15 cm threshold in the source compartment. In this case the hand is still opened when the patient lowered his/her hand to grasp the next block. However, when a patient failed to immediately grasp a block, ES stopped and hand opening was no longer supported. To improve these temporal aspects of support in hand opening, the rule-based system that decides whether or not to stimulate should be adapted in such a way that stroke patients can perform several attempts to grasp a single block.

After stroke, dexterity is affected by several mechanisms. A commonly observed mechanism is a reduced ability to generate wrist and finger extension due to muscle weakness [35] and inappropriate co-activation of finger flexors [36] which makes it difficult to open the hand, or to release a block during the BBT. However, some subjects (S2 and S6) who were able to volitionally open the hand to some extent, experienced difficulty in closing the hand as well, due to muscle weakness in the finger flexors. These patients had difficulty in holding a block. In these cases, support of hand opening by ES or GC has (almost) no beneficial effect on dexterity. Therefore in future research the support of arm and hand function should combine stimulation of finger extension with flexion in a functional way.

Previous studies have combined ES and (robotic) GC during functional tasks and object manipulation [37, 38]. The approach presented in this paper differs from [37, 38] in the way ES is triggered. In [37, 38] subjects triggered ES manually by pushing a button with the non-impaired hand, compared to the automatic, positional triggering in the present study.

Limitations and recommendations

In the present study it was possible to use positional information of the subject's hand relative to the objects that had to be manipulated to trigger the electrical stimulator. However, the present approach was rather coarse since only the dimensions of the compartment that contained the 150 blocks (source) and the empty compartment (target) were used. If the position of a single object that has to be transported or manipulated is known, together with the position of the hand, more accurate control algorithms can be developed. Some subjects, who showed weakness of the finger flexors and as a result had difficulty in holding a block, could have benefited from stimulation of the finger flexors together with the finger extensors. New and more sophisticated algorithms need to be developed that target impairments in hand function more specifically, enabling a patient-tailored approach.

The present study did not find any improvement in dexterity as measured with the BBT, after application of gravity compensation and/or electrical stimulation.

However, results should be interpreted carefully because of the small sample size. For example, some patients experienced fatigue during the BBT. Although the order of measurements had been randomized, fatigue could have influenced the number of transported blocks and therefore the results. In future research, it is recommended to include a more homogeneous group and increase the number of subjects. It is also recommended to measure fatigue of the arm and hand, for example by using a Visual Analog Scale (VAS).

Two subjects experienced diminished tactile feedback. This loss of sensibility is very likely to interfere with performance on a movement task such as the BBT where subjects have to grasp rather small blocks that are likely to be visually blocked by the subject's hand when grasped. In future research it is recommended to assess sensibility of the hand as well or select subjects also based on their level of tactile feedback.

Clinical implication and future research

Some algorithms that were used in the present study to induce hand opening were successful and will be integrated in the ATD. These algorithms will serve as a starting point to develop more sophisticated and more specific control algorithms with improved decision rules to trigger ES more accurately, taking the present findings into account. A possible next step is to combine the robotic arm manipulator with the updated control algorithms for the multichannel electrical stimulator and reassess the influence of GC + ES with the improved system. The ATD has built-in encoders that can be used to calculate the position of the hand. This means that an external system to measure hand position (VICON in the present study) is no longer necessary which makes the ATD more suitable to be deployed in a clinical setting.

In the present study it was possible to induce sufficient hand opening to grasp a wooden block of the BBT, by means of two-channel surface ES in all participating stroke patients. This enables the patient to train several functional movements that require sufficient hand opening, such as reaching for and grasping an object or other task oriented movements. By supporting the arm against gravity, the patient has to deliver an active contribution during reaching tasks, which is more effective than passive performance of movements [39]. Furthermore, to increase the active contribution during grasping, triggering of ES can be done not only by means of positional data, but also by means of activation levels of muscles involved in hand function (EMG triggered ES). After these steps, therapeutic effectiveness of the ATD needs to be evaluated in a longitudinal experiment.

7.5 Conclusion

This feasibility study showed that it was possible to induce sufficient hand opening to grasp a wooden block of the BBT in all participating subjects by means of two-channel surface electrical stimulation. The expected effects of application of gravity compensation on hand opening to result in an instantaneously improved dexterity were not observed. The used algorithms, allowing position-triggered electrical stimulation, allowed only a few patients to benefit from this specific support in hand opening. More research in a larger sample of stroke patients with more specific and more sophisticated control algorithms is needed to further explore beneficial effects on hand function in post stroke rehabilitation.

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Chapter 8

Discussion

THE aim of this thesis is to contribute to the development of a therapeutic rehabilitation robot used in post stroke upper extremity rehabilitation training. Prerequisite for developing a robot with application in post stroke upper extremity rehabilitation is a good understanding of principles in neurorehabilitation. Knowledge of muscle activation while reaching for and grasping of objects is needed, to know how and which movements of the upper extremity need to be supported by the robot. In this section the results of the preceding chapters and the answers on the research questions are discussed. In the following five sections the research questions will be answered, after which the development of the Active Therapeutic Device is discussed and suggestions for future research are made. This chapter ends with the general conclusion of the thesis.

Differences and commonalities between healthy elderly and stroke patients

To better understand which aspects of arm function should be supported by the rehabilitation robot, the first research question addressed the differences and commonalities of muscle activation and kinematics during reaching for and grasping of objects, between healthy elderly and stroke patients. The results presented in chapter 6 showed that stroke patients open the hand in a later phase of the reaching movement [1], compared to the timing of hand opening (THO) in healthy elderly. This was also seen in the Muscle Onset and Offset Profiles (MOOPs), which showed a delayed activation [2] of the m. Abductor Pollicis Brevis (APB) and m. Abductor Pollicis Longus / Extensor Pollicis Brevis (EPB), which oppose and extend the thumb, both needed for a successful hand opening. Stroke patients also had a reduced ability to go in a straight line from the starting position to the target position, as indicated by higher values of the path length ratio. On average, the amount of wrist excursion needed to perform the reach-to-grasp task did not differ between stroke patients and healthy elderly. It is known that especially wrist extension is often impaired in stroke patients [3, 4]. This effect was not clearly observed in the subjects who participated in the study described in chapter 6. A possible explanation is that only mildly impaired stroke subjects were included in the study, since the subjects had to be able to perform the requested movement task.

In addition, the results in chapter 6 showed that healthy subjects have larger variability in wrist excursion in different movement directions compared to stroke subjects. On average, across all movement directions, there was no difference between the two groups, but in the ipsilateral movement direction stroke patients did have smaller wrist excursions than healthy elderly. This movement direction required the largest wrist extension, to prevent the hand from colliding into the cylindrical object. Stroke patients were able to compensate for the lack of wrist extension and excursion by making a more circumferential movement, i.e. an increased Path Length Ratio (PLR) and by opening the hand in a later phase of the movement, i.e. increased Timing of Hand Opening (THO). In this way, compensational strategies were successfully applied to perform the requested movement tasks / activities. Compensational movement strategies to compensate for movement deficits are often seen in people after stroke. For example, many stroke patients use forward trunk movement and shoulder elevation during reaching movements to compensate for a reduced effective arm length due to decreased elbow extension and shoulder horizontal adduction [5]. Compensation may be a means for the stroke patient to achieve better arm function on both the body functions / structure and the activity level when remaining (distal) deficits in arm function are present.

These results give directions for rehabilitation training to focus on, namely opening the hand (finger extension and thumb abduction and opposition), wrist excursion, and compensational strategies in reaching movements. In the section 'Development of an Active Therapeutic Device' a possible solution to train these elements of upper extremity motor control is presented.

Effect gravity compensation training on abnormal synergies

The intended use of an Active Therapeutic Device is to induce improvements in unsupported arm function, which is often affected due to the presence of abnormal coupling between the shoulder and elbow joint [6, 7, 8]. Therefore, the second research question is formulated as: 'Can gravity compensation training affect the influence of abnormal synergies on unsupported arm movements in a sample of chronic stroke patients?'. From previous experiments [9], it is known that application of arm support can instantaneously increase the active range of motion (or work area) of the arm. It was hypothesized that rehabilitation training with arm support could possibly induce improvement in arm function in the unsupported condition. The study described in chapter 3 indeed showed that mildly and moderately impaired stroke patients are able to increase the work area of the arm after 6 weeks of gravity compensated arm training. The increased work area was accompanied by an increased range of motion of the shoulder and the elbow joints. These results are in accordance with a study performed by Chan et al. [10] who also found increased range of motion in the shoulder and elbow joint after a three week period of gravity compensated training. Studies by Sanchez et al. [11] and Housman et al. [12] found improvements in unsupported reaching tasks after a period of training in a gravity compensated environment.

The increased range of motion of the shoulder and the elbow joint is most likely caused by either an increased ability to activate the prime movers of those joints, and/or a reduction in abnormal coupling of those joints. As described in chapter 4, an increased activity of the prime movers or agonists was observed in most patients, instead of a decreased activity of the antagonists, which would have indicated a reduced co-contraction.

Gravity compensation or arm support is a training modality that is incorporated in many upper extremity rehabilitation robotics [13]. Several reviews [13, 14, 15, 16] found positive effects on proximal arm (i.e. shoulder and elbow joints) function after training with rehabilitation robotics. However, the improvements in proximal arm function hardly generalize to improvement of distal arm (i.e. wrist and fingers) function nor to improvement of functional abilities [13, 14, 16]. A possible explanation is that sufficient arm function of both the proximal and the distal arm is required for functional use of the arm. The majority of upper extremity rehabilitation robotics focus on the proximal arm and not on the distal arm, most likely because of the high complexity that is required to support the human hand which has many degrees of freedom [17, 18]. The majority of robotic systems that support activities of the wrist and hand is still in the development phase [17], and (clinical) data from these systems are lacking in a systematic review addressing neurological treatment approaches in stroke rehabilitation interventions [16]. In the same systematic review, a significant effect size of EMG triggered electrical stimulation of the paretic wrist and finger extensors is reported. Neuromuscular electrical stimulation led to improved motor function of the paretic wrist, such as increased muscle strength and increased active range of motion. EMG triggered electrical stimulation on the wrist and finger extensors led to increased arm and hand activities [16]. In other words, EMG triggered electrical stimulation is a promising tool to support hand opening and wrist extension in stroke patients. A logical step is to combine EMG triggered electrical stimulation for distal arm support with gravity compensation for proximal arm support.

Arm support combined with electrical stimulation

Chapter 7 describes a pilot experiment to combine gravity compensation and multichannel electrical stimulation. It was hypothesized that the combination of gravity compensation of the arm, and multichannel surface electrical stimulation of the forearm could lead to an instantaneous functional increase in arm and hand function. For this purpose, arm function was assessed with the Box and Block Test (BBT). Although sufficient hand opening to grasp a 2.5 x 2.5 x 2.5 cm block could be achieved with electrical stimulation in all patients, the BBT scores were not increased during application of electrical stimulation and/or gravity compensation. In other words, an improvement on body structure level (i.e. improved hand opening) does not necessarily lead to improvement on activity level (i.e. more blocks transferred in 1 minute).

A possible explanation why stroke patients did not show functional improvement, is that patients were only supported in hand opening, and not in other aspects of hand motor function, like grasping. During the experiment, it was noticed that patients experienced difficulty in grasping a block. Many patients were unable to make a pincer grasp or precision grasp, which are the most favorable grasps to grasp a single block of the BBT. Some patients tried to grasp a block with a power grasp, but they were not very successful. A reduced sensibility of the distal arm, which is often present in stroke patients, could also negatively affect grasping performance of the blocks of the BBT [19].

It is expected that the patients can benefit more from the electrical stimulation when more sophisticated control algorithms are used. In the study described in chapter 6 an open-loop control scheme was used. Electrical stimulation was switched *on* and *off* based on the position of the hand relative to the position of both segments of the box of the BBT. It is expected that when feedback on hand-opening is used, for example, to control the amount of electrical stimulation, a more natural and effective hand opening can be achieved. In closed-loop control, the amount of hand opening can be controlled based on the difference between the required handopening (i.e. setpoint) and the actual hand opening. When the stroke patient is able to generate sufficient hand opening, the amount of support is small. When the stroke patient is not able to generate sufficient hand opening, the system assists the patient (i.e. assist-as-needed). Preferably, electrical stimulation is triggered by volitional muscle activation of the patient (i.e. EMG-triggered ES) [16].

The feasibility/practical applicability to support hand opening by electrical stimulation is promising. After a short setup time, in each individual patient sufficient hand opening to grasp a block of the BBT was induced by electrical stimulation. To explore the possibilities of sophisticated, EMG triggered control of the electrical stimulator, a good understanding of muscle activation patterns of muscles involved in reaching and grasping of objects is needed.

Autonomous burst detection

As described in chapter 5, it is possible to autonomously detect bursts of sEMG activity and create Muscle Onset Offset Profiles of muscles involved in reaching and grasping objects. This is done in basically three steps. First, sEMG data is band-pass filtered and transferred into the Teager-Kaiser (TK) domain [20]. The Teager-Kaiser Energy Operator (TKEO) is sensitive to the instantaneous amplitude and the instantaneous frequency of the sEMG signal. When a muscle contracts, both the amplitude and the frequency of the measured motor unit action potential signal increase. So, after applying the TKEO, the signal variance of the measured sEMG signal is much higher in the 'muscle contracted' state compared to the 'muscle relaxed' state. In other words, the signal-to-noise ratio is improved, which leads to a more robust burst detector since detection errors are smaller.

Second, the Approximated Generalized Likelihood Ratio (ALGR) algorithm [21] is used to detect changes in signal variance (of the TK signal). The AGLR algorithm calculates a log-likelihood ratio for a sliding window L. When this ratio exceeds threshold h an alarm time is given. In a subsequent step, the maximum likelihood between two alarm times is calculated. The time instance at which the likelihood maximizes is called change time.

Third, these change times are fed into a post processor that determines whether a change time is a muscle onset or muscle offset. For this step, the Root Mean Square (RMS) value of the TK signal between two change times is compared to a predefined threshold. If the RMS values exceeds the threshold, the muscle is regarded as being contracted. If the RMS value is below the threshold, the muscle is regarded as being relaxed. A muscle onset is identified as a transition from the 'relaxed' state to the 'contracted' state. Similarly, a muscle offset is identified as a transition from the 'contracted' state to the 'relaxed' state. The postprocessor also analyzes the change times before a muscle onset and the change times after a muscle offset. Assume that an initial onset is found at change time t_n. Then the postprocessor also analyzes the signal between change times t_{n-1} and t_n. When the variance between t_{n-1} and t_n is smaller than the variance between t_n and t_{n+1}, it is very likely that the muscle started contracting at t_{n-1} instead of t_n and the postprocessor changes the onset from t_n to t_{n-1}. In other words, the postprocessor optimizes the exact timing of muscles onsets and offsets based on the signal variance before and after the onset or offset.

The burst detector as described in chapter 5 and applied to real EMG in chapter 5 and 6 is designed for offline use, i.e. data is recorded and analyzed afterwards. With minor adaptations, the burst detector can also be used for real-time applications such as movement intention detection. The TKEO only requires three samples of (s)EMG, so with a minimal delay of 1 sample time, it can easily run in real-time applications. Since the TKEO is very straightforward, it requires only little computation time, which allows the algorithm to run in control loops with high sample rates. The AGLR algorithm can be easily modified to run in semi-real-time mode, for example by analyzing small blocks of data. For example, when blocks of data with a duration of 100 ms are analyzed, the system is able to analyze 10 blocks of data per second. When epochs of data that are used for analysis are (partly) overlapping, the system can update its outputs more often. The use of overlapping data will increase the computation time. The duration of the epochs data and the amount of overlap determine the sample rate of the control loop. When the update frequency is too low, the user of the rehabilitation device that is controlled by the system will experience delay between the intention of the user and the response of the system. Preferably, this control latency is as small as possible, and temporal delays should not exceed 300 ms [22]. In the case of wearable robotics or assistive orthoses, short latencies are prerequisite for the sense of embodiment of the orthosis [23]. The possibility to timely match movement intention with functional electrical stimulation (FES) assisting specific motor functions allows the use of technology supported assisted devices that support functional movements needed to perform activities of daily living.

It is expected that the burst detector described in chapter 5 can also be used to generate muscle activation patterns of muscles acting on the lower extremity or other body parts. The AGLR algorithm is previously applied to sEMG data obtained from lower extremity muscles of stroke patients [24] to detect onsets in muscle activation. The post processor of the burst detector uses two thresholds Th_{on} and Th_{off} which might need adjustment for use on the lower extremity. In general, muscles of the lower extremity are bigger in size compared to the muscles of the upper extremity. For that reason, the amplitude of sEMG of the lower extremity is expected to be higher than sEMG of the upper extremity. On the other hand, the layer of tissue surrounding the muscles of the lower extremity is most likely thicker compared to the upper extremity, which has an attenuating effect on the measured sEMG. Also the higher impact force of walking can cause movement artefacts in the sEMG signals which are less likely to occur in sEMG obtained from the upper extremity. It is expected that the autonomous burst detector can be easily tuned to objectively generate muscle activation patterns during gait.

One of the design goals of the burst detector was that it can operate autonomously, i.e. without the need for user interaction. This increases the objectivity in the analysis of onset and offset times in EMG analysis and allows a fair comparison of measurement data obtained from different people, across different conditions or obtained at different research centres. To be able to operate autonomously, the burst detector shall be very stable and robust. The TKEO data preconditioning step makes the burst detector sensitive to changes in signal amplitude and frequency content. The AGLR is set fairly sensitive so it reacts to small differences in signal variance. This yields many (false-positive) alarm times from which the rule based post processor selects the onset and offset times of the muscle, based on the surrounding alarm times, current activation level and the electromechanical delay of the muscle. The result is a burst detector that is able to autonomously and objectively create muscle onset and offset profiles.

Outcome measures derived from robotics

Besides electromyography. objective quantification is also important in other aspects of arm function such as kinematics. Therefore, the fifth research question is formulated as 'Which outcome measures derived from rehabilitation robotics can be used to objectively quantify upper extremity function?'. Rehabilitation robotics are equipped with a wide variety of sensors, measuring either kinematics of the robot or arm function of the patient itself. For that reason, the answer to this research question could be quite extensive and the answer will be limited to position sensors that are present in most rehabilitation robots. The circle drawing task that is described in chapter 2 and 3 can be used in any device that measures or calculates the position of the hand. When the position of the hand is known, the area of the circle that is drawn by the patient can be easily calculated. As mentioned in chapter 2, the circle area represents the size of the area where the patient is able to grasp or to manipulate an object. Based on these trajectories, circle roundness can be calculated. The circle roundness highly correlates with the ability of subjects to move out of synergistic movement patterns. This means that even with very low-cost equipment it is possible to objectively quantify arm function of stroke patients. Many other outcome measures can be derived from the hand trajectory. The first time derivative of the position will yield the movement velocity. The number of peaks in movement velocity is negatively correlated to arm function, i.e. fewer peaks mean fewer periods of acceleration or deceleration [25]. The number of peaks in the movement speed profile has previously been used to quantify movement smoothness in stroke patients [25]. The second time derivative yields the acceleration of the hand. Several acceleration metrics have been shown to be responsive to training induced changes in upper extremity function [26]. The third time derivative of the hand position is jerk. This measure has been previously used as a measure of motor performance of both healthy subjects and stroke patients and movement smoothness is related the recovery of stroke patients [27].

Any robot or other measurement system that is able to measure the individual joint angles of the shoulder and the elbow can be used to calculate the amount that patients moved within or out of synergistic movement patterns. One can think of an exoskeleton based rehabilitation robot such as the Dampace (see chapter 2 and 3), Armin or Armeo Power, endpoint controlled robots like the Haptic Master [28] or even a measurement system based on inertial sensors placed on different segments of the arm [29].

Summarizing, the circle drawing task is easily applicable in post stroke upper

Figure 8.1: Prototype of the Active Therapeutic Device (ATD), developed as a joint effort in a consortium consisting of Roessingh Research & Development, Enschede, the Netherlands; University of Twente, Enschede, the Netherlands; Demcon Advanced Mechatronics, Enschede, the Netherlands; Use-Lab, Steinfurt, Germany; tic Medizintechnik, Dorsten, Germany.

extremity rehabilitation. It quantifies arm function (i.e. work area) on a functional level, since it reflects to work area of the arm, i.e. the area where the subject is able to position his hand to graps and/or manipulate objects. The normalized work area correlates strongly with the clinically used Fugl-Meyer assessment [30]. Circle metrics as circle area and roundness can be easily measured and objectively compared.

Development of an Active Therapeutic Device

Findings in this thesis contributed to the development of an Active Therapeutic Device (ATD) [31] intended to train both proximal and distal arm function after stroke, see also Figure 8.1. The ATD is an endpoint controlled robot, equipped with a manually adjustable clock spring which provides a constant supporting force, acting against gravity. A therapist, operator or stroke patient can easily adjust the amount of gravity compensation, tailored to the specific needs of an individual patient. The robot is also equipped with an electric motor connected to a damper which results in a series elastic actuator. This actuator is backdrivable, and can provide both assistive and resistive forces to the patient's arm, which, combined with the force supplied by the clock spring, leads to over- or undercompensation of the patient's arm. The ATD is able to vary the amount of support dynamically during training.

The ATD [31] is equipped with a six degree of freedom loadcell that measures the interaction forces between the subject's forearm and the robot, which enables admittance control of the robot. In admittance control, the patient perceives a certain virtual (haptic) environment. The robot is also equipped with absolute encoders that enable measurement of the angles between the different segments of the robotarm. With known segment lengths of the robot arm, the position of the arm cuff can be calculated. The arm cuff itself is equipped with potentiometers to allow measurement of the orientation of the patient's forearm relative to the robot arm. Based on these values, the position of the patient's hand can be estimated.

Since the position of the patient's hand is known, the ATD can be used to assess arm function by means of the circle drawing tasks as described in chapter 2 and 3. The circle area and roundness can be easily determined, based on the trajectories of the hand. The angles of the elbow and shoulder joint are not measured by the ATD, so it is not possible to directly measure movement within and out of synergistic movement patterns. However, with a biomechanical model (inverse kinematics) of the human arm, or by placing additional sensors on the different arm segments, it might be possible to derive the joint angles of the shoulder and elbow joint from the absolute encoders that measure the angles between the different segments of the robot arm and estimate the synergistic movement patterns.

Besides training the proximal arm, the ATD is also able to train the distal arm (i.e. hand). Training of both the arm and the hand is believed to be most effective to induce functional gains of the upper extremity [32]. To be able to train the hand, the ATD is equipped with a 3-channel electrical stimulator (tic Medizintechnik GmbH & Co. KG, Dorsten, Germany). Parameters controlling timing and amplitude can be set for each individual channel. As described by Westerveld et al. [33], successful opening and closing of the hand to grasp and release objects have been demonstrated with this stimulator, even when the patient or healthy subject was completely passive during the task. The multichannel electrical stimulator is also able to measure volational activation of the muscles, by means of surface electromyography. This enables EMG-triggered stimulation, potentially based based on MOOPs as identified in chapter 6, in which support is given only when the patient needs it, i.e. assist-as-needed control strategy.

Future directions in Active Therapeutic Devices

In the past decades, several Active Therapeutic Devices for post stroke upper extremity rehabilitation have been developed. An extensive overview of robotic devices for upper limb rehabilitation is presented in a review by Maciejasz et al. [34]. Among them were end-point controlled robotics, exoskeletons systems and/or systems equipped with one or more electrical stimulators [35]. It would be very interesting to evaluate the ATD in post stroke rehabilitation and compare it with existing therapeutic devices. Can patients benefit from training with the ATD? Is it possible to induce clinically significant improvements in arm function and hand function on the body function / structure level and on the activity level of the ICF? Is it possible for patients to train safely and effectively in a domestic environment? Currently, it is unknown if and how severely affected stroke patients can benefit from an Active Therapeutic Device that consists of a robotic manipulator for proximal arm support and electrical stimulation for distal arm support. From clinical experiences it is known that functional electrical stimulation (FES) is unfeasible for severe patients who have abnormal or (almost) absent muscle activation patterns. Future research should elaborate if and how severely affected stroke patients can benefit from an ATD.

A related research question is how to implement the ATD in a clinical setting. As can be concluded from several systematic reviews, retraining the upper extremity with currently available rehabilitation robotics is equally effective as conventional rehabilitation training [36]. However, application of rehabilitation robotics can be a cost-effective solution to provide high intensity upper extremity rehabilitation training following stroke [36]. One can think of one physical therapist who can supervise several stroke patients at the same time. In this way, the patients can have more therapy time while the labour costs remain the same. The ATD can be a useful rehabilitation robot to be used in a clinical setting, such as a rehabilitation centre. For example, the ATD can be used to play serious games (also called exergames). The supervisor can adjust the games to the specific needs and capabilities of the individual patient. After that, the patient is able to train semi-independently while both the computer game and the supervisor can provide feedback on performance and/or results to the patient. When multiple ATDs are available at a rehabilitation centre, several stroke patients can play computer games with each other (cooperative games), or against each other (competitive games). Especially the competitive games might increase motivation [37] and can result in an increased therapy dose.

A second approach to increase patient motivation and adherence is to move rehabilitation training from a clinical setting to the domestic environment. In a domestic environment, the frequency and intensity of training could significantly increase, without the need for additional physical therapists, which lowers the burden on healthcare professionals. Increasing the frequency and intensity of training could significantly improve performance following stroke [38]. The ATD is designed to train stroke patients in a domestic environment. When the ATD is also used to assess arm function, for example by means of circle metrics described in chapter 2 and 3, a more reliable measure can be expected when compared to assessment of arm function using (partly) subjective clinical scales. Recent research showed that objective outcome measures such as circle area have greater sensitivity than clinical assessments such as for example the Fugl-Meyer assessment and ARAT [39].

An interesting topic for future research is to combine a therapeutic device with an assistive device. One can think of a wearable orthosis that supports the stroke patient during real-life functional activities. In this case, the patient is assisted by the wearable orthosis while performing (training) functional movements. In other words, the training intensity is maximized and task-specificity is the highest possible. One challenge is to reduce the weight of the heavy parts of such systems, not to hinder the patient while wearing the device. The heavy parts are typically the energy buffers like batteries and the actuators like (servo-) motors. A second challenge is to keep the size of the device small, to prevent collisions and unwanted interactions of the device with the patient's environment. Multichannel electrical stimulation seems a suitable technique to support hand opening and closing following stroke. Only the electrodes and connecting leads have to be placed on the patient's arm, while the heavy parts of the system such as the battery and controller can be placed distant from the arm, for example on the hip. The algorithms used in chapter 5 and 6 can be used to analyze the measured sEMG, possibly detect the intention of the user, and control the output of the electrical stimulator accordingly.

Conclusion

The general aim of the studies included in this thesis is to contribute to the development of a therapeutic rehabilitation robot. Such a robot can also be used to measure arm function of stroke patients. The circle drawing metrics described in chapter 2 and applied in chapter 3 can be used to objectively quantify upper extremity function in stroke patients. Circle area and roundness provide information about the functional work area of the hand and the ability to move out of synergistic movement patterns. Both circle metrics highly correlate with the clinically used Fugl-Meyer assessment.

The results of chapter 3 show that training in a gravity compensated environment led to increased joint excurions of the shoulder and elbow joint during unsupported arm movements. Stroke patients increased the circle area (i.e. work area of the hand) after 6 weeks of training. A decreased strength of involuntary coupling between shoulder and elbow movements might play a role, but the results of chapter 4 showed that most patients have increased their ability to activate prime movers of the arm.

The method to autonomously detect bursts of EMG and generate MOOPs, described in chapter 5 and applied in chapter 6, can be used to objectively quantify upper extremity function in stroke patients and can be used as a tool to study differences in arm function between different groups and/or conditions. Simulation results yielded optimal parameter settings for the burst detector leading to minimal detection errors. The performance of the burst detector improves when the Teager Kaiser Energy Operator is included as data preconditioning step.

The burst detector described in chapter 5 is able to autonomously generate Muscle Onset and Offset Profiles (MOOP) of muscles involved in reach-to-grasp movements. These MOOPs revealed a delayed activation of the Abductor Pollicis Brevis and Abductor Pollicis Longus / Extensor Pollicis Brevis and an early activation of the Flexor Carpi Radialis in stroke patients. Compared to healty subjects, stroke patients process arm and hand movements more serially and have a more curved path towards the target location. The path length ratio, timing of hand opening and the amount of wrist excursion is related to reaching direction. These differences in muscle activation and kinematics can for example be used as input to control (multichannel) electrical stimulators or (soft) robotics to support hand opening and closing during post stroke rehabilitation.

The feasibility study described in chapter 7 shows that with multichannel electrical stimulation sufficient hand opening to grasp a single block of the box and block test can be achieved. The expected effects of application of gravity compensation on hand opening to result in an instantaneously improved dexterity were not observed. The used algorithms, allowing position-triggered electrical stimulation, allowed only a few patients to benefit from this specific support in hand opening and it is recommended to use more sophisticated control algorithms, preferably triggered by EMG, which also support hand closing in future development in technology supported arm and hand training after stroke.

The studies composing this thesis have provided valuable design input for the development of an Active Therapeutic Device (ATD), which is intended to train both proximal and distal arm function after stroke. The ATD is an endpoint controlled robot that is can be used in both clinical settings or domestic environments. The robot supports hand opening (i.e. wrist- and finger extension and thumb opposition and extension) and closing by means of a three channel electrical stimulator. The robot is able to (partly) support the arm against gravity which and can dynamically adjust the amount of support that is given to the patient. The ATD is designed according to the key elements of neuro-rehabilitation.

Hopefully, the findings presented in this thesis, can be 'a reaching hand' and inspire researchers and engineers in developing future technology to support arm- and hand function in stroke patients.

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Appendices

Summary

In **chapter 1** a short overview of the background of stroke and upper extremity rehabilitation afer stroke, is presented. Many stroke patients have to cope with motor problems of the upper extremity such as muscle weakness, spasms, disturbed muscle timing and a reduced ability to selectively activate muscles. After stroke, rehabilitation training aims to re-learn (partly) lost functions and/or learn compensational strategies in order to achieve the highest possible degree of physical and psychological performance. Several key elements of rehabilitation training have been identified such as training intensity, task specific training, active contribution of the patient, exercise variability, ability to make errors, and feedback on performance and results. The

desired, repetitive nature of rehabilitation training led to development of rehabilitation robots to help (physical) therapists with the challenges facing neurorehabilitation. The aim of this thesis is to contribute to the development of a therapeutic rehabilitation robot used in post stroke upper extremity rehabilitation training. The intended use of the robot is to train both arm and hand function by actively supporting the arm against gravity and support hand function by means of multichannel functional electrical stimulation.

Use of rehabilitation robots into research facilities and in clinical practice allows objective measurement and quantification of movement ability of stroke patients. **Chapter 2** showed that circle area, circle roundness and movement within / out of synergistic movement patterns differed between healthy elderly and stroke patients, indicating that these outcome measures are valid measures to assess arm function. This is supported by the strong correlation between these measures and the clinically used Fugl-Meyer assessment in the stroke group.

Chapter 3 describes an experiment to study the effect of training in a gravity compensated environment on unsupported am movements. A group of seven stroke patients received 18 half-hour sessions of gravity compensated reach training. After training, most subjects increased joint excursions of the shoulder and elbow joint, which resulted in significantly increased work area of the hemiparetic arm, as indicated by the normalized circle area. Roundness of the circles and the occurrence of synergistic movement patterns remained similar after the training. The used training setup is simple and affordable and is therefore suitable to use in clinical settings.

To gain more insight in the mechanisms involved in gravity compensation training, muscle activation during a maximal forward reaching task performed before and after the gravity compensation training, is described in **chapter 4**. In this clinical trial, eight chronic stroke patients with limited arm function received the same 18 sessions (30 min) of gravity-compensated reach training as described in chapter 3. Joint angles and muscle activity of eight shoulder and elbow muscles were compared. After training, the maximal reach distance improved significantly by 3.5 % of arm length. Main contributor to the increased forward reaching was an increased elbow extension that was accompanied by an increased elbow extensor activity. In some patients, a reduced cocontraction of biceps and anterior deltoid was involved, although this was not significant on group level.

The study described in **Chapter 5** was performed to investigate the added value of applying the Teager Kaiser Energy Operator (TKEO) as a data pre-processor to a method for autonomous burst detection of sEMG obtained from the arm and hand during sub-maximal movement tasks. Since the TKEO is sensitive to both signal amplitude and frequency, the TKEO may increase the signal to noise ratio of sEMG signals recorded from muscles of the forearm and hand. The burst detector is based on the Approximated Generalized Likelihood Ratio (AGLR) that is able to detect changes in signal variance, combined with a rule-based postprocessor that is able to identify muscle onsets and offsets. Simulations on synthesized electromyographic traces with known onset and offset times were done to obtain optimal settings of the burst detector, leading to minimal detection errors. After the simulations, the optimized burst detector was applied to real surface EMG signals, obtained from arm and hand muscles involved in a submaximal reach-to-grasp task, performed by healthy adults. Muscle Onset and Offset Profiles (MOOP) were generated autonomously based on the detected bursts.

To better understand motor control of the arm and hand of stroke patients with respect to healthy elderly, the study described in **chapter 6** was performed. A group of eighteen healthy elderly and sixteen stroke patients performed functional reach-to-grasp movements, with and without arm support. Objective kinematic outcome measures such as timing of hand opening, path length ratio, wrist excursions and MOOPs were compared between both groups and across conditions. Stroke patients have a more curved path towards the target object than healthy subjects and movements are processed more serially. Compared to healthy helderly, stroke patients have a delayed activation of Abductor Pollicis Brevis and Extensor Pollicis Longus, and an early activation of the Flexor Carpi Radialis. In both stroke patients and healthy elderly, the path length ratio, timing of hand opening and wrist excursions are dependent of movement direction, but not of support condition. Stroke patients seem to compensate for a delayed hand opening with respect to healthy elderly, by making a more circumferential movement towards the target object to prevent colliding into the target object. These temporal differences in muscle activation between healthy elderly and stroke patients can serve as input to control assistive and/or therapeutic rehabilitation robot system or multi-channel electrical stimulators to support hand opening and -closing.

In an explorative study, described in **chapter 7**, arm support or gravity compensation was combined with multichannel electrical stimulation of muscles involved in opening of the hand. For this purpose, a group of eight stroke patients performed the Box and Blocks Test (BBT) with and without arm support and electrical stimulation. The position of the subject's hand and the box of the BBT were measured with VICON. Positional data was sent in real-time to the computer that controlled a multichannel electrical stimulator. Since the position of the hand relative to the BBT was known, hand opening for grasp and release of small objects was supported by electrically stimulating the m. Extensor Digitorum and the m. Abductor Pollicis Brevis. In all patients, it was possible to induce sufficient hand opening for grasping a block of the BBT by means of ES. There was no direct improvement in dexterity as measured by the BBT. More sophisticated control algorithms, stimulating both flexors and extensors, are needed to explore beneficial effects of GC and ES on hand function in post stroke rehabilitation.

Finally, in **chapter 8**, the main findings and conclusions of this thesis were discussed, along with suggestions for clinical implications and future research. The studies composing this thesis have provided valuable design input for the development of an Active Therapeutic Device (ATD), which is designed according to the key elements of neuro-rehabilitation. The robot supports hand opening (i.e. wrist- and finger extension and thumb opposition and extension) and closing by means of a three channel electrical stimulator. The robot is able to (partly) support the arm against gravity, and can dynamically adjust the amount of support that is given to the patient. Hopefully, the findings presented in this thesis will inspire researchers and engineers in developing future technology to support arm- and hand function in stroke patients.

Samenvatting

In **hoofdstuk 1** wordt de achtergrond informatie van een Cerebro-Vasculair Accident (CVA) en de revalidatie die daarop volgt beschreven. De meerderheid van de CVA-patiënten kampt met motorische problemen als gevolg van een CVA. Enkele voorbeelden hiervan zijn spierzwakte, spasticiteit, verstoorde timing van spieractivatie en een beperkte selectiviteit van aansturing. Het doel van revalidatie is om de (gedeeltelijk) verloren functies weer te herstellen of om compensatie strategiën aan te leren, zodat een zo hoog mogelijke mate van zelfstandigheid verkregen wordt. De effectiviteit van revalidatie-interventie is afhankelijk van trainingsintensiteit, taakspecificiteit, de mate waarin de patiënt zelf een actieve bijdrage levert, variabiliteit in training, de mogelijkheid tot het maken van fouten en het krijgen van feedback op de uitvoering en het resultaat. Het herhalende karakter van revalidatie-oefeningen heeft geleid tot ontwikkeling van revalidatie robotica. Het doel van dit proefschrift is om een bijdrage te leveren aan de ontwikkeling van een trainingsrobot voor de bovenste extremiteit voor revalidatie na een CVA. De robot is bedoeld om zowel de arm als de hand te trainen door middel van zwaartekrachtcompensatie en meerkanaals functionele elektrostimulatie.

Door het gebruik van revalidatierobotica in de klinische praktijk en in onderzoekscentra is het mogelijk om armfunctie van CVA-patiënten objectief te kwantificeren. **Hoofdstuk 2** laat zien dat cirkel-oppervlakte, rondheid en de mate waarin mensen binnen en buiten synergistische patronen bewegen verschillen tussen gezonde ouderen en CVA-patiënten, waardoor deze uitkomstmaten geschikt zijn om armfunctie te kwantificeren. Dit wordt ondersteund door de sterke correlatie tussen bovengenoemde uitkomstmaten en de Fugl-Meyer assessment die in de klinische praktijk gebruikt wordt.

Hoofdstuk 3 beschrijft een experiment waarin het effect van het trainen in een zwaartekracht-gecompenseerde omgeving op armfunctie onderzocht werd. Een groep van zeven CVA-patiënten kreeg 18 sessies van een half uur waarin reiktaken getraind werden, terwijl de arm ondersteund werd tegen de zwaartekracht. Na de trainingsperiode hadden de meeste proefpersonen meer bewegingsvrijheid in het schouder- en elleboogewricht. Dit resulteerde in een significant toegenomen werkbereik van de hand, zoals weergegeven door de genormaliseerde cirkeloppervlakte. De rondheid van de cirkels en de mate waarin buiten synergistische patronen bewogen werd, bleven onveranderd na training. De gebruikte technologie is eenvoudig en goedkoop waardoor het goed toepasbaar is in de klinische praktijk.

Om meer inzicht te krijgen in de werkingsmechanismen van zwaartekracht-gecompenseerde training, zijn in **Hoofdstuk 4** spieraanspanningspatronen bestudeerd. Deze patronen zijn opgenomen tijdens een maximale voorwaartse reiktaak die zowel voor aanvang als na afloop van de training uitgevoerd werd. In deze studie deden 8 CVA-patiënten met beperkte armfunctie mee die dezelfde training ontvingen als beschreven in hoofdstuk 3. Gewrichtshoeken en spieractivatie van 8 schouder- en elleboogspieren werden vergeleken voor en na training. Na de training was de maximale reikafstand significant toegenomen met 3.5 % van de armlengte. De belangrijkste bijdrage kwam door een toegenomen elleboog-strekking en toegenomen activiteit van de elleboog-strekker. Sommige patiënten lieten een verminderde co-contractie tussen de biceps en de deltoïdeus anterior zien, maar dit effect was niet significant op groepsniveau.

Het doel van de studie beschreven in **Hoofdstuk 5** was om te onderzoeken of het toepassen van de Teager-Kaiser Energy Operator (TKEO) een gunstig effect heeft op een autonome burst-detectie voor sEMG signalen, die gemeten zijn op de arm en hand tijdens sub-maximale bewegingstaken. Omdat de TKEO zowel gevoelig is voor de amplitude en frequentie-inhoud van een signaal, kan de TKEO zorgen voor een toename in de signaal-ruisverhouding van sEMG signalen gemeten op de arm en de hand. De burst-detector is gebaseerd op de Approximated Generalized Likelihood Ratio (AGLR) die veranderingen in signaal variantie kan detecteren. Vervolgens identificeert een post-processor de onsets en offsets van de spier. Aan de hand van simulaties van sEMG signalen met bekende onsets en offsets zijn de optimale parameters bepaald die leidden tot minimale detectie fouten. Vervolgens is de geoptimaliseerde burst-detector toegepast op spiersignalen gemeten op de arm en de hand tijdens een submaximale reik- en grijptaak, uitgevoerd door gezonde ouderen. Muscle Onset en Offset Profielen (MOOPs) werden autonoom gegenereerd op basis van de gedetecteerde bursts.

De studie die beschreven staat in **Hoofdstuk 6** is uitgevoerd om beter inzicht te krijgen in de verschillen in aansturing van spieren in de arm en de hand tussen CVA-patiënten en gezonde ouderen. Hiervoor hebben 18 gezonde ouderen en 16 CVA-patiënten functionele reik- en grijptaken uitgevoerd, zowel met als zonder zwaartekracht-compensatie. Objectieve uitkomstmaten zoals timing van hand opening, path length ratio, pols-excursie en MOOPs zijn vergeleken tussen beide groepen en tussen verschillende condities. Ten opzichte van gezonde ouderen bewegen CVA-patiënten meer in een omtrekkende beweging naar hun doel, en de verschillende componenten van de beweging worden meer serieel uitgevoerd. Daarbij laten CVA-patiënten een verlate activatie van de abductor pollicis brevis en de extensor pollicis longus zien, en juist een vervroegde activatie van de flexor carpi radialis. In beide groepen zijn de path length ratio, timing van hand opening en de pols excursie afhankelijk van de bewegingsrichting, maar niet van zwaartekrachtcompensatie. Om te voorkomen dat CVA-patiënten met hun hand tegen het doelobject botsen, compenseren zij voor de verlate handopening door een meer omtrekkende beweging naar het doelobject te maken. De temporele verschillen in spieractivatie tussen CVA-patiënten en gezonde ouderen kunnen als input dienen om ondersteunende en/of therapeutische revalidatierobotica of meerkanaals elektrostimulatoren aan te sturen, die zowel het openen als het sluiten van de hand kunnen ondersteunen.

De exploratieve studie in **Hoofdstuk 7** beschrijft hoe zwaartekrachtcompensatie gecombineerd is met meerkanaals elektrostimulatie voor het openen van de hand. Een groep van 8 CVA-patiënten voerde de Box and Block Test (BBT) uit, met en zonder zwaartekracht compensatie en met en zonder meerkanaals elektrostimulatie. Tijdens het experiment werd zowel de positie van de hand als van de BBT gemeten met VICON. Deze positiedata werd in realtime naar een computer gestuurd die vervolgens de elektrostimulator aanstuurde. Omdat de positie van de hand ten opzichte van de BBT bekend was, kon het openen van de hand voor het grijpen en loslaten van kleine objecten ondersteund worden door op de juiste momenten de extensor digitorum en de abductor pollicis brevis elektrisch te stimuleren. Op die manier was het bij alle patiënten mogelijk om voldoende handopening te creëren om een blokje van de BBT te pakken. Helaas was er geen direct effect van de zwaartekracht compensatie en elektrostimulatie op handfunctie zoals gemeten met de BBT. De verwachting is dat hiervoor geavanceerdere aansturings-algoritmes nodig zijn, die zowel de flexoren als de extensoren kunnen ondersteunen.

Tenslotte worden in **Hoofdstuk 8** de belangrijkste bevindingen van dit proefschrift vermeld en bediscussieerd. Daarnaast wordt de klinische relevantie besproken en worden aanbevelingen gedaan voor toekomstig onderzoek. De resultaten van de onderzoeken die beschreven zijn in dit proefschrift, hebben belangrijke design input geleverd voor de ontwikkeling van een Active Therapeutic Device (ATD). Deze revalidatierobot is ontwikkeld volgens de belangrijkste principes van de neurorevalidatie. De robot kan het openen en sluiten van de hand ondersteunen door middel van een 3-kanaals EMG-getriggerde elektrostimulator. Daarnaast kan de robot de arm (gedeeltelijk) ondersteunen tegen de zwaartekracht en kan de mate van ondersteuning dynamisch worden aangepast gedurende de training. Hopelijk inspireert dit proefschrift onderzoekers en ingenieurs om nieuwe technologie te ontwikkelen voor de ondersteuning van arm- en handfunctie na een beroerte.

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Curriculum Vitæ

Thijs Krabben werd geboren op 20 oktober 1979 in Winterswijk en groeide op in het Achterhoekse Lichtenvoorde. De middelbare school volgde hij aan het Marianum in Groenlo waar hij in 2000 zijn VWO-diploma behaalde. In 2004 heeft hij zijn HTS-diploma Elektrotechniek met differentiaties 'Medische Elektrotechniek' en 'Multimediatechniek' behaald aan de Saxion Hogeschool in Enschede. Aansluitend heeft hij de master 'Biomedical Engineering' met als differentiatie 'Human Function Technology' gedaan aan de Universiteit Twente. De afsluitende afstudeeropdracht heeft hij tussen september 2007 en september 2008 uitgevoerd bij Roessingh Research & Development in Enschede. Binnen deze afstudeeropdracht heeft hij onder andere gekeken naar het effect van zwaartekrachtcompensatie training op arm functie bij chronische CVA patiënten. Daarnaast heeft hij een trainingsopstelling gebouwd waarmee CVA patiënten reikbewegingen kunnen oefenen door middel van een motiverend computerspel. Na het behalen van dit diploma is hij in november 2008 als promovendus in dienst gekomen bij Roessingh Research & Development. Tijdens dit promotietraject heeft hij onderzoek gedaan naar het gebruik van robotica, meerkanaals elektrostimulatie en motiverende computerspellen en het effect hiervan op arm- en handfunctie bij CVA-patiënten. Dit proefschrift is het eindresultaat van het promotieonderzoek.

Na de periode bij Roessingh Research & Development heeft hij bij ingenieursbureaus Demcon en Mecon gewerkt aan de ontwikkeling van diverse medische hulpmiddelen. Momenteel werkt hij als mechatronic system engineer bij MILabs in Utrecht, waar hij werkt aan de ontwikkeling van een klinische SPECT-scanner.

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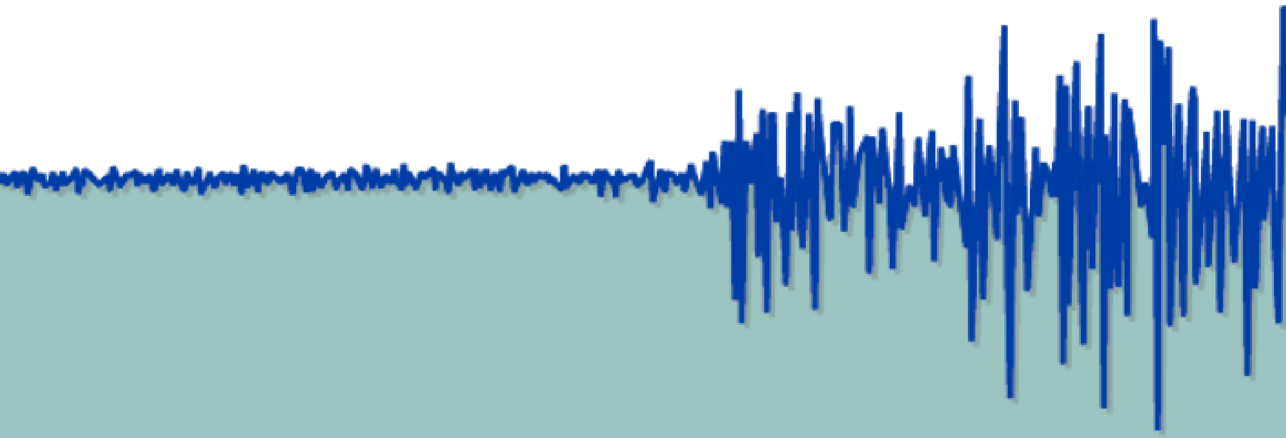

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