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Effects of Movement Context on Reach-Grasp-Lift Motion and Grip Force after Stroke

Stacey DeJong

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EFFECTS OF MOVEMENT CONTEXT ON
REACH-GRASP-LIFT MOTION AND GRIP FORCE

AFTER STROKE

by

Stacey Lynn DeJong

A dissertation presented to the
Graduate School of Arts and Sciences
of Washington University in
partial fulfillment of the
requirements for the degree
of Doctor of Philosophy

May 2011

Saint Louis, Missouri

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ABSTRACT OF THE DISSERTATION

Effects of Movement Context on
Reach-Grasp-Lift Motion and Grip Force
after Stroke

by

Stacey Lynn DeJong

Doctor of Philosophy in Arts and Sciences

(Movement Science)

Washington University in St. Louis, 2011

Dr. Catherine E. Lang, Chairperson

Loss of upper extremity function after stroke is a significant problem resulting in enormous personal, societal, and economic costs. Neurophysiological discoveries over several decades have revealed great potential for use-dependent neural adaptation, and have revitalized the search for training strategies that optimize recovery. Although task-specific repetitive practice is recognized as a key stimulus to promote upper extremity function after stroke, choices of what to practice and how to practice remain challenging and poorly guided by evidence. This research was inspired by evidence in healthy individuals, that movement can be altered by characteristics of the task and the environment, together referred to as the movement context. The purpose of this research was to determine whether motor performance of the paretic upper extremity is affected by two specific movement context variations: 1) preferred speed versus fast, and 2) unilateral versus bilateral.

Using electromagnetic motion tracking and pressure sensor quantification of grip force, we assessed upper extremity task performance in people with post-stroke hemiparesis. To evaluate effects of movement speed, we compared paretic-limb performance of a reach-grasp-lift task at a self-selected preferred speed to the same task performed as fast as possible. People with hemiparesis were able to move faster than their preferred speed, and when they did, movement quality was better. Reach paths were straighter, finger movements were more efficient, and the fingers opened wider. To evaluate effects of the bilateral movement context, we compared paretic-limb performance of a reach-grasp-lift-release task unilaterally versus bilaterally. We found no immediate improvement in the bilateral context. We further explored effects of the bilateral movement context by measuring maximal and submaximal grip force capacity using grip dynamometers. Unlike healthy controls and unlike the non-paretic side, the paretic side of people with hemiparesis produced more maximal force in the bilateral condition. In a submaximal task, however, the bilateral condition did not enhance the paretic side's contribution. These results suggest that emphasizing speed during post-stroke rehabilitation may be worthwhile, that the bilateral movement context has little immediate impact on task performance, and that the paretic limb may benefit from the bilateral condition only at high force levels.

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Dedication

This dissertation is dedicated to my Mom

Marjorie Carol DeJong

**an intelligent, strong woman,
who taught me that I could do anything I set my mind to,
who encouraged me to keep my options open,
and who would have been so proud**

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Chapter 1

Upper extremity movement after stroke:

Could moving faster or bilaterally affect performance?

INTRODUCTION

Loss of upper extremity function after stroke is a significant problem

Each year in the United States, about 795,000 people experience a stroke, including about 610,000 first attacks and 185,000 recurrent strokes. Survival time averages five to seven years when stroke occurs between the ages of 60 and 80 years, and exceeds one year in 75-80% of all cases (Lloyd-Jones et al., 2010). Although the incidence of stroke has declined slightly over the past 50 years (Carandang et al., 2006), survival rates have increased dramatically (Lloyd-Jones et al., 2010), and prevalence is expected to continue on an upward trend (Brown et al., 2006). In 2005, 6.5 million people in the United States were living with the aftermath of stroke (Lloyd-Jones et al., 2010). Estimated costs of stroke for 2009 total \$68.9 billion, including \$45.9 billion in direct costs and \$23 billion in lost productivity (Lloyd-Jones et al., 2010).

Upper extremity paresis affects 70-85% of stroke survivors (Dobkin, 2004; Mayo et al., 2002). At six months post stroke, 54% report difficulty with instrumental activities of daily living, and 65% report restricted participation in community life (Mayo et al., 2002). Findings from focus groups and structured interviews indicate that stroke survivors view upper extremity impairment as a critical but neglected issue, associated with disappointment, frustration, and an enormous sense of loss (Barker and Brauer, 2005). Clearly, efforts to ease the personal, societal and economic burden of stroke are needed.

All domains of disability are affected

Post-stroke hemiparesis affects upper extremity movement at all levels of the disability spectrum (Goljar et al.). Neuronal loss, due to either ischemic infarct or hemorrhage, disrupts the neural network that governs limb movement, and thereby limits capacity for corticomotor neuron activation, transmission of descending neural signals, and subsequent muscle activation. Primary impairments of body functions include weakness (diminished capacity for muscle force generation), diminished ability to regulate and coordinate muscle activation according to the spatial and temporal requirements of specific motor tasks, sensory deficits, and spasticity. Muscle activation is diminished (Canning et al., 2000; McCrea et al., 2005; Wagner et al., 2007a), movement speed is reduced (Beer et al., 2000; Cirstea et al., 2003; Dewald and Beer, 2001; Lang et al., 2005; Levin, 1996; Reisman and Scholz, 2003; Wagner et al., 2007a), and synergistic movement patterns constrain multijoint movements proximally and distally (Cirstea et al., 2003; Ellis et al., 2005; Lang and Beebe, 2007; Lang and Schieber, 2004; Li et al., 2003; Schieber et al., 2009).

Activity limitations (difficulties with executing tasks) and participation restrictions (problems with involvement in life situations) are also common after stroke, and are related to upper extremity impairments (Faria-Fortini et al., 2011; Gunaydin et al., 2006; Wagner et al., 2007b; Wagner et al., 2006). Activity limitations are typically measured using clinical rating scales such as the Action Research Arm Test (Lyle, 1981), Wolf Motor Function Test (Wolf et al., 2005), or Jebsen-Taylor Test of Hand Function (Jebsen et al., 1969). Participation measures include ratings of quality of life (Williams

et al., 1999), the Stroke Impact Scale (Duncan et al., 1999; Lai et al., 2002), and the Canadian Occupational Performance Measure (Dedding et al., 2004; Law et al., 1990).

Recovery occurs mostly within the first 6 months and is often incomplete

Typically within the first six months post-stroke, partial functional improvement occurs, through remediation of impairments and through the development of compensatory movement strategies (Krakauer, 2005; Kwakkel et al., 2004; Levin et al., 2009). Consistently across studies, severity of initial impairment has been shown to be the best predictor of recovery, with more severe deficits associated with less improvement (Beebe and Lang, 2009; Chen and Winstein, 2009; Duncan et al., 1992; Harris and Eng, 2007; Nijland et al., 2010). Outcomes are generally better for cortical lesions than for subcortical lesions, and are poorest when stroke affects the posterior limb of the internal capsule (Feys et al., 2000; Kwakkel et al., 2003; Shelton and Reding, 2001; Wenzelburger et al., 2005). The time course of stroke recovery typically follows an exponential curve, with relatively rapid functional and impairment level gains during the first six months post-stroke, largely due to spontaneous neurological recovery (Kwakkel et al., 2004). A plateau phase follows, during which additional gains are smaller and occur more slowly. Recovery of upper extremity movement is often incomplete. Only about one-third of stroke survivors who initially show hemiparesis will achieve full functional recovery (Olsen, 1990; Parker et al., 1986; Twitchell, 1951; Wade et al., 1983).

Task-specific repetitive practice drives neural adaptation and recovery

Neuroscientific discoveries over the past several decades have shown that the brain undergoes a continual process of reorganization, strongly influenced by behavioral experience, in healthy individuals and particularly in those with recent neural injury (Kleim and Jones, 2008; Nudo, 2007). These discoveries have renewed interest in the idea that greater motor recovery may be possible after stroke, and that it may be possible to restore function through return of normal movement patterns instead of through compensatory strategies (Cramer, 2008; Krakauer, 2005; Kwakkel et al., 2004; Levin et al., 2009). Repetitive training is a powerful behavioral stimulus for driving use-dependent neural adaptation in animals (Butefisch et al., 2000; Kleim et al., 2004; Monfils et al., 2005; Nudo et al., 1996), and in humans (Askim et al., 2009; Jang et al., 2003; Liepert et al., 2000; Schaechter et al., 2002). Clinicians and researchers now seek to identify the parameters of physical training that maximize neural adaptation and allow individuals to approach their potential in terms of motor control and function. Important features of training include acquisition of skills that are salient for the individual, and repetition of the newly learned skills at an adequate intensity (Kleim and Jones, 2008).

Current standards of care for post-stroke rehabilitation include sensorimotor training to improve upper extremity function, particularly in cases of mild or moderate hemiparesis, and for those showing signs of ongoing recovery (Teasell et al., 2003). It has become increasingly clear that task-specific repetitive practice of relevant motor skills has the potential to drive brain reorganization toward optimal functional performance (Shepherd, 2001; Urton et al., 2007). Rehabilitation protocols that include repetitive task-specific training can produce gains in upper extremity function early after

stroke (Harris et al., 2009; Winstein et al., 2004; Wolf et al., 2006), and at later time points as well (Page et al., 2008; Pang et al., 2006; Platz et al., 2001; Taub et al., 2006a).

Evidence to guide rehabilitation remains inadequate

Although task-specific repetitive practice is clearly a key stimulus to promote motor learning, the choices of what to practice and how to practice remain challenging and poorly guided by evidence. Optimal methods to implement task-specific training remain debatable, and the effects of altering specific characteristics of task performance are largely unknown. This research is inspired by findings in healthy people that upper extremity performance can be altered by characteristics of the task and the environment, together referred to as the movement context (Ansuini et al., 2006; Rearick et al., 2003; Santello and Soechting, 1998). Two specific contextual variations are explored: 1) effects of altering movement speed, and 2) effects of performing tasks bilaterally instead of unilaterally. The following pages summarize prior investigations into the effects of these two movement context variations.

FASTER SPEED MAY IMPROVE UPPER EXTREMITY PERFORMANCE

Speed is rarely emphasized during rehabilitation

Most of the time, rehabilitation includes task performance at a self-selected preferred speed. Although slow, insufficient muscle activation is a hallmark of hemiparesis (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck and Andreassen, 1980; Young and Mayer, 1982), the speed of task performance is rarely emphasized in either clinical or experimental intervention

protocols. Reasons for this are unclear, but may stem from concerns about how hyperactive stretch reflexes or speed-accuracy trade-offs may affect movement quality. In healthy people, however, instructions to move faster result in more efficient reaching movements that are produced with greater force (Adam, 1992; Fisk and Goodale, 1984; Rival et al., 2003), despite the well-described speed-accuracy trade-off relating movement speed to endpoint spatial errors in a variety of motor tasks (Battaglia and Schrater, 2007; Bootsma et al., 1994; Fitts, 1954; van Veen et al., 2008; Walker et al., 1993).

Moving faster alters reaching and grasping in healthy people

A defining feature of hemiparesis is weakness due to insufficient neural activation, and studies of people without hemiparesis support the idea that moving quickly may increase neural drive. For example one study showed increased grip force when healthy participants performed a lift-and-transport task faster than their preferred speed, (Iyengar et al., 2009). In another study, when healthy participants were asked to emphasize speed over accuracy, their reach path was smoother (i.e. composed of fewer movement units), and the same effect was found on the non-paretic side of people with hemiparesis (Lin et al., 2008).

Moving faster may enhance paretic-limb performance after stroke

Little attention has been given to the potential effects of movement speed on upper extremity performance in people with post-stroke hemiparesis. One recent study explored the coordination between reaching and grasping in twelve people with

hemiparesis moving at their preferred speed compared to their fastest possible speed (van Vliet and Sheridan, 2007). The participants with hemiparesis were able to increase their movement speed by about 35%, and improved their reaching performance. Faster movements were associated with increased opening of the hand, and a greater percentage of the reach duration was spent in the acceleration phase. This indicates a difference in control strategy, since movement during the acceleration phase is largely driven by central neural commands, and the deceleration phase generally involves feedback-dependent error correction. Given these findings, we sought to determine whether faster movement speeds would have other beneficial or detrimental effects on paretic-limb task performance after stroke, as reported in Chapter 2.

THE BILATERAL MOVEMENT CONTEXT MAY IMPROVE UPPER EXTREMITY PERFORMANCE

Bilateral training is a relatively new intervention paradigm

Most therapeutic activities that constitute traditional post-stroke rehabilitation involve the use of the paretic arm by itself, or the use of both arms in a complimentary, asymmetrical fashion (McCombe Waller and Whittall, 2008). Constraint-induced movement therapy, for example, emphasizes unilateral task performance by the paretic limb and intentionally limits participation by the non-paretic limb (Lin et al., 2007; Page et al., 2008; Taub et al., 2006a; Wolf et al., 2006). In contrast, bilateral training paradigms include simultaneous task performance by both limbs, symmetrically or reciprocally, in an attempt to capitalize on the effects of interlimb coupling and thereby

improve paretic limb performance (Cauraugh and Kim, 2002; Lin et al., 2010; Mudie and Matyas, 2000; Stinear and Byblow, 2004; Whittall et al., 2000).

Over the past decade, several research groups have investigated the potential benefits of practicing movements bilaterally instead of unilaterally after stroke. These studies began in the late 1990's, when Mudie and Matyas serendipitously discovered that practice of bilateral simultaneous movements seemed to improve recovery (Mudie and Matyas, 1996; Mudie and Matyas, 2000). Twelve single-case experiments were reported, each showing immediate and sustained improvements in upper extremity task performance as a result of bilateral practice. Movement impairment was assessed through visual observation of videotapes, using a rating scale that was specifically developed for use in the study. Examiners who were unaware of training status used a five-point rating scale to assess multiple aspects of movement quality (i.e. 'joint ranges at the point of reaching the target, straightness and smoothness of trajectory, accuracy of targeting, synchrony of limb parts, quality of grasp, and presence of extraneous movements'). Using interrupted time series analysis, rapid improvement in motor performance was evident when participants switched from unilateral to bilateral practice of three upper extremity tasks. Further, the rate of improvement over multiple sessions was greater when practice was performed bilaterally. Although this study generated interest in bilateral training among the rehabilitation research community, implementation into clinical practice has not been widespread.

Outcomes of bilateral training show efficacy but not superiority

Numerous outcome studies have followed the initial investigations into bilateral training. These studies are summarized in Table 1, clustered according to research groups. A few main findings emerge when comparing across studies. First, distinctly different intervention protocols are considered within the general category of bilateral training. For example, in the initial studies, Mudie and Matyas utilized repetitive practice of block placement, simulated drinking, and peg targeting as the training method (Mudie and Matyas, 2000). Other groups have since utilized similar task practice regimens (Desrosiers et al., 2005; Lewis and Byblow, 2004; Lin et al., 2010; Morris et al., 2008; Stoykov et al., 2009; Summers et al., 2007). In contrast, Whittall and colleagues developed the BATRAC method (Bilateral Arm Training with Rhythmic Auditory Cueing), which involves cyclical pushing and pulling of handles symmetrically and reciprocally, combined with use of a metronome for pacing (Whittall et al., 2000). Cauraugh and colleagues compared unilateral versus bilateral active wrist and finger extension contractions, combined with electrical stimulation (Cauraugh and Kim, 2002), and Stinear and colleagues employed a custom-built device whereby passive movement of the paretic wrist was driven by active non-paretic wrist movement. These protocols all incorporate the bilateral movement condition, involving the non-paretic limb for the purpose of improving paretic-limb performance. Given their differences, however, outcomes and generalizability may differ as well.

A second main finding that emerges from review of outcome studies is that although many cohort studies report improvement after bilateral training, when bilateral training is compared to alternative training protocols, potential benefit of the bilateral

condition itself is much less clear. Gains in upper extremity function, strength, range of motion, and daily use have been reported after bilateral training programs lasting between one and six weeks (Cauraugh and Kim, 2002; Cauraugh et al., 2005; Lewis and Byblow, 2004; Lin et al., 2009; Lin et al., 2010; Morris et al., 2008; Richards et al., 2008; Senesac et al., 2010; Stinear and Byblow, 2004; Summers et al., 2007; Whittall et al., 2011).

Larger, more recent clinical trials, however, have not supported bilateral training as being any more effective than other dose-matched training protocols (Lin et al., 2009; Lin et al., 2010; Morris et al., 2008; Whittall et al., 2011). Thus bilateral training may be effective, but no more effective than other forms of training.

A third main finding is that different training protocols may improve different aspects of upper extremity movement. For example, a recent randomized controlled trial compared bilateral training with constraint-induced movement therapy (CIMT) in people with chronic stroke (Lin et al., 2009). After three weeks of training, participants in the bilateral training group showed more improvement in the portion of the Fugl-Meyer Assessment that addresses proximal arm function, compared to the CIMT group. Those in the CIMT group improved more on the Motor Activity Log and on the activities of daily living domain of the Stroke Impact Scale. Lin et al. hypothesized that bilateral training may uniquely improve proximal arm movement, making it a better treatment option for some stroke survivors, while CIMT may be preferred for others. Similarly, in one study dexterity improved less in a bilaterally trained group compared to a unilaterally trained group (Morris et al., 2008), and in another study the Upper Arm Function subscale of the Motor Assessment Scale improved after bilateral training but not after unilateral training (Stoykov et al., 2009). Task specificity may also impact observed

effects. For example, McCombe-Waller and colleagues showed faster and smoother bilateral reaching after BATRAC training, but faster unilateral reaching after dose-matched therapeutic exercise (McCombe Waller et al., 2008).

Effects of unilateral versus bilateral training on task performance are unclear

Although many studies have explored outcomes of bilateral training, few have included kinematic measures, and none have confirmed the immediate changes in movement quality originally reported (Mudie and Matyas, 2000). Two studies indicate decreased reach duration and increased peak velocity after bilateral training (Cauraugh et al., 2005; Lin et al., 2010). Cauraugh et al. further reported decreased deceleration time, and Lin et al. reported a more direct reach path. Summers et al. measured reach duration, peak velocity, curvature of the arm trajectory, and elbow angle during reaching tasks before and after six sessions of either bilateral or unilateral training (Summers et al., 2007). No significant group differences were found for any of the kinematic parameters, although the pre-post decrease in reach duration approached significance in the bilaterally trained group only.

Paretic-limb reaching is faster in the bilateral context

Three single-session studies have directly compared bilateral versus unilateral reaching movements in people with post-stroke hemiparesis (Harris-Love et al., 2005; McCombe Waller et al., 2006; Rose and Winstein, 2005). In each case, improved temporal symmetry was evident in the bilateral movement condition, due to increased velocity on the paretic side and decreased velocity on the non-paretic side, relative to

each side's unilateral performance. These findings were attributed to interlimb coupling effects, whereby the two upper extremities are thought to be controlled as a single coordinative unit with tendencies toward spatial and temporal symmetry (Kelso et al., 1979). These studies indicate that people with stroke retain at least some degree of interlimb coordination, which potentially could be exploited to improve paretic-limb performance. Smoothness of the reaching trajectory was evaluated in one additional single-session study, in which three of six people with chronic mild hemiparesis showed fewer discontinuous reach trajectories in bilateral movement trials compared to those performed unilaterally (Cunningham et al., 2002).

Mechanisms for improved performance in the bilateral context have been proposed

Several mechanisms have been suggested to explain the possible benefits of practicing movements bilaterally instead of unilaterally after stroke (Carson, 2005; Cauraugh and Summers, 2005; McCombe Waller and Whittall, 2008; Mudie and Matyas, 2000). Activation of corticospinal pathways in the lesioned hemisphere may be facilitated during bilateral symmetrical movements due to 1) activation of neural network components shared by the two sides, 2) interlimb coupling effects whereby the two sides share a single motor command, or 3) by normalization of interhemispheric and intracortical inhibitory influences on the lesioned hemisphere that are exaggerated after stroke (Murase et al., 2004; Stinear et al., 2008; Stoykov and Corcos, 2009). In addition, activation of ipsilateral corticospinal pathways from the non-lesioned hemisphere to the paretic limb may be increased during bilateral movement.

Specific effects of the bilateral context on task performance are largely unknown

A more complete characterization of differences between bilateral and unilateral task performance may help to determine which stroke survivors are most likely to benefit from bilateral training, and may provide insight into the neurophysiological mechanisms involved. Since the immediate effects that Mudie and Matyas visually observed form the basis of investigation into the use of bilateral training, it is important to confirm and quantify those effects, and to identify specifically which parameters of performance are affected. However, no studies to date have fully examined kinematic or kinetic differences in performance of bilateral versus unilateral tasks within a single testing session. As described in Chapter 3, we sought to determine whether, within a single session, moving bilaterally instead of unilaterally enhances paretic-limb performance of a reach-grasp-lift-release task, and to identify specifically which parameters of performance might be enhanced.

The bilateral context diminishes maximal muscle force production in healthy people

In contrast to the possible facilitory effects of bilateral movement discussed above, studies of healthy adults indicate that voluntary force production is diminished, rather than facilitated, when homologous muscles on the left and right sides contract simultaneously rather than individually. This phenomenon, termed the ‘bilateral deficit’, has been demonstrated across age groups, genders, muscle groups and contraction types in numerous studies, which are summarized and listed chronologically in Table 2. In most, but not all of the studies, maximal force was between 3 and 25% less when contractions were performed bilaterally compared to unilaterally (for exceptions see

(Hakkinen et al., 1997; Hakkinen et al., 1995; Herbert and Gandevia, 1996; Jakobi and Cafarelli, 1998; Khodiguian et al., 2003)). The bilateral deficit is a flexible, use-dependent phenomenon that increases with unilateral training and decreases with bilateral training (Howard and Enoka, 1991; Kuruganti et al., 2005; Taniguchi, 1997; Taniguchi, 1998; Weir et al., 1995).

Interhemispheric inhibition underlies the bilateral deficit

Since bilateral versus unilateral differences in force production are consistently accompanied by corresponding differences in cortical activation and electromyographical recordings, it is likely that a supraspinal mechanism diminishes neural drive during bilateral contractions (Howard and Enoka, 1991; Oda and Moritani, 1995; Post et al., 2007; Taniguchi et al., 2001; Van Dieen et al., 2003). This hypothesis has been supported by twitch-interpolation studies showing a lower percentage of maximal activation utilized during voluntary bilateral contractions compared to those performed unilaterally (Herbert and Gandevia, 1996; Van Dieen et al., 2003).

Interhemispheric inhibition, specifically, is thought to be the predominant mechanism underlying the bilateral deficit phenomenon (Archontides and Fazy, 1993). During unilateral activity, a high level of cortical activation in one hemisphere has an inhibitory influence on the homologous cortical area in the opposite hemisphere (Asanuma and Okuda, 1962; Duque et al., 2005a). Anatomical studies, which illustrate the topographical arrangement of transcallosal fibers, support this theory by showing connectivity between functionally equivalent cortical regions (Zarei et al., 2006). This provides evidence of a pathway by which the bilateral deficit can affect simultaneous

contractions of homologous muscles, but does not affect contractions involving different muscles on the two sides of the body (Howard and Enoka, 1991). Existence of the bilateral deficit phenomenon suggests that during maximal bilateral symmetrical contractions, both sides mutually inhibit each other, limiting the intensity of cortical activation and thereby limiting maximal muscle force production.

The bilateral deficit may be altered on the paretic side after stroke

Two published reports address the influence of the bilateral movement condition on upper extremity force production after stroke (Li et al., 2003; McQuade et al., 2008). In one study, ten people with chronic hemiparesis performed unilateral and bilateral maximal isometric elbow flexion contractions (McQuade et al., 2008). Force produced by the non-paretic limb was diminished by 15% during bilateral contractions, consistent with the bilateral deficit expected in healthy individuals. The paretic limb, however, produced an equal amount of force during unilateral versus bilateral contractions. These findings suggest that the bilateral condition might result in disinhibition of the paretic limb after stroke. In the other study, however, the paretic and non-paretic sides both showed a bilateral deficit (approximately 23%), as did healthy controls during a multi-finger force production task (Li et al., 2003). As described in Chapter 4, we sought to determine how the bilateral movement context affects maximal and submaximal grip force on the paretic side of people with post-stroke hemiparesis, as compared to their non-paretic side and to healthy individuals.

Mechanisms for lack of a paretic-limb bilateral deficit have been proposed

Since interhemispheric inhibition underlies the bilateral deficit in healthy people, if inhibitory influences acting on the lesioned hemisphere are reduced after stroke, that could explain a lack of bilateral deficit on the paretic side. Substantial evidence from studies using transcranial magnetic stimulation, however, shows that interhemispheric inhibition of the lesioned hemisphere remains intact after stroke and may be exaggerated (Butefisch et al., 2008; Duque et al., 2005a; Murase et al., 2004; Perez and Cohen, 2009). It is therefore unlikely that lack of a bilateral deficit on the paretic side can be explained by disrupted interhemispheric inhibitory influence onto the lesioned motor cortex.

Alternatively, it is possible that the effect of interhemispheric inhibition might be offset and even reversed by increased activation of alternative descending pathways in the bilateral condition. Indirect connections involving secondary motor cortical areas, uncrossed corticospinal projections to the paretic limb, and / or cerebellar circuits may be recruited to a greater extent when movements are performed bilaterally. This possibility was proposed by McQuade and colleagues (McQuade et al., 2008), and is supported by imaging studies of bilateral training outcomes (Luft et al., 2004; Whitall et al., 2011; Wu et al., 2010). For example, a recent randomized clinical trial demonstrated a greater increase in activation of the ipsilesional supplementary motor and anterior cingulate areas after bilateral training, compared to dose-matched therapeutic exercise (Whitall et al., 2011). Thus recruitment of alternative motor pathways is a plausible mechanism whereby the bilateral deficit may not be observed on the paretic side.

SCOPE OF THESIS

This research was undertaken to determine whether motor performance of the paretic upper extremity is affected by two specific movement context variations: 1) preferred speed vs. fast, and 2) unilateral vs. bilateral. In Chapter 2, we explored effects of movement speed by comparing paretic-limb performance of a reach-grasp-lift task at the participant's self-selected preferred speed to the same task performed after instructions to move as fast as possible. In Chapter 3, we questioned whether the paretic limb would perform a reach-grasp-lift-release task differently when the non-paretic limb also performed the same task at the same time (i.e. in the bilateral context). In Chapters 2 and 3, kinematic and kinetic aspects of task performance were characterized using an electromagnetic tracking system to assess motion and a pressure sensor to quantify grip force. Since neural control of grasping may vary depending on the type of grip and level of force produced (Ehrsson et al., 2000; Kutz-Buschbeck et al., 2001), and since grip type could therefore influence movement context effects, we evaluated two grip types that differ in the level of precision required and the amount of force produced (palmar and 3-finger). In Chapter 4, we investigated the apparent conflict between: 1) ample evidence of diminished muscle activation in the bilateral condition in healthy individuals; 2) reports of improved performance and training effects in the bilateral condition for the paretic limb of people post-stroke; and 3) discrepant findings regarding the presence or absence of the bilateral deficit phenomenon after stroke. We used grip dynamometers to question how the bilateral movement context affects maximal and submaximal grip force production on the paretic versus non-paretic sides of people with hemiparesis. Results

from these investigations are interpreted, integrated, and discussed in Chapter 5, with emphasis on implications for rehabilitation.

Table 1. Studies evaluating outcomes of bilateral training after stroke

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
Mudie MH, Matyas TA, Tijs E La Trobe University, Victoria Australia					
(Mudie and Matyas, 1996)	8 single-case experiments multiple baseline interrupted time series analysis	n = 8 hemiparesis 3 – 78 weeks post-stroke 7 male, 1 female age 56 – 83 years	5 x/wk, 8 wks Unilateral, then bilateral symmetrical practice of block placement, simulated drinking, and peg targeting	Observational ratings of movement impairment from randomly ordered videos of unilateral paretic-limb task performance recorded each session	Stable performance during unilateral practice phase Immediate improvement and increased rate of improvement upon beginning bilateral practice
(Mudie and Matyas, 2000)	12 single-case experiments multiple baseline interrupted time series analysis (same 8 included in Mudie & Matyas 1996, plus 4),	n = 12 hemiparesis 4 – 78 weeks post-stroke 9 male, 3 female age 56 – 83 years	5 x/wk, 6 – 8 wks Unilateral, then bilateral symmetrical practice of block placement, simulated drinking, and peg targeting	Observational ratings of movement impairment from randomly ordered videos of unilateral paretic-limb task performance recorded each session	Stable performance during unilateral practice phase Immediate improvement and increased rate of improvement upon beginning bilateral practice
(Mudie and Matyas, 2001)	Single session Randomized controlled comparison	n = 36 'dense' hemiplegia randomly assigned to 2 intervention groups 26 male, 10 female age 42 – 90 years	5 isometric shoulder abduction or wrist extension contractions either unilaterally (control group) or bilaterally (experimental group)	Integrated EMG from middle deltoid or extensor carpi radialis longus during unilateral isometric contraction	No difference across groups

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
(Tijs and Matyas, 2006)	5 single-case experiments multiple baseline interrupted time series analysis	n = 5 hemiparesis 2 – 20 months post-stroke 3 male, 2 female age 29 – 75 years	25 – 40 daily sessions repetitive practice of 3 copying (writing) tasks	Quality of paretic limb movement during unilateral copying (writing), based on pen tilt and pen movement on a digitizing pad	No improvement during or after bilateral training
Whitall J, McCombe Waller S, Luft A University of Maryland, Baltimore, MD					
(Whitall et al., 2000)	Cohort pre vs. post training	n = 14 hemiparesis > 1 year post-stroke 8 male, 6 female age 44 – 89 years	3 x/wk, 6 wks BATRAC (Bilateral arm training with rhythmic auditory cueing, pushing and pulling handles symmetrically, then reciprocally, with trunk restrained)	Fugl-Meyer Upper Extremity Motor Performance Test, Wolf Motor Function Test, University of Maryland Arm Questionnaire for Stroke, strength, range of motion	Improved paretic-limb functional motor performance after training and 8 weeks later. Few gains in strength and range of motion
(McCombe Waller and Whitall, 2004)	Cohort pre vs. post training Reference group of age and gender matched healthy controls, tested once but not trained	n = 9 hemiparesis > 6 months post-stroke 5 male, 5 female age not reported	3 x/wk, 6 wks BATRAC	Rate and timing consistency of finger tapping done unilaterally, bilaterally symmetrically, and bilaterally reciprocally	Improved paretic-limb fine motor control in 2 of 4 participants with mild stroke severity Improved non-paretic limb fine motor control regardless of severity

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
(Luft et al., 2004)	Small randomized controlled trial	n = 21 hemiparesis randomly assigned to 2 training groups 1 – 39 years post-stroke 12 male, 9 female age 62 ± 13 years	3 x/wk, 6 wks BATRAC versus dose-matched therapeutic exercise (DMTE)	Fugl-Meyer Upper Extremity Test Wolf Motor Arm Test fMRI during elbow flexion and extension	No group difference on functional tests After BATRAC, increased activation of precentral and postcentral gyri on non-lesioned side and cerebellum on lesioned side
(McCombe Waller et al., 2008)	Small randomized controlled trial	n = 18 hemiparesis randomly assigned to 2 training groups 1 – 20 years post-stroke 7 male, 11 female age 37 – 83 years	3 x/wk, 6 wks BATRAC versus DMTE	Kinematics of unilateral and bilateral reaching, Fugl-Meyer Upper Extremity Test, Modified Wolf Motor Arm Test	Functional gains in both groups Task-specific effects on reaching Faster and smoother bilateral reach after BATRAC Faster unilateral reach after DMTE
(Whitall et al., 2011)	Randomized controlled trial	n = 92 (38 for fMRI) hemiparesis randomly assigned to 2 training groups BATRAC group: 5 ± 4 yrs post-stroke age 60 ± 10 years DMTE group: 4 ± 5 yrs post-stroke age 58 ± 13 years	3 x/wk, 6 wks BATRAC versus DMTE	Fugl-Meyer Upper Extremity Test Wolf Motor Function Test Time fMRI	Small functional gains, equal across groups Greater activation in several secondary motor cortical areas in the BATRAC group vs. DMTE

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
Richards LG, Senesac CR University of Florida, Gainesville, FL					
(Richards et al., 2008)	Cohort Pre vs. post training	n = 14 9 male, 5 female 1 – 14 years post-stroke age 38 – 80 years	4 x/wk, 2 wks Modified BATRAC (modBATRAC) using same device, different mechanical stops and training schedule	Fugl-Meyer Upper Extremity Test Wolf Motor Function Test Motor Activity Log	No change on Fugl-Meyer Upper Extremity Test or Wolf Motor Function Test Increased paretic arm use reported on Motor Activity Log
(Senesac et al., 2010)	Cohort Pre vs. post training	n = 14 9 male, 5 female 1 – 14 years post-stroke age 38 – 80 years	4 x/wk, 2 wks modBATRAC	Kinematic measures of 2 bilateral reach-to-target tasks, 1 with symmetrical spatial demands, 1 asymmetrical	Increased velocity and smoother, straighter hand paths after training Similar findings for the 2 tasks tested
Lin KC, Wu CY National Taiwan University, Taipei, Taiwan					
(Lin et al., 2009)	Small randomized controlled trial	n = 60 34 male, 26 female age 23 – 81 years hemiparesis randomly assigned to 3 groups Time since stroke approximately 20 ± 20 months	5 x/wk, 3 wks bilateral arm training of functional tasks symmetrically and alternating (BAT) vs. unilateral constraint induced movement therapy (CIMT) vs. compensation and unilateral therapeutic exercise (Control)	Fugl-Meyer Upper Extremity Test Functional Independence Measure (FIM) Motor Activity Log (MAL) Stroke Impact Scale (SIS)	Bilateral group improved more than other groups on Fugl-Meyer proximal part score CIMT group improved more than other groups on MAL and SIS activities of daily living subscales

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
(Lin et al., 2010)	Small randomized controlled trial	n = 33 19 male, 14 female age approximately 54 ± 13 years hemiparesis Randomly assigned to 1 of 2 groups 6 – 67 months post-stroke	5 x/wk, 3 wks BAT vs. standard occupational therapy including fine motor and compensatory practice and neurodevelopmental techniques (Control)	Kinematic measures of 1 unilateral and 1 bilateral task Fugl-Meyer Upper Extremity Test FIM MAL	Better performance of both tasks after BAT vs. Control Greater Fugl-Meyer gains after BAT vs. Control No group difference for FIM or MAL
(Wu et al., 2010)	Small randomized controlled trial	n = 6 5 male, 1 female age 45 – 68 years 9 – 57 months post stroke Randomly assigned to 2 groups in parent study (Lin et al., 2009)	5 x/wk, 3 wks BAT vs. CIMT	Fugl-Meyer Upper Extremity Test Action Research Arm Test Motor Activity Log fMRI during finger and elbow flexion and extension	Improved motor function and varied patterns of fMRI change Cerebellar activation increased in 3 of 4 BAT participants, decreased in the 2 CIMT participants
Cauraugh JH, Summers JJ University of Florida, Gainesville, FL					
(Cauraugh and Kim, 2002)	Small randomized controlled trial	n = 25 21 male, 4 female mean age 64 years hemiparesis mean 39 months post-stroke randomly assigned to 3 training groups	2 x/wk, 2 wks unilateral vs. bilateral active wrist and finger extension with EMG-triggered electrical stimulation. Controls did only unilateral movement	Box and Block Test Reaction Time Ability to sustain muscle contraction	Greater gains in all measures for the group who did bilateral training with electrical stimulation vs. the other 2 groups

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
(Cauraugh et al., 2005)	Small randomized controlled trial	n = 26 13 male, 13 female randomly assigned to 2 training groups Bilateral training: 4 ± 2 yrs post-stroke age 63 ± 11 years Unilateral training: 5 ± 4 yrs post-stroke age 69 ± 10 years 5 healthy controls: age 54 ± 14 years	2 x/wk, 2 wks unilateral vs. bilateral active wrist and finger extension with EMG-triggered electrical stimulation. Control group did no intervention	Kinematic measures of transverse plane target aiming movements	Improved aiming after bilateral vs. unilateral training Evidence of intra-limb transfer from distal bilateral training to proximal motor performance
(Summers et al., 2007)	Small randomized controlled trial	n = 12 (7 for TMS) hemiparesis randomly assigned to 2 training groups 7 male, 5 female age 43 – 82 years	Daily for 6 days unilateral vs. bilateral dowel placement task, moving vertical dowel from table onto shelf	Kinematics of upper extremity movements Modified Motor Assessment Scale TMS cortical maps and resting thresholds	Improved performance in bilateral group only Decreased non-lesioned cortex map volume linked to motor gains, mainly in bilateral group
Stinear JW, Lewis GN, Stoykov ME University of Auckland, Auckland, New Zealand					
(Lewis and Byblow, 2004)	Cohort AB design where A = unilateral and B = bilateral training	n = 6 4 male, 2 female age = 42 – 84 years hemiparesis 1 – 47 months post- stroke	Daily for 4 wks practice of 3 tasks selected from a list, unilaterally for first 8 – 13 days, then bilaterally	2 components of the Fugl-Meyer Upper Extremity Test Observational analysis of task performance based on video TMS cortical maps	No change in Fugl- Meyer scores Task performance improved with unilateral practice, Inconsistent effects of bilateral training TMS inconclusive

Author, Year	Design	Participants	Intervention	Outcome Measures	Results
(Stinear and Byblow, 2004)	Cohort Pre vs. post training (Pre-post statistical analysis as one group, despite 2 training protocols)	n = 9 randomly assigned to 2 training groups 7 male, 2 female age 48 – 84 years hemiparesis 2 – 84 months post-stroke	6 x/day, 4 wks active-passive bimanual movement therapy (APBT) Paretic wrist passive flexion and extension driven by active non-paretic wrist, via a custom built device	3 components of the Fugl-Meyer Upper Extremity Test Muscle strength TMS cortical maps and resting thresholds	Improved Fugl-Meyer scores Decreased non-lesioned cortex map volume No strength change
(Stoykov et al., 2009)	Small randomized controlled trial	n = 24 16 male, 8 female Hemiparesis Randomly assigned to 2 groups Bilateral: 10 ± 5 years post-stroke, age 64 ± 13 years Unilateral: 10 ± 10 years post-stroke age 65 ± 11 years	3 x/wk, 8 wks repetitive practice of the same 6 upper extremity tasks either unilaterally or bilaterally	3 Subscales of the Motor Assessment Scale (MAS) – Upper Limb Motor Status Scale (MSS) Strength	Only bilateral group improved on the Upper Arm Function subscale of the MAS Both groups improved strength and MSS with no group difference

Morris JH University of Dundee, Dundee, UK					
(Morris et al., 2008)	Randomized controlled trial	n = 97 61 male, 36 female Mean age 68 years Hemiparesis 2 – 4 weeks post-stroke randomly assigned to 1 of 2 groups	5 x/wk, 6 wks unilateral vs. bilateral repetitive practice of 4 upper extremity tasks	Action Research Arm Test (ARAT) Rivermead Motor Assessment Nine-Hole Peg Test (9HPT) Modified Barthel Index	No group difference immediately after training 3 months later, lower ARAT pinch subscale and 9HPT in Bilateral group vs. Unilateral group
Desrosiers J University of Sherbrooke, Quebec, Canada					
(Desrosiers et al., 2005)	Small randomized controlled trial	n = 41 19 male, 22 female Mean age 73 years Hemiparesis 10 – 60 days post-stroke Randomly assigned to 1 of 2 groups	15 – 20 sessions of usual arm therapy plus repetitive practice of unilateral and symmetrical bilateral tasks vs. equal dose of usual therapy only	Motor impairment, strength, dexterity, coordination, function, ADL's Upper extremity functional test for the elderly (TEMPA)	No group differences Both groups showed improved functional independence, impairment, arm disability

Table 2. Studies investigating the bilateral deficit in healthy people

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Vandervoort et al., 1984)	n = 10 young adult	Isokinetic and isometric knee extension	9% Bilateral Deficit (BD) for isometric force 49% BD for fast isokinetic force (424 degrees/second)	BD exists and is increased during fast isokinetic contractions vs. isometric Bil. condition may affect fast-twitch motor units more than slow-twitch
(Howard and Enoka, 1991)	n = 22 3 groups: weight lifters, cyclists, untrained young adult	Isometric knee extension Arm-leg task combined knee extension with contralateral elbow flexion	No BD for arm-leg task 8 % BD for untrained group No BD for cyclists 6 % bilateral facilitation for weight lifters	BD affects only homologous contralateral muscle groups BD is altered by training status and can reverse, becoming bilateral facilitation after bilateral, symmetrical training BD has a neural mechanism
(Oda and Moritani, 1994)	n = 11 young adult right handed	Isometric elbow extension	4-5 % BD for force on left 9-10% BD for force on right Greater BD on right vs. left	BD exists for isometric elbow extension BD affects dominant side more than non-dominant side
(Hakkinen et al., 1995)	n = 33 3 groups based on young, middle or older age	Isometric knee extension	No BD for force or EMG	No BD for isometric force or EMG Similar findings across age groups
(Oda and Moritani, 1995)	n = 8 young adult right handed	Isometric hand grip	5 % BD for force 8 – 10 % BD for EMG Decreased movement related cortical potentials during bil. vs. uni. grip	BD exists for isometric hand grip BD is likely due to interhemispheric inhibition

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Weir et al., 1995)	n = 17 2 groups young adult	Eccentric knee extension before and after unilateral eccentric training vs. no training	11% BD during eccentric testing Unilateral eccentric training increased strength and BD	BD exists for eccentric contractions BD increased after unilateral eccentric training
(Herbert and Gandevia, 1996)	n = 11 young adult	Isometric thumb adduction	Voluntary activation was approximately 90% of maximum obtained via TMS twitch interpolation No BD for force	No BD of thumb adduction force or % activation Voluntary activation failure is at least partially due to suboptimal corticospinal drive
(Hakkinen et al., 1997)	n = 78, 7 groups based on gender and young, middle, or older age	Isometric and concentric knee extension	No BD for force or EMG	No BD for isometric or concentric knee extension force or EMG Similar findings across genders Similar findings across age groups
(Taniguchi, 1997)	n = 62 9 groups based on training protocols (3 groups for each of 3 training tasks) young adult	Isometric grip or isokinetic arm or leg extension power (80 degrees/second) before and after uni. vs. bil. training of the same movements	Baseline BD: 0 – 2 % for handgrip 9 – 10 % for arm extension 7 – 18 % for leg extension Trained limb BD increased by 1 – 5 % after uni. training, decreased by 0 – 9 % after bil. training	Greater BD for arm and leg extension than for handgrip Training effects are task-specific Unilateral training increases BD Bilateral training decreases BD Similar effects across muscle groups
(Weir et al., 1997)	n = 16 2 groups young adult	Concentric knee extension before and after unilateral concentric training vs. no training	3 – 10 % BD during concentric testing Unilateral concentric training increased strength but reversed BD.	BD exists for concentric contractions BD reversed, became bilateral facilitation, after unilateral concentric training

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Jakobi and Cafarelli, 1998)	n = 20 young adult untrained	Isometric knee extension 25, 50, 75, 100% of maximum	No BD for force, rate of force generation, EMG, coactivation, EMG/force ratio, or % activation (twitch interpolation)	No BD, isometric knee extension Similar pattern across measures BD likely has neural mechanism
(Taniguchi, 1998)	n = 39 5 groups based on training protocols (2 groups for each of 2 training tasks and one control group) young adult	Isokinetic (80 degrees/second) arm and leg extension power before and after uni. vs. bil. training of chest press vs. leg press, vs. no training	Baseline BD: 1 – 10 % for chest press 9 – 15 % for leg press Trained limb BD increased by 2 – 9 % after uni. training, decreased by 2 – 6 % after bil. training	Training effects are task-specific Unilateral training increases BD Bilateral training decreases BD
(Taniguchi et al., 2001)	n = 12 young adult right handed	Concentric index finger flexion reaction time	4% BD for reaction time on dominant side Non-significant 2% BD on non-dominant side EEG BD during movement execution, not preparation	BD affects reaction time BD greater on dominant side Lower cortical activation during bilateral vs. unilateral movement execution
(Li et al., 2001)	n = 12 young adult right handed	Isometric flexion of fingers individually or in various multi-finger combinations	11 – 16% BD for force Larger BD for asymmetrical finger combinations (14%) vs. symmetrical (11%)	BD affects multi-finger flexion force Finger flexion BD is greater when the active fingers differ across sides

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Latash et al., 2002)	n = 10 young adult right handed	Isometric flexion of fingers individually or in various multi-finger combinations	5 – 15% BD for force Larger BD for asymmetrical finger combinations (10%) vs. symmetrical (5%)	BD affects multi-finger flexion force Finger flexion BD is greater when the active fingers differ across sides
(Cresswell and Ovendal, 2002)	N = 28 young adult	Isokinetic (60 degrees/second) knee extension and flexion	17 % BD for extension torque 8 – 14 % BD for extensor EMG No BD for flexor torque or flexor EMG	BD exists for isokinetic knee extension torque and EMG, but not knee flexion BD not explained by antagonist muscle activation
(Khodiguian et al., 2003)	n = 17 young adult	Isometric and Myotatic patellar reflex-induced knee extension	No BD for isometric force 9 % BD for reflex force 17 % BD for reflex EMG	No BD for reflex knee extension force Contribution of spinal circuitry to BD is unclear since there was no force BD
(Van Dieen et al., 2003)	n = 22 young adult	Isometric finger flexion Isometric knee extension	Knee extension: 4 – 10 % BD for force 1 – 18 % BD for EMG Finger flexion: 20 – 22 % BD for force 20 % BD for EMG Force BD moderately correlated with EMG BD and with activation deficit shown by twitch interpolation	BD exists for isometric finger flexion and knee extension Similar patterns for force, EMG and level of voluntary activation BD not explained by postural instability or attention Magnitude of BD is large enough to be functionally important

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Kuruganti et al., 2005)	n = 33, 4 groups based on gender and young or older age	Isokinetic (45 degrees/second) knee extension and flexion before and after bilateral strengthening program	Baseline BD: 27 % for extension force 33 % for flexion force After bilateral training, knee extension BD decreased by 14 % but knee flexion BD did not change	BD exists for isokinetic knee extension and knee flexion force Bilateral training decreases BD, but effect may depend on muscle group Similar findings across age groups Similar findings across genders
(Hay et al., 2006)	n = 5 young adult	Concentric horizontal leg press jumps against 100% and 200% body weight	13 – 28 % BD for ground reaction impulse 25 – 36 % BD for hip power 6 – 39 % BD for work at hip, knee, ankle 6 – 21 % BD for EMG	BD exists for dynamic multi-joint movement Similar pattern across measures Variable BD magnitude across muscles
(Kuruganti and Seaman, 2006)	n = 8 adolescents, compared to previously reported data	Isokinetic (45 degrees/second) knee extension and flexion	26 % BD for extension force 24 % BD for flexion force No BD for EMG	BD exists for isokinetic knee extension and knee flexion force BD exists in adolescent females Similar findings across age groups
(Post et al., 2007)	n = 22 young adult right handed	Isometric index finger abduction	2 – 4 % BD for force 3 – 10 % BD for EMG Decreased intensity of precentral gyrus fMRI during bilateral vs. unilateral movement	Similar pattern across measures of force, EMG, cortical activation Source of the BD lies upstream of the primary motor cortex
(Magnus and Farthing, 2008)	n = 8 adult	Concentric leg press, Isometric hand grip	12 % BD for leg press 1 % BD for hand grip Increased core muscle EMG during leg press vs. grip	BD exists for concentric leg press and isometric hand grip Postural stability demands may influence BD

Authors	Participants	Muscle group / Contraction Type	Results	Conclusions / Comments
(Yamauchi et al., 2009)	n = 24 2 groups based on young or older age	Isometric leg press Isotonic concentric leg press at 10 – 80 % of maximal isometric force	21 – 23 % BD for isometric hip/knee extension force 16 – 19 % BD for isometric hip/knee extension power Force/velocity plots show larger BD at high force/ low velocity	BD exists for isometric and isotonic concentric hip/knee extension force and power Similar findings across age groups

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Chapter 2

The need for speed:

Better movement quality during faster task performance after stroke

This chapter has been submitted:

DeJong SL, Schaefer SY, Lang CE (submitted, *Neurorehabilitation and Neural Repair*).

The need for speed: Better movement quality during faster task performance after stroke.

ABSTRACT

Background: Although slow and insufficient muscle activation is a hallmark of hemiparesis post-stroke, movement speed is rarely emphasized during upper extremity rehabilitation. Moving faster may increase intensity of task-specific training, but positive and/or negative effects on paretic-limb movement quality are unknown. **Objective:** To determine whether moving quickly instead of at a preferred speed either enhances or impairs paretic limb task performance after stroke. **Methods:** Sixteen people with post-stroke hemiparesis and 11 healthy controls performed reach-grasp-lift movements at their preferred speed and as fast as possible, using palmar and 3-finger grip types. We measured durations of the reach and grasp phases, straightness of the reach path, thumb-index finger separation (aperture), efficiency of finger movement, and grip force.

Results: As expected, reach and grasp phase durations decreased in the fast condition in both groups, showing that participants were able to move more quickly when asked.

When moving fast, the hemiparetic group had reach durations equal to those of healthy controls moving at their preferred speed. Movement quality also improved. Reach paths were straighter and peak apertures were greater in both groups in the fast condition. The group with hemiparesis also showed improved efficiency of finger movement.

Differences in peak grip force across speed conditions did not reach significance.

Conclusions: People with hemiparesis are able to move faster than they choose to, and when they do, movement quality is improved. Simple instructions to move faster could be a cost-free and effective means of increasing rehabilitation intensity after stroke.

Keywords: hemiparesis, speed, kinematics, upper extremity, motor control, reach-to-grasp

INTRODUCTION

The neurological system is known to be highly adaptable and capable of transforming functionally and structurally after injury, in a use-dependent manner (Adkins et al., 2006; Jones et al., 2009; Mueller and Maluf, 2002; Nudo et al., 1996). Clinicians and researchers alike now seek to identify the parameters of physical training that maximize neural adaptation and allow individuals to approach their potential in terms of motor control and function. For people with stroke, intensity of rehabilitation is often insufficient, as revealed by the many clinical trials that show less improvement after standard care compared to more intense experimental training protocols (Duncan et al., 2003b; Harris et al., 2009; Kuys et al., ; Kwakkel et al., 1999; Macko et al., 2005; Sunderland et al., 1992; Wolf et al., 2006). While the frequency and duration of therapy sessions are largely limited by cost constraints, the content of each session remains an area in which clinicians can potentially enhance effectiveness through careful decision making, guided by evidence.

For upper extremity rehabilitation post-stroke, repetitive task-specific training is a key stimulus to promote neural adaptation and recovery (Askim et al., 2009; Jang et al., 2003; Liepert et al., 2000; Schaechter et al., 2002). Optimal intensity requires sufficiently challenging tasks, repeated an adequate number of times, in a manner that elicits improved performance. Although slow, insufficient muscle activation is a

hallmark of hemiparesis (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck and Andreassen, 1980; Young and Mayer, 1982), the speed of task performance is rarely emphasized in either clinical or experimental intervention protocols. Reasons for this are unclear, but may stem from concerns about how hyperactive stretch reflexes or speed-accuracy trade-offs may affect movement quality.

Only two studies have questioned the effects of movement speed on upper extremity task performance after stroke. In one, faster paretic limb movements were associated with increased opening of the hand, and a larger percentage of the reach duration was spent in the acceleration phase (van Vliet and Sheridan, 2007). In another, non-paretic limb reaching trajectories were smoother (i.e. fewer movement units) when speed was emphasized over accuracy (Lin et al., 2008). Similar findings have been demonstrated in healthy participants (Adam, 1992; Fisk and Goodale, 1984; Rival et al., 2003) and people with other movement disorders (Rand et al., 2000), but have not been adequately investigated in the paretic limb of people post-stroke.

The purpose of this study, therefore, was to determine whether moving quickly instead of at a preferred speed either enhances or impairs performance of a reach-grasp-lift task by the paretic limb of people with post-stroke hemiparesis. Based on previous findings, we expected that participants would be able to increase their movement speed when asked. We hypothesized that faster movements would be associated with improved movement quality, as measured by reach path straightness, thumb-finger separation (aperture), efficiency of finger movement, and grip force. Two grip types were included, and a group of healthy adults provided control data for comparison. If faster speeds

benefit performance without negative consequences, simple instructions to move faster could be a cost-free and effective means of increasing intensity and maximizing the therapeutic dose of activity contained within each therapy session.

METHODS

Participants

Sixteen people with hemiparesis due to stroke were recruited from the St. Louis metropolitan area via the Brain Recovery Core Database and the Cognitive Rehabilitation Research Group Stroke Registry at Washington University, and from local support groups for people with stroke. Potential participants were included if they 1) had been diagnosed with ischemic or hemorrhagic stroke by a stroke neurologist, 2) had persistent hemiparesis, as evidenced by upper extremity Medical Research Council muscle test scores that were at least one muscle grade lower on the paretic side compared to the non-paretic side, 3) had residual reaching and grasping ability sufficient to participate in the study procedures, and 4) had the ability to follow 2-step commands. We excluded people who 1) had severe aphasia as indicated by a score of 2 or 3 on the Best Language item of the National Institutes of Health Stroke Scale (NIHSS), 2) had severe hemispatial neglect, as indicated by a score of 2 on the Extinction and Inattention item on the NIHSS, 3) had musculoskeletal or other medical conditions besides stroke that limited either upper extremity, or 4) were unable to give informed consent.

For comparison, eleven healthy adults were recruited from the Volunteer for Health Research Participant Registry at Washington University. Volunteers were

included if they 1) were at least 30 years old, 2) had no known neurological disease, and 3) had no disability or injury affecting their upper extremity on either side. This study was approved by the Washington University Human Research Protection Office, and all participants provided informed consent prior to beginning the study.

Clinical Assessments

Clinical tests were used to describe the participants with post-stroke hemiparesis (Table 3). We assessed upper extremity function using the Action Research Arm Test (ARAT) on the paretic side (Lang et al., 2006a; Lyle, 1981; Yozbatiran et al., 2008) and the Activities of Daily Living and Hand Function domains of the Stroke Impact Scale, version 3.0 (Duncan et al., 1999; Lai et al., 2002) (SIS). Maximum grip strength was measured on each side using a Jamar grip dynamometer in its second position (Fess, 1992; Schmidt and Toews, 1970). Maximum pinch strength was measured on each side with a Jamar hydraulic pinch gauge positioned between the thumb and the lateral side of the index finger middle phalanx (Mathiowetz et al., 1985; Werle et al., 2009). Sensation on the palmar surface of the distal index finger was evaluated using Semmes-Weinstein monofilaments (Bell-Krotoski, 1991). Spasticity of the elbow flexors was assessed on the paretic side using the Modified Ashworth Scale (Bohannon and Smith, 1987).

Experimental Procedures

For each participant, data collection was completed in a single session. Upper extremity movement and grip force were measured during reach-grasp-lift movements in

preferred speed and fast conditions using palmar and 3-finger grip types. These grip types were chosen because they have been well characterized as two discrete patterns of prehension with different levels of accuracy and precision, and because they represent a range of actions observed in daily life (Ehrsson et al., 2000; Landsmeer, 1962; Napier, 1956; Pouydebat et al., 2008). We tested the contralesional, paretic upper extremity of hemiparetic participants, and one randomly selected side for control participants. The object that was grasped by the tested side consisted of a custom-fabricated vertical cylinder (3.4 cm diameter, 11.3 cm height) attached to a rectangular base (13.5 by 6 cm) that was designed to hold a Tekscan I-scan electronic interface (Tekscan, Inc. South Boston, MA). The cylindrical portion of the object was covered with a Tekscan pressure sensor (11.18 by 11.18 cm, 1936 sensels, spatial resolution 15.5 sensels/cm²). Combined weight of the object and electronics was 420 grams. Pressure data were collected at 100 Hz. Measurement of grip force is a novel use of pressure sensor technology. This method was chosen instead of a more typical strain gauge system because it does not require that participants place their hand or fingers on specific locations, and instead allows for more natural grasping performance. A disadvantage of the pressure sensor system is that it only measures grip forces (normal forces) and is unable to measure load forces (tangential or shear forces). For use in this study, we believed that the advantage of capturing natural movements outweighed the disadvantage of limiting our force analysis to grip (i.e. normal) forces.

Three-dimensional movements of the tested upper extremity and the object were captured at 50 Hz using an electromagnetic tracking system (The MotionMonitor,

Innovative Sports Training, Chicago, IL). Nine sensors were attached to the trunk and upper extremity, as follows: 1) trunk: midline below the sternal notch, 2) upper arm: proximal to the lateral epicondyle, bisecting the upper arm mass, 3) forearm: midpoint between the radial and ulnar styloids on the dorsum of the forearm, 4) hand: midpoint of the third metacarpal on the dorsum of the hand, and 5 through 9) thumb and fingers: on the nail of each digit. One additional sensor was attached to the object, at the base of the cylindrical portion.

Participants were seated in a chair with back support for all data collection (Figure 1). A table was placed with its closest edge across the participant's mid-thighs and the height was adjusted to be as low as possible without contacting the thighs, in order to allow clearance of the table edge while reaching. The object was placed on the table at a standardized distance from the participant (90% of the length of the arm from shoulder to wrist). In the frontal plane, the object was aligned with the mid-clavicle.

Four trial types were collected, each characterized by the preferred speed or fast movement condition and by the type of grip (i.e. palmar preferred speed, palmar fast, 3-finger preferred speed, and 3-finger fast). We collected preferred speed trials before fast trials in order to capture unbiased natural performance, and randomized the order in which palmar and 3-finger trials were collected within each speed condition. Prior to each trial, the participant was instructed to rest both hands in their lap with thumb and fingers together, wait for the word 'go', then grasp and lift the object, hold it above the table for about 5 seconds until the examiner said 'done', then put it down and return to the starting position. No speed-related instructions were provided prior to preferred

speed trials. Before each fast trial, the participant was instructed to wait for the word ‘go’, then complete the reach-grasp-lift movement as fast as possible while still being able to complete the task. Verbal instruction and demonstration was also provided regarding grip type. Three trials of each type were recorded consecutively, with approximately 10 seconds of rest between trials.

Analysis

Pressure data were converted to grams of force, using Tekscan software to multiply recorded pressure by the sensor’s spatial area. After low-pass filtering of kinematic data at 6 Hz using a second-order Butterworth filter, sensor position data were extracted using MotionMonitor software (Innovative Sports Training, Chicago, IL). Subsequent analysis was then completed using custom software written in MATLAB (The MathWorks, Inc., Natick, MA).

Durations of movement phases were determined based on hand velocity, force on the object, and object position (Figure 1C). The reach phase began when velocity of the hand sensor first exceeded 5 mm/s, and ended when force on the object first exceeded 5 grams. Pre-lift delay began at the end of the reach, and ended when the vertical position of the object increased by 3 mm from its initial value. Other variables of interest included the reach path ratio, peak aperture, aperture path ratio, and peak grip force. Reach path ratio was defined as the length of the actual path of the forearm sensor during the reach phase, divided by the length of a straight line path. A reach path ratio close to one indicates a straight, direct reach, achieved through coordination of shoulder flexion

and elbow extension movements. Reach path ratios greater than one indicate greater curvature, typically resulting from temporally decoupled shoulder and elbow movements. Peak aperture was the maximum three-dimensional distance between sensors on the thumbnail and the index fingernail during the reach phase. Aperture path ratio quantified the smoothness/efficiency of thumb and index finger movement during the reach phase, and was calculated as follows, modified from Lang et al., 2005 (Lang et al., 2005) and Lang et al., 2006 (Lang et al., 2006b):

$$\text{Aperture Path Ratio} = \frac{\text{Sum of the absolute values of all changes in aperture during the reach phase}}{(\text{Peak aperture} - \text{aperture at beginning of reach}) + (\text{Peak aperture} - \text{aperture at end of reach})}$$

An aperture path ratio equal to one indicates smooth and direct separation of the thumb and index finger to the maximum aperture value, followed by smooth and direct closing onto the object. Higher values indicate abnormal, inefficient opening and closing of the thumb and index fingers, typically seen when participants make multiple attempts to open their hand and then close it on the object. Peak grip force was defined as the maximum force applied to the object. Reliability of kinematic reaching variables has been shown to be adequate in healthy individuals and people with post-stroke hemiparesis (Caimmi et al., 2008; Wagner et al., 2008). In a recent evaluation of a reach-to-grasp task that resembled the task used in the current study, excellent reliability was reported for reach duration, reach path ratio, and peak aperture ($r > 0.75$) in a group of people with hemiparesis after stroke (Patterson et al., In Press).

Variables were calculated separately for each trial. Each participant's performance in each movement condition was represented by the mean of three trials.

Kolmogorov-Smirnov tests were used to determine whether data were normally distributed. Since all data met the normality assumption ($p > 0.05$), parametric statistics were used. For each variable, $2 \times 2 \times 2$ repeated measures analysis of variance was used to determine effects of movement condition (preferred speed vs. fast), grip type (3-finger vs. palmar), and group (control vs. hemiparesis). Statistica software was used for normality testing and analysis of variance (Version 6.1 Statsoft Inc., Tulsa, OK), and the criterion for significance was set at $p < 0.05$. Effect sizes were calculated for statistically significant differences between speed conditions using Hedges' g , which is equal to the mean difference between conditions divided by the pooled unbiased standard deviation.

RESULTS

Characteristics of the 16 participants with hemiparesis are provided in Table 3. Time since stroke ranged from two weeks to nine years, and was less than four months in all except four participants. Severity of sensorimotor impairment and functional limitation ranged from mild to moderate, as shown by the strength measures and scores on the ARAT and SIS assessments. Eleven healthy adults also participated, including five males and six females between 34 and 81 years of age (mean 54.9 ± 15.2 years). Nine were right handed and two were left handed, by self report. Random selection of the side to be tested resulted in six rights and five lefts. The dominant side was tested in six participants (five right-handed, one left-handed).

Effects of movement speed

As expected, participants in both groups were able to move faster when asked (Figure 2). Difference values between speed conditions and ANOVA results are presented in Table 4. Reach duration (Figure 2A) was 40% shorter in the fast condition in the hemiparetic group (post-hoc $p < 0.05$, $g = 1.26$), and 47% shorter in the fast condition in the control group (post-hoc $p < 0.05$, $g = 1.54$). Within each speed condition, reach durations were longer in the hemiparetic group compared to controls (post hoc $p < 0.05$). When moving fast, however, the hemiparetic group showed reach durations equal to those of healthy controls moving at their preferred speed (post-hoc $p = 0.93$). Pre-lift delay (Figure 2B) was 37% shorter in the fast condition in the hemiparetic group (post-hoc $p < 0.05$, $g = 1.24$), and 52% shorter in the fast condition in the control group (post-hoc $p < 0.05$, $g = 1.51$).

Improvements in movement quality were also evident during faster task performance. Representative data from individual participants with hemiparesis are shown in Figure 3. In the fast condition, reach trajectories were straighter than they were in the preferred speed condition (Figure 3A, left panel vs. right panel). Curved reach paths in the preferred speed condition indicate impaired coordination and temporal dissociation of shoulder flexion and elbow extension movements during reaching. Efficiency of finger movement was also improved in the fast condition, shown by smoother aperture traces (Figure 3B, left panel vs. right panel) and quantified by a decrease in the aperture path ratio.

Group data for the measures of movement quality are shown in Figure 4.

Difference values between speed conditions and ANOVA results are presented in Table 4. Both groups showed lower (better) reach path ratios and greater peak apertures in the fast condition compared to the preferred speed condition (main effect of speed, $p < 0.05$, hemiparetic group $g = 0.37$ for reach path ratio and 0.24 for peak aperture, control group $g = 0.48$ for reach path ratio and 0.62 for peak aperture). In the hemiparetic group only, aperture path ratios were lower (better) in the fast condition compared to the preferred speed condition ($g = 0.75$). Although the main effect of movement speed on peak grip force approached significance ($p = 0.06$), post hoc testing failed to find a difference between speed conditions in either group (hemiparetic group $p = 0.94$, control group $p = 0.20$). Visual inspection of data indicated that improvements in movement quality in the fast condition were similar in the four participants who had sustained strokes less than four months previously compared with the twelve participants who had sustained strokes more recently.

Effects of group and grip type

Some additional significant effects of group and grip type were also found (Table 4). Pre-lift delays and reach path ratios were greater in the hemiparetic group than in controls (main effects of group, $p < 0.05$, Figures 2B and 4A, respectively), regardless of speed condition (no group x condition interactions). Differences between groups did not reach significance for aperture path ratio, peak aperture, or grip force (Figures 4B, 4C, and 4D).

In the hemiparetic group only, reach duration and pre-lift delay were longer during 3-finger grip trials compared to palmar grip trials (post-hoc $p < 0.05$). In both groups, peak aperture and peak grip force were greater during palmar grip trials compared to 3-finger grip trials (main effect of grip $p < 0.05$). Grip type did not affect reach path ratios or aperture path ratios significantly in either group.

DISCUSSION

Faster is possible

This study demonstrated that people with mild to moderate post-stroke hemiparesis are able to increase their movement speed upon request, and when they do, movement quality is improved. Reach paths are straighter, finger movements are more efficient, and the fingers open wider. These measures of task performance are known to be altered after stroke and have the potential for recovery (Lang et al., 2005; Lang et al., 2006b). As most of our participants were within a few months post-stroke, our findings suggest that incorporating the fast movement condition into rehabilitation may improve movement quality during training and thus may contribute to improved outcomes.

Shorter reach durations and pre-lift delays in the fast condition demonstrate that people with hemiparesis can voluntarily increase their rate of muscle activation in order to approach the movement speeds of healthy individuals. Slow and insufficient muscle activation is a fundamental movement problem after stroke (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck and Andreassen, 1980; Young and Mayer, 1982), and people with hemiparesis often choose to use their opposite

limb instead when the paretic limb is too slow or unreliable (Taub et al., 2006b). Aside from any potential improvements in movement quality, aiming to increase paretic limb movement speed is itself a reasonable goal of upper extremity rehabilitation.

Faster is better

This is the first study to demonstrate improved paretic-limb coordination during faster movement, as shown by the reach path and aperture path ratios. For peak aperture, our results echo those of van Vliet and Sheridan (van Vliet and Sheridan, 2007), who also showed wider finger opening during fast movements in healthy controls and people post-stroke. For the comparison across speeds in the hemiparetic group, effect size was large for aperture path ratio ($g \geq 0.8$), medium for reach path ratio ($0.3 \leq g \leq 0.5$), and small for peak aperture ($g \leq 0.3$). No detrimental effects of the fast movement condition were observed. These results suggest that fast training may not only increase rates of muscle activation, but may also improve the spatiotemporal pattern of activation that controls proximal and distal multi-joint movements. In addition, fast training may allow for more task repetitions during the same allotted therapy time, as has been explored recently in a proof-of-concept trial (Birkenmeier et al., 2010).

Although outcomes of fast training have not been examined in the upper extremity, studies of gait training post-stroke may provide valuable insight. In a large randomized clinical trial, walking speeds in people with hemiparesis were dramatically increased when participants were simply informed of their fast walking speed each day during inpatient rehabilitation (Dobkin et al., 2010). In another study, participants were

able to walk 165% faster than their preferred speed over-ground, and faster walking was associated with improved symmetry, increases in joint excursions and muscle activations, and less compensatory paretic-limb circumduction (Lamontagne and Fung, 2004). Cardiovascular fitness, walking endurance and functional mobility have also been shown to increase much more after speed-intensive gait training compared to a less intense protocol (Macko et al., 2005). Outcomes of upper extremity task specific training might improve as well, given faster training speeds.

Limitations

Recruitment into the hemiparetic group in this study was limited to people who were able to perform reach-grasp-lift movements with both palmar and 3-finger grip types. Participants were, therefore, mildly to moderately impaired, and the results may not generalize to people with more severe hemiparesis. Our investigation of the fast movement condition was limited to kinematic and kinetic characteristics of task performance. It is possible that muscular, neurological, and/or cardiorespiratory fatigue may limit implementation of fast task-specific training, particularly in certain individuals with comorbidities. This investigation was also limited to the within-session effects of different movement conditions, and did not explore training effects across multiple sessions. Further investigation into the feasibility, safety, and potential benefits of incorporating the fast movement condition into task-specific training appears warranted.

Conclusions

In summary, this study showed that people with mild to moderate hemiparesis post-stroke are able to perform upper extremity reach-grasp-lift tasks substantially faster than their preferred movement speed and, further, that movement quality is enhanced during faster movements. No detrimental effects were observed in the fast condition. Simple instructions to move faster could be a cost-free and effective means of increasing the intensity of task specific training after stroke. Further studies of feasibility, safety and therapeutic effects are needed.

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Figure 1. Assessment of task performance. Illustration of the experimental set-up and a participant beginning (A) and finishing (B) the reach-grasp-lift task with a 3-finger grip. C) Example data from one trial. Vertical dashed lines demonstrate division of the task into movement phases. The reach phase began when velocity of the hand sensor first exceeded 5 mm/sec and ended when grip force first exceeded 5 grams. Pre-lift delay began at the end of the reach and ended when the vertical position of the object increased by 3 mm from its initial value.

Figure 1

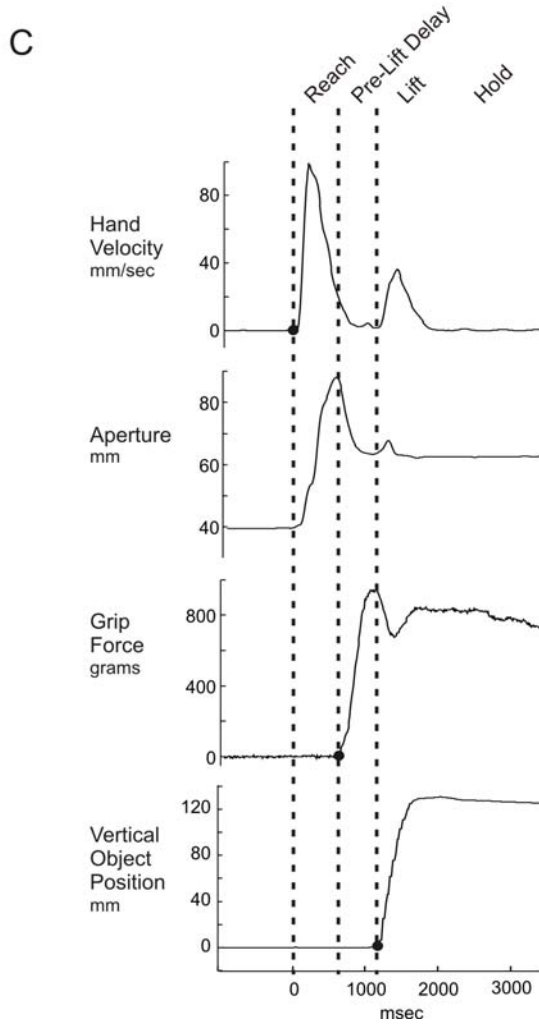
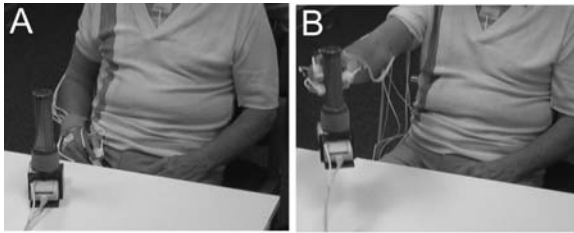


Figure 2. Comparison of phase durations in the preferred speed versus fast conditions. Values are means \pm 1 standard error. Reach duration (A) and pre-lift delay (B) were shorter in the fast condition, in both groups. Reach duration was longer in the hemiparetic group compared to controls. When moving fast, however, the hemiparetic group had reach durations equal to that of the control group moving at their preferred speed.

Figure 2

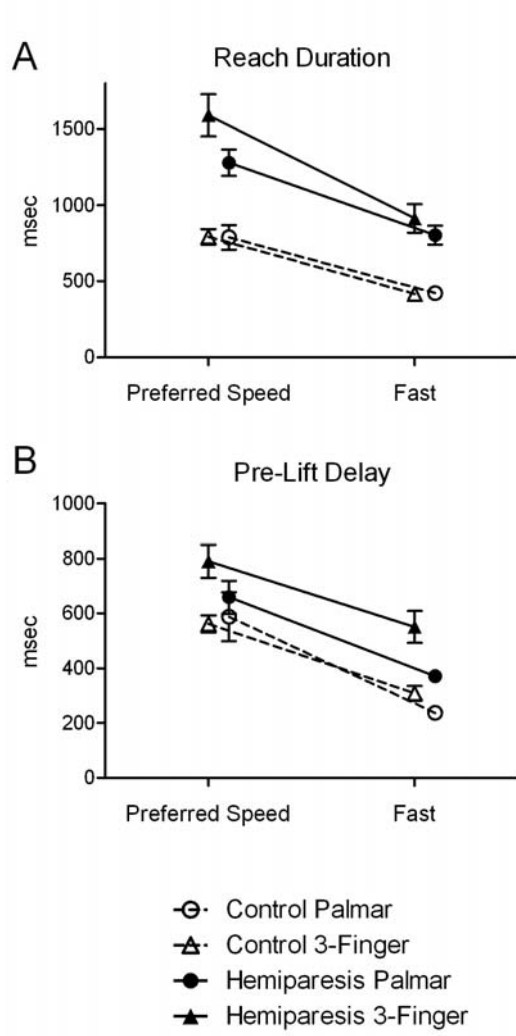
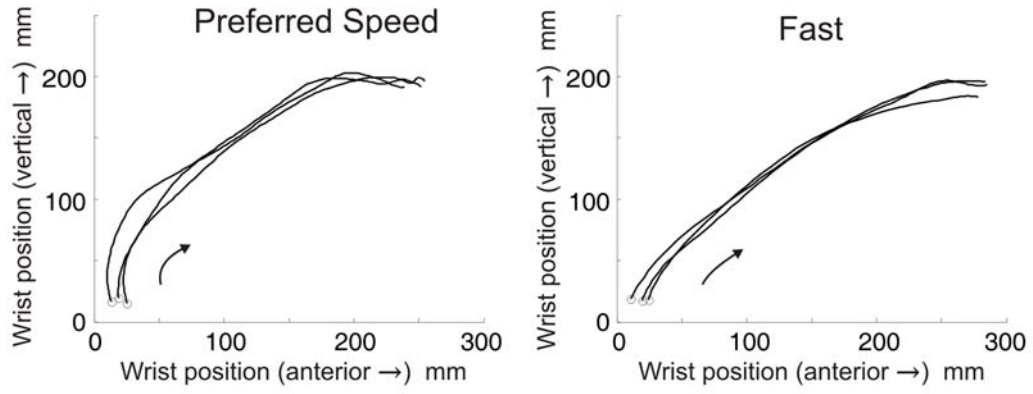


Figure 3. Examples of improved movement quality during the fast condition in individual participants with hemiparesis. A) Trajectories of the wrist sensor in the sagittal plane. Reach paths were straighter during three fast trials (right panel) compared to three preferred speed trials (left panel). Curved reach paths indicate impaired coordination and temporal dissociation between shoulder flexion and elbow extension during reaching. B) Improved efficiency of finger movement, seen as smoother aperture traces during three fast trials (right panel) compared to three preferred speed trials (left panel). Smoothness of the aperture trace is quantified by the aperture path ratio.

Figure 3

A



B

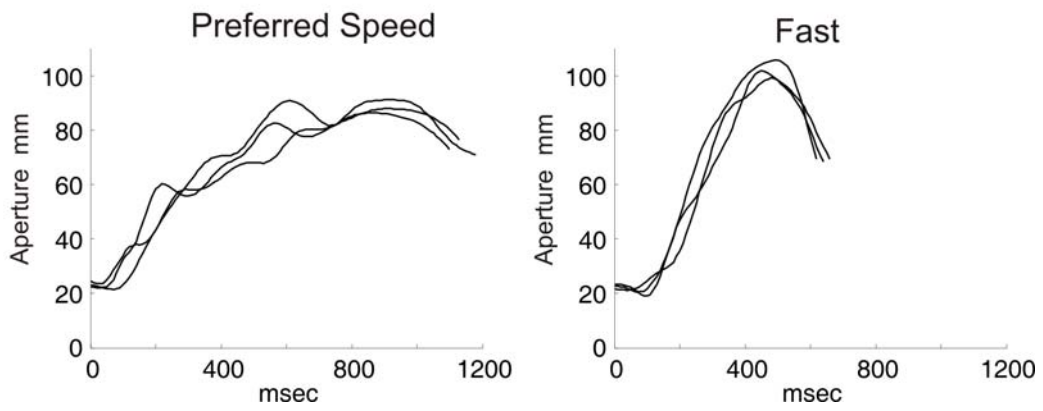


Figure 4. Comparison of movement quality in the preferred speed versus fast conditions. Both groups showed lower reach path ratios (A) and greater peak apertures (C) in the fast condition compared to the preferred speed condition. In the hemiparetic group only, aperture path ratios were lower in the fast condition compared to the preferred speed condition (B).

Figure 4

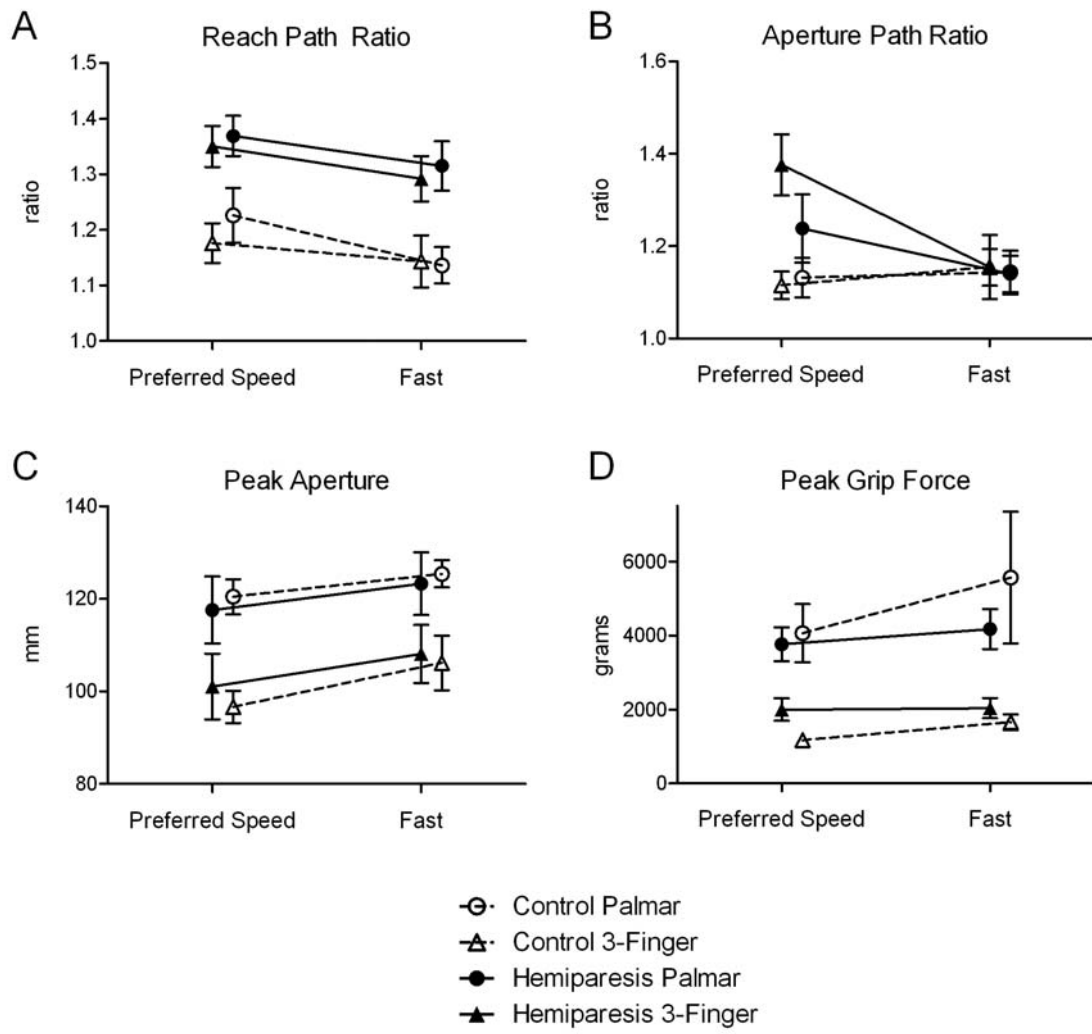


Table 3. Characteristics of participants with hemiparesis^a

Age, years	59 ± 11 (39 – 88)
Gender, n	
Male	9
Female	7
Paretic side, n	
Dominant	11
Non-dominant	5
Right	8
Left	8
Type of stroke	
Ischemic	14
Hemorrhagic	2
Time since stroke (median, range)	1.2 months (2 weeks – 9.4 years)
Grip strength	
paretic side in kg	21.9 ± 8.8 (10.0 – 36.0)
paretic side as % of non-paretic	69 ± 26 (37 – 112)
Pinch strength	
paretic side in kg	5.5 ± 1.9 (2.0 – 8.0)
paretic side as % of non-paretic	70 ± 21 (29 – 114)
Sensation ^b , n	
2.83	6
3.61	6
4.31	2
6.25	2
Spasticity ^c , n	
0	8
1	6
2	1
4	1
Action Research Arm Test ^d	41 ± 10 (20 – 53)
Stroke Impact Scale ^e	
Activities in a Typical Day	62 ± 15 (43 – 88)
Hand Function	50 ± 21 (0 – 85)

^a Data are mean ± standard deviation (range), except where otherwise noted.

^b Size of the smallest Semmes Weinstein monofilament sensed in 3 of 5 trials on the anterior distal index finger on the paretic side

^c Modified Ashworth Scale score for the elbow flexors on the paretic side

^d Paretic side. Range of possible scores is 0 to 57, 57 = normal

^e Range of possible scores is 0 to 100, 100 = normal

Table 4. Effects of movement speed on task performance^a

	Group	Difference between Fast and Preferred Speed Conditions	
		Palmar Grip	3-Finger Grip
Reach Duration (msec) ^{b c d e f}	Hemiparesis	-476 ± 79	-677 ± 104
	Control	-365 ± 81	-375 ± 40
Pre-Lift Delay (msec) ^{b c d f}	Hemiparesis	-288 ± 64	-239 ± 80
	Control	-351 ± 86	-253 ± 49
Reach Path Ratio ^{b c}	Hemiparesis	-0.05 ± 0.03	-0.06 ± 0.03
	Control	-0.09 ± 0.03	-0.03 ± 0.03
Peak Aperture (mm) ^{c d}	Hemiparesis	6 ± 3	7 ± 4
	Control	5 ± 4	9 ± 6
Aperture Path Ratio ^{c e}	Hemiparesis	-0.10 ± 0.05	-0.22 ± 0.06
	Control	0.01 ± 0.03	0.04 ± 0.08
Peak Grip Force (grams) ^d	Hemiparesis	412 ± 302	42 ± 66
	Control	1500 ± 1286	486 ± 213

^a Data are mean ± standard error. Negative numbers indicate lower values in the fast condition. Positive numbers indicate higher values in the fast condition.

^b Main effect of group, $p < 0.05$

^c Main effect of preferred vs. fast speed, $p < 0.05$

^d Main effect of grip, $p < 0.05$

^e Speed x group interaction effect, $p < 0.05$

^f Grip x group interaction effect, $p < 0.05$

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Chapter 3

Comparison of unilateral versus bilateral upper extremity task performance after stroke

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Comparison of unilateral versus bilateral upper extremity task performance after stroke.

ABSTRACT

Previous studies have suggested that moving bilaterally instead of unilaterally may improve paretic limb performance after stroke. In this single-session study, we compared unilateral vs. bilateral performance of a reach-grasp-lift-release task in people with post-stroke hemiparesis and healthy controls. Motion analysis variables included durations of the reach, grasp, and release phases, reach path straightness, maximum thumb-index finger aperture, efficiency of finger movement, and peak grip force. We found no evidence of immediate improvement in paretic-limb performance in the bilateral condition. In both groups, release duration was increased when participants moved bilaterally instead of unilaterally, possibly representing a divided-attention effect. Other variables did not differ across conditions. Our findings suggest little immediate impact of the bilateral condition on motor performance.

Keywords: motor control, hemiparesis, kinematic, reach, grasp

INTRODUCTION

Advances in restorative neuroscience have revealed immense potential for use-dependent neural adaptation after stroke and have renewed the search for training methods that optimize recovery. For people with hemiparesis, although task-specific repetitive practice is clearly a key stimulus to promote motor learning, the choices of what to practice and how to practice remain challenging and poorly guided by evidence. Current standards of care for post-stroke rehabilitation include sensorimotor training (Teasell et al., 2003), but optimal methods to implement such training remain debatable, and the effects of altering specific characteristics of task performance are largely unknown. Most therapeutic activities that constitute traditional post-stroke rehabilitation involve the use of the paretic arm by itself, or the use of both arms in a complimentary, asymmetrical fashion (McCombe Waller and Whitall, 2008). Constraint-induced movement therapy emphasizes unilateral task performance by the paretic limb and intentionally limits participation by the non-paretic limb (Wolf et al., 2006). In contrast, bilateral training paradigms include simultaneous task performance by both limbs, symmetrically or reciprocally, in an attempt to capitalize on the effects of interlimb coupling and thereby improve paretic limb performance (Harris-Love 2005, Mudie and Matyas 1996, 2000, Whitall et al., 2000). Because of the potential impact on rehabilitation and recovery, it is important to understand how moving bilaterally instead of unilaterally affects motor performance.

Interest in bilateral training began more than a decade ago, based on a case series of twelve people with post-stroke hemiparesis (Mudie and Matyas 1996, 2000). After

several sessions of practicing multijoint upper extremity tasks with only the paretic upper extremity, participants began practicing the same tasks using both upper extremities simultaneously and symmetrically. Raters quantified motor impairment by visually analyzing video recordings of task performance and rating various movement characteristics, each on a five-point scale. The observational scale included assessments of “joint ranges at the point of reaching the target, straightness and smoothness of the trajectory, accuracy of targeting, synchrony of limb parts, quality of grasp and presence of extraneous movements” (Mudie and Matyas, 2000). Upon beginning the bilateral training, each participant showed an immediate improvement as well as an increased rate of improvement across sessions.

Since those initial findings were reported, other investigators have demonstrated gains in upper extremity function, strength, range of motion, and daily use after bilateral training programs lasting between one and six weeks (Whitall et al., 2000, Lewis and Byblow, 2004, Stinear and Byblow, 2004, Cauraugh and Kim, 2002, Cauraugh et al., 2005, Summers et al., 2007, Richards et al., 2008, Lin et al., 2009, 2010, Morris et al., 2009, Senesac et al., 2010, Whitall et al., 2011). Larger, more recent clinical trials, however, have not supported bilateral training as being any more effective than other dose-matched training protocols (Lin et al., 2009, 2010, Morris et al., 2009, Whitall et al., 2011). Some have suggested that bilateral training may improve certain aspects of upper extremity movement (e.g. proximal joint motion) more than unilateral training does, and therefore may be more beneficial for certain individuals (Lin et al., 2009).

Several mechanisms have been suggested to explain the possible benefits of practicing movements bilaterally instead of unilaterally after stroke. Activation of corticospinal pathways in the lesioned hemisphere may be facilitated during bilateral symmetrical movements, due to 1) activation of neural network components shared by the two sides, 2) interlimb coupling effects whereby the two sides share a single motor command, or 3) by normalization of interhemispheric and intracortical inhibitory influences on the lesioned hemisphere that are exaggerated after stroke (Stinear et al. 2008, Murase et al., 2004, Stoykov and Corcos, 2009). In addition, activation of ipsilateral corticospinal pathways from the non-lesioned hemisphere to the paretic limb may be increased during bilateral movement.

Although many studies have explored functional and impairment level outcomes of bilateral training, few have included kinematic measures, and none have confirmed the immediate changes in movement quality during task performance originally reported by Mudie and Matyas (2000). After multisession bilateral training programs, three reports indicate decreased reach duration and/or increased peak velocity (Cauraugh et al., 2005, Lin et al., 2009, Senesac et al., 2010), one study showed decreased deceleration time during reaching (Cauraugh et al., 2005), and two showed a more direct reach path (Lin et al., 2009, Senesac et al., 2010). In a comparison of bilateral training vs. unilateral training outcomes, however, Summers et al. (2007) found no differences across groups in reach duration, peak velocity, curvature of the arm trajectory, or elbow angle.

Three within-session comparisons of bilateral vs. unilateral reaching alone (without grasping) have demonstrated greater paretic arm peak velocity in the bilateral

movement condition, for people with mild or moderate post-stroke hemiparesis (Harris-Love et al. 2005, Rose and Winstein 2005, McCombe Waller et al., 2006). Also using a within-session design, Cunningham et al. (2002) reported that three of six people with chronic mild hemiparesis showed fewer discontinuous reach trajectories in bilateral movement trials compared to those performed unilaterally. A more complete characterization of differences between bilateral and unilateral task performance is needed for a better understanding of how the bilateral movement condition affects movement, and to help indicate which people with hemiparesis are most likely to benefit from bilateral training.

The purposes of this study were to determine, within a single session, whether moving bilaterally instead of unilaterally enhances performance of the paretic limb in people with post-stroke hemiparesis, and to identify specifically which parameters of performance are enhanced. We hypothesized that upper extremity movements performed bilaterally would be associated with faster and more direct reaching, more efficient finger movement, increased separation of the thumb and index finger, faster grasp formation and release, and grip force closer to that of healthy controls, compared to movements performed unilaterally. Using three dimensional motion analysis methods, we assessed timing, movement, and grip force during reach-grasp-lift-release movements. Two grip types were included, and a group of healthy adults provided control data for comparison.

METHODS

Participants

Sixteen people with hemiparesis due to stroke were recruited from the St. Louis metropolitan area via the Brain Recovery Core Database and the Cognitive Rehabilitation Research Group Stroke Registry at Washington University, and from local support groups for people with stroke. Potential participants were included if they 1) had been diagnosed with ischemic or hemorrhagic stroke by a stroke neurologist, 2) had persistent hemiparesis, as evidenced by upper extremity Medical Research Council muscle test scores that were at least one muscle grade lower on the paretic side compared to the non-paretic side, 3) had residual reaching and grasping ability sufficient to participate in the study procedures, and 4) had the ability to follow 2-step commands. We excluded people who 1) had severe aphasia as indicated by a score of 2 or 3 on the Best Language item of the National Institutes of Health Stroke Scale (NIHSS), 2) had severe hemispatial neglect, as indicated by a score of 2 on the Extinction and Inattention item on the NIHSS, 3) had musculoskeletal or other medical conditions besides stroke that limited either upper extremity, or 4) were unable to give informed consent.

For comparison, twelve healthy adults were recruited from the Volunteer for Health Research Participant Registry at Washington University. Volunteers were included if they 1) were at least 30 years old, 2) had no known neurological disease, and 3) had no disability or injury affecting their upper extremity on either side. This study was approved by the Washington University Human Research Protection Office, and all participants provided informed consent prior to beginning the study.

Clinical Assessments

Clinical tests were used to describe the participants with post-stroke hemiparesis (Table 5). We assessed upper extremity function using the Action Research Arm Test (ARAT) on the affected side (Lyle 1981, Lang et al., 2006, Yozbatiran et al., 2008) and the Activities of Daily Living and Hand Function domains of the Stroke Impact Scale, version 3.0 (Duncan et al., 1999, Lai et al., 2002). Maximum grip strength was measured on each side using a Jamar grip dynamometer in its second position (Schmidt and Toews 1970, Fess, 1992). Maximum pinch strength was measured on each side with a Jamar hydraulic pinch gauge positioned between the thumb and the lateral side of the index finger's middle phalanx (Mathiowetz et al., 1984, Werle et al., 2009). Sensation on the palmar surface of the distal index finger was evaluated using Semmes-Weinstein monofilaments (Bell-Krotoski 1991). Spasticity of the elbow flexors was assessed on the affected side using the Modified Ashworth Scale (Bohannon and Smith 1987).

Experimental Procedures

For each participant, data collection was completed in a single session lasting approximately two hours. Upper extremity movement and grip force were measured during reach-grasp-lift-release movements in bilateral and unilateral conditions using palmar and 3-finger grip types. These grip types were chosen because they have been well characterized as two discrete patterns of prehension with different levels of accuracy and precision, and because they represent a range of actions observed in daily life (Napier

1956, Landsmeer 1962, Tucker and Ellis, 1996, 2004, Ehrsson et al., 2000, Pouydebat et al. 2010). We tested the paretic upper extremity of participants with hemiparesis, and one randomly selected side for control participants. The object that was grasped by the tested side consisted of a custom-fabricated vertical cylinder (3.4 cm diameter, 11.3 cm height) attached to a rectangular base (13.5 cm by 6 cm) that was designed to hold a Tekscan I-scan electronic interface (Tekscan, Inc. South Boston, MA). The cylindrical portion of the object was covered with a Tekscan pressure sensor (11.18 x 11.18 cm, 1936 sensels, spatial resolution 15.5 sensels/cm²). Combined weight of the object and electronics was 420 grams. Pressure data was collected at 100 Hz. An identical object without the pressure sensor was grasped by the non-tested side during bilateral movement trials. Measurement of grip force is a novel use of pressure sensor technology. This method was chosen instead of a more typical strain gauge system because it does not require that participants place their hand or fingers on specific locations, and instead allows for more natural grasping performance. A disadvantage of the pressure sensor system is that it only measures grip forces (normal forces) and is unable to measure load forces (tangential or shear forces). For use in this study, we believed that the advantage of capturing natural movements outweighed the disadvantage of limiting our force analysis to grip (i.e. normal) forces.

Three-dimensional movements of the tested upper extremity and the object were captured at 50 Hz using an electromagnetic tracking system (The MotionMonitor, Innovative Sports Training, Chicago, IL). Nine sensors were attached to the trunk and upper extremity, as follows: 1) trunk: midline below the sternal notch, 2) upper arm:

proximal to the lateral epicondyle, bisecting the upper arm mass, 3) forearm: midpoint between the radial and ulnar styloids on the dorsum of the forearm, 4) hand: midpoint of the third metacarpal on the dorsum of the hand, and 5 through 9) thumb and fingers: on the nail of each digit. One additional sensor was attached to the object, at the base of the cylindrical portion.

Participants were seated in a chair with back support for all data collection (Figure 5). A table was placed with its closest edge across the participant's mid-thighs and the height was adjusted to be as low as possible without contacting the thighs, in order to allow clearance of the table edge while reaching. The object was placed on the table at a standardized distance from the participant (90% of the length of the arm from shoulder to wrist). In the frontal plane, the object was aligned with the mid-clavicle. For bilateral trials, these criteria also determined placement of the non-instrumented object placed on the opposite side.

Four trial types were collected in random order, each characterized by the unilateral or bilateral movement condition and by the type of grip (i.e. palmar unilateral, palmar bilateral, 3-finger unilateral, and 3-finger bilateral). Prior to each trial, the participant was instructed to rest both hands in his or her lap with thumb and fingers together, wait for the word 'go', then grasp and lift the object, hold it above the table for about 5 seconds until the examiner said 'done', then put it down and return to the starting position. Further verbal instruction and demonstration was also provided regarding grip type and the bilateral or unilateral movement condition. Three trials of each type were recorded consecutively, with approximately 10 seconds of rest between trials.

Analysis

Pressure data were converted to grams of force, using Tekscan software to multiply recorded pressure by the sensor's spatial area. After low-pass filtering of kinematic data at 6 Hz using a second-order Butterworth filter, sensor position data were extracted using MotionMonitor software (Innovative Sports Training, Chicago, IL). Subsequent analysis was then completed using custom software written in MATLAB (The MathWorks, Inc., Natick, MA).

Durations of movement phases were determined based on hand velocity, force on the object, and object position, as follows (Figure 5B). The reach phase began when velocity of the hand sensor first exceeded 5 mm/s, and ended when force on the object first exceeded 5 grams. Pre-lift delay began at the end of the reach, and ended when the vertical position of the object increased by 3 mm from its initial value. Duration of the release phase was calculated as the difference between the time when the object returned to within 3 mm of its initial vertical position, and the time when force on the object returned to within 5 grams of its baseline value. In some cases, force returned to baseline prior to the object reaching a final stable position. In these cases, the calculated duration of the release phase was negative, indicating release of the object before it was placed securely on the table. In other cases, the object reached a stable position before force returned to baseline, yielding a positive release phase duration.

Other variables of interest included reach path ratio, peak aperture, aperture path ratio, and peak grip force. Reach path ratio was defined as the length of the actual path of the forearm sensor (just proximal to wrist joint) during the reach phase, divided by the

length of a straight line path. A reach path ratio close to one indicates a straight, direct reach, and a value greater than one indicates greater curvature of the reach path. Peak aperture was the maximum three-dimensional distance between sensors on the thumbnail and the index fingernail during the reach phase. Aperture path ratio quantified the smoothness/efficiency of thumb and index finger movement during the reach phase, and was calculated as follows (modified from Lang et al., 2005 and Lang et al., 2006b):

$$\text{Aperture Path Ratio} = \frac{\text{Sum of the absolute values of all changes in aperture during the reach phase}}{(\text{Peak aperture} - \text{aperture at beginning of reach}) + (\text{Peak aperture} - \text{aperture at end of reach})}$$

An aperture path ratio equal to one indicates smooth and direct separation of the thumb and index finger to the maximum aperture value, followed by smooth and direct closing onto the object. Higher values indicate abnormal, inefficient opening and closing of the thumb and index fingers, typically seen when participants make multiple attempts to open their hand and then close it on the object. Peak grip force was defined as the maximum force applied to the object. Reliability of kinematic reaching variables has been shown to be adequate in healthy individuals and people with post-stroke hemiparesis (Caimmi et al., 2008 Wagner, et al, 2008). In a recent evaluation of a reach-to-grasp task resembling the task used in the current study, Patterson et al. (In press) reported excellent reliability for reach duration, reach path ratio, and peak aperture ($r > 0.75$) in a group of people with hemiparesis after stroke.

Variables were calculated separately for each trial. Each participant's performance in each movement condition was represented by the mean of three trials. Kolmogorov-Smirnov tests were used to determine whether data were normally

distributed. Since all data met the normality assumption ($p > 0.05$), parametric statistics were used. For each variable, $2 \times 2 \times 2$ repeated measures analysis of variance was used to determine effects of movement condition (unilateral vs. bilateral), grip type (3-finger vs. palmar), and group (control vs. hemiparetic). Statistica software was used for normality testing and analysis of variance (Version 6.1 Statsoft Inc., Tulsa, OK), and the criterion for significance was set at $p < 0.05$.

Statistical power was analyzed for the unilateral vs. bilateral comparisons in the hemiparetic group. Observed effect sizes were calculated using Cohen's d , which is equal to the mean difference between conditions divided by the pooled standard deviation. For each variable, the sample size that would have been needed to achieve statistical significance was estimated using G*Power3 software (Faul et al., 2007), a paired t test design, observed effect sizes, and assumptions that power = 0.80 and 2-tailed alpha = 0.05.

RESULTS

Characteristics of the 16 participants with hemiparesis are provided in Table 5. Time since stroke ranged from two weeks to nine years, and was less than four months in all except three participants. Severity of sensorimotor impairment and functional limitation ranged from mild to moderate, as shown by the strength measures and scores on the ARAT and SIS assessments. Twelve healthy adults also participated, including six males and six females between 32 and 81 years of age (mean 53.0 ± 15.8 years). Ten were right handed and two were left handed, by self report. Random selection of the side

to be tested resulted in seven rights and five lefts. The dominant side was tested in seven participants (six right-handed, one left-handed).

Unilateral vs. bilateral effects

Results for each of the seven variables are presented in Table 6. The primary comparison of interest for this study (unilateral vs. bilateral performance), was tested via the main effect of condition and the condition by group interaction effect. Contrary to our hypothesis, none of the variables showed improved motor performance in the bilateral condition, in either group. This finding is illustrated graphically in Figure 6 A-G. One variable, release duration, was significantly different in the unilateral vs. bilateral conditions (Figure 6C). Participants in both groups took longer to release the object when moving bilaterally instead of unilaterally (effect size $d = 0.74$, collapsed across groups and grip types). For another variable, reach duration, a significant condition by group interaction was found. Post-hoc testing, however, failed to find a difference between the unilateral and bilateral conditions for either group ($p = 0.17$ for the hemiparetic group, $p = 0.57$ for the control group). No main effects of condition or condition by group interaction effects were found for the other variables.

Observed effect sizes for unilateral vs. bilateral comparisons in the hemiparetic group are presented in Table 7. The only large effects ($d \geq 0.5$) were for release duration, which was greater during bilateral compared to unilateral trials, in both grip types. Effect size was medium ($0.3 \leq d \leq 0.5$) for reach path ratio in palmar grip trials, which tended to be lower in the bilateral condition although the mean difference did not reach

significance. The remaining effect sizes were small ($0.1 \leq d \leq 0.3$) or minimal ($d < 0.1$). For all variables except release duration, a substantially larger sample would be required in order for the observed effects to reach statistical significance (Table 7).

Effects of group and grip type

Significant effects of group and grip type are indicated in Table 6. As expected, reach duration and reach path ratio were greater in the hemiparetic group compared to the controls (effect sizes $d = 1.36$ and $d = 1.00$, respectively), across conditions and grip types. In the hemiparetic group only, pre-lift delay was greater for the 3-finger grip compared to the palmar grip, across conditions (effect size $d = 0.91$). Reach duration was greater for the 3-finger grip compared to the palmar grip, across conditions and groups (effect size $d = 0.60$). Peak aperture and peak grip force were greater for the palmar grip compared to 3-finger grip, across conditions and groups (effect sizes $d = 1.38$ and $d = 0.97$, respectively).

DISCUSSION

In this single-session study, we found no evidence of an immediate improvement in paretic-limb performance of a reach-grasp-lift-release task when participants with hemiparesis moved bilaterally instead of unilaterally. The only significant difference across the unilateral vs. bilateral conditions was for release duration, which was prolonged in the bilateral condition. Post-hoc power analysis showed that the observed

effects for most variables were small and would not have reached statistical significance unless the sample size was much larger.

Rapid improvements in paretic limb motor performance, observed visually in the initial case studies of bilateral training (Mudie and Matyas 1996, 2000), were not confirmed in this study using three-dimensional motion analysis methods. Several possible explanations merit exploration. First, it is possible that the variables chosen to quantify motor performance in this study captured different movement characteristics than the observational scale used in the initial studies. This possibility is unlikely however because there are clear parallels between the two methodologies. For example, reach path ratio is a measure of trajectory smoothness/straightness. The current study quantified multiple aspects of motor performance, including several movement characteristics that were likely not assessed in the earlier studies (e.g. pre-lift delay, aperture path ratio, peak grip force).

A second possibility is that the objective and precise quantitative motion capture methodology used here may have provided a more accurate assessment than observational ratings. This would imply that the immediate effects of the bilateral movement condition may indeed be quite small or non-existent. This second possibility is supported by evidence of only moderate agreement ($r^2 \geq 0.46$) between therapists' visual observational ratings of hand path indirectness and motion analysis quantification of the reach path ratio (Bernhardt et al., 1998). Similar comparisons have not been reported for the other variables we measured.

A third possibility is that bilateral training effects emerge over the course of many repetitions within a session and thus are not detectable unless bilateral practice trials precede assessment. Certain forms of experience-dependent neural adaptation (e.g. alterations in cortical excitability, strengthening of pre-existing latent synaptic connections) can occur on a relatively short time scale, but require repeated movement practice (Kleim and Jones, 2008). Since we tested each condition using only a few trials, we are unable to determine whether many bilateral repetitions would have improved paretic limb performance in the bilateral condition by the end of a session.

The fourth possibility is that the reach-grasp-lift-release task chosen for this study may not have adequately challenged the motor abilities of the participants with hemiparesis. Of the variables we studied, only reach duration and reach path ratio differed significantly across groups, despite the motor impairment and functional deficits confirmed by clinical tests in the participants with hemiparesis. A more difficult assessment task may have accentuated motor deficits, potentially revealing greater differences between unilateral and bilateral task performance. The challenge here however, is that all participants may not have been able to complete a more difficult task, thereby restricting the study of behavioral changes across conditions to only the most mildly affected individuals. This is a dilemma faced during use of many highly-quantitative behavioral assessments in various patient populations.

Previous single-session studies have shown faster paretic-limb reaching in the bilateral condition, a finding that was not apparent in our results (Harris-Love et al. 2005, Rose and Winstein 2005, McCombe Waller et al., 2006). Differences in speed-related

instructions may explain why that effect did not reach significance in our study. In each of the previous studies, reaching movements were performed as fast as possible, and in our study participants moved at their natural, self-selected speed. In the previous studies, increased paretic limb speed during bilateral reaching has been attributed to interlimb coupling effects, whereby the two upper extremities are thought to be controlled as a single coordinative unit with tendencies toward spatial and temporal symmetry (Kelso et al. 1979). After stroke, temporal symmetry of bilateral reaching is enhanced via faster paretic limb movement and slower non-paretic limb movement, relative to each side's unilateral performance. Interlimb coupling effects may be less apparent at slower speeds, thus explaining why we did not observe a decrease in reach duration in the bilateral condition during natural, self selected speed reaching. Although we may have been able to elicit greater interlimb coupling effects by asking participants to move as fast as possible, their natural self-selected speed movements are more likely to represent most movements performed during rehabilitation and in daily life.

Release duration was increased in the bilateral condition, across both groups and grip types. This may represent an effect of divided attention, as participants may have alternated their gaze between the two objects as both were returned to the table and released at the same time. Slow, difficult grip release is a common problem experienced by many people with stroke, and this finding suggests that the bilateral movement condition may further impede performance.

Expected effects of grip type were also observed in this study. In both groups, movements using palmar grip were characterized by shorter reach durations, increased

peak apertures, and increased peak grip force, as compared to movements using 3-finger grip. These differences are consistent with previous reports and with the fundamental differences between grip types used for power vs. precision (ie. palmar vs. 3-finger) (Castiello et al., 1993, Napier, 1956, Johansson, 1996, Flanagan et al., 1999, Ehrsson et al., 2000, Pouydebat et al., 2008). The only grip effect that differed across groups was for pre-lift delay. In the hemiparetic group only, pre-lift delay was longer during 3-finger grips compared to palmar grips. This may reflect difficulty with dexterity and finger individuation, which are common impairments post-stroke.

Conclusions

Because we found no evidence of improved paretic limb performance during bilateral vs. unilateral conditions in this single-session study, we are unable to infer which characteristics of motor performance, if any, may be most likely to change after bilateral training. Differences between unilateral and bilateral performance may be too small to observe in a simple single-session comparison across conditions. It is possible that bilateral training effects accrue over the course of a training session to produce measurable change, and that small changes within training sessions add up over multiple sessions to produce more pronounced, longer lasting effects. Alternatively, training bilaterally may produce little or no improvement in paretic limb performance beyond that achieved with unilateral paretic-limb training, as recent clinical trials have indicated (Lin et al., 2009, Morris et al. 2009, Whitall et al., 2011).

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Figure 5. Assessment of motor performance. A) Illustration of the experimental set-up and a participant performing the reach-grasp-lift-release task with a palmar grip in unilateral (upper row), and bilateral (lower row) conditions. B) Example data from one trial. Vertical dashed lines demonstrate division of the task into movement phases. The reach phase began when velocity of the hand sensor first exceeded 5 mm/sec (time = 0) and ended when grip force first exceeded 5 grams. Pre-lift delay began at the end of the reach and ended when the vertical position of the object increased by 3 mm from its initial value. Duration of the release phase was the time difference between the object returning to within 3 mm of its initial vertical position, and force on the object returning to within 5 grams of its initial value.

Figure 5.

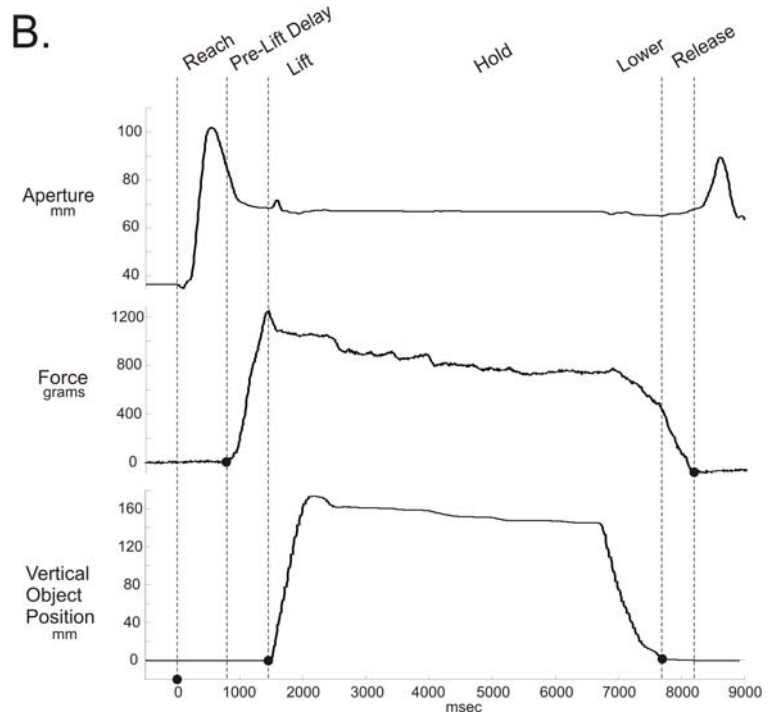


Figure 6. Comparisons of reach-grasp-lift-release task performance when moving unilaterally versus bilaterally. Values are means \pm 1 standard error. The only variable that differed across the unilateral versus bilateral conditions was release duration (panel C). Participants in both groups took longer to release the object when moving bilaterally instead of unilaterally.

Figure 6.

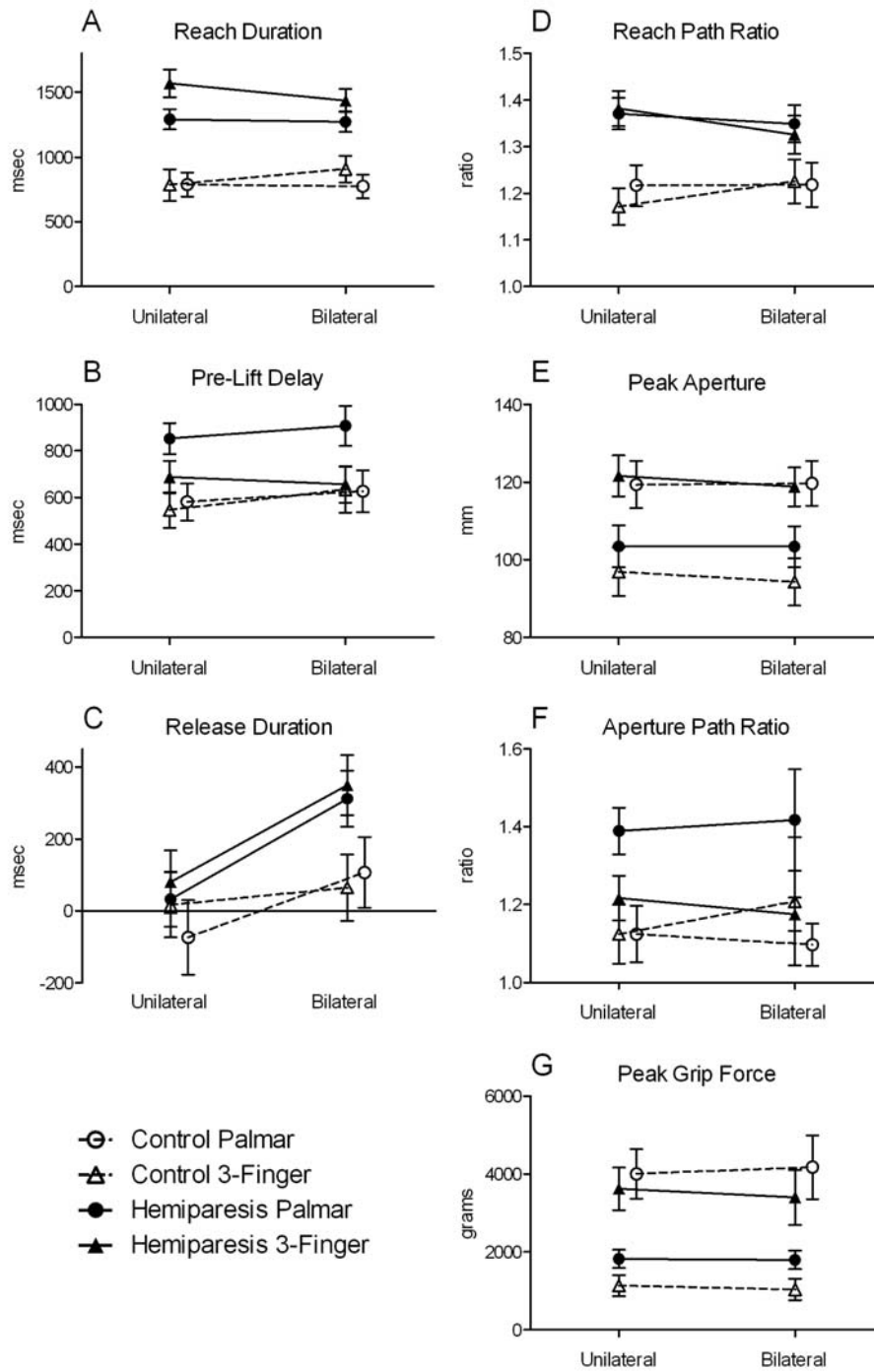


Table 5. Characteristics of participants with hemiparesis

Age (years)	58 ± 11 (38 – 88)
Gender	9 Male, 7 Female
Tested side	10 Dominant 6 Non-dominant 8 Right 8 Left
Type of stroke	14 Ischemic 2 Hemorrhagic
Years since stroke	1.2 ± 2.7 (0.04 – 9.2)
Grip strength (paretic side in kg)	21.8 ± 8.9 (10.0 – 36.0)
Grip strength (paretic side as % of non-paretic side)	67 ± 27% (34 – 113)
Pinch strength (paretic side in kg)	5.2 ± 2.3 (0 – 8)
Pinch strength on paretic side (paretic side as % of non-paretic side)	65 ± 27% (0 – 114)
Sensation †	2.83 n = 7 3.61 n = 5 4.31 n = 2 6.65 n = 2
Spasticity ‡	0 n = 8 1 n = 7 2 n = 1
Action Research Arm Test on paretic side *	41 ± 9 (24 – 53)
Stroke Impact Scale ** Activities in a Typical Day Subscale	62 ± 15 (43 – 88)
Stroke Impact Scale ** Hand Function Subscale	49 ± 22 (0 – 85)

Mean ± 1 standard deviation (range)

† Size of the smallest Semmes Weinstein monofilament sensed in 3 of 5 trials on the anterior distal index finger on the paretic side

‡ Modified Ashworth Scale score for the elbow flexors on the paretic side

* Range of possible scores is 0 to 57, 57 = normal

** Range of possible scores is 0 to 100, 100 = normal

Table 6. Effects of unilateral vs. bilateral movement condition, group, and grip type

	Group	Unilateral Palmar	Bilateral Palmar	Unilateral 3-Finger	Bilateral 3-Finger
Reach Duration (msec) * ‡ §	Hemiparesis	1291 ± 80	1272 ± 79	1570 ± 106	1435 ± 89
	Control	787 ± 92	774 ± 91	785 ± 122	906 ± 103
Pre-Lift Delay (msec) ∫	Hemiparesis	688 ± 69	657 ± 78	853 ± 66	908 ± 86
	Control	582 ± 79	627 ± 90	547 ± 76	634 ± 99
Release Duration (msec) †	Hemiparesis	81 ± 87	349 ± 83	32 ± 77	312 ± 78
	Control	-73 ± 103	107 ± 98	17 ± 91	65 ± 92
Reach Path Ratio *	Hemiparesis	1.38 ± 0.04	1.33 ± 0.04	1.37 ± 0.03	1.35 ± 0.04
	Control	1.22 ± 0.04	1.22 ± 0.05	1.17 ± 0.04	1.23 ± 0.05
Peak Aperture (mm) ‡	Hemiparesis	122 ± 5	119 ± 5	103 ± 5	103 ± 5
	Control	119 ± 6	120 ± 6	97 ± 6	94 ± 6
Aperture Path Ratio	Hemiparesis	1.22 ± 0.06	1.17 ± 0.04	1.39 ± 0.06	1.42 ± 0.13
	Control	1.12 ± 0.07	1.10 ± 0.05	1.12 ± 0.08	1.21 ± 0.16
Peak Grip Force (grams) ‡	Hemiparesis	3625 ± 549	3400 ± 707	1824 ± 234	1798 ± 237
	Control	4007 ± 634	4175 ± 816	1140 ± 270	1036 ± 274

Mean ± 1 standard error

† Main effect of unilateral vs. bilateral condition, $p < 0.05$

§ Condition x group interaction effect, $p < 0.05$

* Main effect of group, $p < 0.05$

‡ Main effect of grip, $p < 0.05$

∫ Grip x group interaction effect, $p < 0.05$

Table 7. Effect sizes for comparisons of unilateral vs. bilateral conditions in participants with hemiparesis

	Palmar		3-Finger	
	Observed Effect Size	Estimated N	Observed Effect Size	Estimated N
Reach Duration	0.05	>1000	0.28	101
Pre-Lift Delay	0.12	569	0.15	348
Release Duration	0.80	15	0.88	13
Reach Path Ratio	0.33	73	0.13	456
Peak Aperture	0.12	521	0.00	na*
Aperture Path Ratio	0.21	183	0.06	>1000
Peak Grip Force	0.12	569	0.02	>1000

* not applicable, since effect size was 0

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Chapter 4

The bilateral movement condition facilitates maximal but not submaximal paretic-limb grip force in people with post-stroke hemiparesis

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The bilateral movement condition facilitates maximal but not submaximal paretic-limb grip force in people with post-stroke hemiparesis

ABSTRACT

Although healthy individuals have less force production capacity during bilateral muscle contractions compared to unilateral efforts, emerging evidence suggests that certain aspects of paretic upper limb task performance after stroke may be enhanced by moving bilaterally instead of unilaterally. In this study, we questioned whether the bilateral movement condition affects grip force differently on the paretic side of people with post-stroke hemiparesis, compared to their non-paretic side and compared to both sides of healthy young adults. Within a single session, we compared: 1) maximal grip force during unilateral versus bilateral contractions on each side, and 2) the force contributed by each side during a 30% submaximal bilateral contraction. Healthy controls produced less grip force in the bilateral condition, regardless of side ($p < 0.05$, -2.4% change), and similar findings were observed on the non-paretic side of people with hemiparesis ($p < 0.05$, -4.5% change). On the paretic side, however, maximal grip force was increased by the bilateral condition ($p < 0.05$, +11.3% change). During submaximal bilateral contractions in each group, the two sides each contributed the same percentage of unilateral maximal force ($p = 0.36$ for controls, $p = 0.25$ for the hemiparetic group). These findings suggest that during maximal, but not submaximal force production, the paretic limb may benefit from the bilateral movement condition.

Keywords: interhemispheric inhibition, bilateral deficit, strength, human

INTRODUCTION

In healthy adults, maximal voluntary force production is diminished, generally 3 – 25%, when homologous muscles on the left and right sides contract simultaneously rather than individually. This phenomenon, termed the ‘bilateral deficit’, has been demonstrated for flexor and extensor muscle groups of the upper and lower extremities, and affects force production during all types (e.g. isometric, concentric, eccentric, isokinetic) of maximal contractions (Hay et al., 2006; Herbert and Gandevia, 1996; Howard and Enoka, 1991; Kuruganti et al., 2005; Kuruganti and Seaman, 2006; Latash et al., 2002; Li et al., 2001; Magnus and Farthing, 2008; Oda and Moritani, 1994; Oda and Moritani, 1995; Taniguchi, 1998; Van Dieen et al., 2003; Vandervoort et al., 1984; Weir et al., 1995; Yamauchi et al., 2009). The bilateral deficit is present in both young and older adults (Kuruganti and Seaman, 2006; Li et al., 2003; Owings and Grabiner, 1998; Yamauchi et al., 2009), and is a flexible, use-dependent phenomenon that increases with unilateral training and decreases with bilateral training (Howard and Enoka, 1991; Jakobi and Chilibeck, 2001; Kuruganti et al., 2005; Taniguchi, 1997; Taniguchi, 1998; Weir et al., 1995).

Evidence supports interhemispheric inhibition as the predominant mechanism underlying the bilateral deficit phenomenon (Archontides and Fazey, 1993). During unilateral activity, a high level of cortical activation in one hemisphere has an inhibitory influence on the homologous cortical area in the opposite hemisphere (Asanuma and Okuda, 1962; Duque et al., 2005b). This effect, which suppresses mirror movements and supports motor control of intentionally unilateral actions, occurs via transcallosal connections between homologous cortical areas. Existence of the bilateral deficit

phenomenon suggests that during maximal bilateral symmetrical contractions, both sides mutually inhibit each other, limiting the intensity of cortical activation and thereby limiting maximal muscle force production.

A separate body of literature from people with hemiparesis after stroke indicates that insufficient muscle activation is a key impairment that underlies loss of function. Stroke disrupts connectivity within the neural network that controls voluntary movement and as a result, diminishes the capacity to produce descending neural drive. People with post-stroke hemiparesis have reduced maximal force production capacity (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck and Andreassen, 1980; Young and Mayer, 1982), and impaired regulation of submaximal force levels during skilled movement (Canning et al., 2000; Gowland et al., 1992; Kamper and Rymer, 2001; Lang and Schieber, 2004; Wagner et al., 2007a).

Rehabilitation of the upper extremity after stroke involves repetitive task-specific training, implemented through one of many well-described approaches (Birkenmeier et al., 2010; Duncan et al., 2003a; Harris et al., 2009; Lin et al., 2009; Taub et al., 2006a; Winstein et al., 2004; Wolf et al., 2006). One such approach advocates repetitive practice of upper extremity tasks in a bilateral, symmetrical fashion, such that simultaneously moving the non-paretic limb might improve performance and recovery of the paretic limb (Mudie and Matyas, 1996; Mudie and Matyas, 2000). This intervention paradigm is supported by reports of improved paretic-limb kinematics during bilateral reaching (Cunningham et al., 2002; Harris-Love et al., 2005; McCombe Waller et al., 2006; Rose and Winstein, 2005), and improved paretic-limb strength, range of motion, function, and daily use after multi-session bilateral training programs (Cauraugh and Kim, 2002;

Cauraugh et al., 2005; Lewis and Byblow, 2004; Lin et al., 2009; Lin et al., 2010; Mudie and Matyas, 2000; Stewart et al., 2006; Stinear and Byblow, 2004; Summers et al., 2007; Whitall et al., 2000). Clear benefits over alternative interventions, however, have not been consistently demonstrated (Coupar et al., 2010; Desrosiers et al., 2005; Lin et al., 2009; Lin et al., 2010; Morris et al., 2008; Whitall et al., 2011).

Several mechanisms have been suggested to explain the possible benefits of practicing movements bilaterally instead of unilaterally after stroke. Since there is overlap between the neural networks that control unilateral movements on the two sides, inclusion of the non-paretic limb in simultaneous symmetrical task performance may activate shared components. As a result, the crossed and / or uncrossed corticospinal pathways contributing to paretic limb movement may be disinhibited or facilitated in the bilateral condition (Carson, 2005; Cauraugh and Summers, 2005; McCombe Waller and Whitall, 2008; Mudie and Matyas, 2000; Whitall et al., 2000). Interhemispheric and intracortical inhibition of the lesioned hemisphere is known to be exaggerated after stroke, and may be lessened after bilateral training (Cauraugh and Summers, 2005; Duque et al., 2005a; Murase et al., 2004; Stinear et al., 2008; Stoykov and Corcos, 2009; Summers et al., 2007). In addition, paretic limb performance may be enhanced via interlimb coupling, whereby a single shared motor command may govern both limbs during bilateral movement (Al-Senawi and Cooke, 1985; Cauraugh and Summers, 2005; Cohen, 1970; Kelso et al., 1981; Mudie and Matyas, 2000).

Two published reports address the influence of the bilateral movement condition on upper extremity force production after stroke (Li et al., 2003; McQuade et al., 2008). In one, the paretic side produced the same amount of elbow flexor force regardless of

whether the maximal contraction was performed unilaterally or bilaterally. Force produced by the non-paretic side was, on average, 15% lower in the bilateral condition (McQuade et al., 2008). These findings, combined with the bilateral deficit phenomenon in healthy individuals, suggest that the bilateral condition may result in disinhibition of the paretic limb after stroke. In the other study, however, the paretic and non-paretic sides both showed a bilateral deficit (approx. 23%), as did healthy controls during a multi-finger force production task (Li et al., 2003).

Here, we investigated the apparent conflict between: 1) ample evidence of diminished muscle activation in the bilateral condition in healthy individuals; 2) reports of improved performance and training effects in the bilateral condition for the paretic limb of people post-stroke; and 3) discrepant findings regarding the presence or absence of the bilateral deficit phenomenon after stroke. The purpose of this study was to determine how the bilateral movement condition affects maximal and submaximal grip force in people with post-stroke hemiparesis. Based on prior studies of bilateral training and suggested neural mechanisms, we hypothesized that the paretic side would benefit from the bilateral movement condition, and would therefore show no reduction in maximal grip force during bilateral efforts compared to unilateral efforts. We included a control group of healthy young adults for comparison, and expected that they would produce less maximal grip force when contracting bilaterally instead of unilaterally. Since most skilled movements utilize a small percentage of maximal force generating capacity (Wagner et al., 2007a), we included a submaximal task that required participants to maintain a pre-determined force level, using both hands to simultaneously grip separate dynamometers. We hypothesized that the paretic limb could benefit from the

submaximal bilateral movement condition, and if so, would utilize a higher percentage of its maximal unilateral grip force compared to the non-paretic limb, which would utilize a lower percentage of its maximal unilateral grip force.

MATERIALS AND METHODS

Participants

Sixteen people with hemiparesis due to stroke were recruited from the St. Louis metropolitan area via the Brain Recovery Core Database and the Cognitive Rehabilitation Research Group Stroke Registry at Washington University, and from local support groups for people with stroke. Potential participants were included if they had been diagnosed with stroke and had persistent upper extremity hemiparesis, demonstrated by Medical Research Council muscle test scores that were at least one grade lower on the paretic side compared to the non-paretic side. Potential participants were excluded if they 1) had severe aphasia as indicated by a score of 2 or 3 on the Best Language item of the National Institutes of Health Stroke Scale (NIHSS), 2) had severe hemispatial neglect, as indicated by a score of 2 on the Extinction and Inattention item on the NIHSS, 3) were unable to follow 2-step commands, 4) had musculoskeletal or other medical conditions besides stroke that limited either upper extremity, or 5) were unable to hold a grip dynamometer once it was placed in their hand. Since the bilateral deficit has been shown to be influenced by weight training and other similar athletic activities (Howard and Enoka, 1991; Kuruganti et al., 2005; Taniguchi, 1997; Taniguchi, 1998), we also excluded people who participated in weight training, rock climbing, racquet sports,

rowing, or any similar activities involving the upper extremities, at any time within the past year.

Fifteen healthy young people also participated, in order to provide reference values and to verify the presence of a bilateral deficit affecting grip force using the instrumentation and protocol employed in this study. Volunteers were included if they 1) were between 20 and 35 years old, 2) had no history of any neurological disorder or musculoskeletal condition affecting their upper extremity on either side, and 3) had not participated in weight training or other similar activities within the past year. This study was approved by the Washington University Human Research Protection Office, and all participants provided informed consent prior to enrollment.

Clinical Measurements

Clinical scales were used to describe the sample of people with post-stroke hemiparesis. We assessed upper extremity function using the Action Research Arm Test (Lang et al., 2006a; Lyle, 1981; Yozbatiran et al., 2008) and the Activities of Daily Living and Hand Function domains of the Stroke Impact Scale, version 3.0 (Duncan et al., 1999; Lai et al., 2002). Sensation on the palmar surface of the distal index finger was evaluated on the paretic side using Semmes-Weinstein monofilaments (Bell-Krotoski, 1991). Spasticity of the wrist flexors was assessed on the paretic side using the Modified Ashworth Scale (Bohannon and Smith, 1987). When possible, medical records were reviewed to identify lesion locations.

Maximum grip strength was measured in all participants using a Jamar grip dynamometer in its second position (Fess, 1992; Schmidt and Toews, 1970). For each

side, we recorded the average score achieved in three unilateral attempts, each separated by 15 seconds of rest. This common clinical method of assessing grip strength was used in addition to the experimental protocol described below, since the Jamar method allows comparison of our participants to published normative data (Bohannon et al., 2006) and to other studies of people with post-stroke hemiparesis.

Instrumentation

For the experimental protocol, grip force was measured using two Biopac strain gauge hand dynamometers, shown in Figure 7D (Model SS25, Biopac Systems, Inc., Goleta, CA). The same two dynamometers were used throughout the study. Each dynamometer was paired with a custom-designed differential amplifier that applied a low pass filter at 10 Hz and a gain of 2000. Signals were sampled at 20 Hz with an A/D converter (Model USB-1208LS, Measurement Computing Corp., Norton, MA). Prior to the study, linear response characteristics were verified and scale factors were determined for each dynamometer/amplifier pair using calibration weights ranging from 0 to 218 N and procedures recommended by the manufacturer. Zero offsets were determined immediately prior to each data collection session, by collecting five seconds of data with no load applied to the dynamometers. Because of differences in design and response characteristics, the Biopac dynamometers yielded different grip force values compared to the Jamar method, although recordings from the two methods were highly correlated ($r = 0.91$). The Biopac design employs a strain gauge at one end of the dynamometer, resulting in attenuation of grip forces that occur at a distance from the strain gauge. In contrast, the Jamar dynamometer, which is commonly used in clinical settings, consists

of a hydraulic dual-post design capable of measuring all grip force exerted along the length of its handle.

Data acquisition was accomplished using custom software created with LabVIEW 8.2 (National Instruments Corp., Austin, TX). The LabVIEW program randomly assigned which dynamometer would be used in each hand, randomly selected the order of conditions presented to the participant (left unilateral, right unilateral, or bilateral), and controlled the duration of each grip force trial and rest break. The program also applied the previously determined calibration parameters and stored the data to a file.

Positioning

All data for each participant were collected within a single session. The participant was seated in a chair with a table in front and a pillow behind their back. Table height was adjusted to allow for symmetrical positioning of both upper extremities with approximately 30 degrees of flexion, abduction, and internal rotation at the shoulders, 60 degrees of flexion at the elbows, and neutral forearm supination / pronation. Versa-Form vacuum-molded pillows (Patterson Medical Products, Inc., Bolingbrook, IL) were used to provide firm support and to maintain this position throughout the data collection process (Figure 7A). This standardized positioning was intended to minimize postural adjustments and compensatory movements that might otherwise affect grip force production, and to ensure constant positioning across all trials. A laptop computer on a cart was placed in front of the table, for viewing by the participant.

Maximal Grip Force Measurements

Maximal grip force was assessed first. A computer-generated random sequence specified the order of three conditions (left unilateral, right unilateral, and bilateral). The sequence was repeated three times, yielding nine trials. Each effort was separated by two minutes of rest, to minimize fatigue. Before each trial, the examiner placed a dynamometer in the hand(s) corresponding to the condition being tested and carefully positioned the upper edge of the dynamometer in the web space between the thumb and index finger. For unilateral trials, only the hand participating in the trial held a dynamometer, and the participant was encouraged to relax the other hand.

The participant was then instructed to watch the computer screen, wait for a green light to appear, and then squeeze as hard as possible with the appropriate hand(s). Visual feedback was provided on the screen in real time, using meters that displayed the force generated by each hand (Figure 7B). The examiner also verbally encouraged maximum effort by yelling ‘Go, go, go’ loudly for the 5-second duration of each trial. After all maximal trials were completed, a 4-minute rest period was provided.

Submaximal Grip Force Measurements

Because upper extremity task performance generally utilizes only a small percentage of maximal force production capacity (Wagner et al., 2007a), we questioned whether potential effects of the bilateral movement condition on maximal force would also be observed in a submaximal task. In preparation for submaximal trials, the LabVIEW program determined peak grip force for each maximal trial, then averaged within trial types to obtain average peak grip force on each side for the unilateral and

bilateral conditions. A target force level for the submaximal trials was calculated according to the following equation:

$$30\% \text{ Submaximal Target} = (0.30)(\text{Left average unilateral grip force} + \text{Right average unilateral grip force})$$

Data collection resumed with submaximal testing, which was performed only in the bilateral condition. On-screen visual feedback for the submaximal trials consisted of one meter in the center of the screen (Figure 7C), which displayed the total amount of force produced by the two hands combined, and was scaled so that the participant's target force level corresponded with the vertical position of the meter's needle. Given this feedback, the participant was unaware of how much force was contributed by each hand, but could see whether they were achieving the target force level with the two hands combined. Prior to each trial, the examiner placed a dynamometer in each hand and instructed the participant to watch the computer screen, wait for a green light to appear, then squeeze with both hands, hard enough to make the needle point straight up. Participants were encouraged to use both hands, but no instructions were provided regarding distribution of effort or symmetry of force production. Three submaximal trials were completed, each separated by one minute of rest. Each trial ended once the participant maintained total grip force within $\pm 2\%$ of their 30% submaximal target force level for three seconds.

Analysis

Statistical analyses were performed using Statistica software (Version 6.1, StatSoft Inc., Tulsa, OK). A normal distribution of each variable was verified using the Kolmogorov-Smirnov test. Statistical significance was assumed when $p < 0.05$.

Peak grip force was determined for each maximal grip force trial, then averaged across the three repetitions of each condition. This yielded average peak grip force values for each side in the unilateral and bilateral movement conditions. For each group, effects of unilateral vs. bilateral condition and side on average peak grip force were evaluated using 2 condition x 2 side repeated measures analysis of variance. The condition factor compared the unilateral vs. bilateral conditions. The side factor compared the paretic vs. non-paretic sides of participants with hemiparesis and the non-dominant vs. dominant sides of controls. Both factors were within-subjects and were considered fixed effects. For significant interactions, Fisher LSD post-hoc tests were used to determine the significance of mean differences. Using this analysis, our hypothesis would be supported by a significant interaction effect in the hemiparetic group, showing diminished maximal grip force in the bilateral condition on the non-paretic side, but not on the paretic side.

Analysis of each submaximal trial was restricted to the 3-second interval during which the combined force of the two sides remained within the target range ($30\% \pm 2\%$ of the participant's maximal unilateral grip force on the two sides combined). For each side, the average amount of force recorded during that interval was determined for each trial, averaged across the three submaximal trials, then expressed as a percentage of the average peak grip force measured during maximal unilateral trials on that side. This

percentage of unilateral maximal force that was utilized during submaximal trials served as the dependent variable in paired t-tests that tested for a difference between the two sides (paretic vs. non-paretic for participants with hemiparesis, non-dominant vs. dominant for controls). Using this analysis, our hypothesis would be supported by a significant difference between sides in the hemiparetic participants, whereby the paretic side would utilize a higher percentage of its unilateral maximal force and the non-paretic side would utilize a lower percentage of its unilateral maximal force. Lack of a significant difference would signify that the paretic side's submaximal grip force production was not enhanced by the bilateral condition.

RESULTS

Sixteen people with hemiparesis participated in this study. Demographics and results of clinical tests are provided in Table 8. Time since stroke varied from 6 weeks to 9.6 years, and exceeded 6 months in all except 3 participants. The group comprised a wide range of sensorimotor impairment and functional limitation, ranging from mild to severe. Lesion locations also varied, including five cortical, five subcortical, two that were both cortical and subcortical, and four unknown. As measured with a Jamar grip dynamometer, grip force on the paretic side ranged from 8 to 68% of the non-paretic side.

Fifteen controls also participated, including 8 females and 7 males between 22 and 30 years of age (mean 24.4 ± 1.8 years). All were right-handed, by self report. Jamar grip strength on the dominant (right) side was 40.6 ± 12.5 kg. On the non-dominant (left) side, Jamar grip strength was 38.0 ± 13.1 kg, and was 93.3 ± 8.8 % of the dominant side.

Representative data showing maximal unilateral and bilateral grip force from one control and one participant with hemiparesis are shown in Figure 8. Each side of the control participant (8A) produced more peak grip force when contracting unilaterally than it did during bilateral contractions. The same pattern was seen on the non-paretic side of the participant with hemiparesis (8B). On the paretic side, however, peak force was greater during the bilateral effort.

Average findings in each group are shown in Figure 9. In the control group, average peak grip force was 2.4% less during bilateral trials than during unilateral trials (main effect of condition, $p = 0.04$), thus confirming the presence of a bilateral deficit affecting grip force. The effect of the bilateral vs. unilateral condition did not vary across the two sides (no condition x side interaction, $p = 0.60$, comparison not shown, pooled across sides in Figure 9). As expected in the control group, grip force was greater on the dominant side compared to the non-dominant side (main effect of side, $p = 0.05$).

In the hemiparetic group, the effect of condition differed across the two sides (condition x side interaction, $p = 0.01$). On the non-paretic side, average peak grip force was less during bilateral trials than during unilateral trials (post-hoc $p = 0.04$, -4.5% change). On the paretic side, average peak grip force was greater during bilateral trials than during unilateral trials (post-hoc $p = 0.04$, +11.3% change).

Results of submaximal grip force trials are shown in Figure 10. Representative data from one control (10A) and one participant with hemiparesis (10B) show the time course of force generation on each side, including the last three seconds of each trial, during which the combined force of the two sides was maintained within the target range. The control participant achieved the target force level utilizing roughly 30% of each

side's maximum unilateral force. The participant with hemiparesis, however, primarily used their non-paretic hand. Figure 10C shows averaged data for each side in each group. The grip force contributed by each side is expressed as a percentage of that side's maximal unilateral force. In each group, the percentage of unilateral maximal force utilized during submaximal trials did not differ across the two sides (control group $p = 0.36$, hemiparetic group $p = 0.25$). This lack of difference between the two sides indicates that submaximal grip force was neither diminished nor facilitated by the bilateral movement condition. Contrary to our hypothesis, the paretic side did not use a higher percentage of maximal unilateral force (paretic mean = 24.2%, non-paretic mean = 31.5%). Thus there was no evidence of paretic limb facilitation in the submaximal condition.

DISCUSSION

We sought to reconcile the conflict inherent in: 1) ample evidence of diminished muscle activation in the bilateral condition in healthy individuals; 2) reports of improved performance and training effects in the bilateral condition for the paretic limb of people post-stroke; and 3) discrepant findings regarding the presence or absence of the bilateral deficit phenomenon after stroke (see Introduction). Results from both sides of control participants and the non-paretic side of participants with hemiparesis confirmed the presence of the bilateral deficit phenomenon affecting maximal grip force production. On the paretic side, the bilateral condition resulted in increased maximal force production compared to the unilateral condition. This finding supported and even extended our hypothesis that that the paretic side would benefit from the bilateral movement condition.

In contrast, in the submaximal task, the bilateral condition did not facilitate the paretic limb's contribution. Instead, each side contributed approximately the same percentage of its respective maximal unilateral force.

An important finding of this study is that the maximal bilateral movement condition actually enhanced force production on the paretic side in people with post-stroke hemiparesis. This finding extends results of a similar investigation, in which no bilateral deficit was found during maximal elbow flexor force production in twelve people with chronic mild/moderate hemiparesis (McQuade et al., 2008). In addition to showing similar results in a more distal muscle group, our findings further suggest that the effect may be facilitation, rather than disinhibition, since our participants exceeded their unilateral paretic-limb performance during bilateral contractions. Together, these studies support the idea that the bilateral movement condition does not have the same negative effect on maximal descending neural drive in the lesioned hemisphere that it does in the non-lesioned hemisphere and in healthy controls. Conflicting findings have been reported in one study (Li et al., 2003), in which seven people with hemiparesis showed a 23% bilateral deficit affecting multi-finger flexion force on the paretic side. These differing results are difficult to explain based on the muscle group or participant characteristics, but may be related to differences in methods used to calculate the bilateral deficit.

Although interhemispheric inhibition (IHI) underlies the bilateral deficit phenomenon in healthy individuals, studies using transcranial magnetic stimulation have shown that IHI from the non-lesioned hemisphere toward the lesioned hemisphere remains intact and may be exaggerated after stroke (Butefisch et al., 2008; Duque et al.,

2005a; Murase et al., 2004; Perez and Cohen, 2009). Diminished IHI, therefore, is not a likely mechanism for the lack of a bilateral deficit on the paretic side in people with hemiparesis.

Instead, we propose that the effect of IHI might be offset and even reversed by increased activation of alternative descending pathways in the bilateral condition. Indirect connections involving secondary motor cortical areas, uncrossed corticospinal projections to the paretic limb, and / or cerebellar circuits may be recruited to a greater extent when movements are performed bilaterally. Imaging studies support this idea (Luft et al., 2004; Whitall et al., 2011; Wu et al., 2010). For example, a recent randomized clinical trial demonstrated a greater increase in activation of the ipsilesional supplementary motor and anterior cingulate areas after bilateral training, compared to dose-matched therapeutic exercise (Whitall et al., 2011).

In contrast to our results in the maximal force production task, there was no evidence of facilitation of the paretic limb during the submaximal task. Instead, each side contributed approximately the same percentage of its maximal unilateral force. This finding is important given the fact that daily upper extremity actions typically require only a small percentage of maximal force generating capacity (Wagner et al., 2007a). It is not clear from current literature if the bilateral deficit phenomenon is present during submaximal force production in healthy individuals. Inferences that it is present have been made based on high-speed isokinetic testing, which limits force levels by exploiting the force/velocity relationship of muscle contractions (Vandervoort et al., 1984; Yamauchi et al., 2009). Nevertheless, our findings suggest that the bilateral movement condition may have little or no effect on force production during typical activities.

Limitations of this study include the heterogeneity of participants in terms of stroke severity, time since stroke, and lesion location. Although the sample size was small, statistical power was adequate for testing of our hypotheses. Limited information was available regarding lesion size, location, and pathways affected. Since the study included only behavioral measurement, without functional imaging, the relative contributions of different neural pathways to force production could not be delineated.

In summary, the bilateral condition resulted in increased maximal grip force production on the paretic side of people with post-stroke hemiparesis, but decreased maximal grip forces on the non-paretic side and on both sides of healthy controls. In a submaximal bilateral grip task, as might be expected during daily activities, each side contributed an equal percentage of its respective maximal unilateral force, thus showing no enhancement of paretic-limb performance in the submaximal bilateral task. Given the absence (McQuade et al., 2008) or possible reversal (in the present study) of the well-described bilateral deficit phenomenon on the paretic side, combined with prior evidence of intact IHI toward the lesioned hemisphere after stroke, we suggest that alternative motor pathways may be activated to a greater extent when maximal efforts are performed bilaterally instead of unilaterally.

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Disclosures

Neither author has any conflict of interest related to this manuscript.

Figure 7. Experimental assessment of grip strength. A) Illustration of the experimental set-up and a participant performing a right unilateral maximal grip force trial. Versa-Form vacuum molded pillows maintained consistent positioning of the upper extremities throughout the data collection session. B) During maximal trials, on-screen meters provided real time visual feedback of grip force produced by each side. C) During submaximal trials, one meter in the center of the screen provided real time visual feedback of the force produced by both hands combined. Given this feedback, the participant was unaware of how much force each hand contributed, but could see whether the combined force was within the target range. D) Biopac grip dynamometer.

Figure 7.

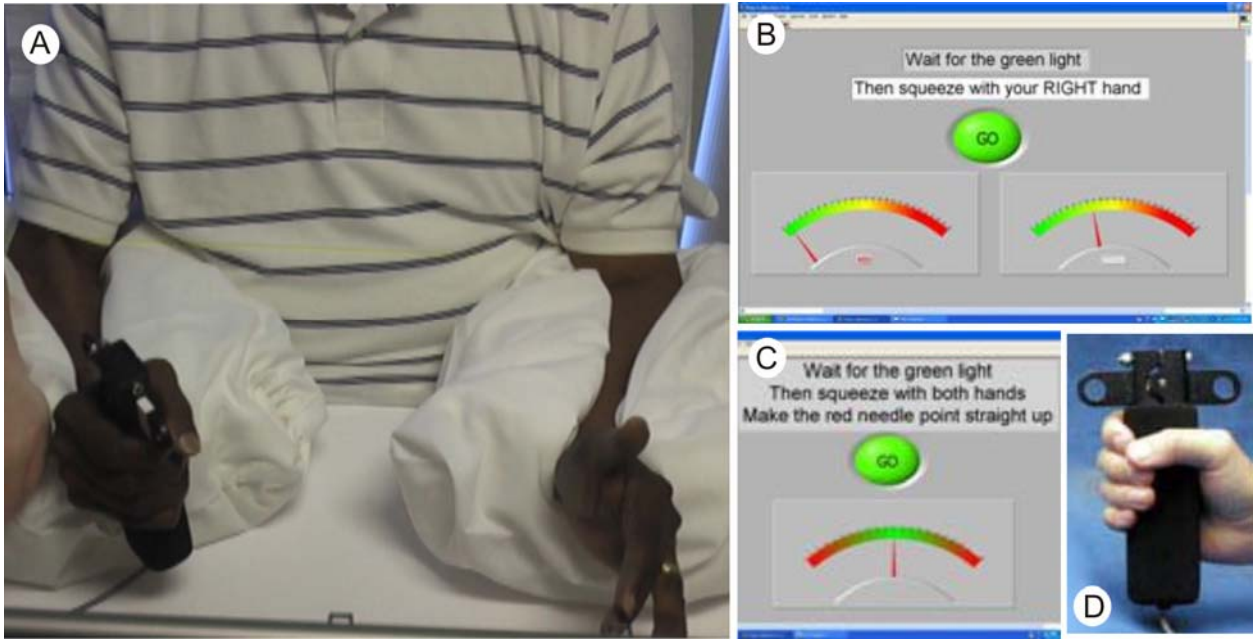


Figure 8. Maximal grip force (kg) in the unilateral and bilateral conditions in one control participant (A) and one person with hemiparesis (B). Each graph represents a 5-second trial. Arrows and numerical values indicate peak force (kg). On the non-paretic side of the person with hemiparesis, and on each side of the healthy young adult, grip force was diminished in the bilateral condition compared to the unilateral condition. The paretic side, however, produced greater peak grip force in the bilateral condition than it did in the unilateral condition.

Figure 8.

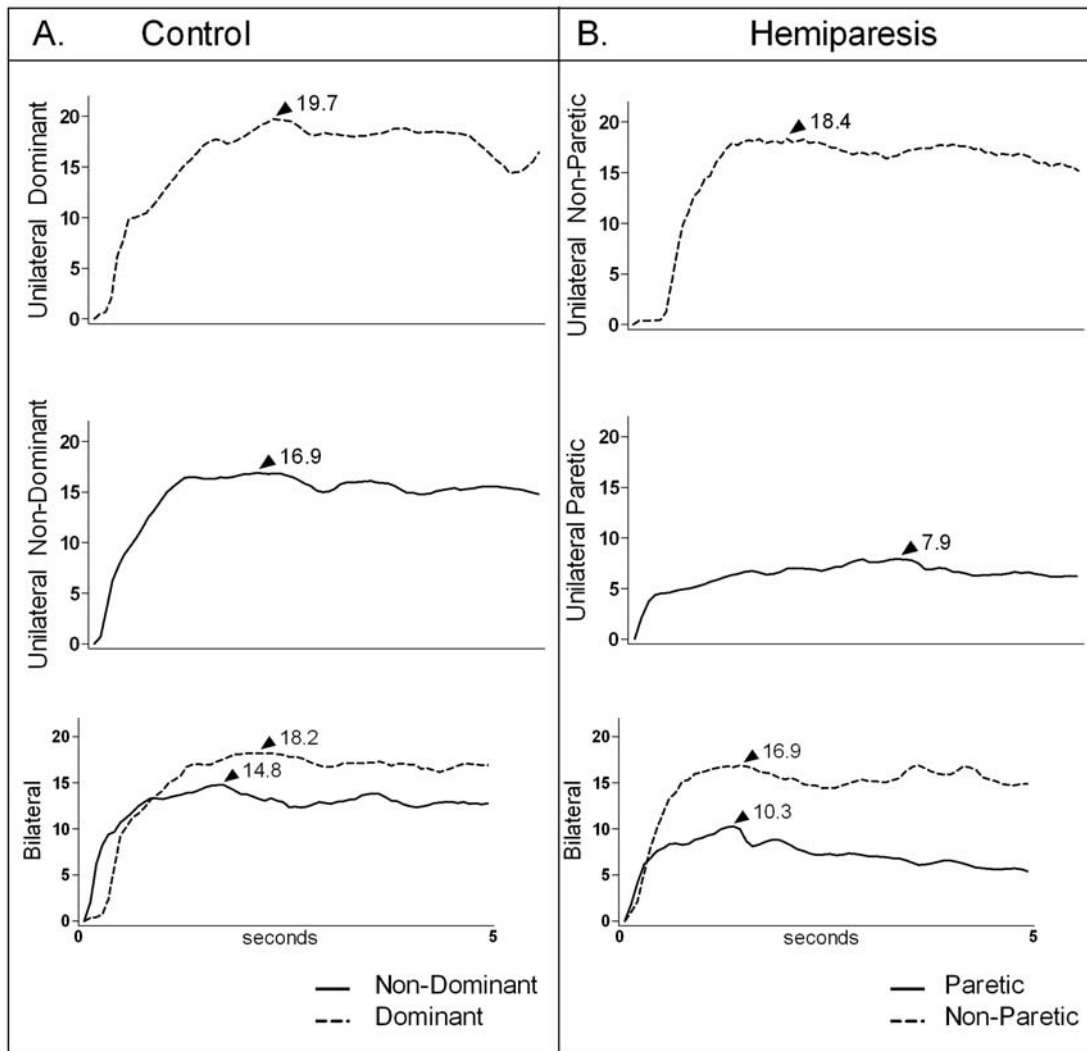


Figure 9. Maximal grip force (kg) in unilateral and bilateral conditions (mean \pm 1 SE). In the control group (●), peak grip force was 2.4% less in the bilateral condition than it was in the unilateral condition. For the group of participants with hemiparesis, the effect of condition differed between the two sides. The non-paretic side (■) showed 4.5% less peak grip force in the bilateral condition compared to the unilateral condition. On the paretic side (□), grip force was 11.3% greater in the bilateral condition.

Figure 9.

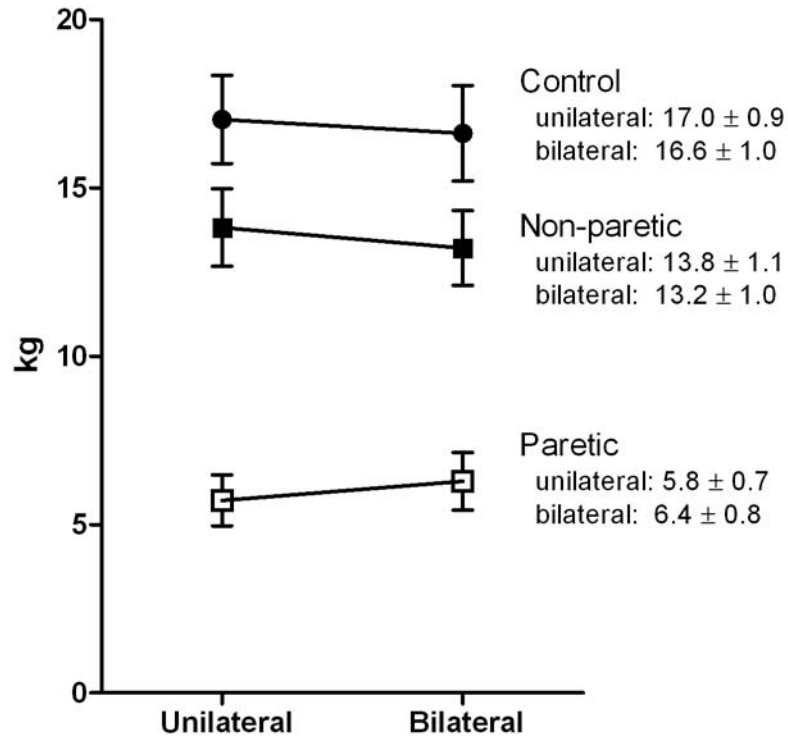


Figure 10. Submaximal grip force in the bilateral condition in one control (A) and one person with hemiparesis (B). The last 3 seconds of data represent the interval during which grip force of the two hands combined was maintained within the target range. Numbers indicate the amount of force each side contributed during that interval, expressed as a percentage of that side's maximal unilateral grip force. Group data (C), show no significant difference between sides in either group ($p > 0.05$). The lack of a significant difference between sides in the participants with hemiparesis suggests that the bilateral condition did not enhance submaximal grip force production on the paretic side.

Figure 10.

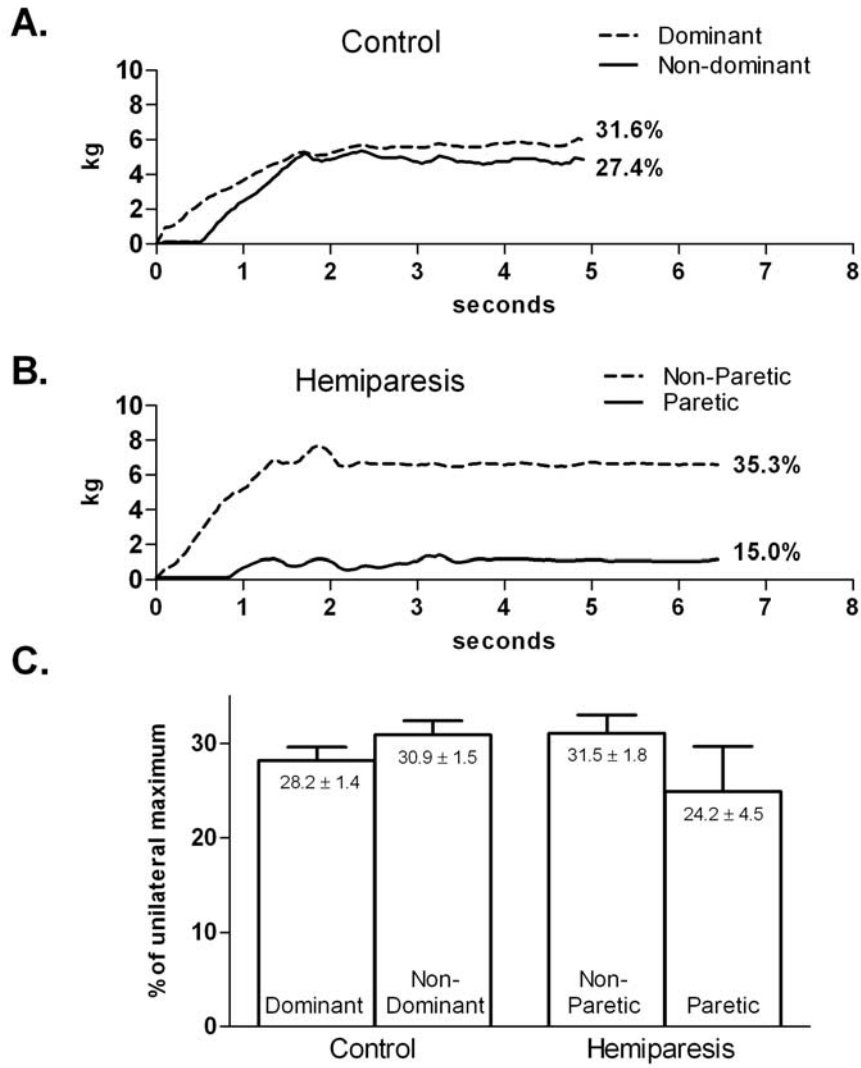


Table 8. Characteristics of participants with hemiparesis

Age (years)	62 ± 13 (47 – 91)
Gender	10 male 6 female
Type of stroke	13 ischemic 3 hemorrhagic
Months since stroke	34 ± 34 (1.5 – 115)
Paretic side	6 right / 10 left 8 dominant / 8 non-dominant
Dominant side	12 right / 4 left
Jamar grip strength on paretic side (kg)*	14.7 ± 7.6 (2.0 – 27.0)
Jamar grip strength on non-paretic side (kg)*	34.3 ± 11.7 (19.0 – 60.3)
Jamar grip strength on paretic side (as % of grip strength on non-paretic side)	42.2 ± 17.9 (8.0 – 68.2)
Sensation (size of smallest Semmes Weinstein monofilament sensed in 3 of 5 trials)	2.83 n = 8 3.61 n = 4 4.31 n = 1 4.56 n = 2 6.65 n = 1
Spasticity †	0 n = 8 1 n = 2 2 n = 4 3 n = 2
Action Research Arm Test ‡	34.4 ± 16.2 (8 – 56)
Stroke Impact Scale Activities in a Typical Day Subscale §	66.3 ± 15.2 (35 – 98)
Stroke Impact Scale Hand Function Subscale §	48.1 ± 25.0 (5 – 85)

Values are mean ± 1 standard deviation (range), unless otherwise noted

* Maximal isometric grip strength assessed during unilateral contractions with a Jamar grip dynamometer in its second position.

† Modified Ashworth Scale score of the wrist flexors on paretic side. 0-4 point scale where 0 = normal resistance to passive movement

‡ Paretic side, 0-57 point scale where 57 = normal upper extremity function

§ 0-100 point scale where 100 = normal activity or hand function

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Chapter 5

Summary of Major Findings

MAJOR FINDINGS

In Chapter 2, we questioned whether moving quickly instead of at a preferred speed either enhances or impairs performance of a reach-grasp-lift task by the paretic limb after stroke. Our results showed that people with mild to moderate post-stroke hemiparesis were able to increase their movement speed upon request, and that when they did, movement quality was improved. We demonstrated, using reach durations and pre-lift delays, that people with hemiparesis can voluntarily increase their rate of muscle activation in order to approach the movement speeds of healthy individuals. Further, faster movements were associated with straighter reach paths, more efficient finger movements, and increased opening of the hand during reaching. This is the first study to show improved paretic-limb coordination during faster movement. No detrimental effects of the fast movement context were observed.

In Chapter 3, we sought to determine whether moving bilaterally instead of unilaterally enhances performance of the paretic limb in people with post-stroke hemiparesis. Further, we examined several aspects of performance in order to determine which specific parameters might be enhanced. In this single-session comparison, we found no evidence of immediate improvement in paretic-limb performance in the bilateral condition, despite the many outcome studies that suggest effectiveness of bilateral training. Contrary to our hypotheses, release duration was increased when participants moved bilaterally instead of unilaterally, possibly representing a divided-attention effect. Other variables did not differ across conditions. Our findings suggest little immediate impact of the bilateral condition on motor performance.

In Chapter 4, we investigated the apparent conflict between: 1) evidence of diminished muscle activation in the bilateral condition in healthy individuals; 2) reports of improved performance and training effects in the bilateral condition for the paretic limb of people post-stroke; and 3) discrepant findings regarding the presence or absence of the bilateral deficit phenomenon after stroke. Similar to healthy controls, the non-paretic side of people with hemiparesis produced less grip force in the bilateral condition, as expected. On the paretic side, however, maximal grip force was greater in the bilateral condition. Since prior studies show intact interhemispheric inhibition of the lesioned hemisphere after stroke, we propose that greater recruitment of alternative motor pathways in the bilateral condition may underlie this effect. During submaximal bilateral contractions, the two sides each contributed an equal percentage of unilateral maximal force, thus showing no evidence that the bilateral condition facilitates submaximal paretic-limb force production. These findings suggest that during maximal, but not submaximal force production, the paretic limb may benefit from the bilateral movement condition.

LIMITATIONS

For the studies in Chapters 2 and 3, recruitment was limited to people who were able to perform reach-grasp-lift movements with both palmar and 3-finger grip types. Participants were therefore mildly to moderately impaired, and our results may not generalize to people with more severe hemiparesis. People with mild and moderate impairments post-stroke, however, are most likely to recover function (Beebe and Lang,

2009; Kwakkel et al., 2003; Smania et al., 2007), and thus may be most likely to benefit from rehabilitation services.

Also for the studies in Chapters 2 and 3, our investigations were limited to the within-session effects of altering the movement context, and did not explore training effects either within the testing session or across multiple sessions. In the comparison of movement speeds, our novel results showing better coordination during faster movements suggest that an emphasis on speed may be an effective strategy to enhance outcomes. A proof-of-concept trial thus appears warranted. Conversely, for the comparison of unilateral versus bilateral performance, numerous training studies have already preceded this within-session comparison. One potential explanation for our lack of significance is that effects of the bilateral context may emerge over the course of practice and thus may not be observable until after training occurs.

In all three studies, our sample sizes were small and thus may have limited our ability to detect small effects. Particularly in the comparison of unilateral versus bilateral task performance, where no statistically significant improvements were observed in the bilateral movement context, probability of a Type 2 statistical error was a concern. Post-hoc power analysis, however, indicated that effect sizes were quite small, and that a much larger sample size would have been required to detect differences between conditions.

Small sample sizes also clearly precluded our ability to evaluate how participant characteristic might influence the effects we observed. For example, time since stroke, severity of motor deficits, lesion location, and handedness may be important modifiers, but could not be statistically evaluated. Relationships between these variables and

movement context effects were examined graphically, however, as shown in the appendices, and no strong relationships were apparent.

For the comparison of unilateral versus bilateral grip force production in Chapter 4, the participants were heterogeneous in terms of time since stroke, severity of motor impairment, and lesion location. This can be considered a limitation, since neural network connectivity is clearly affected by these variables. As shown in the appendices, effects of these variables were evaluated graphically, with no clear patterns emerging. Our significant findings despite the heterogeneity of the group suggests that the bilateral context may facilitate maximal grip force on the paretic side across the range of participant characteristics.

In all three studies, our evaluations were limited to behavioral assessments. Discussions of potential mechanisms therefore rely on prior neurophysiological and neuroanatomical investigations, and no mechanistic conclusions can be delineated.

CLINICAL IMPLICATIONS AND SIGNIFICANCE

Our comparison of preferred speed versus fast upper extremity performance has clear implications for clinical rehabilitation. Since slow and insufficient muscle activation is a fundamental movement problem after stroke (Frontera et al., 1997; Gemperline et al., 1995; Jakobsson et al., 1992; Rosenfalck and Andreassen, 1980; Young and Mayer, 1982), and since people with hemiparesis often choose to use their opposite limb when the paretic limb is too slow or unreliable (Taub et al., 2006b), increasing movement speed is itself a reasonable goal. Beyond that, our findings show better coordination both proximally and distally during faster movements. Emphasizing

speed during upper extremity training therefore may be beneficial in two ways. First, enhanced movement quality during training may lead to better restoration of normal movement patterns as opposed to recovery of function via compensatory strategies. Second, moving faster may allow for more repetitions of task specific training during each therapy session, thus increasing the dose of practice achieved. Moving faster may be a cost-free and effective mean of increasing rehabilitation intensity after stroke.

Implications of our unilateral versus bilateral comparisons are less clear. Because we found no evidence of improved paretic limb performance during bilateral versus unilateral performance of a reach-grasp-lift-release task in our single-session study, we are unable to infer which characteristics of motor performance, if any, may be most likely to change after bilateral training. Our results engender skepticism regarding the rapid gains in movement quality visually observed by Mudie and Matyas. Along with studies of interlimb coordination, these early clinical observations provided a basis upon which bilateral training clinical trials have proceeded for over ten years (Mudie and Matyas, 2000). Given recent relatively large randomized clinical trials that have not supported bilateral training as being any more effective than other forms of upper extremity training (Lin et al., 2009; Morris et al., 2008; Whittall et al., 2011), our support of the null hypothesis illustrates the importance of progressively staging pilot studies in rehabilitation research (Dobkin, 2009). Ideally, multiple pilot studies using more objective methodology and rigorous design could have explored within-session and short-term effects on a variety of tasks, prior to investment in clinical trials. Although absence of within-session differences does not rule out the existence of potentially important training effects, results of additional pilot studies could have been used to optimize

protocol development, choice of outcome measures, and participant selection in clinical trials.

Our comparison of grip force in the unilateral versus bilateral contexts offers insight into the process of neural activation post-stroke. We showed, in a maximal force generation task, that the paretic arm responds differently to the bilateral movement context, as compared to the non-paretic limb and to both limbs of healthy controls. This suggests that at high levels of activation, the balance of inputs onto the motor cortex is shifted in the direction of greater excitability. Although our results could be explained by either disinhibition or facilitation, prior studies showing intact interhemispheric inhibition toward the lesioned cortex suggest that a facilitory mechanism is more likely. We propose that perhaps alternative, indirect motor pathways, which are strengthened after stroke through neuroplastic mechanisms (Nudo, 2006), may be activated to a greater extent in the bilateral movement context than they are during unilateral movement. Further, our null findings in the submaximal task suggest that those alternative motor pathways may contribute to force production mainly at high levels of activation.

SUGGESTIONS FOR FUTURE STUDIES

Based on our findings, a proof-of-concept investigation of speed-intensive task specific training appears warranted. While our study provides preliminary evidence supporting the fast movement context as a way to elicit better movement quality and increase intensity of training after stroke, further study is needed to confirm the findings and to determine feasibility, safety and potential benefits of speed-intensive training. This concept has been addressed indirectly in a recent trial of high-repetition task-specific

training (Birkenmeier et al., 2010). In order to complete at least 300 repetitions of upper extremity tasks within each one-hour therapy session, participants likely moved more quickly than they otherwise would have. A cohort of 13 people with chronic hemiparesis showed significant gains in upper extremity function after six weeks of training, with minimal reports of pain and fatigue, and no adverse events. A similar trial that includes specific instructions to move as fast as possible would be worthwhile, and should include kinematic outcome measures combined with assessment at the level of activities and participation. People with other neurological disorders might also benefit from speed-related instructions, thus potential effects on performance and recovery should be explored.

Based on the literature review of bilateral training presented in Chapter 1, an intervention study that combines multiple treatment approaches would also be worthwhile, to see if their training effects are somewhat additive. For example, bilateral training and constraint induced movement therapy (CIMT) each may be effective, and are thought to stimulate neural adaptation through different mechanisms. Bilateral training may stimulate and strengthen indirect motor pathways involving secondary motor cortical areas (Luft et al., 2004; Whitall et al., 2011; Wu et al., 2010), and CIMT may reduce interhemispheric inhibition of the lesioned cortex by restricting sensory and motor activity on the non-lesioned side. Perhaps intervention that includes both strategies may lead to more motor gains than either paradigm in isolation. Further, based on a randomized controlled trial comparing the two interventions, Lin and colleagues suggested that CIMT may be more effective for manual dexterity and activities of daily living, while bilateral training may be more effective for proximal arm movement.

Combining the two strategies may allow participants to practice a range of tasks that better represent the multitude of activities performed by the upper extremities in real-world daily life.

To further explore effects of the bilateral movement condition on maximal and submaximal force production, studies using different methodologies are needed to examine mechanisms. For example, comparison of functional MRI data during unilateral versus bilateral maximal force production may clarify whether alternative pathways are activated to a greater extent in the bilateral context. Additional investigations using transcranial magnetic stimulation could further examine how cortical activation evolves as force production progresses from submaximal to maximal levels.

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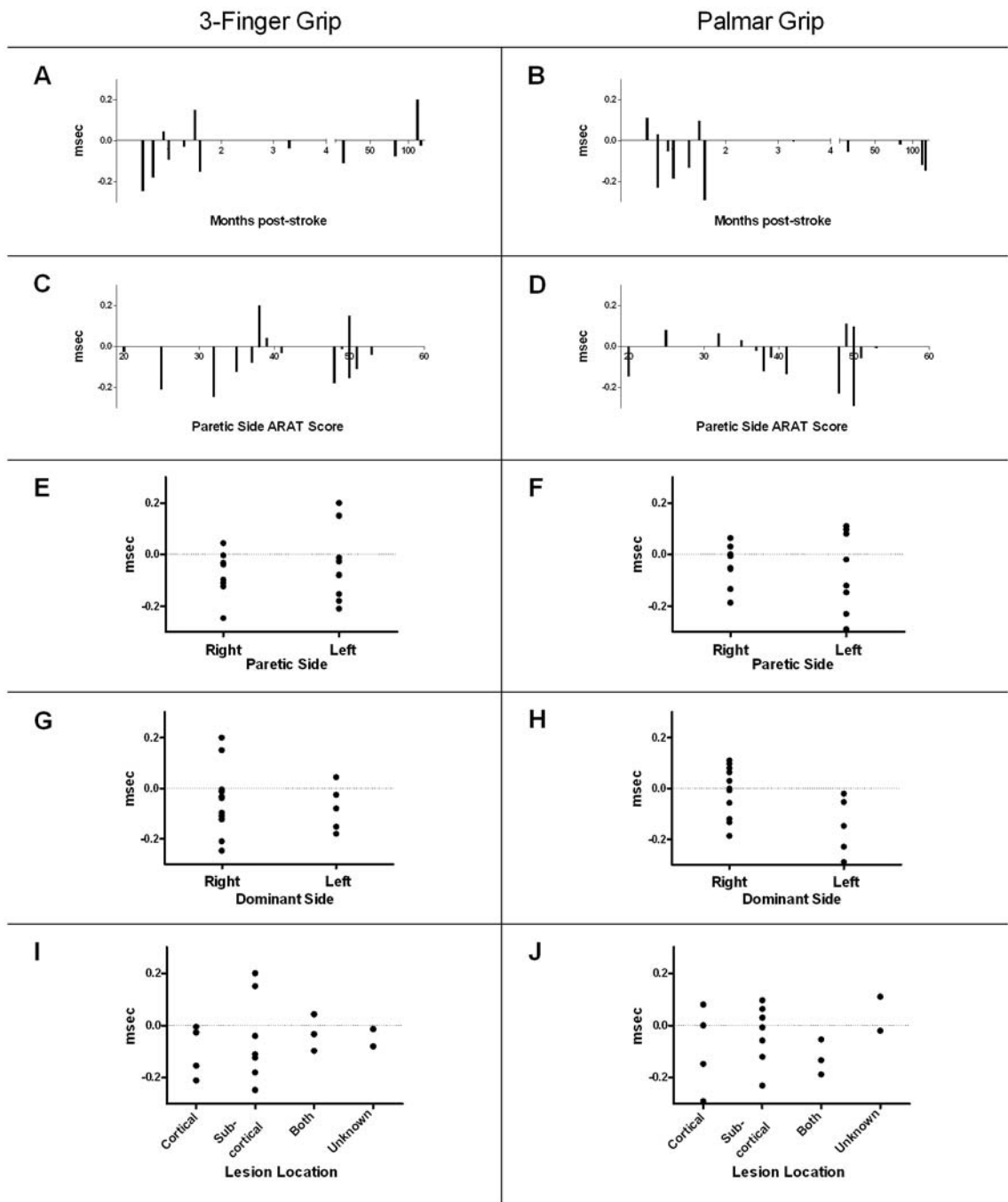
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Appendices

Since the effects of movement contexts on motor performance may be influenced by participant characteristics, and given our small sample size, these potential effects were evaluated graphically for selected variables, as shown in Figures 11-16. Each figure shows the effects of time post-stroke (A,B), the paretic side's ARAT total score as an index of severity (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J). In each case the change score, or difference across movement contexts, is shown on the y-axis. For the preferred speed vs. fast comparison in Chapter 2, effects of participant characteristics are shown for the two kinematic measures of coordination: Reach Path Ratio (Figure 11), and Aperture Path Ratio (Figure 12). For the unilateral vs. bilateral comparison in Chapter 3, two timing variables and one coordination measure are shown (Reach Duration in Figure 13, Release Duration in Figure 14, and Reach Path Ratio in Figure 15). Figure 16 shows the effects of participant characteristics on the Bilateral Deficit. For each variable, no strong evidence emerged linking movement context effects to participant characteristics.

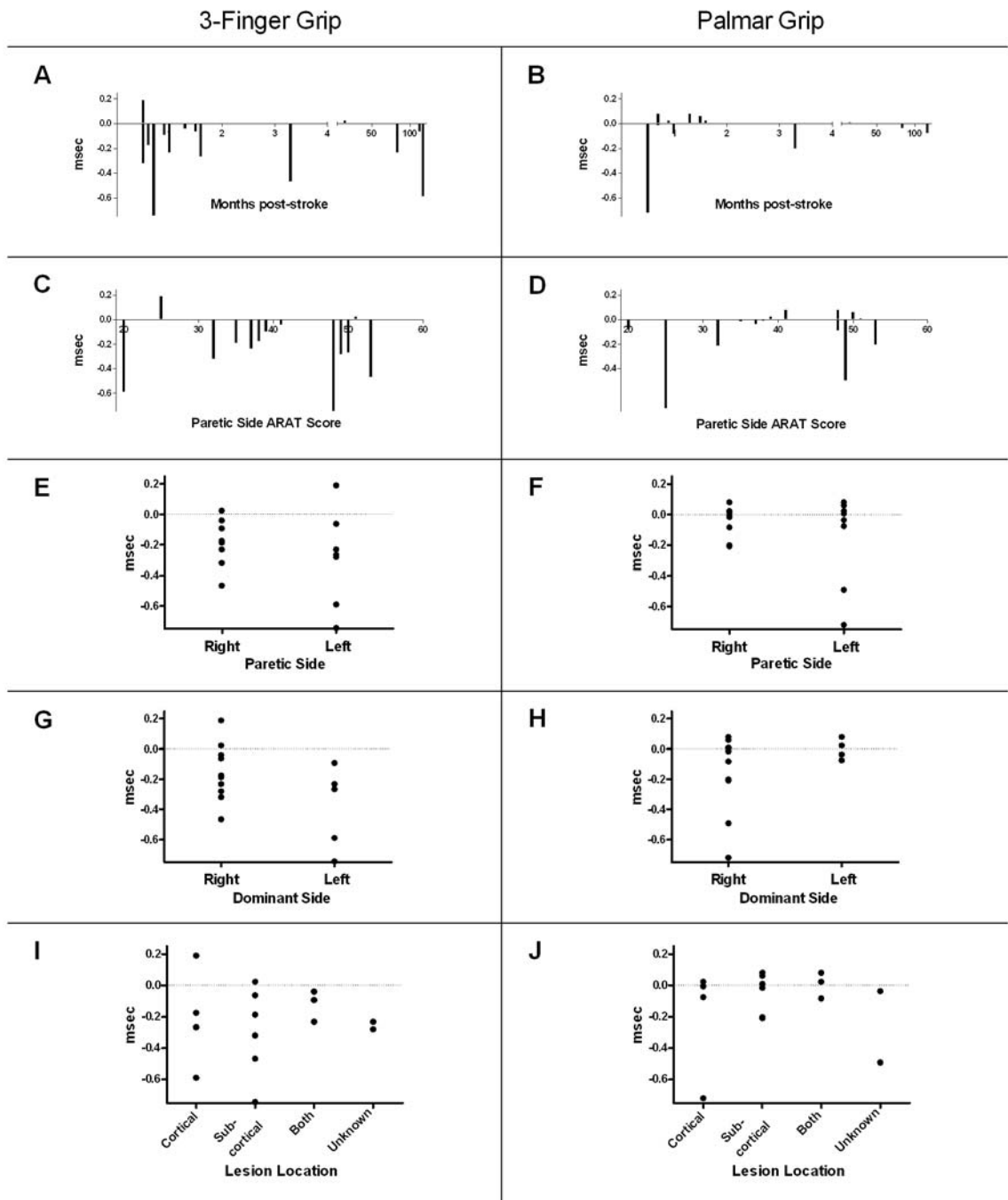
Calibration information is presented for the Tekscan I-scan pressure sensor in Figure 17, and for the Biopac grip dynamometers in Figure 18.

Figure 11. Effects of participant characteristics on **Reach Path Ratio** across **Preferred-Speed vs. Fast** Movement Contexts



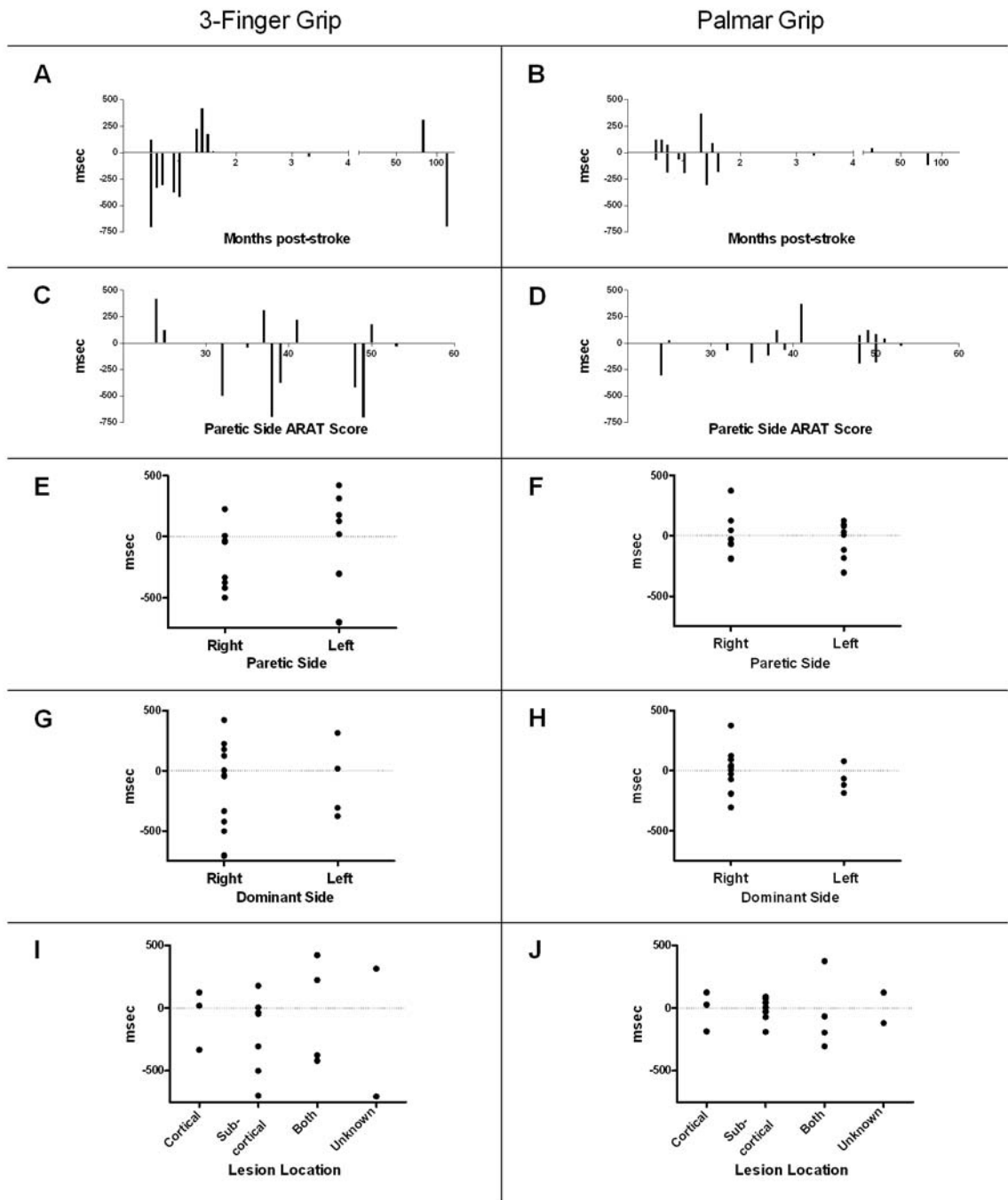
Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the effect of preferred-speed vs. fast movement context on the reach path ratio.

Figure 12. Effects of participant characteristics on **Aperture Path Ratio** across **Preferred-Speed vs. Fast** Movement Contexts



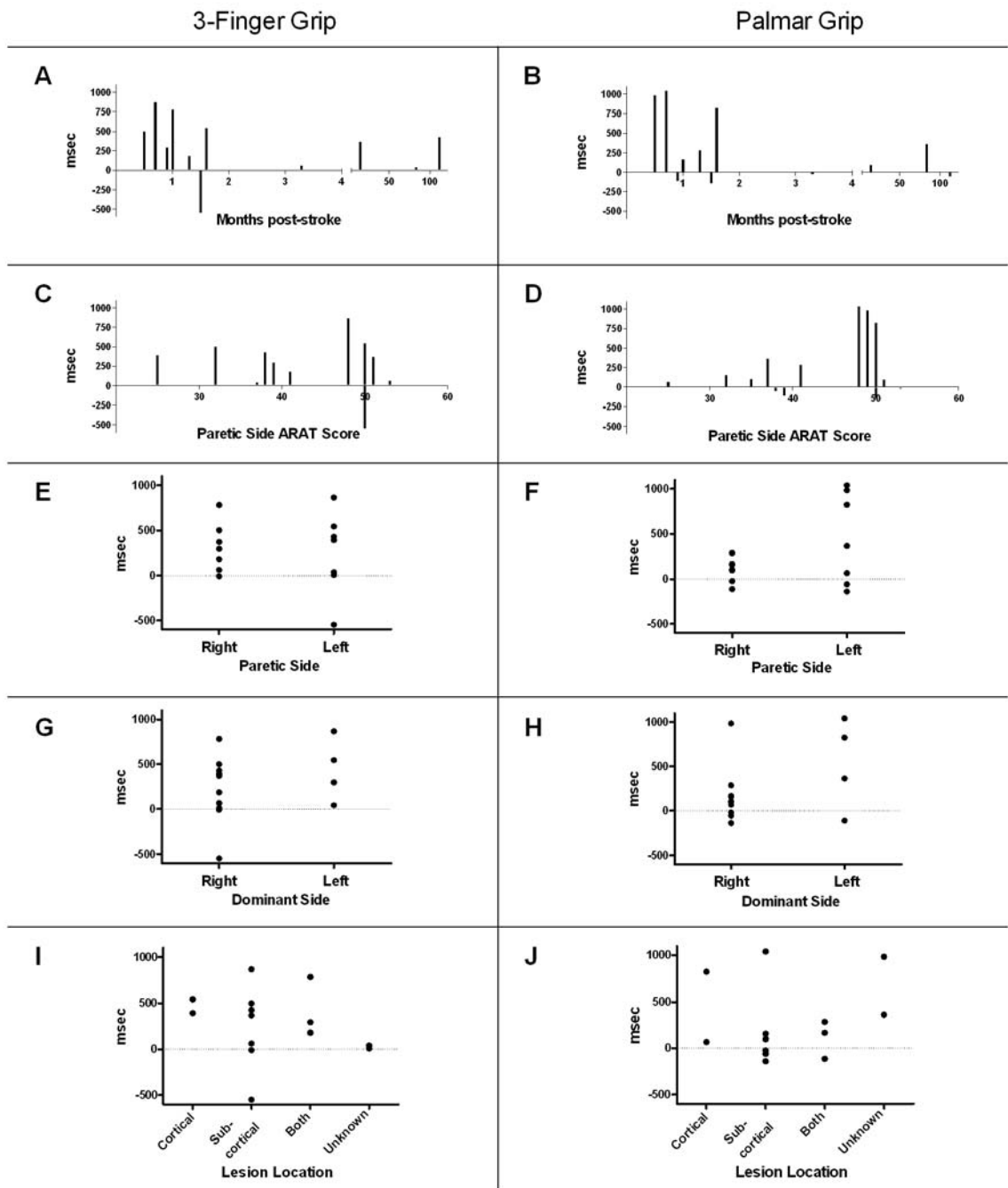
Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the effect of preferred-speed vs. fast movement context on the aperture path ratio.

Figure 13. Effects of participant characteristics on **Reach Duration** across **Unilateral vs. Bilateral** Movement Contexts



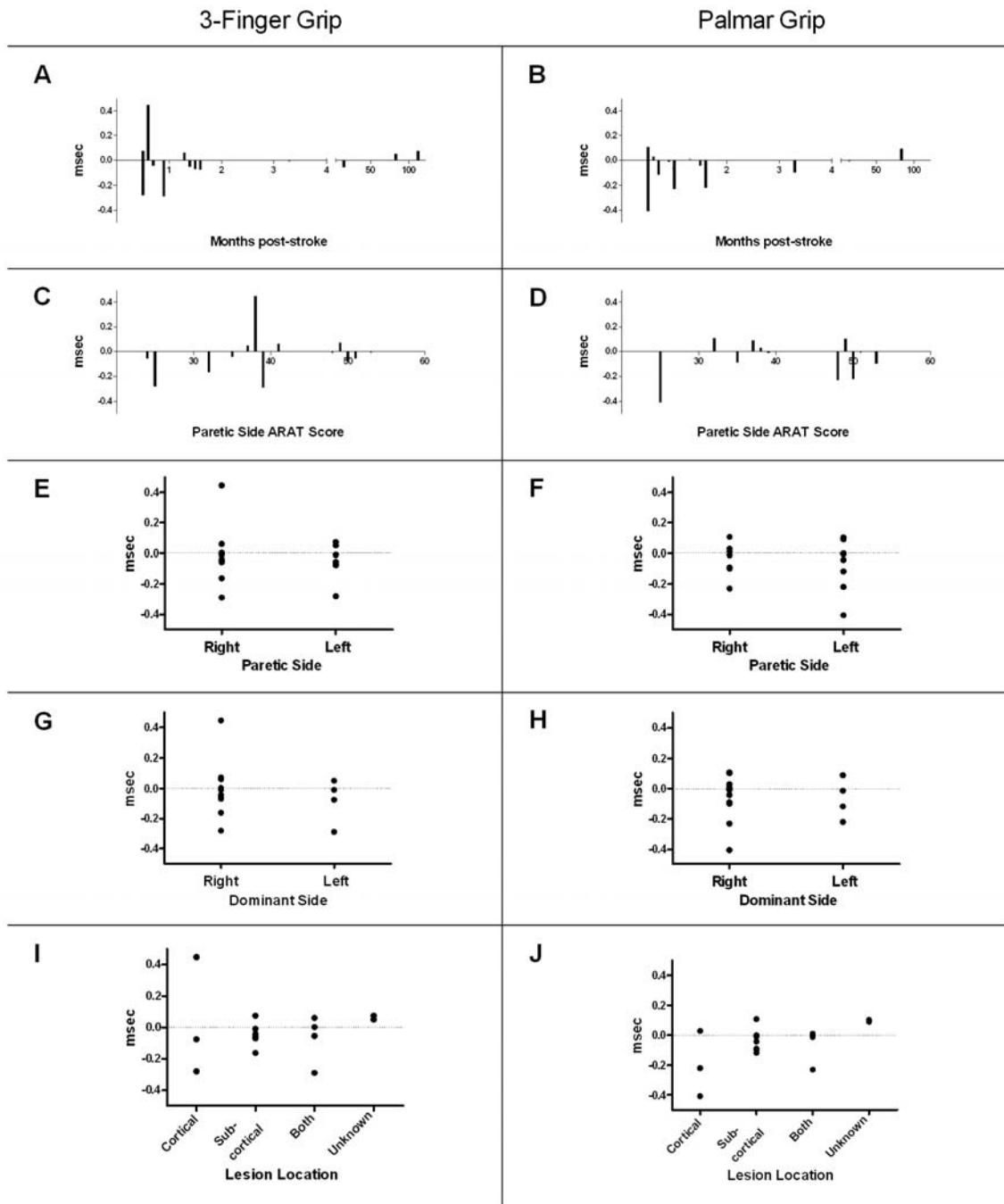
Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the effect of unilateral vs. bilateral movement context on reach duration.

Figure 14. Effects of participant characteristics on **Release Duration** across **Unilateral vs. Bilateral** Movement Contexts



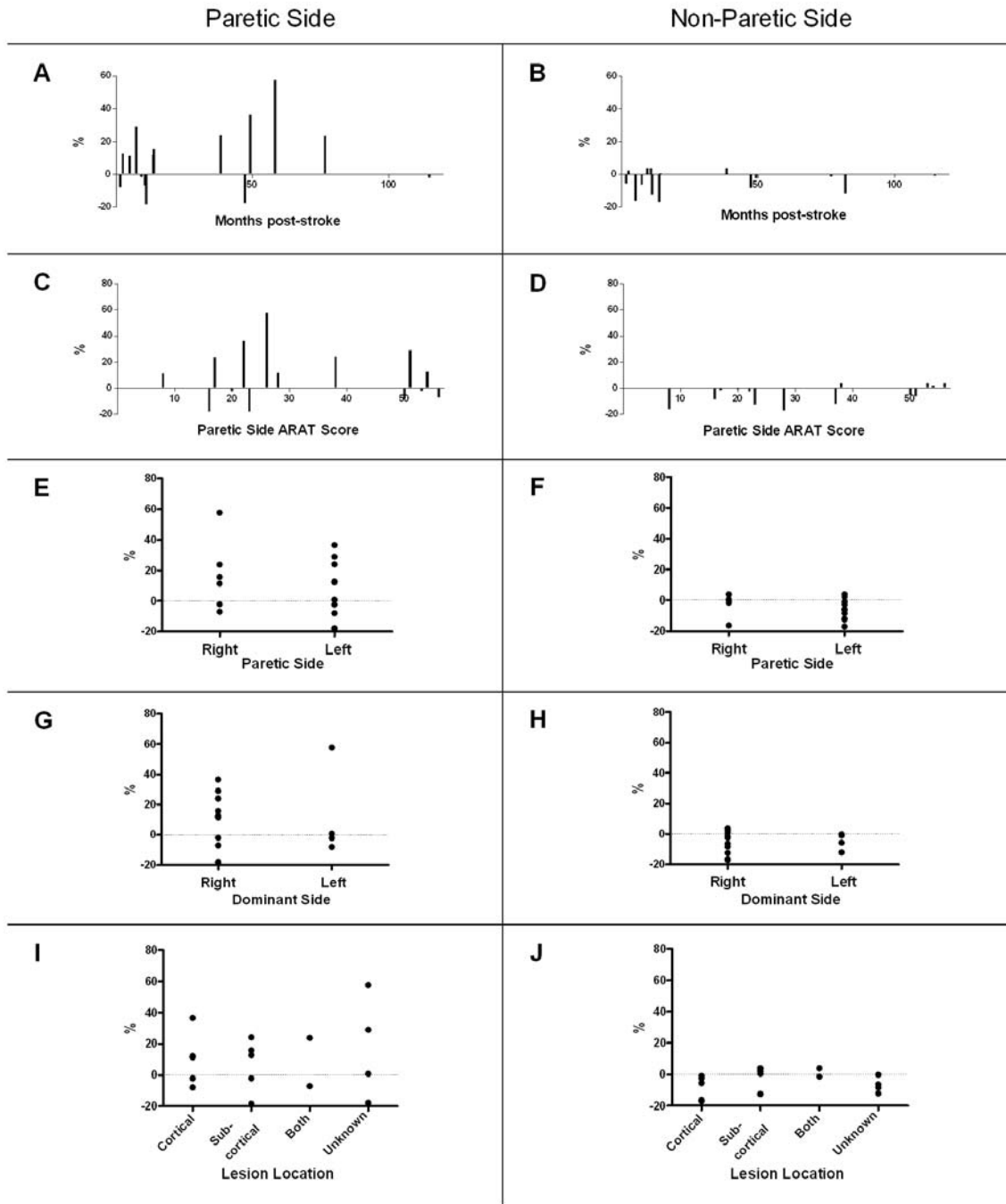
Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the effect of unilateral vs. bilateral movement context on release duration.

Figure 15. Effects of participant characteristics on **Reach Path Ratio** across **Unilateral vs. Bilateral** Movement Contexts



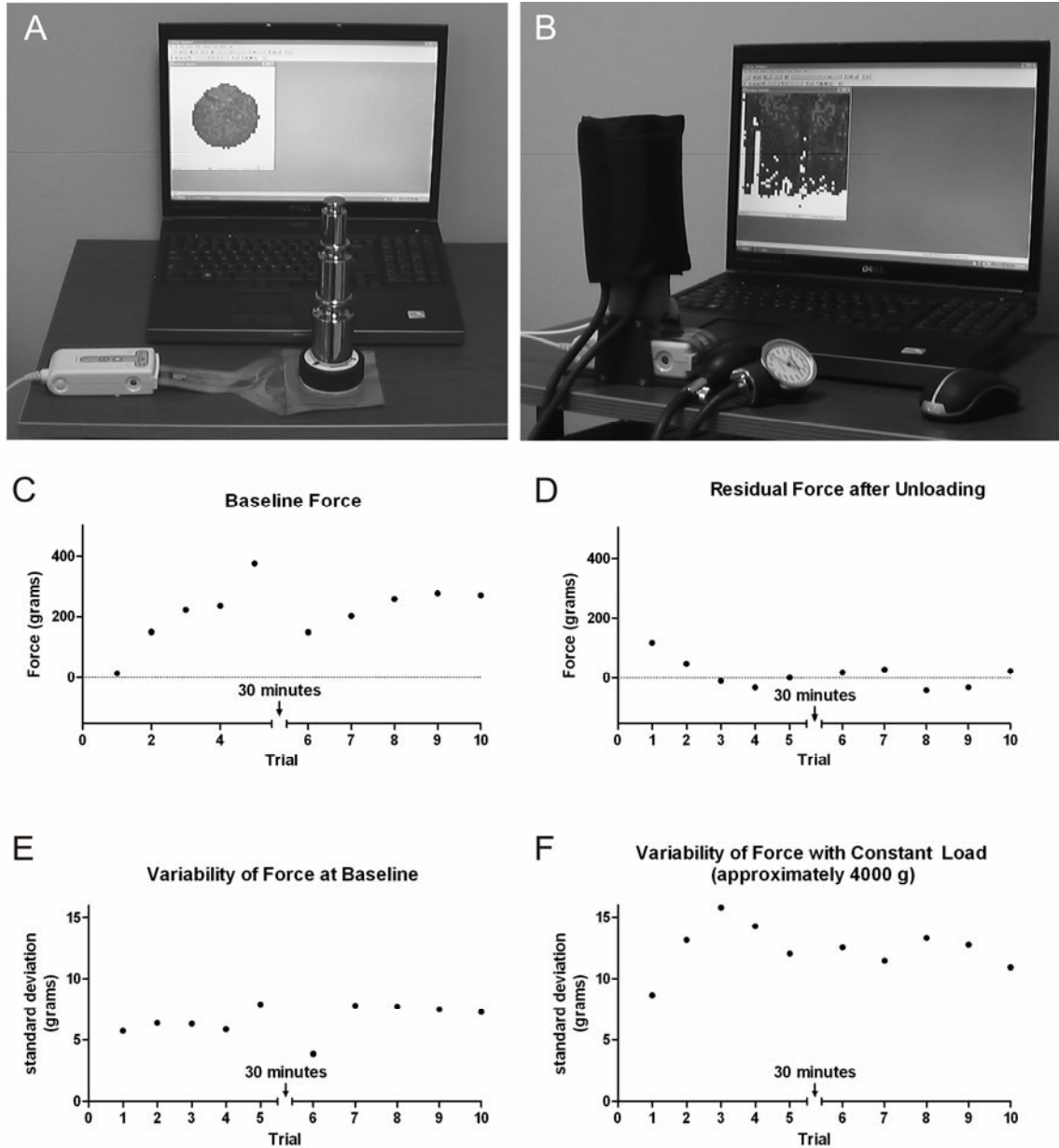
Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the effect of unilateral vs. bilateral movement context on the reach path ratio.

Figure 16. Effects of participant characteristics on the **Bilateral Deficit**



Participant characteristics including time post-stroke (A,B), severity of motor deficits (C,D), paretic side (E, F), dominant side (G, H), and lesion location (I, J), had no clear relationship with the bilateral deficit (the effect of unilateral vs. bilateral movement context on grip force) on either side.

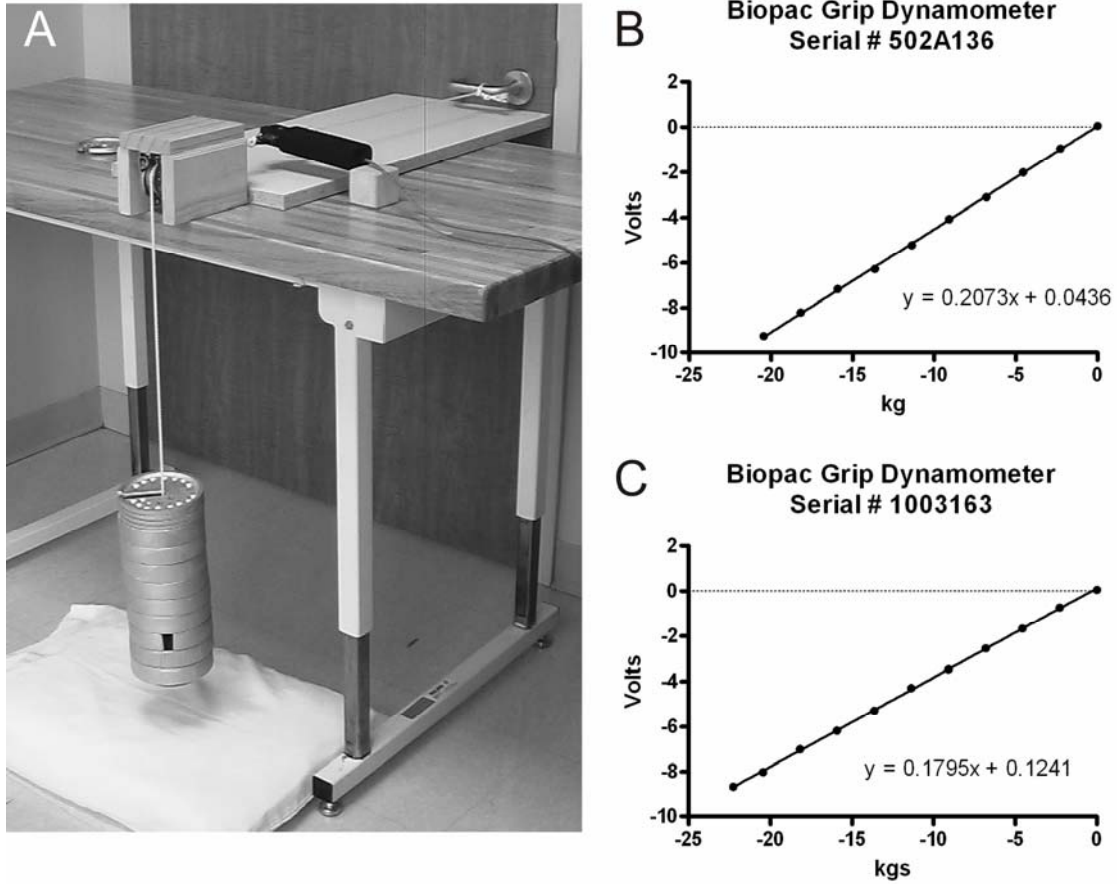
Figure 17. Calibration and Variability of the Tekscan I-scan Pressure Sensor



A) A Tekscan I-scan Model 5101-10 pressure sensor (Tekscan, Inc., South Boston, MA) was calibrated according to manufacturer recommendations, using the linear calibration method, 2164 grams of stacked weights, and thin layers of foam above and below the sensor. Saturation pressures determined in 5 consecutive calibration trials within a single session differed by 1.5% or less. B) After the sensor was attached to the vertical cylinder using spray adhesive (3M General Purpose 45, 3M, St. Paul, MN), variability was evaluated within and between trials, in a manner similar to our intended use during data collection. During each of ten trials, data was collected during a 5 second baseline,

5 seconds during which a constant load of approximately 4000 grams was maintained using a blood pressure cuff, and 5 seconds after the cuff was removed. Thirty minutes elapsed between trials 5 and 6. Results were converted from pressure to grams of force using Tekscan software. C) Recorded force prior to loading varied considerably, increasing from trial to trial and decreasing during the 30 minute break. D) During each trial, recorded force did not return precisely to its baseline value. Residual forces ranged from +118 grams to -42 grams. These characteristics of the pressure sensor were accounted for in our data collection and analysis methods. In addition to 'zeroing' the sensor at the beginning of each session using the Tekscan software's 'Tare' function, MATLAB code was used to subtract baseline force on a trial-by-trial basis. Variability of force (noise) was evaluated during the baseline (E) and loaded (F) intervals. The standard deviation of recorded force was low in both cases, averaging 6 grams when the sensor was not loaded and 12 grams during a constant load of approximately 4000 grams.

Figure 18. Calibration of the Biopac grip dynamometers



A) Scale factors were determined for two Biopac grip dynamometers according to manufacturer recommendations (Biopac Systems Inc., Goleta, CA). For each dynamometer, calibration weights, ropes and a pulley were used to apply tension directly across the strain gauge. Voltage was recorded for 30 seconds at each increment, and the mean was plotted against the applied tension (B and C). Scale factors were determined and were programmed into the LabVIEW data acquisition software. The LabVIEW routine included a 10-second baseline trial at the beginning of each session and subtracted the baseline force from subsequent trials.

Serial # 502A136
 Scale factor: 2.1927 kg/V
 Precision: 0.0214 kg
 Std. Dev. with 0 kg: 0.01 kg
 Std. Dev. with 20.45 kg: 0.06 kg

Serial # 1003163
 Scale factor: 2.5323 kg/V
 Precision: 0.0247 kg
 Std. Dev. with 0 kg: 0.01 kg
 Std. Dev. with 20.45 kg: 0.06 kg