Hand and arm coordination during reach to grasp after stroke.

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ABSTRACT

Coordination of hand and arm movements in reach to grasp has been extensively studied in normal volunteers. The research explores kinematic impairments of reach to grasp in patients with lesions involving the parietal cortex and cerebellum; brain areas considered important for controlling hand and arm coordination. The effectiveness of current targeted interventions is reviewed and a novel intervention tested in a proof of concept pilot study.

Following a brief theoretical and methodological overview (Chapter 1), the first study (Chapter 2) demonstrates that even though movements of people with parietal lobe and cerebellar lesions are characterised by prolonged duration and longer trajectories, coordination, expressed by correlation between kinematic features of transport and grasp, is comparable to controls. Coordination is also largely preserved after perturbations to the transport component. Slower movements, potentially controlled by other brain areas may compensate for latent impairments in hand and arm coordination.

A systematic review (Chapter 3) identifies functional therapy, electrical stimulation and robot training as potential interventions for improving hand and arm coordination after stroke. However, insufficient evidence and heterogeneity in terms of the stroke population prevents definitive conclusions regarding effectiveness.

A second empirical study (Chapter 4) examines a novel treatment approach by way of treatment targeted towards patients with these specific lesions. The treatment design was motivated by the lesion specific impairments identified (Chapter 2) together with a lack of clear evidence regarding treatment effectiveness for particular patient groups (Chapter 3). The study shows that high intensity, repetitive practice of reach to grasp with auditory rhythmic cueing is well tolerated by a sample of stroke patients with moderate upper limb impairments. Findings such as shorter wrist path trajectories

provide early indications for improved motor control during reach to grasp. Results suggest however a need for more challenging practice with higher dosage particularly as reach to grasp movements, which are performed as fast as possible remain prolonged, despite training that emphasizes progression of speed.

The concluding chapter (Chapter 5) provides an overview of the thesis and presents directions for future research, including investigation of the effect of competing attentional resources upon hand and arm coordination after stroke.

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CHAPTER 1: BACKGROUND

Please note that small extracts within chapter 1 are drawn from a paper recently accepted by Neurorehabilitation and Neural Repair (van Vliet, Carey et al. 2012) and these extracts are the authors own work.

Introduction

Stroke is defined as 'rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin'(Hatano 1976). The impact of stroke worldwide is enormous. Given that neuronal loss within the brain network is irreversible stroke is the leading cause of disability (Ward and Cohen 2004). Recovery of motor function following stroke is dependent upon the capacity of surviving structures and networks to generate a signal (Ward and Cohen 2004) and upon functional reorganization which may involve the peri-infarct and secondary motor areas taking on a new role (Ward, Brown et al. 2003). In patients with more motor impairment (the term motor impairment used by (Johansen-Berg, Rushworth et al. 2002) refers to delays in a simple index finger response time to a visually cued task and inability to make individual finger movements on a choice task), recovery may also involve recruitment of the contralesional dorsal premotor cortex (Johansen-Berg, Rushworth et al. 2002).

Rehabilitation has the potential to influence this reorganization and to promote recovery (Teasell, Bayona et al. 2006), but the scientific rational behind upper limb stroke rehabilitation is still in its infancy (Pomeroy and Tallis 2002). Stroke treatments are typically generic as opposed to tailored to the individual (van Vliet, Carey et al. 2012) and more intuitive rather than evidence based (Teasell, Bayona et al. 2006). Recovery of arm function after stroke is variable, often poor (de Pedro-Cuesta, Widen-Holmqvist et al. 1992; Dean 1992; Nakayama, Jorgensen et al. 1994; Kwakkel, Kollen et al. 2004), for example only 38% of people who received rehabilitation were found to recover some hand dexterity at 6 months (Kwakkel, Kollen et al. 2003). Hence there is a need to develop effective

treatments with a sound theoretical underpinning of the mechanisms which cause reach to grasp (RTG) deficits and the proposed effects (Krakauer, Carmichael et al. 2012). One option for refining treatment techniques is to explore the effects of specific interventions targeted to individual patients based upon their lesion location (van Vliet, Carey et al. 2012).

Paresis, which is the most common neurological impairment, is experienced by around 80% of acute stroke patients (Lawrence, Coshall et al. 2001). Depending upon the amount of damage to the corticospinal system (Ward, Newton et al. 2006) upper limb function may become slow or paralysed. Hemiparetic muscles show a reduction in the number of motor units recruited and slowing of the discharge rates during voluntary contraction as a result of damage to the corticospinal system and consequent loss of corticospinal input to the motoneuron pool (Jakobsson, Edstrom et al. 1991; Jakobsson, Grimby et al. 1992). Stroke may also cause specific coordination deficits between the hand and the arm which are important for successful reach to grasp (RTG) (Michaelsen, Jacobs et al. 2004; van Vliet and Sheridan 2007; Wu, Chou et al. 2008).

Coordination is defined (Diedrichsen, Criscimagna-Hemminger et al. 2007) as a 'state dependent control process in which motor commands to one effector depend upon the predicted state of another effector' a process that combines efferent copies of motor commands with afferent sensory signals to produce a representation of the current status of the peripheral motor system. Reaching for an object comprises transportation and grasp and coordination between these components is essential for everyday activities, such as grasping a cup of liquid without spillage. After stroke RTG movements may be limited and appear clumsy. For example (Jeannerod 1994) a patient may knock over the target object either because the reach continues after contact, the fingers close before contact or the fingers close too late.

Studies in healthy adults (Jeannerod 1984; Wallace SA 1990; Gentilucci, Castiello et al. 1991; Castiello, Bennett et al. 1998) have demonstrated spatiotemporal coordination between phases of reach and grasp. For example, the timing of the final adjustment to the grasp aperture normally occurs at the peak deceleration phase of transport. After stroke the temporal coupling between key events in

prehension can be disrupted (van Vliet and Sheridan 2007). The study demonstrated that coordination between reach and grasp in a heterogenous group of stroke patients was not as tightly coupled as age matched controls. For example the correlation between the time of maximum aperture and peak deceleration was lower than controls when grasping a small cup at fast speed. To date however relatively little attention has been paid to the specific coordination deficits following stroke and thus the need for further investigation.

Although the exact mechanism of hand and arm coordination during RTG is poorly understood, there is a growing understanding within neuroscience of the central nervous system control of RTG and effects of central nervous system pathology on this coordination, for reviews see (Castiello 2005; Grafton 2010). This knowledge is potentially useful for therapists attempting to retrain movements of the hand and arm for successful coordination after stroke. The present chapter provides an overview of the current understanding of central nervous system motor control of RTG coordination in healthy subjects, including proposed models of RTG and brain structures identified as being involved, specifically the parietal lobe and the cerebellum. The RTG deficits associated with lesions affecting these brain areas in particular are explored in order to generate more targeted interventions for RTG coordination deficits based upon specific lesion location. It begins with a description of some of the methodologies employed to investigate RTG coordination and the challenges facing neurorehabilitation.

Methodologies used to investigate RTG coordination

Our understanding of brain function is dependent upon the available technology. The earliest approach to understanding brain function was to correlate deficits in function with post-mortem analysis of damaged brain areas, typically after stroke. One prominent case example reported by Broca in 1861 (in (Arbib 2006)) involved a patient with expressive aphasia for whom post mortem analysis revealed a lesion in the posterior part of the left inferior frontal gyrus. Consequently the posterior part of the left inferior frontal gyrus was considered an important brain area for expressive language. Whilst providing important insights, these studies were limited, firstly in the ability to

differentiate between the processing centre (brain area responsible for the execution of a behaviour) and overlap within a widely distributed network supporting that function. Secondly, these studies fail to determine whether the area in question subserves just one or multiple functions.

Animal studies (Lawrence and Kuypers 1968; Brinkman and Kuypers 1972; Haaxma and Kuypers 1975; Rizzolatti, Camarda et al. 1988; Rizzolatti, Gentilucci et al. 1990) provided investigators with control over the size and location of lesions. Neuropsychological findings in split-brain monkeys suggested that the motor control of the proximal and distal segments of the upper limb were organized functionally (Lawrence and Kuypers 1968; Brinkman and Kuypers 1972; Haaxma and Kuypers 1975). When forced to use ipsilateral eye and hand to control prehension directed at a food target the monkeys demonstrated intact reaching with impairments in grasping; while grasp was performed accurately when using contralateral eye and hand control. It was proposed that the distal musculature is under the control of the contralateral primary motor cortex whereas more proximal musculature is controlled bilaterally. This area of research continues to make important contributions the literature although animal brain structure and function are not directly comparable with humans.

Some of the methodological issues were overcome by studies involving multiple patients with lesions of the same location (Ghika, Ghika-Schmid et al. 1998; Serrien and Wiesendanger 1999; Brandauer, Hermsdorfer et al. 2008) to reveal overlap. Similarly, cases of double dissociation (lesion A affects function X but not Y and lesion B affects function Y not X) provided new insights (Ivry, Keele et al. 1988; Goodale, Milner et al. 1991). Further understanding, particularly of the time course over which particular brain areas are involved in reach and grasp movements, came from the ability to produce temporary disruptions using repetitive transcranial magnetic stimulation (TMS) in healthy volunteers (Tunik, Frey et al. 2005; Rice, Tunik et al. 2007; Vesia, Yan et al. 2008). With this method, a repetitive pulsed focal magnetic field produced over an area of cortex, results in temporary suppression of function of that brain area. The high temporal resolution of TMS enables the investigator to study the direct consequence of disruption to cortical activity with manipulations occurring at discrete stages during the RTG behaviour. For example, rapid corrections in response to

changes in object position were disrupted when TMS was applied within 65ms of the object perturbation to the anterior inferior parietal sulcus (Tunik, Frey et al. 2005). The most direct evidence of the function of different brain areas has come from functional imaging techniques, such as functional magnetic resonance imaging (fMRI). These determine blood-oxygen-level-dependent (BOLD) contrast that is the changes in blood flow which are linked to increased metabolism of brain areas involved during visually guided reach to grasp.

Motion capture is proving to be a particularly insightful tool for quantifying upper limb function (Raghavan, Petra et al. 2006; Schettino, Adamovich et al. 2006; Nowak 2008) and for monitoring treatment effects on motor performance (Lin, Wu et al. 2007). The work began with Eadweard Muybridge (1830-1904) and a series of cameras placed in a row which captured the trotting motion of a horse (Wing and Beek 2004). Shortly after Etienne-Jules Marey (1830-1904) developed a single camera capable of taking multiple pictures (Wing and Beek 2004). Video recordings, which were subject to error when measured directly from the video screen can now be converted to digital form for greater accuracy. The data from markers placed upon anatomical landmarks and stored as coordinates at each frame can be used to calculate the relationship between body parts during movement. With the development of high speed film Jeannerod (Jeannerod 1981; Jeannerod 1984) used data extracted from the displacement of markers on the wrist and fingers to differentiate between transport (movement of the hand to the target location) and grasp (shaping the hand according to object size) components, which gave rise to a wealth of research on human reach-to-grasp.

3D kinematic analysis now employs optoelectronic systems which track either passive markers (a series of infra-red cameras captures light reflected from markers covered with retro-reflective material) or active markers (markers with individual power packs which actively transmit infra-red rays to a receiving camera system). Optoelectronic systems provide accurate computer-generated quantitative information regarding segmental and joint displacement, speed and acceleration. Visual representation of the movement quality is lost using this system, but importantly it can be used to determine selective motor control (Teulings, Contreras-Vidal et al. 1997), movement

variability (Sabatini 2002) and movement smoothness (Hogan, Bizzi et al. 1987). In short, kinematic analysis can help to determine the capacity for motor control and coordination. This thesis develops methods for studying impaired coordination in stroke patients using 3D kinematic analysis.

One way of demonstrating the degree of coordination between the hand and the arm is to look at the correlations between the absolute timing of key temporal events of transport and grasp (Marteniuk, Leavitt et al. 1990; Paulignan, MacKenzie et al. 1990; Gentilucci, Chieffi et al. 1992) . Pilot data here for example (Appendix A1.1) showed a linear positive relationship between the time of peak velocity and the time of maximum aperture (Pearsons' correlation coefficient of 0.7). A perfect correlation (1.0) is unlikely since there is normally some variance to one or other effector which cannot be be accounted for, such as fatigue or attending to hand opening but not to transport. In addition there may be unexplained individual differences and changes, which might be context dependent and occur over time with learning. Another way of showing functional coupling between the respective trajectories is to examine the normalised timing of kinematic landmarks (for example the time to maximum aperture occurs at a fixed ratio of 75% to 80% of the total movement time) (Jeannerod 1984). This is comparable to gait analysis where people might look at the percentage of time during the gait cycle, which is spent in stance or swing phase.

The challenge for neurorehabilitation.

The role of therapy is to limit stoke disability by maximising cortical reorganization and promoting recovery which is balanced with maximising function through compensation. A lack of clear guidelines regarding individual interventions in stroke rehabilitation has recently been highlighted as a problem facing therapists treating people with upper limb weakness (NICE 2011), although the draft report suggests clear evidence for the considered use of constraint induced therapy, functional electrical stimulation, repetitive task training and functional strength training. Further research (Pollock, Legg et al. 2000) (Viana and Teasell 2012) has identified barriers to the implementation of evidence based therapy. Such barriers include uncertainty regarding the reliability of stroke research (Pollock, Legg et al. 2000) and the gains seen actually being attributed to the result

of specific treatments (Viana and Teasell 2012). Furthermore, results from the Randomised Controlled Trials (RCTs), which are considered the gold standard in research, are not easily translated into clinical practice due to the heterogeneity of patients (Schreiber and Stern 2005). That is to say, studies with heterogeneity in terms of lesion location, chronicity and level of impairment make it difficult to detect specific treatment effects. Studies examining treatment effects upon homogenous patients groups in terms of lesion location for example could contribute to the development of clearer guidelines and implementation of more evidence based therapy.

The evidence base for neuro-rehabilitation is relatively new and evidence based therapy is not as highly developed as other sciences (Pomeroy and Tallis 2002). There is a demand for more preliminary research to investigate which patients might benefit from what dose of well described interventions (Pomeroy and Tallis 2002). Some practice recommendations for example (Barreca 2001) have been drawn from evidence which associates poor arm recovery with severe paresis and poor motor function (Nakayama, Jorgensen et al. 1994; Hendricks, van Limbeek et al. 2002; Kwakkel, Kollen et al. 2003); anterior circulation infarcts, right hemispheric strokes, homonymous hemianopia, visual gaze deficits and visual inattention (Kwakkel, Kollen et al. 2003). The mechanisms mediating recovery remain uncertain (Kolb, Teskey et al. 2010), although emerging models of recovery may help identify which patients are most likely to benefit from a particular treatment. For instance, relative integrity of the cortico-spinal tract (CST) may indicate intense unilateral exercise, whereas patients with damage to the CST may benefit most from augmented or bilateral therapy (Stinear and Ward 2013).

Standard treatments are largely based upon the clinical assessment of function and presenting impairments in muscle strength, tone, sensation and coordination (van Vliet, Carey et al. 2012). Another approach, that of matching interventions to individuals based upon the lesion location has the potential to compliment standard treatments and improve outcomes (van Vliet, Carey et al. 2012). Whilst impairment measures such as Fugl-Meyer (Prabhakaran, Zarahn et al. 2008) and finger extension (Nijland, van Wegen et al. 2010) have a good correlation with prognosis, the exact nature of

the lesion might enable a more refined approach to individual prognosis and patient management. Therefore neuroimaging in combination with clinical and neurophysiological assessments is likely to contribute to a more important role in stroke rehabilitation in the future (Krakauer 2005; Stinear and Ward 2013).

Following observations of impaired RTG coordination in patients with stroke a few training suggestions have been made (van Vliet and Sheridan 2007), for example stroke patients should practice the use of grasp and transport together to facilitate the activation of temporally linked commands. Motor behaviour needs to be flexible in a variety of environmental conditions and is organised around behavioural goals, so practice should involve grasping objects of different sizes at a variety of locations. This task orientated approach is supported by the classic interpretation of coordination in RTG (Jeannerod 1984) which suggests that neural processes controlling the transport and grasp components are independent but coordinated so that the expected duration to the target, of each of these trajectories is adjusted and temporally matched. Further knowledge of how particular brain regions disrupt RTG coordination will improve our understanding of the neural networks involved and the potential mechanisms for recovery. Such work may help with the development of more specific guidelines for training RTG coordination.

Brain regions identified in planning and controlling RTG (Winstein, Wing et al. 2003) include posterior parietal cortex, and the cerebellum. It is not clear from current understanding how different lesion locations affect the disruption of reach-to-grasp, although there are a small number of studies looking at the populations separately (Jakobson, Archibald et al. 1991; Rand, Shimansky et al. 2000; Zackowski, Thach et al. 2002; Milner, Dijkerman et al. 2003). Lesion specific studies may provide greater insight into the RTG coordination deficits but to our knowledge, coordination of reach-to-grasp in groups with different lesion locations has not been compared using the same paradigm. This knowledge is important for understanding the problems of different patients presenting with stroke in the clinic, and for the design of treatment interventions targeted towards the different groups. In the

next section an outline of the research involving RTG movements in healthy participants is provided, which has fuelled the drive to investigate lesion specific deficits.

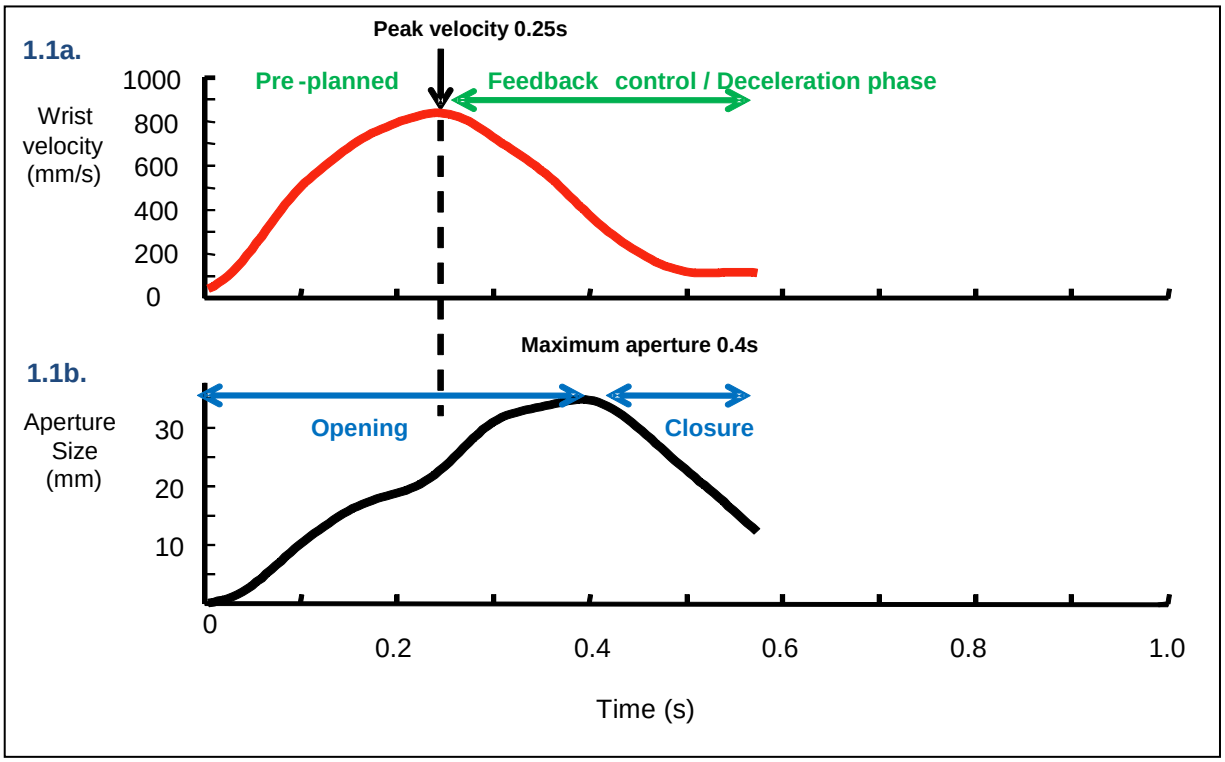
Coordination of reach to grasp in healthy participants

Skilled reach-to-grasp requires temporal and spatial coordination between multiple joints of the hand, elbow and shoulder, as well as eye and trunk movements. The final phase of movement depends upon the integration of visual and proprioceptive information to execute accurate motor control, to make on-line adjustments and to respond to changes in the environment (Gentilucci, Toni et al. 1994). Healthy participant studies (Jeannerod 1984; Gentilucci, Castiello et al. 1991; Castiello, Bennett et al. 1993; Hoff and Arbib 1993; Rosenbaum, Meulenbroek et al. 1999) demonstrate characteristic patterns, which suggest for example that although the arm and hand are controlled separately, they are coordinated according to key temporal and spatial events. This view is based upon observations that hand movement for opening is correlated in time with onset of transport and that maximum hand aperture is linked to peak deceleration. It has also been shown that the magnitude of grasp aperture is adjusted to the size of the object intended for manipulation, the speed of the movement (Wing, Turton et al. 1986) and the movement end goal (Ansuini, Santello et al. 2006).

For a given movement the hand follows a characteristic path as it moves towards an object, described as the 'transport' component (Jeannerod 1984). Transport can be defined as the change in position over time of the hand and is commonly depicted by the velocity and acceleration profiles plotted against absolute time (usually in milliseconds (ms) or against normalised movement duration (each time point is expressed as a percentage of total movement duration). Peak velocity (PV) normally occurs within 50% of movement duration thus generating a hand velocity profile, which appears asymmetric (Figure 1.1a). Wrist velocity profiles which show this characteristic asymmetrical pattern indicate a ballistic pre-planned phase followed by controlled deceleration under visual guidance (Jeannerod 1981). The time to PV is often described as 'ballistic' meaning it is assumed to be driven by muscle commands that are not corrected by feedback and are probably fully planned and specified before movement onset (Nagasaki 1989). The time after PV is thought to be controlled in a

feedback manner whereby visual or proprioceptive information made available to the central nervous system (CNS) after the movement begins is used to correct the movement according to task goals and environmental demands. The time after PV is described as the 'deceleration' phase, while the hand slows in readiness to grasp the object. Peak velocity and deceleration occur earlier when smaller objects are grasped with precision grip (Castiello, Bennett et al. 1993). Paulignan (Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991) observed that variability of the wrist path trajectory was not distributed evenly during trials and that the greatest variability corresponded with time of peak velocity.

Figure 1.1a. Wrist velocity profile and 1.1b. grip aperture profiles. Examples from healthy control participant grasping an object, sized 15mm located 35cm away. In this example peak wrist velocity (800mm/s) occurs at 43% of the total movement duration (0.58s). Maximum grip aperture in this case is 35mm and occurs at approximately 69% of the movement duration.



During reach to grasp, the hand typically opens once and then closes on the object, referred to as the 'grasp' component and is described as the change over time of the distance between the index finger and thumb markers (Figure 1.1b). The maximum grasp aperture (MA) tends to exceed the object diameter by about 20% (Jeannerod 1981) and increases with the speed of the movement (Wing,

Turton et al. 1986). The timing of hand opening and closing is adjusted according to the movement end goal (Ansuini, Santello et al. 2006) and maximum grasp aperture occurs at around 50-70% of the movement duration (Jeannerod 1984). Object size and movement speed influence the timing and size of maximum aperture. The size of aperture increases for more rapid movements in compensation for increased variability when there is less time for visual feedback (Wing, Turton et al. 1986).

Transport and grasp must be coordinated to ensure that the object is grasped successfully. This coordination is partly defined by an invariant temporal relationship between the two components, where the start time of the opening of the hand is correlated with the start time of hand movement towards the object (Jeannerod M 1982; Jeannerod 1984; van Vliet and Sheridan 2007) (e.g. Pearsons correlation coefficients varying between 0.8 - 0.91 and the time of maximum hand opening is correlated with the time of peak deceleration of the hand (Jeannerod 1984; Castiello, Bennett et al. 1993) (e.g. Pearsons correlation coefficients varying between 0.76 - 0.89 (Jeannerod 1984)). As well as the coupling of MA and PD, a relationship has been demonstrated between MA and peak velocity, where although PV occurs prior to MA the two events are significantly correlated (Wallace SA 1990).

Temporal invariance is important for everyday tasks to prevent displacement or knocking over objects. An optimum level of variability (Stergiou, Harbourne et al. 2006) within individual's patterns of movement may however be considered to be a purposeful and functional property of an adapting neuromuscular system, helping to overcome anatomical and physiological changes. Movement patterns with excessive variation may be considered unstable or inefficient; whereas minimal variability may be associated with rigidity and unchanging movements. In both cases the performer may lack the potential to adapt to errors and perturbations or to learn within a changing environment.

Studies involving mechanical perturbation of the arm (Haggard and Wing 1995; Rand, Shimansky et al. 2004) or deliberate manipulation of the object location (Paulignan, Mackenzie et al. 1991; Alberts, Saling et al. 2002) and/or object size (Paulignan, Jeannerod et al. 1991; Castiello, Bennett et al. 1993; Bennett and Castiello 1995; Castiello, Bennett et al. 1998; Roy, Paulignan et al.

2006; Hesse and Franz 2009; van de Kamp, Bongers et al. 2009) have provided further evidence of the close temporal relationship between the reach and grasp components. When either reach or grasp is disturbed, for example by manipulations of object size (Paulignan, Jeannerod et al. 1991), or object location (Paulignan, Mackenzie et al. 1991), a deliberate double opening and closing manoeuvre (Timmann, Stelmach et al. 1996), increasing speed of transport (Wing, Turton et al. 1986), obstacles placed in the hand's path (Saling, Alberts et al. 1998) or mechanical perturbations of the arm (Haggard and Wing 1995; Rand, Shimansky et al. 2004) there is compensating adjustment made to the other component. For example following perturbation of the object size (Paulignan, Jeannerod et al. 1991) the deceleration phase of the wrist velocity profile was prolonged and in some cases appeared to consist of a secondary sub-movement which implied a comparative and correction process between the two components.

In addition to object size and distance, the orientation at which the fingers grasp the object presents further complexity for prehensile planning and execution. A small number of studies (van Bergen, van Swieten et al. 2007; Sangole and Levin 2008) show that the degree of hand rotation affects overall movement duration and this will interact with the timing of transport and grasp components. Thus the motor output for the coordination of reach to grasp involves a larger number of degrees of freedom, consisting of at least three separate components, transport, rotation and grasp that occur concurrently within a given time window. For the purposes of this preliminary investigation the thesis will be restricted to the binding of the two components of transport and grasp, which constitute the main focus of recent research in this area. It will be limited to unimanual coordination and to movements of the shoulder, elbow wrist, hand and digits in order to provide a detailed analysis of these components. Future research might consider other important aspects such as the impaired coordination of rotation and coordination of the hand and arm with other body parts such as the trunk and the other arm.

It should be noted that the majority of studies informing our knowledge of reach to grasp in the healthy population have been conducted with young people; however stroke predominantly affects

older people. One study (Bennett and Castiello 1995) has shown that although the control of reach to grasp in the older population resembles the younger controls, there are differences in their reaching kinematics (longer movement duration, deceleration time, lower peak velocity and peak deceleration) and in some aspects of their response to perturbation of object size, due most probably to slower processing of feedback, and/or weakness. For this reason it is important for studies to use age matched controls.

Speculative models of hand and arm coordination for reach to grasp

It is important to consider how complex actions such as reach to grasp are processed. In the healthy adult reach to grasp movement is considered relatively automatic, in the sense that it requires little attention to the details of the movement (Lang and Bastian 2002). The dual route model of cortical processing (Mishkin and Ungerleider 1982; Goodale and Milner 1992; Milner and Goodale 1993; Milner, Paulignan et al. 1999; Milner and Goodale 2008) distinguishes between vision for perception and vision for action. This classic theory (Mishkin and Ungerleider 1982; Goodale and Milner 1992) has proposed two separate streams for visual processing of objects, namely the 'what' pathway for object identification and the 'where for action' pathway for its egocentric and allocentric location for the purpose of manipulation. The former 'ventral stream' passes from the occipital lobe through the temporal lobe, whilst the latter 'dorsal stream' projects from the occipital lobe through the parietal and frontal lobes. The concept of two visual streams is supported by patient studies (Goodale and Milner 1992; Pisella, Vighetto et al. 2001; Grea, Pisella et al. 2002; Carey, Dijkerman et al. 2006; Frak, Paulignan et al. 2006) involving a visual form agnostic patient (DF) visual ataxia (AT), which have revealed a double dissociation. The literature for example (Milner and Goodale 2008), reports that DF is able to manipulate objects in a skilled way but has difficulty reporting the object parameters, whilst AT is accurate in object perception but has impairments associated with reach and grasp. When a delay is imposed, optic ataxia patients exhibit an improvement in reaching, which it is argued (Milner and Goodale 2008) is achieved by relying more on the cognitive control offered by the ventral stream than on the impaired automatic control of the dorsal stream. By contrast Hesse, Ball &

Schenk (Hesse, Ball et al. 2012) opposed the view of a double-dissociation based on the observation that peripheral vision is impaired in the visual form agnostic patient DF in a similar way to patients with optic ataxia.

The dual route model has recently been refined (Milner and Goodale 2008) and now offers a robust framework from which it is assumed that cortical visual information for reach to grasp is largely processed via the 'dorsal stream'. A development of the classic dual stream model of organization for prehension movements proposed two separately controlled parallel input-output visuomotor processing channels, which are linked for key temporal events. The traditional visuomotor channel hypothesis (Jeannerod 1988; Hoff and Arbib 1993) proposed independent control of the visuomotor transformations associated with reaching and grasping. The first motor control program for coordinated action (Arbib 1981) proposed that perceptual information and motor schemas are matched according to the task and sensory environment. The model posits that maximum aperture is synchronised with the temporal ending of the reach movement. Coordination between the reach and grasp components is temporally based with object interaction by planning a consistent enclosure time, that is the time from maximum aperture to object grasp. Independent motor schemas, one for the arm to transport the hand towards the object and the second for preshaping of the hand, activated concurrently based upon perceptual schema output regarding location, size and orientation. On completion of the fast initial phase of hand transport the final stage of the grasping schema is engaged to shape the fingers under control of visual and tactile feedback. During the transport phase hand orientation and grip size are matched according to the perceived object properties to embrace the object for a stable grip.

A hierarchical arrangement of motor control processes has been suggested (Wang and Stelmach 1998). This is consistent with the model proposed by Hoff & Arbib (Hoff and Arbib 1993), where reach and grasp components are governed by independent motor synergies with a higher level control system responsible for their integration. Substantive data both from computer simulation and real subjects (Hoff and Arbib 1993; Castiello, Bennett et al. 1998; Vilaplana and Coronado 2006)

support the idea that the reach is planned with respect to the expected duration to the target, via a consistent enclose time of the hand. There is a two-way interaction between the neural processes controlling transport and grasp, so that the expected duration to the target, of each of these trajectories, is compared and adjusted so that they are temporally matched. For example, when both object size and location are 'perturbed' at movement onset, MA and PD are both delayed in order to allow them to be temporally matched again after adjustment to each component has been made (Castiello, Bennett et al. 1998). The expected duration to the target may be determined from an abstract representation stored in memory referred to as motor schema (Schmidt 1975). Alternatively, the expected duration may be derived from internal models (Kawato 1999), acquired and stored in part by the cerebellum. Forward internal models predict sensory consequences from efferent copies of a given motor command, whereas for inverse internal models the output motor command is projected from the desired sensory state (Kawato 1999). These neural mechanisms help to explain coordinated movements which are performed too quickly to be executed exclusively under feedback control (Kawato 1999).

An alternative state-space coordination model (Haggard and Wing 1991; Haggard and Wing 1995; Haggard and Wing 1998; Saling, Alberts et al. 1998; Wang and Stelmach 1998; Wang and Stelmach 2001), assumes that adjustments to grasp aperture following a perturbation in reach are made to maintain a consistent spatial relationship between the two components. In contrast to the Hoff and Arbib model (Hoff and Arbib 1993), Alberts (Alberts, Saling et al. 2002) found that perturbation in transport alters enclosure time, whereas the aperture-closure distance did not alter significantly. There is more support for the idea of distance from the object being more of a controlling parameter than the time to close the hand, for example time taken to close the hand remained constant over varying reaching amplitudes in one study (Gentilucci, Chieffi et al. 1992) although contrasting data shows increasing time to contact with increasing object size (Zaal, Bootsma et al. 1998). The grasp aperture seems to be modulated according to the distance to the object, because the enclosure distance is relatively invariant under a variety of task conditions such as alterations of object distance, presence/absence of objects (Alberts, Saling et al. 2002) and different involvement of body segments

(Wang and Stelmach 1998). In further support of the state-space control model (Haggard and Wing 1998; Saling, Alberts et al. 1998), Wang & Stelmach (Wang and Stelmach 1998) reported invariance in the closing-aperture distance, despite changes to the transport distance related to the involvement of trunk movement. It was speculated (Wang and Stelmach 1998) that both spatial and temporal factors are utilized by a higher level synergy, which incorporates independent synergies for reach and grasp in a coordinated movement pattern.

Aperture closure may be governed by the kinematic state of parameters, which include hand distance to target, velocity and acceleration and grip aperture magnitude (Alberts, Saling et al. 2002; Rand, Smiley-Oyen et al. 2006; Rand, Squire et al. 2006). A common control law governing this interaction in different task conditions has yet to be published. Recently, from experimental data of RTG, Rand (Rand, Squire et al. 2006) has found evidence for a law which states when hand distance to the object becomes less than a linear function of aperture size, hand velocity and hand acceleration, grasp closure will be initiated. This law matched data well for the hand closing phase when both distance and speed were varied.

Alternative models for control of the hand have been proposed. One contrary view (Smeets and Brenner 1999; Smeets and Brenner 2001) suggests that the hand and arm are controlled by a single mechanism composed of a generalized reaching movement, involving independent finger trajectories for optimum contact with the surface of the object. This alternative view has gained additional support from an experiment where response to an obstacle placed near the target object was guided more by placement of individual digits than grasp aperture (Biegstraaten, Smeets et al. 2003). Using an obstacle avoidance task (Mon-Williams and McIntosh 2000) two opposing models of prehension control have directly been compared. The study largely supported the traditional visuomotor channel hypothesis (Jeannerod 1988). A ‘third-way’ hypothesis was proposed (Mon-Williams and McIntosh 2000) which retains aspects of the two theories; such that the control system transports either the tip of the thumb or the tip of the index finger with relatively independent control of the grip formation. Finally, some evidence (Santello and Soechting 1997; Vilaplana and Coronado

2006) suggests that grasp can be described by a small number of postural synergies and may be controlled based on a temporal weighting of these synergies. Analysis of grasp movements involving different hand postures combined with and without vision or sensory input for example (Santello and Soechting 1997) suggested that the hand is controlled as a single unit.

Coordination of RTG requires the central nervous system (CNS) to receive information about the movement so that adjustments can be made. Feedback from vision and proprioception can be used in the latter stage of the movement to guide the hand as it moves towards the object. Evidence that this sensory information is used to aid coordination comes from studies of deafferented patients who, when deprived of vision, demonstrate a delayed grasp onset, longer grasp closure time, increased deceleration time and reopening of grasp (Gentilucci, Toni et al. 1994; Simoneau, Paillard et al. 1999). However, the minimum time needed for a motor response of this feedback to occur is estimated at about 100ms (Jeannerod 1988). Prior to this time there is evidence for a mechanism to make early adjustments in the trajectory. This works by comparing target position with an instantaneous internal estimate of hand position (internal model), and this information is used to modify the ongoing motor command (Desmurget, Epstein et al. 1999; Desmurget and Grafton 2000). Reaching movements involve both these processes, with very fast movements presumably relying more on feedforward control.

Brain areas and pathways involved in RTG coordination

Motor coordination for prehension relies upon a complex neural network with different brain structures each contributing a specific role in RTG function. Particular aspects of motor coordination are disturbed when certain parts of the network are lesioned after stroke. The following subsection will outline the importance of the parietal lobe and the cerebellum for the coordination of reach to grasp. Following sections will describe RTG deficits identified in stroke patients with particular reference to patients with damage to these brain areas.

Parietal involvement in RTG coordination

Two parietofrontal neural circuits have been identified in primates that contribute to the control of coordination of transport and grasp. For proximal muscles involved in transport, a medial circuit is described, which is concerned with object location. The medial circuit is associated with areas of the superior parietal lobule (area 'MIP'/PRR (parietal reach region)) and the dorsal premotor Brodmann area 6. For the distal musculature involved in grasping, a lateral circuit is described which is concerned with the size and shape of the object. The lateral circuit is associated with the inferior parietal lobule (in particular the anterior intraparietal area) and the ventral premotor area 6 (Fattori, Breveglieri et al. 2009). Overlap exists so that both circuits are partially involved in both processes and the dorsomedial pathway contributes to the integration of the two components (Fattori, Raos et al. 2010; Vesia and Crawford 2012).

The posterior parietal cortex (PPC) has specialised areas for reaching. It is involved in spatial monitoring (Buneo, Jarvis et al. 2002), as evidence suggests that internal spatial monitoring is lost in monkeys with lesions involving the PPC, area 7 (Batista and Andersen 2001). Humans with PPC lesions show directional errors in reaching (Binkofski, Dohle et al. 1998). Because humans with such lesions also show problems with grasp formation, it has been suggested that the PPC has a role in coordination as the hand nears the target (Mackay WA 1992). Mechanisms for controlling the pre-shaping of grasp are thought to be located within the anterior intraparietal sulcus in the PPC (Binkofski, Dohle et al. 1998). The PRR neurons within the PPC are selectively activated during reaches and are thought to encode target location (Batista and Andersen 2001). Results from studies using TMS have suggested the PPC may be involved in computing current motor error to allow updating of muscle activation pattern (Desmurget, Epstein et al. 1999), so this area could be involved in the comparison of timing of transport and grasp. The parietal cortex appears to play a dual role in feed-forward and feedback control of reach to grasp; transforming visual information into a motor plan (Crawford, Henriques et al. 2011) and making online corrections according to visual feedback (Iacoboni 2006).

Cerebellum involvement in RTG coordination

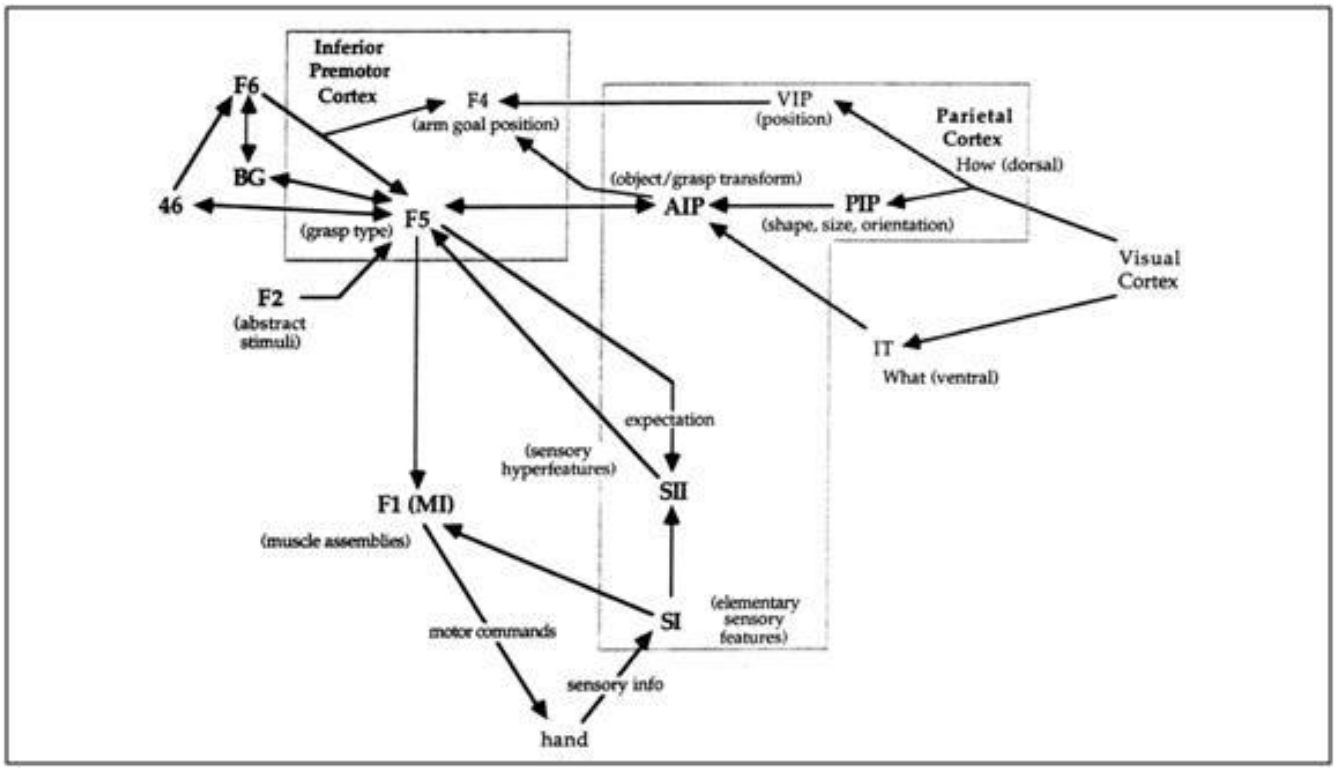
It has been proposed that the cerebellum provides an internal state estimate or sensory prediction used for the online control of movements (Miall 1998; Ebner and Pasalar 2008; Miall and King 2008). These predictive state estimates are used to coordinate actions by the different effectors including the eye, the hand and the arm (Miall and Wolpert 1996). The cerebellum may integrate the independent motor processes for reach and grasp into one common motor program (Jakobson, Archibald et al. 1991; Saling, Alberts et al. 1998). As previously indicated it is unclear whether reach to grasp depends either upon a precise central timing mechanism or alternatively an internal positional representation of handpath (Wolpert and Kawato 1998; Miall and Reckess 2002; Hore and Watts 2005) or both. The cerebellum may adjust the relative strength and timing of muscle activations based upon internal predictions about the likely outcome of the effector (Miall, Weir et al. 1993; Wolpert and Kawato 1998). The cerebellum, (particularly the posterior part of lobule VI, extending into lobule V of the anterior arm area and the posterolateral cerebellum) (Donchin, Rabe et al. 2012) is also important for making rapid adjustments to perturbations by modifying automatic movements that are dependent upon visual sensory information. The cerebellum probably plays a greater role in controlling learned, automatic movements which require little attention to detail. In comparison to controls cerebellar subjects showed marked degradation of a practiced movement when required to focus attention towards an audio letter sequence task (Lang and Bastian 2002). These findings, indicate firstly that the cerebellum may be important for shifting movement performance of attention demanding tasks controlled by higher order structures (i.e., more prefrontal lobe involvement), to a more automatic state. Secondly the cerebellum may be important for the execution of these movements based upon learned internal representations of the motor pattern.

Other areas involved in RTG coordination

Other areas which are active during RTG include the supplementary motor area (SMA) (Binkofski, Dohle et al. 1998) and the Basal Ganglia (BG). According to the Fagg-Arbib-Rizzolatti-Sakata FARS model *(Fagg and Arbib 1998) (see figure 1.2) the SMA (F6*) prepares the ventral pre-

motor regions for action and initiates the execution of the program; and the Basal Ganglia are involved in the selection of the motor program and managing motor sequencing, although these two processes may not be mutually exclusive. The red nucleus (via the rubrospinal tract) appears to influence control of metacarophalangeal extension at the appropriate phase of limb transport (Gibson AR 1998; van Kan and McCurdy 2002). Further active areas include the posterior limb of the internal capsule (Wenzelburger, Kopper et al. 2005) and the reticular formation, rostral mesencephalon and superior colliculus (Gibson AR 1998). Based upon the neural connections, it is speculated that these are involved in mediating sensorimotor transformation from intention (spatial coordinates) to action (motor signals). With respect to action, EMG studies involving macaques (Park, Belhaj-Saif et al. 2001; Saleh, Takahashi et al. 2012) have revealed overlap between reach and grasp areas in the upper limb area of the primary motor cortex. Both proximal and distal musculature are activated by single neurons according to spatiotemporal patterns of coordinated reach to grasp movements as opposed to single joint movements (Saleh, Takahashi et al. 2012).

Figure 1.2. The complete FARS *(Fagg-Arbib-Rizzolatti-Sakata)* model (Fagg and Arbib 1998). The primary areas are IT (inferotemporal cortex), VIP (ventral intraparietal), PIP (posterior intraparietal), AIP (anterior intraparietal), area 46, BG (basal ganglia), F1 (primary motor cortex), F2 (dorsal premotor cortex), F4 and F5 (of the inferior premotor cortex) and F6 (pre SMA).



Coordination of reach to grasp in people with stroke

This thesis will be restricted to the discussion of studies examining movement with the arm contralateral to the lesion, as these are of most interest to the clinician. The majority of existing studies of coordination after stroke have involved participants who might be described as heterogeneous in that they have symptoms of hemiparesis in common (i.e. unilateral weakness and slowness) but their lesions might be quite varied (e.g. more or less localised to the motor cortex and/or corticospinal tract) or even not documented, except from the clinical examination based on signs and symptoms. These will be discussed first, followed by the small number of existing lesion specific studies. Heterogenous groups have demonstrated a longer movement duration (Thielman, Dean et al. 2004; Lang, Wagner et al. 2005; van Vliet and Sheridan 2007), increased deceleration phase (Farne, Roy et al. 2003; van Vliet and Sheridan 2007), decreased movement smoothness (increased number of peaks in the velocity profile, or its derivatives, acceleration and jerk) (Thielman, Dean et al. 2004)

both indicating a reliance on feedback rather than feedforward control (Nagasaki 1989), lower peak velocity (Lang, Wagner et al. 2005; Nowak, Grefkes et al. 2007; van Vliet and Sheridan 2007), increased variability of size and timing of peak velocity (vanVliet, Kerwin et al. 1995) and larger endpoint errors (Lang, Wagner et al. 2005; van Vliet and Sheridan 2009), compared to normal. For grasp, there is increased variability of maximum aperture size (Lang, Wagner et al. 2005; van Vliet and Sheridan 2007) and maximum aperture can occur earlier than normal (Lang, Wagner et al. 2005; Nowak, Grefkes et al. 2007). There is a cost to efficiency with such abnormalities, implied by optimization models for explaining movement control, such as minimum jerk (Flash and Hogan 1985) torque change (Uno, Kawato et al. 1989) or variance of final arm position (Harris and Wolpert 1998).

There are few studies that specifically address the temporal coupling between components. One study (van Vliet and Sheridan 2007) compared stroke and healthy subjects reaching for cups of different sizes. Although start of aperture and start of transport were significantly correlated in this heterogenous group of patients with stroke, this correlation was significantly weaker than in healthy subjects when reaching for a larger cup. For coupling of MA and PD, these events were significantly correlated in stroke subjects but the correlation was weaker than healthy subjects when reaching fast for a small cup. Wu et al also found an impaired ability to adjust timing of grasp for different sized objects (Wu, Chou et al. 2008).

Michaelsen et al (Michaelsen, Jacobs et al. 2004) found temporal coordination to be mostly intact in a mixed group of patients, with the MA and time of MA, expressed as percentage of movement duration, and the temporal delay between time to PV and time to MA, expressed as percentage of movement duration, not significantly different to healthy subjects. However, four out of the 19 patients showed abnormal timing of grasp, with two patients keeping the grasp aperture constant throughout transport, and two suddenly opening the hand at the end of transport. Another study (Sangole and Levin 2009), showed delays in palmar aspect (oblique, distal transverse and longitudinal arches) hand pre-shaping which normally conforms with the object prior to reaching

maximum finger aperture. The authors suggest impaired coordination between the modulation of anticipatory hand shaping and changes in finger aperture after stroke.

Because of hemispheric specialization, patients with right-sided lesions may have more difficulty in processing visual feedback for movement adjustments, than those with left sided lesions. One study (Winstein and Pohl 1995) found that participants with right sided lesions experience more difficulty with the closed loop phase of an aimed movement, prior to target contact, when visual processing is necessary for accuracy. Further work suggests a left hemisphere specialization for the visuomotor transformation of grasp preshaping and a right hemisphere specialization for transport-grasp coordination (Tretriluxana, Gordon et al. 2009).

The ability to adjust one component in response to perturbations in the other is also affected by stroke. When transport speed is increased, stroke patients open the hand wider as do healthy individuals (Wing, Turton et al. 1986) and MA occurs later in the movement, but the latter adjustment is not as large as in healthy subjects (van Vliet and Sheridan 2007). The stroke participant may therefore have trouble responding to changes in object size. Although there may be some preservation of the control strategy for coordination of reach to grasp, as has been shown for other aspects of upper limb motor control (Beer, Dewald et al. 2000; Mihaltchev, Archambault et al. 2005).

Knowledge gained from studies of heterogenous groups of patients is useful, but there is also a growing amount of information about the effect of lesions in specific areas involved in control of reach to grasp. This research is potentially of great use to therapists, who are likely in the future to be able to direct targeted therapies to patients with different lesions, and this will be summarised in the next sections.

Coordination of reach to grasp in participants with parietal lesions

A clinical assessment of 32 patients with parietal stroke (Ghika, Ghika-Schmid et al. 1998) reveals abnormal anticipatory hand shaping, dysmetria, striking hypertonia with unpredictable variations toward hypotonia in the first 5 days, followed by hypotonia, and laterodeviation or

levitation of the arm (when held in a extended position in front of the body). More specific to reach to grasp, Binkofski (Binkofski, Dohle et al. 1998) describes the deficits of 6 subjects with stroke affecting the lateral bank of the anterior intraparietal sulcus in the PPC. These patients show poor preshaping of the hand in the acceleration phase, increased and more variable aperture in the deceleration phase, and a later maximum grasp aperture as percentage of movement duration, compared to healthy subjects, but almost normal velocity profiles, indicating the performance of transport was preserved. Jeannerod also found that transport is preserved after a posterior parietal lesion whereas the grasp shows deficits including a larger than normal maximum aperture (Jeannerod 1986; Jeannerod 1994). A lesion in the dorsal posterior parietal cortex as reported in a single case study, causes a lack of the usual modulations to changes in object size and location (Roy, Stefanini et al. 2004). Patients with lesions in the superior parietal lobe and adjacent intraparietal sulcus commonly demonstrate optic ataxia, where misreaching (missing the target) and larger than normal maximum aperture (Jakobson, Archibald et al. 1991) occurs to peripheral vision targets while looking at a central fixation point, but when fixating the target, no misreaching occurs (Wolpert, Goodbody et al. 1998).

Coordination of reach to grasp in participants with Cerebellar lesions

Damage to the cerebellum appears to disrupt the temporal program for coordinated multi-joint movement. For example ball-throwing inaccuracy in cerebellar patients is associated with variable and delayed finger opening and ball release times (Timmann, Watts et al. 1999). In another trial of pointing movements (Topka, Konczak et al. 1998) cerebellar patients show more variable endpoints, and longer movement durations, with lower peak hand acceleration and a longer deceleration phase, in comparison to healthy subjects. Notably these deficits are accentuated during fast movements. After cerebellar stroke deficits observed during movements to predictable and unpredictable targets suggest the cerebellum has a greater role in planning goal directed aiming movements rather than updating the ongoing movement (Fisher, Boyd et al. 2006). The hypermetria and loss of coordinated joint action associated with cerebellar damage are thought to occur as a result of impaired predictive

control (Miall 1998). Furthermore unilateral cerebellar lesions are known to affect aimed movements of both arms (Immisch, Quintern et al. 2003; Fisher, Boyd et al. 2006) therefore RTG deficits might be expected bilaterally.

To date few studies have examined reach to grasp movements in cerebellar patients. One study involving patients with cerebellar degeneration demonstrates slowed movements with more deviant trajectories and larger hand apertures during reach to grasp (Brandauer, Hermsdorfer et al. 2008). Since the cerebellum is known to be involved in the coordination of complex movements, it is suggested that cerebellar impairments disrupt the relationship between transport and grasp aperture (Rand, Shimansky et al. 2000). Rand et al tested reach to grasp in the hand ipsilateral to the lesion, in six patients with cerebellar lesions and healthy controls. Both fast and comfortable paced RTG movements either to a vertical dowel or to a small cross were made to examine the effects of accuracy constraints. For healthy controls the time between peak wrist velocity and maximum grasp aperture is highly consistent across conditions, whereas for cerebellar patients the relationship is variable regardless of the accuracy requirement. This group also show multiple peaks in the hand velocity profile and maximum grasp aperture (expressed as a percentage of movement duration) occurs earlier and is larger than for healthy subjects. In terms of the relationship between transport and grasp, the time from peak velocity to time to maximum aperture is significantly smaller in cerebellar subjects.

Distinct deficits have been found in the coupling of reach and grasp movements in cerebellar subjects (Zackowski, Thach et al. 2002) which suggest that the cerebellum may be involved in combining the two movements into a single motor program. There is within and between subject variability of time to MA, which occurs both before and after peak deceleration. MA is also higher and shows multiple peaks, which respectively could suggest compensation and correction for inaccurate movements. Decomposition or sequencing of movements may be the result of impaired parallel processing between the shoulder, elbow and hand (Timmann, Watts et al. 1999) or abnormal on-line processing of proprioceptive information during RTG (Shimansky, Saling et al. 1997).

In summary, there is some preservation of the temporal coordination of reach to grasp after mild to moderate cortical and cerebellar stroke, however a number of motor deficits have also been described. Research suggests that lesions involving the cerebellum may disrupt the control law governing the spatiotemporal coordination for prehension, although further studies are necessary to confirm this. The main types of lesions that will impact on coordination of reach to grasp will involve the parietal lobe, or cerebellum. More studies are needed of coordination in specific lesion groups to increase depth of understanding of different lesion effects, so as to inform future more targeted therapies than we have at present. Previous studies have not directly compared the RTG deficits of these two patient groups with lesions to either the parietal lobe or cerebellum. Motion tracking of RTG affords a quantitative and objective measurement of motor deficit which is sensitive to small performance changes (Krakauer 2005). This comparison may provide new insights on which to base more targeted interventions.

Broad research questions

It is known that the parietal cortex and the cerebellum both play an essential role in goal directed hand movement (Sakata, Taira et al. 1997; Rand, Shimansky et al. 2000). To our knowledge however, there is no one study which has compared the effects of parietal and cerebellar lesions upon reach and grasp coordination. It is suggested that further work is required to identify the specific effects of different areas of brain damage upon upper limb function and to consider possible implications for rehabilitation. Consequently the first experimental study in Chapter 2 aims firstly to compare specific RTG coordination impairments associated with patients following stroke involving either the right parietal lobe or cerebellum. In healthy subjects (Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991), perturbation of one of the components of transport or grasp has shown that another component is adjusted in response. Using the same paradigm this Phase I study also aims to quantify how these patients adjust reach-to-grasp when hand transport is perturbed in order to verify whether the online adjustments necessary for good coordination are intact. This knowledge is important for clinicians attempting to understand the problems of different patients

presenting with stroke. It is important for researchers for more informed evaluation of current treatments and for the design of novel treatment interventions targeted towards different patient groups.

A systematic literature review (Chapter 3) establishes a profile of existing treatments used to correct coordination deficits in the arm after stroke and to determine their effectiveness**.** Insufficient evidence was identified to provide strong recommendations about the effect of interventions for improving hand and arm coordination after stroke. The review follows systematic guidelines produced by the Joanna Briggs Institute (JBI) and represents collaborative work. Trudy Pelton was the lead author, Professor van Vliet the second reviewer and Dr Hollands acted as the third independent reviewer. The paper has been peer reviewed and published in both the Joanna Briggs Institute Library of Systematic Reviews (Pelton, Van Vliet et al. 2011) and the International Journal of Evidence Based Medicine (Pelton, van Vliet et al. 2011).

There is strong evidence that the effects of rehabilitation following stroke are highly specific (Bayona, Bitensky et al. 2005; Foley, Teasell et al. 2005-2013). Understanding the specific impairments of reach and grasp will help to develop more refined treatment strategies for therapists and researchers. The current work contributes to the growing body of evidence, which shows potential for rehabilitation even in chronic stroke and aims to provide direction for upper limb treatment of patients with mild to moderate hemiplegia. In Chapter 4, a second experimental study measures the effectiveness of a specific intervention targeted for the rehabilitation of reach and grasp after either right parietal or cerebellar stroke. The novel treatment design incorporated evidence of the effectiveness of current methods for rehabilitation of RTG after stroke (Chapter 3) together with knowledge of the specific coordination deficits associated with the lesions to the right parietal lobe or cerebellum (Chapter 2). Unlike previous work the intervention is targeted at hypothesized mechanisms for specific coordination deficits. The effect of metronome cued RTG functional practice in patients with mild to moderate impairment is measured in a Phase I proof of principle case study

design involving 6 patients. The study concluded that metronome cued RTG functional practice was well tolerated and showed some potential for improved motor control of reach to grasp.

The present chapter has described how the hand and arm movements are normally coordinated to control skilled RTG movements. It is clear from the above overview that both the cerebellum and the parietal lobe play an integral role in the neural network for coordinated RTG. It is less clear how damage to the specific regions compares in an objective measure of RTG. A comparison between healthy controls and stroke patients with lesions to the either the cerebellum or right parietal lobe of is presented in the following chapter. Motion tracking was used as a sensitive and quantitative measure for potential differences. The experimental study examined the ability to coordinate direct RTG movements and movements to an object where the target location was perturbed immediately after movement onset.

CHAPTER 2: A COMPARISON OF PREHENSION DEFICITS FOLLOWING EITHER A RIGHT PARIETAL OR CEREBELLAR LESION.

Abstract

Background: Control of transport to grasp requires coordination between the components of hand transport towards the object and hand shaping to enclose it; however the mechanism is poorly understood and the differential contributions of the cerebellum and parietal lobe have not been identified. Objectives: Contrasting impairments to transport to grasp (RTG) coordination were examined in patients following either right parietal or cerebellar lesions during unperturbed and perturbed movements. Method: A two-factor design with one between subject factor (right parietal stroke; cerebellar stroke; controls) and one within subject factor (presence or absence of perturbation) examined correction processes used to maintain coordination between transport to grasp in the presence of an object location perturbation. Sixteen chronic stroke participants (8 with right parietal lesions and 8 with cerebellar lesions) were matched in age (mean=61years; standard deviation=12) and hand dominance with 16 healthy controls. Infrared cameras recorded the motion of hand and arm movements during unperturbed baseline trials (10) and unpredictable trials (30) in which the target was unpredictably displaced to the left (5) and right (5) or remained fixed (30). Results: Despite prolonged movements and spatial variability in patients with either parietal or cerebellar lesions, the correlations between key temporal events of the transport and grasp components during both unperturbed and perturbed trials were comparable to age matched controls. Conclusion: Coordination between the hand and arm was controlled in these patients even though normally it might be controlled by the parietal lobe and or cerebellum. Perhaps structures such as the PPC were undamaged in these participants. Alternatively impaired coordination was compensated for in a predictive way with slowed movements, as faster movements would increase interaction torques. A third possibility is that coordination was previously impaired but had recovered by the time of testing.

Introduction

Coordination is a crucial part in successful control of transport to grasp. There are several aspects of coordination involved, for example the arm with the trunk, the shoulder with the elbow and the hand with the arm, the latter of which is the focus of the present study. The shaping of the hand to the object by one set of muscles relies heavily on predicting the movement of the arm, moved by another set of muscles (Diedrichsen, Criscimagna-Hemminger et al. 2007). Studies in healthy adults (Jeannerod 1984; Wallace SA 1990) have demonstrated spatiotemporal coordination between phases of reach and grasp, suggestive of a single coordinated unit. Contrasting evidence in favour of independence between the transport and grasp components (Marteniuk, Leavitt et al. 1990; Gentilucci, Castiello et al. 1991; Jakobson and Goodale 1991; Kudoh, Hattori et al. 1997), has shown that the two motor programs may not be so tightly coupled. For instance (Gentilucci, Castiello et al. 1991), correlations between the time of peak deceleration and the time of maximum hand aperture were not reliable across different conditions where transport and grasp were manipulated by the distance and type of grasp.

It is known that the parietal cortex and the cerebellum both play an essential role in goal directed hand movement (Sakata, Taira et al. 1997; Rand, Shimansky et al. 2000). To our knowledge however, there is no one study which has compared the effects of cortical and cerebellar lesions upon transport and grasp coordination. Studies using kinematic analysis and involving patients with specific lesion location may help to determine detailed effects of damage to brain regions and pathways upon upper limb function. This first experimental study aimed to identify specific RTG coordination impairments associated with either right parietal or cerebellar lesions. The study aimed to further test coordination between the arm and the hand in these participants following a perturbation to the transport component. In Control participants (Paulignan, Mackenzie et al. 1991) the hand movement should adjust in response to rapid changes in object location.

Research involving a heterogenous group of stroke patients with mild impairments, has investigated the spatiotemporal relationships between transport and grasp (VanVliet and Sheridan

2007). Movements were performed at both fast and preferred speeds and to small and larger objects. The time of maximum aperture and time of peak deceleration correlated significantly ($p<0.05$) in all conditions for both groups, although some of the correlations were numerically small (Pearson product-moment correlation co-efficient r for the two groups ranged from 0.3 to 0.71). The study demonstrated that coordination between transport and grasp in patients was not as tightly coupled for stroke as with age matched controls. In the condition which most challenged accuracy (i.e. the fast paced condition with small objects) the two events were more highly correlated in healthy participants. The study by van Vliet (VanVliet and Sheridan 2007) examined coordination of transport to grasp in patients with uncontrolled lesion location, whereas the following subsections involve patient contrast studies.

Coordination of transport to grasp in participants with parietal lesions

Previous research has established an important role for the parietal lobe in the coordination between the hand and arm during RTG movements (Mackay WA 1992; Desmurget, Epstein et al. 1999; Fattori, Breveglieri et al. 2009) and specific RTG deficits following parietal lesions (Jeannerod 1994; Binkofski, Dohle et al. 1998; Frak, Paulignan et al. 2006). Jeannerod (Jeannerod 1986) found that transport was preserved after a posterior parietal lesion whereas the grasp showed deficits including a larger than normal maximum aperture. A lesion in the dorsal posterior parietal cortex, in a single case study, caused a lack of the usual modulations to changes in object size and location (Roy, Stefanini et al. 2004). Another study which assessed the impairments of 32 patients with parietal stroke (Ghika, Ghika-Schmid et al. 1998) using videotape recordings, revealed abnormal anticipatory hand shaping and dysmetria. Binkofski (Binkofski, Dohle et al. 1998) described the deficits of 6 subjects with stroke affecting the lateral bank of the anterior intraparietal sulcus in the PPC. These patients showed poor pre-shaping of the hand in the acceleration phase, increased and more variable aperture in the deceleration phase, and a later maximum grasp aperture as percentage of movement duration, compared to control subjects, but almost normal velocity profiles, indicating the performance of transport was preserved. The transport component may also be impaired after damage

to the parietal lobe. Patients with lesions in the superior parietal lobe and adjacent intraparietal sulcus commonly demonstrate optic ataxia, where mistransporting (missing the target) and larger than normal maximum aperture (Jakobson, Archibald et al. 1991) occurs. This is normally observed during transport to peripheral vision targets whilst maintaining a central fixation point; when allowed to fixate to the target, no mistransporting occurs(Wolpert, Goodbody et al. 1998). A recent review (Buneo and Andersen 2006) indicates that the PPC plays a role to convert sensory information into motor commands and also for integrating sensory input with previous and ongoing motor commands to maintain a continuous estimate of arm state that can be used to update present and future movement plans. Recent studies (Desmurget, Epstein et al. 1999; Tunik, Frey et al. 2005) involving transcranial magnetic stimulation (TMS) in control participants, have evidenced the important contribution of the parietal lobe to the online monitoring and adjustment of the reaching and grasping actions.

Coordination of transport to grasp in participants with cerebellar lesions

Since the cerebellum is known to be involved in the coordination of complex movements, it has been hypothesised that cerebellar impairments disrupt the relationship between transport and grasp aperture (Rand, Shimansky et al. 2000). Rand et al (2000) tested transport to grasp in the hand ipsilateral to the lesion, in six patients with cerebellar lesions. Greater variability was seen in the hand velocity profile of cerebellar participants, with several velocity peaks compared to control subjects. Maximum grasp aperture (expressed as a percentage of movement duration) occurred earlier and was larger than for control subjects. In terms of the relationship between transport and grasp, the time from peak velocity to time to maximum aperture was significantly smaller and more variable in cerebellar subjects.

In another trial of pointing movements (Topka, Konczak et al. 1998) patients showed more variable endpoints, and longer movement durations, with lower peak hand acceleration and deceleration and a longer deceleration, compared to control subjects and these deficits were accentuated in fast movements. The role of the cerebellum is likely to be greater in the planning rather than updating of aimed movements. For example, Fisher et al (Fisher, Boyd et al. 2006) found that

cerebellar subjects had errors in target direction and amplitude specification, despite ample preparation time, whereas final position was minimally impaired suggesting preserved ability to adapt or update the movements. Cerebellar damage would result in more importance being placed upon on-line correction which would result in a longer deceleration phase. Conversely, the cerebellum is also implicated in updating goal-directed movements (Wolpert and Kawato 1998; Donchin, Rabe et al. 2012).

During transport and grasp patients with cerebellar degeneration have demonstrated slower movements, a more deviant trajectory and a larger hand aperture (Brandauer, Hermsdorfer et al. 2008). Distinct deficits have been found in the coupling of the transport and grasp movements in cerebellar subjects (Rand, Shimansky et al. 2000; Zackowski, Thach et al. 2002) which suggest that the cerebellum may be involved in combining the two movements into a single motor program. The cerebellar group showed within and between subject variability of time to MA which occurred both before and after PD. MA for this group was also larger and showed multiple peaks which respectively could suggest compensation and correction for inaccurate movements. Alternatively, decomposition or sequencing of movements may be the result of impaired parallel processing between the shoulder, elbow and hand (Timmann, Watts et al. 1999) or abnormal on-line processing of proprioceptive information during RTG (Shimansky, Saling et al. 1997).

To summarise, there is some preservation of the temporal coordination of transport to grasp after mild to moderate parietal or cerebellar stroke, however a number of motor deficits have also been described. Research suggests that lesions involving the cerebellum may disrupt the control law governing the spatiotemporal coordination for prehension, although further studies are necessary to confirm this. The main types of lesions that will impact on coordination of transport to grasp will involve the parietal lobe, or cerebellum. There is a paucity of patient contrast studies which have examined the correlation between timing events of arm and hand during RTG movements. More studies are needed of coordination in specific lesion groups to increase depth of understanding of different lesion effects, so as to inform future more targeted therapies than we have at present.

Object perturbation

In contrast to the studies described in previous sections which used correlation between the hand and arm in naturally varying transport and grasp, the aim of perturbing the object is to cause the subject to begin one direction of movement, then alter the direction during movement. Perturbing the location of the target allows examination of the resulting temporal adjustments made to the grasp component. Adaptation for a new spatial position of an object after perturbation may involve modification of pre-defined program(Goodale, Pelisson et al. 1986) .This paradigm has previously been informative of coordination of transport-to-grasp in control subjects, as it tests ability to adjust timing of grasp for alteration to hand transport. Paulignan et al (Paulignan, MacKenzie et al. 1990; Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991) found that unexpected perturbations in the object location during transport to grasp produced adjustments to both the transport and grasp components. Paulignan et al concluded that the two components are coordinated spatiotemporally. In control subjects also (Gentilucci, Chieffi et al. 1992), perturbation of either one of the components of transport or grasp at movement onset has shown that the other component is adjusted in response.

The premise of a tight-coupling between the two components as based upon correlations even though they were not always numerically large and prompted the development of a model for the temporal coordination of transport and grasp (Hoff and Arbib 1993). The model describes the interaction between the two components under a variety of conditions, including perturbation. The transport and grasp components are controlled by two independent neuromotor synergies, which in turn are coordinated by a higher-level synergy that includes both spatial and temporal factors.

Perturbation studies involving changes to object location or size at movement onset have shown that the adjustment of transport occurs before the grasp component (Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991; Gentilucci, Chieffi et al. 1992; Castiello, Bennett et al. 1993; Kudoh, Hattori et al. 1997). A comparison between straight and curved prehensile movements (Haggard and Wing 1998) which included perturbation, suggested a scheduling of motor control

systems, whereby grasp aperture processing was based upon transport information. A hierarchical organization of transport over grasp was proposed. An alternative organization where transport is considered secondary to grasp has been raised (Roy, Paulignan et al. 2006; van de Kamp, Bongers et al. 2010) following observations that the coordination mechanisms are more efficient to correct for grasp size than for location perturbation.

Using the same object location paradigm as reported by Paulignan 1991(Paulignan, Mackenzie et al. 1991), the present study aimed to quantify how patients with right parietal or cerebellar lesions adjust transport-to-grasp when hand transport is perturbed and to verify whether the online adjustments necessary for good coordination are intact. This knowledge is important for understanding the problems of different patients presenting with stroke in the clinic, and to consider the potential benefit of treatment interventions targeted towards different patient groups.

There is limited understanding about the mechanisms for on-line modification of transporting movements and the involvement of specific regions or pathways of the brain (Hesse and Franz 2009). Transport goals are represented in the parietal region and have to be rapidly switched in response to perturbation (Snyder, Batista et al. 2000). On-line corrections during target errors depend upon the integrity of the posterior parietal cortex (Desmurget, Epstein et al. 1999). Pisella et al (Pisella, Grea et al. 2000) provide patient evidence for the involvement of the parietal lobe in rapid modifications of pointing movements. It was observed in a single case study that whilst unperturbed movements were normal in a patient with bilateral PPC lesions, on-line adjustments during perturbed movements were slow and deliberate.

Evidence suggests that the cerebellum plays an integral role visuomotor adaptation. For example (Donchin, Rabe et al. 2012) patients with focal cerebellar lesions showed impaired motor learning of a cursor movement task with the handle of a Robot when a proportion of the trials involved perturbations to either the visual rotation of the cursor or a force field of the manipulandum. Similarly (Tseng, Diedrichsen et al. 2007), the path travelled during pointing is less efficient than controls following on-line correction of movements in responsee to perturbation. Furthermore (Day,

Thompson et al. 1998) patients with cerebellar lesions show that reaching path corrections based upon visual sensory information are characterized by excessive deviations and abnormal oscillations.

In summary the coordinated control of transport to grasp with object location perturbation is a multi faceted challenge. It involves the integration of sensory signals from multiple modalities (principally visual information concerning the object and its relative position; and proprioceptive information about the position of the arm and the hand). It requires the feedforward selection of perhaps one or two coupled motor commands for transport and grasp together with a forward representation of the desired movement. Smooth movement is dependent upon online updating of the initial pattern of muscle activation and detection of error between the actual positions of object relative to the hand. Large errors which are instigated by the introduction of a perturbation require either rapid modification of an ongoing motor program or rapid onset of a new motor program and cessation of the old motor program.

The above studies are inconclusive as to whether the hand and arm are coordinated as a single unit or as two closely linked but independent motor programs. It is also unclear whether coordination is controlled by spatial and/or temporal parameters and which area or areas and pathways of the brain are responsible for coordinating the two components. Since the research suggests that both the PPC and the cerebellum are involved in the process (Desmurget and Grafton 2000) the present study will compare transport to grasp coordination and the response to object location perturbation in patients with parietal and cerebellar lesions with age and hand matched controls.

It was hypothesised that for unperturbed transport-to-grasp the wrist velocity profiles of control participants would show a characteristic symmetrical pattern indicative of a ballistic pre-planned movement, followed by controlled deceleration under visual guidance. These subjects would demonstrate temporal coordination during transport to grasp based upon intact processing of visual and proprioceptive information and predictive state dependent estimates which facilitate coordinated control of the concurrent motor schemas for the hand and arm. Specifically the time of maximum hand aperture was expected to be linked with time of peak velocity and the time of deceleration.

Control subjects would also show parameterization for the object size with maximum hand aperture generally 20% greater than the diameter of the object (Jeannerod 1981), which in this case was 1.5cm.

In response to perturbations in object location the control group would demonstrate rapid movement modification and temporal rescaling is anticipated due to the temporal linking between the two motor schemas. It was expected that perturbation of object location would influence both transport and grasp components. Peak wrist velocity would occur earlier for perturbed movements and with lower amplitude. Modification of the grasp program would appear as a double peak in the amplitude of grasp aperture profile. The amplitude of the first peak was expected to be smaller and occur earlier than the single peak observed during unperturbed movements. The timing of the last peak velocity was expected to correlate with the last aperture peak.

During unperturbed trials a parietal lobe lesion was expected to cause the wrist velocity profile to appear asymmetrical; as a result of the prolonged deceleration phase required for a more corrective mode of movement control, mediated partly with vision as opposed to the movement being mainly pre-programmed. Impaired sensory perception and or integration would contribute to spatial errors and reduced movement smoothness detected by multiple velocity peaks and increased movement trajectory. Overall movement time was therefore expected to be longer and peak velocity will be early and reduced. With intact state dependent estimation parietal participants were expected to demonstrate preserved temporal coordination between the hand and arm but the key temporal events were expected to show more variance between them than for control participants. It was anticipated that parietal stroke participants would show poor control for aperture parameterization based upon impaired visual and proprioceptive mapping and difficulties processing visual information during the deceleration phase. On-line corrections to target location perturbation would be slow and deliberate after parietal lobe damage due to difficulties mapping the new transport goal and compensation. Parietal lobe stroke patients were expected to retain an element of temporal rescaling as the state dependent coordination between the motor schemas for the hand and arm remains intact.

The correlation between key events for transport and grasp was expected to be weak for participants with cerebellar lesions as a result of faulty internal state estimation and impaired coordination of the different effectors. In contrast to the controls, spatial and temporal variability was expected to be high, movement time would be increased and peak velocity reduced in the absence of predicted sensory outcome motor commands and poor on-line adjustments. Due to abnormal velocity control (Haggard, Jenner et al. 1994; Rand, Shimansky et al. 2000) time to maximum aperture and time to aperture onset were expected to be early and variable, similarly maximum aperture would be larger and more variable. It was anticipated that cerebellar participants would demonstrate multiple peaks in wrist velocity and aperture size as a result of multiple on line corrections prior to grasp and movement decomposition or sequencing. Overall manipulation time would be longer than for controls. The cerebellum is important for modifying automatic movements which are dependent upon concurrent visual and proprioceptive sensory information and require rapid adjustments to perturbations. Based upon poor state estimation for coordination between different effectors it was hypothesised that there would be disruption to the temporal coordination with no evidence of temporal rescaling between the hand and the arm on the second sub-movement. It was expected that these participants with intact sensory integration but impaired modification programming would adopt an alternative strategy that would be a slow and deliberate correction to perturbation, since rapid cerebellar corrections are likely to result in inaccuracies this group would perhaps substitute a fast response under cerebellar control with more delayed cortical control.

In summary right parietal lobe patients were expected to demonstrate preserved temporal coordination during unperturbed movements and temporal rescaling after perturbation. In contrast cerebellar patients were expected to show asynergia, temporal variance between transport and grasp and a lack temporal rescaling after perturbation.

Methods

Setting

Data collection and analysis took place in the 'SyMoN' laboratory based in the Behavioural Brain Sciences Centre at the University of Birmingham, UK.

Design

The experiment was conducted in a single session and employed a two-factor design with one between subject factor (parietal, cerebellar, and healthy) and one within subject factor (presence or absence of perturbation). A within subject design has the advantage of being more efficient at showing a significiant difference if present although it is potentially liable to carry-over effects conditioned by perturbation, which might not appear if a between subject design were used.

Participants

Participants were recruited consecutively from 6 Birmingham Hospitals and from a local database of stroke patients within the School of Psychology. Potential volunteers were identified either by local clinicians, the UK Stroke Research Network or the PI (a research physiotherapist) whilst visiting the involved stroke wards and searching the database. The study was inclusive in terms of time since stroke. Diagnosis was confirmed by computed tomography (CT) scan when possible or the medical report which needed to state the involvement of either the right parietal lobe or cerebellum. Inclusion criteria: (1) cerebellar or right parietal stroke of ischemic or haemorrhagic origin, confirmed by CT scan (2) a score of 6 or more on the arm section of the Rivermead Motor Assessment (RMA), i.e. transport forward, pick up tennis ball, release at mid thigh on affected side x 5 (3) Informed consent. Exclusion criteria: (1) cognitive dysfunction preventing understanding of the task, (2) concurrent medical problems which prevent repetitive transporting (e.g. shoulder pain). Medical files were reviewed and potential candidates were interviewed by the PI to assess the RMA. Viable participants were invited to the laboratory for the experimental assessment. We aimed to

recruit 15 stroke patients to each patient group plus 30 Control participants matched according to age, gender and hand dominance. Clinical examination was undertaken by the research physiotherapist and included Fugl-Meyer Upper Extremity Motor Function (Fugl-Meyer, Jaasko et al. 1975); Revised Nottingham Sensory Assessment (NSA) (Lincoln, Jackson et al. 1998); Nottingham Extended Activities of Daily Living (NEADL) (Nouri and Lincoln 1987); classical testing procedures for tactile extinction (light touch with fingers to the subjects hand) (Tucker and Bigler 1989) and visual extinction (in which the patient fixates the examiner's nose, the examiner's arms are outstretched, and the patient has to detect movements of the examiner's index finger on either or both sides) (Baylis, Driver et al. 1993), Modified Ashworth Scale (MAS)(Bohannon R 1987) and the Medical Research Council scale (MRC) (Compston 2010) strength test of the more involved upper limb. Upper limb range of movement (ROM) was recorded as either full or reduced relative to the less involved side. Stroke participants and controls were also assessed for the time taken to complete the 10Hole Peg Test (10HPT) (Turton and Fraser 1986).

Protocol

Seated close to a table edge and the sternum in line with the start position, participants were instructed to perform fast, accurate, transport-to-grasp movements with the more affected arm using a precision grip between the thumb and index finger where possible. Participants were encouraged to lift the object 2-4cm off the table before replacing it in the approximate same position. The hand starting position with the pads of the index finger and thumb touching was from a pressure-sensitive switch close to the body in the saggital axis. Reaches were to perspex cylinders, (10cm height x 1.5 cm in diameter), in 3 locations: 10°, 30° or 50° to the opposing side of midline, each 35 cm from the start position. Following 6 practice trials and 10 unperturbed control trials, two blocks of 30 experimental trials ensued with a 5 minute rest period between the 2 blocks as necessary. Each block consisted of a randomised sequence of 20 unperturbed trials to the 30° cylinder, 5 trials perturbed to the 10° cylinder and 5 trials perturbed to the 50° cylinder. A visual fixation light indicated the start of each trial. Participants were instructed to move as soon as they saw the illumination of the 30° object

which occurred at a random time ranging between 500 and 2000 ms after the start of each trial. Perturbation occurred at movement onset by illumination of the 10° or 50° cylinders, via release of a start switch under the hand.

Data acquisition

Data was captured using a Qualysis ProReflex MCU240 3D (Qualysis 2006) motion analysis system with four infrared cameras and a sample rate of 200Hz. The operation was controlled by an external trigger in Matlab and the data processed using Qualisys Track Manager software. Two cameras were positioned two above the table and two in front. Data from reflective markers on the wrist (radial styloid process), the index finger nail, the thumb nail and the sternal notch was processed using custom Matlab programmes. Data was filtered using a Butterworth zero-phase forward and reverse digital filter with a cut-off of 8Hz. Trajectory, velocity, and acceleration were calculated from the 3 dimensional coordinates of each marker.

Reaction time (RT) was defined as the time (s) between the illumination onset of the 30° object and the wrist onset time (the time at which the wrist marker resultant (across x,y,z) velocity exceeded a threshold of 25mm/s for 5 consecutive frames). This method ensured the beginning of a voluntary movement was captured as opposed to an irrelevant movement that was linked to the depression of the start switch. Movement time (MT) was characterised by the time (s) between wrist onset and object lift-off (the time at which the velocity of the object exceeded 25mm/s for 5 consecutive frames in the vertical dimension). The offset time has previously been defined by the time at which the wrist stops moving forwards or the time when the grasp aperture reaches a stable value, but these methods fail to capture the ability to grasp the object properly. Grasp aperture was calculated as the maximum Euclidean distance between the markers on the thumb and index finger relative to the starting aperture distance. The maximum amplitude (mm) was defined as the maximum aperture (MA) and the time (s) at which this occurred was recorded was defined as the time of maximum aperture (TMA). The time at which the aperture velocity (differentiation of the distance between the finger and the thumb)

exceeded 25mm/s for 5 consecutive frames relative to the wrist start time was termed the aperture onset.

The wrist path trajectory (WPT) was defined as the sum of the distance (mm) between each frame from wrist onset to object-lift off. The absolute closure distance (CD) was calculated as the cumulative distance (mm) from MA to object lift off. CD was also expressed as a proportion of the total movement distance (CD%). Similarly the trunk distance (TD) was calculated as the sum of the distance (mm) travelled by the trunk marker between each frame.

Peak wrist velocity (PV mm/s) referred to the absolute maximum amplitude of the tangential wrist velocity. Peak deceleration (mm/s) was defined as minimum tangential wrist acceleration. The times at which peak velocity (TPV) and peak deceleration (TPD) occurred were expressed as absolute (s) and proportional (% movement duration) values.

Movement smoothness was quantified by the number of peaks in the tangential wrist velocity and the aperture size. Peaks were detected using a standard 'Peakdet.m' (delta 0.5) Matlab file (Eli Billauer, 3.4.05 Explicitly not copyrighted, released to the public domain; Any use is allowed) and counted if the difference between the peak and the preceding 'valley' (minimum value) exceeded 15% of the global maximum amplitude (Kahn, Zygman et al. 2001). The number of identified wrist velocity and aperture size peaks was recorded. For each component the time of the last peak prior to object lift-off was also recorded.

Statistical analysis

Unrelated sample t-tests were used to compare group characteristics such as age, time taken to complete the 10HPT and time since stroke. Similarly Mann Whitney tests were performed on the scores for Fugl-Meyer UE motor function, NEADL, MRC muscle strength grading and NSAS. The number of participants in each patient group with tactile extinction, visual extinction or reduced ROM was also recorded.

Analysis involved a two-way mixed ANOVA design with group (Control, Parietal, Cerebellar) as the unrelated factor and condition (Unperturbed and Perturbed) as the related factor. Post hoc comparisons employed Bonferonni correction. Pearson product moment correlation coefficients were used to examine the temporal relation between transport and grasp. Within-group correlation coefficients were calculated separately for each condition between the absolute time of maximum velocity peak and the absolute time of maximum grasp aperture; the absolute time of peak deceleration and the absolute time of maximum grasp aperture and finally between the absolute time of the last velocity peak and the last aperture peak. Pearson's r were later transformed to Fisher z: $z_r = (1/2)[\log_e(1+r) - \log_e(1-r)]$.

Independent t tests ($p<0.05$) were used to perform the following comparisons: effect of perturbation (perturbed vs. unperturbed trials) in cortical patients compared to controls; the same comparison of cerebellar patients to controls; effect of perturbation in cortical compared to cerebellar patients.

Fugl-Meyer scores (Fugl-Meyer, Jaasko et al. 1975) have previously been associated with a good prognosis for recovery after stroke (Prabhakaran, Zarahn et al. 2008). It was therefore considered of additional interest to observe the correlation between clinical impairment according to Fugl-Meyer scores and the RTG movement variables. This information may help to identify the most objective and sensitive variable for RTG function that could guide prognosis and measure performance. Stepwise multiple regressions were used to determine the relationships between multiple movement variables as predictors of movement time within groups.

Results

Results Overview

Firstly an outline of the participant recruitment process and characteristics of the included participants is provided. General features of the transport to grasp movement are and described with specific details of both the transport and the grasp components. Results are illustrated in the form of

velocity profiles and bar charts. Finally, measures of hand and arm coordination are presented in terms of the relationship between key events of transport and grasp. For simplification the two groups of age, sex and handedness matched data from control participants were pooled.

Recruitment (Figure 2.1)

A total of 57 patients were screened by the principle investigator and 16 patients (8 Parietal and 8 Cerebellar) were recruited. Due to difficulty recruiting cerebellar stroke participants the inclusion criteria were widened to include patients with cerebellar/pontine lesions.

Participants (Table 2.1)

Unrelated sample t-tests revealed no statistical age differences between the control group (N=16, M=62yrs, SD=13), the parietal group (N=8, M=59yrs, SD=13) or the cerebellar group participants (N=8, M=62yrs, SD=10). Mean time to complete the 10HPT was significantly faster (t_{13} =2.580, $p<0.05$) for control participants (M=12s, SD=2) than for the stroke patients (M=27s, SD=24). Unrelated sample t-tests revealed no significant time difference for the 10HPT between the two patient groups. Time since stroke was significantly (t_{14}=3.002, $p=0.01$) longer for the parietal group than the cerebellar group. Mann-Whitney U-tests showed no statistical difference between patient groups in terms of the Fugl-Meyer, EADL and muscle strength. A significant difference ($p<0.01$) in the Nottingham Sensory Assessment was found between the two patient groups; the parietal group demonstrated sensory impairment whereas for the cerebellar group sensation was globally intact. The parietal group included 5 participants with tactile extinction and 2 participants with visual extinction. There were no visual or tactile extinction problems identified in the cerebellar group. Active range of movement was reduced in one participant in the parietal group and 2 participants in the cerebellar group.

Figure 2.1 Recruitment flow diagram

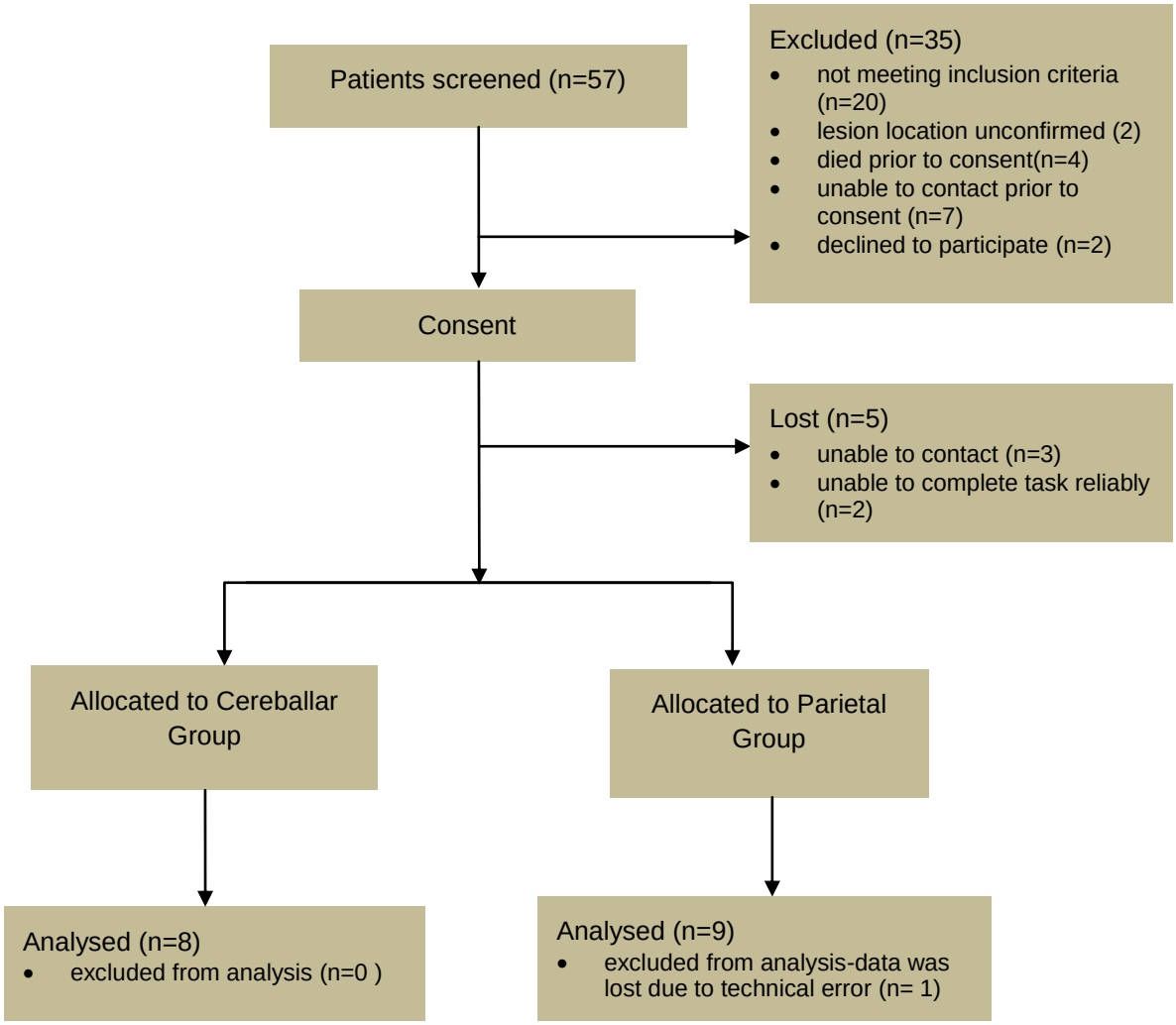


Table 2.1 Participant characteristics

Group	Lesion	Time since stroke (mths)	Age (yrs)	10 HPT (s)	NSA (9)	NEADL (63)	FMUL (66)	Extinction		FROM (y/n)	MAS (5)	Oxford Muscle (5)
								Tactile (y/n)	Visual (y/n)			
Parietal												
1	R P	25	55	52	5	48	48	n	n	y	0	4
2	R P-T	131	75	16	6	26	64	n	y	y	0	4
3	R F-P	22	62	33	6	40	55	y	n	y	0	5
4	B/L P	24	33	19	0	33	55	y	n	y	0	5
5	R P	68	55	15	6	53	65	y	y	y	0	4
6	R P	48	61	104	2	33	45	y	n	n	2	4
7	R P	124	57	17	4	32	58	y	n	y	1	4
8	R P	30	72	14	9	41	62	n	n	y	2	4
N=8		**59 (45)**	**59 (13)**	**34 (31)**	**5 (3)**	**38 (9)**	**57 (7)**	**5**	**2**	**1**	**3**	**4.3 (0.5)**
Cerebellar												
1	CP-A	24	60	14	9	63	63	n	n	y	0	5
2	R Cb	4	64	14	9	54	64	n	n	y	0	5
3	Pontine	12	66	19	9	53	44	n	n	n	2	4
4	R Cb	6	63	17	9	24	55	n	n	n	0	3
5	L Cb	3	61	18	9	46	64	n	n	y	0	5
6	L Cb	3	45	54	9	28	46	n	n	n	0	4
7	Cb	24	81	17	9	33	64	n	n	n	0	4
8	Cb	6	56	13	9	50	64	n	n	n	0	4
N=8		**10 (9)**	**62 (10)**	**21 (14)**	**9 (0)**	**44 (14)**	**58 (9)**	**0**	**0**	**2**	**1**	**4.3 (0.8)**

10 HPT (s) = time taken to complete 10 hole peg test performed with tested upper limb. NSA (Nottingham sensory assessment score) for the hand consisting of – Light touch, pin prick and stereognosis (0= absent, 1 impaired, 2 normal); and proprioception (0- absent, 1 appreciation of movement (wrong direction), 2 Direction of movement (<10 degrees), 3 Joint position sense (<10 degrees)). NEADL (Nottingham extended ADL index). Group average from a maximum of 63 = 21 activities (0=Not at all, 1with help, 2 alone with difficulty, 3 alone easily)FMUL (Fugl-Meyer Assessment upper limb section). Extinction (n) – y=yes, n=no positive signs of tactile and visual extinction.
FROM (Full active range of movement) y=yes, n=no.
MAS (Modified Ashworth Scale) - 0=No increase in muscle tone; 1=min resistance at end of range; 2=slight increase min resistance in second half of movement; 3increase in muscle tone through most of range; 4=passive movement difficult; 5=rigid
Oxford Scale Muscle Strength – 1=Flicker of movement; 2=Movement through full range but not against gravity; 3=movement through full range against gravity; 4=movement through full range with some resistance; 5=movement through range with full resistance.

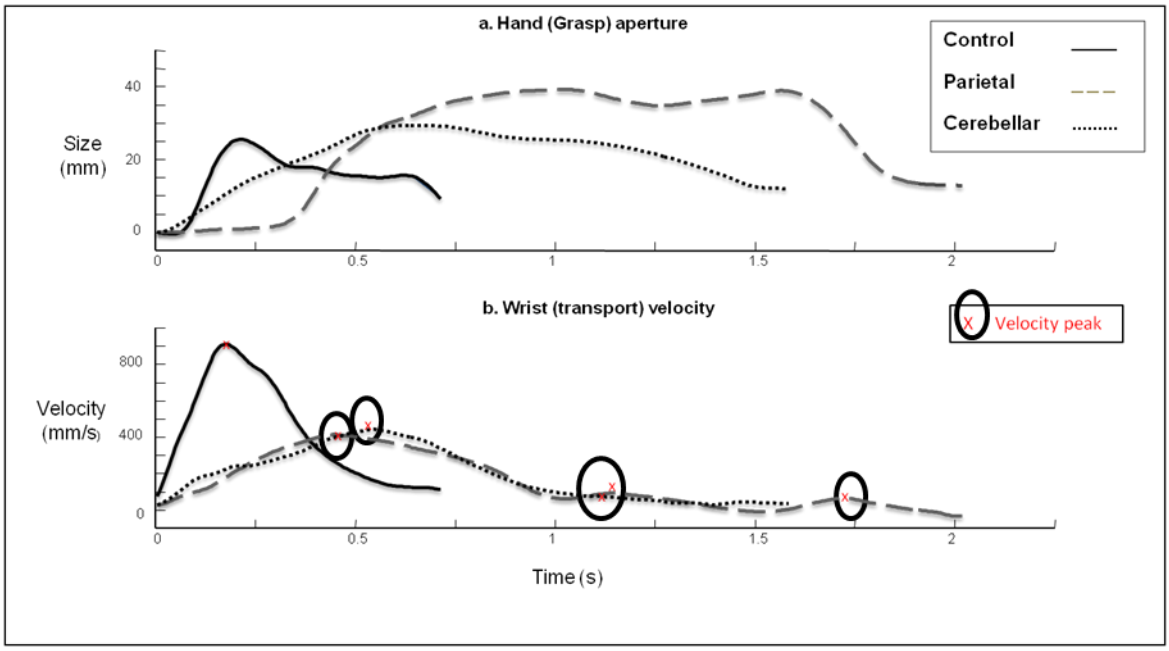
General movement characteristics

Example profiles of hand (grasp) aperture size and wrist (transport) velocity are illustrated in Figure 2.2. The wrist velocity profile (Figure 2.2b) for the control participant shows a characteristic symmetrical pattern with a single peak, indicative of a ballistic pre-planned phase followed by controlled deceleration under visual guidance. In comparison to the controls the parietal stroke participant demonstrates a large amplitude for grasp aperture and the maximum aperture occurs

relatively early in the movement. Poor control for aperture parameterization may result from impaired visual mapping or difficulties with sensory integration typical after a lesion to the parietal lobe. For a patient with a parietal lobe lesion the wrist velocity profile appears to be skewed to the left because peak velocity occurs relatively early in prehension. The overall movement time is longer and the wrist peak velocity is much lower than for the control participant. The prolonged low velocity phase suggests a more corrective mode of movement control, mediated with visual feedback as opposed to the movement being mainly pre-programmed. The transport profile for the parietal participant also shows three wrist velocity peaks suggesting corrective movement for spatial errors.

The aperture onset of the cerebellar (Figure 2.2a) stroke participant appears relatively early and is more gradual than the two comparison profiles. Maximum aperture is larger than the control participant but smaller by comparison to the parietal participant. In contrast to the control wrist velocity profile the movement time is increased and peak velocity is reduced for the cerebellar participant. The wrist velocity profile shows a prolonged deceleration phase and fluctuations (although less distinct than the parietal participant) supporting on line correction for errors in transport prior to grasp.

Figure 2.2 Sample hand (grasp) aperture (a) and wrist (transport) velocity profiles (b) for fast transport-to-grasp movements. Lines represent one trial each for a control (black solid line), a Parietal stroke participant (grey dashed line), and a Cerebellar stroke participant (black dotted line).



Group Comparisons: Transport component.

The group data (Controls, Parietal and Cerebellar) and the effect of condition (Baseline, Unperturbed 30', Perturbation 10' and Perturbation 50') upon parameters of the transport component are shown in Figures 2.3 to 2.8 pages 69-71.

There was a reliable ($F_{2, 29}$=12.957, p<0.01) group difference in the reaction time (figure 2.3). Movement onset was consistently delayed for the parietal group (mean (M)=0.7s, standard error (SE)=0.1) in comparison to the average time (M=0.4s, SE=0.04) for controls (baseline t_7=-3.321, p=0.01; unperturbed t_{22}=-4.868, p<0.01; perturbed 10° t_{22}=-2.856, p<0.01 and perturbed 50° t_{22}=-2.856, p<0.01). Movement onset for the cerebellar group (M=0.60s, SE=0.06) was similarly delayed (baseline t_{22}=-3.316, p=0.01; unperturbed t_{22}=-4.088, p<0.01; perturbed 10° t_{22}=-2.387, p<0.05 and perturbed 50° t_9=-4.046, p<0.01). There was no statistical difference between the two patient groups. The coefficient of variation (M=37, SE=2.7) for the movement delay time was similar between groups. A reliable ($F_{2,29}$=8.967, p<0.01) group difference in the average movement duration (figure

2.4) was observed. As predicted the mean time between movement onset and lift off was quicker for control participants (M=0.83s, SE= 0.13) than for patients with parietal lesions (M=1.72s, SE=0.18) most reliably so after the baseline trials (baseline t_7=-2.238, p=0.06; unperturbed t_7=-2.930, p<0.05; perturbed 10° t_8=-3.156, p=0.01 and perturbed 50° t_7=-2.983, p<0.05). Comparisons between the cerebellar group (M=1.39s, SE=0.18) and controls yielded similar differences (baseline t_7=-2.185, p=0.06; unperturbed t_8=-2.872, p<0.05; perturbed 10° t_9=-3.233, p=0.01; and perturbed 50° t_{10}=-4.345, p<0.01). There were no statistical differences between the two patient groups. The coefficient of variation for movement time was similar between groups.

With further regard to the transport component, as was anticipated the mean peak velocity (M=684mm/s, SE=37) was reduced significantly ($F_{2, 29}$=13.795, p<0.01) after stroke (figure 2.5). The average peak velocity for the parietal group (M=555mm/s, SE=53) was significantly lower than for controls (M=823mm/s, SE= 37) in each condition (baseline t_{22}=3.582, p<0.01; unperturbed t_{22}=3.907, p<0.01; perturbed 10° t_{22}=3.640, p<0.01 and perturbed 50° t_{22}=3.865, p<0.01). For the cerebellar group peak velocity (M=537mm/s, SE=53) was also consistently lower than controls (baseline t_{22}=4.596, p<0.01; unperturbed t_{22}=4.764, p<0.01; perturbed 10° t_{22}=4.874, p<0.01 and perturbed 50° t_{22}=4.159, p<0.01). There was no statistical difference between the two patient groups.

We found no difference in variability of peak velocity between groups. There was a between group difference ($F_{2, 29}$=3.810, p<0.05) in the average WPT (M=393mm, SE =9). The mean WPT (figure 2.6) was longer for the parietal group (M=432mm, SE=16) than for the control group (baseline not significant; unperturbed t_{22}=-2.200, p<0.05; perturbed 10° t_{22}=-2.330, p<0.05 and perturbed 50° t_{22}=-2.648, p=0.01). The WPT of the parietal group was also longer than that of the cerebellar group, but reliably so for just the perturbed 50°trials (baseline not significant; unperturbed not significant; perturbed 10° t_{14}=-2.018 p=0.06; perturbed 50° t_{14}=-2.234 p<0.05). The mean WPT of the cerebellar group (M=376, SE=16) was more similar to that of controls (M=383mm, SE= 11). We found no group difference in the coefficient of variation for the resultant distance. For the normalised time to peak velocity (figure 2.7) there was a between group effect ($F_{2,29}$=4.159, p<0.05) which highlighted

the prolonged deceleration phase after stroke. Peak velocity occurred comparatively early particularly in the parietal group (Controls M=36%, SE=2; Parietal M=28%, SE=2; Cerebellar M=32%, SE=2). Peak velocity occurred reliably early for the parietal group in comparison to controls (baseline t_{22}=-2.817, p=0.01; unperturbed t_{22}=-2.145, p<0.05; perturbed 10° t_{22}=-2.159, p<0.05 and perturbed 50° t_{22}=-2.208, p<0.05). In contrast, there were no differences between controls and the cerebellar group. We found no significant differences in % PV between the two patient groups.

The mean number of wrist velocity peaks (M=1.9, SE=0.2; figure 2.8) was higher ($F_{2, 29}$=3.415, p<0.05) after stroke (Controls M=1.3, SE=0.2; Parietals M=2.4, SE=0.3 and Cerebellar M=1.9, SE=0.3). Pairwise comparisons showed there to be significantly more wrist velocity peaks for the parietal group than for controls (p<0.05), whilst the number of velocity peaks was more similar between controls and the cerebellar group. Independent t-tests however showed that due to the unequal variance, group comparisons were not significant between controls and the parietal group. Comparisons between the controls and the cerebellar participants yielded a significant difference for the perturbed 10° trials only *(*t_{22}=-2.672 p<0.05). There was no significant difference in the number of velocity peaks between the patient groups. Anterior trunk displacement (M=45mm, SD=52, figure 2.13) was higher for stroke participants however the group difference in amplitude was not significant (Controls M=31mm, SE=10; Parietal M=51mm, SE=14 & Cerebellar M=68mm, SE=14). There was no difference in the coefficient of variation between the three groups.

Group Comparisons: Grasp component

The group data (Controls, Parietal and Cerebellar) and the effect of condition (Baseline, Unperturbed 30, Perturbation 10' and Perturbation 50') upon parameters of the grasp component are shown in Figure 2.9 to 2.15 pages 72-75

With regard to the grasp component, there was a main effect ($F_{2,29}$=3.902, p<0.05) of group upon grasp onset time (figure 2.9) with early aperture onset (baseline NS; unperturbed t_{14}=-2.338, p<0.05; perturbed 10° t_{14}=-2.351, p<0.05 & perturbed 50° t_{14}=-2.413, p<0.05) observed in the

cerebellar group (M=-0.036, SE=0.038) in comparison to the parietal group (M=0.115, SE=0.038) for which the onset was delayed. We found no significant differences for either of the patient groups in comparison to controls (M=0.049, SE=0.027). Overall the mean maximum aperture (figure 9. M=59mm, SD=18) was similar between the control group (M=57mm, SE= 4) and the stroke patient groups (Parietal M=65mm, SE=6 and Cerebellar M=55mm, SE=6). There was a tendency (t_9=-2.042, p=0.73) for increased variability in the parietal group (M=15%, SD=6.0) when compared to controls (M=10%, SD=2.9) during the unperturbed trials only.

On average TMA% (figure 2.11) was comparable between stroke patients and controls (Controls M=71%, SE= 2; Parietal M=67%, SE=3; Cerebellar M=66%, SE=3). The timing was found to be more variable however in the parietal group in comparison to controls during baseline trials (t_{22}=-2.957, p<0.01). There was also a tendency for more variability in the cerebellar group during perturbed 10° trials (t_{22}=-2.00, p=0.058) in contrast to controls.

Overall the mean number of aperture peaks (figure 2.12) was comparable between stroke participants and controls (Controls M=1.4 peaks, SE=0.04; Parietal M=1.4 peaks, SE=0.06 and Cerebellar M=1.4 peaks, SE=0.06). Absolute CD (figure 2.14) was greatest for the parietal group but there was no significant group effect (Controls M=44mm, SE=8; Parietal M=76mm, SE=12 & Cerebellar M=59mm, SE=12). The absolute CD was also more variable for the parietal group (M=51%, SE=6) than the cerebellar group (M=45%, SE=6) and controls (M=38%, SE=4) but this was not significant. CD% (figure 2.15) was higher in the stroke participants but there was no significant group difference (Controls M=12%, SE=2; Parietal M=17%, SE=2; Cerebellar M=16%, SE=2). CD% appeared more variable for the parietal group (M=50%, SE=6) than the cerebellar group (M=39%, SE=6) and controls (M=39%, SE=4) but there was no main effect for group.

Comparison between Conditions

As was expected the reaction time (M=0.5s, SD=0.2) was similar for each condition, whereas the average movement time (M=1.2s, SD=0.6) was longer ($F_{3, 87}$=8.747, p<0.01) in response to a perturbation in the object location.

Comparison between Conditions: Transport component

Peak wrist velocity showed a main effect for condition ($F_{3, 29}$=7.592, p<0.01). Overall the peak velocity (figure 2.5) during baseline trials (M=682mm/s, SE=33.7) was higher (p<0.05) than for all other conditions and for perturbed 10°trials (M=606mm/s, SE=29) it was lower (p<0.01) than the other conditions. The average peak velocity was however similar between the unperturbed (M=635mm/s, SE=28) and perturbed 50° trials (M=630mm/s, SE=28). Perturbation in the object location significantly ($F_{3, 29}$=24.323, p<0.01) increased the overall WPT (figure 2.6). There was a statistical difference (p<0.01) in WPT between the two perturbed conditions (perturbed 10° M=404mm, SE=10 and perturbed 50° M=426mm, SE=8) but no difference between baseline (M=382mm, SE=11) and unperturbed trials (M=377mm, SE=8). The normalised time to peak velocity (figure 2.7) was significantly ($F_{3, 87}$=8.447, p<0.01) different between conditions. The %TPV for perturbed 10° trials (M=28%, SE=2) was earlier than baseline (M=34%, SE=2, p<0.05); unperturbed (M=34%, SE=2, p<0.01) and perturbed 50° trials (M=31%, SE=1, p=0.06).

It was assumed that in response to a perturbation in the object location there would be a normal adjustment to the wrist profile resulting in a second velocity peak. Indeed we found a reliable effect of condition ($F_{3, 87}$=33.357, p<0.01) with more wrist velocity peaks (figure 2.8) observed for perturbed 10° trials (M=2.1, SE=0.2) and perturbed 50° trials (M=2.1, SE=0.2) than for unperturbed (M=1.5, SE=0.2) and baseline trials (M=1.6, SE=0.2).

Comparison between Conditions: Grasp component

As was assumed there was no main effect of condition effect on the aperture onset time (figure 2.9). Perturbation of the object location had a reliable effect ($F_{3, 87}$=4.128, p<0.01) upon the size of the maximum grasp aperture (figure 2.10) and a significant condition and group interaction was observed ($F_{3,87}$=3.360, p<0.01). Maximum aperture for perturbed 10° trials (M=61mm, SE=3) and perturbed 50° trials (M=59mm, SE=3) was significantly (p<0.01 and p<0.05 respectively) larger than for unperturbed trials (M=56mm, SE=3). For the normalised time to maximum aperture TMA% (figure 14) a significant main effect of condition ($F_{3, 87}$=5.282, p<0.05) was observed (Baseline M=65%, SE=2; Unperturbed M=67%, SE=3; Perturbed 10° M=71%, SE=2; Perturbed 50° M=68%, SE=2). Pairwise comparisons showed that maximum aperture occurred significantly (p<0.01) later for perturbed 10° trials than at baseline.

There was a significant main effect of condition ($F_{3, 87}$=31.508, p<0.01) upon the number of aperture peaks (figure 2.12) suggesting that perturbation of transport resulted in the adjustment of the grasp aperture. A significant group and condition interaction ($F_{6, 87}$=3.064, p<0.01) was observed. Comparisons between controls showed a significantly greater number of peaks for the parietal group (baseline t_{22}=-2.864, p<0.01) and the cerebellar group (baseline t_{22}=-4.152, p<0.01) during the initial baseline trials. Following the baseline trials the number of aperture peaks was similar for the three groups. Trunk movement was not significantly affected by the perturbation and there was no interaction effect upon the anterior trunk displacement (figure 2.13).

The absolute CD (figure 2.14) was smaller for perturbed trials but the difference between conditions was not significant (Baseline M=60mm, SE=7; Unperturbed M=63mm, SE=7; Perturbed 10° M= 57mm, SE=8 & Perturbed 50° M=59mm, SE=7). On average CD% (figure 2.15) was also similar for each condition (Baseline M=15%, SE=1; Unperturbed M=16%, SE=2; Perturbed 10° M=14%, SE=2; Perturbed 50° M=13%, SE=1).

Figures 2.3 to 2.15 pages 69-75 Effect of group (Control, parietal, cerebellar) and condition (Baseline, Unperturbed 30', Perturbed 10' and Perturbed 50' upon Reaction Time (Figure 2.3), Movement Time (Figure 2.4),Peak velocity (Figure 2.5), Wrist path trajectory distance (Figure 2.6), Normalised time to peak velocity (Figure 2.7), Number of wrist peaks (Figure 2.8), Aperture onset relative to wrist onset (Figure 2.9), Maximum aperture (Figure 2.10), Normalised time to maximum aperture (Figure 2.11), Number of aperture peaks (Figure 2.12) , Anterior Trunk Displacement (Figure 2.13) Aperture Closure Distance (Figure 2.14) and Normalised aperture closure distance (Figure 2.15).

Figure 2.3: Bar chart: Group Mean (SE): Reaction Time

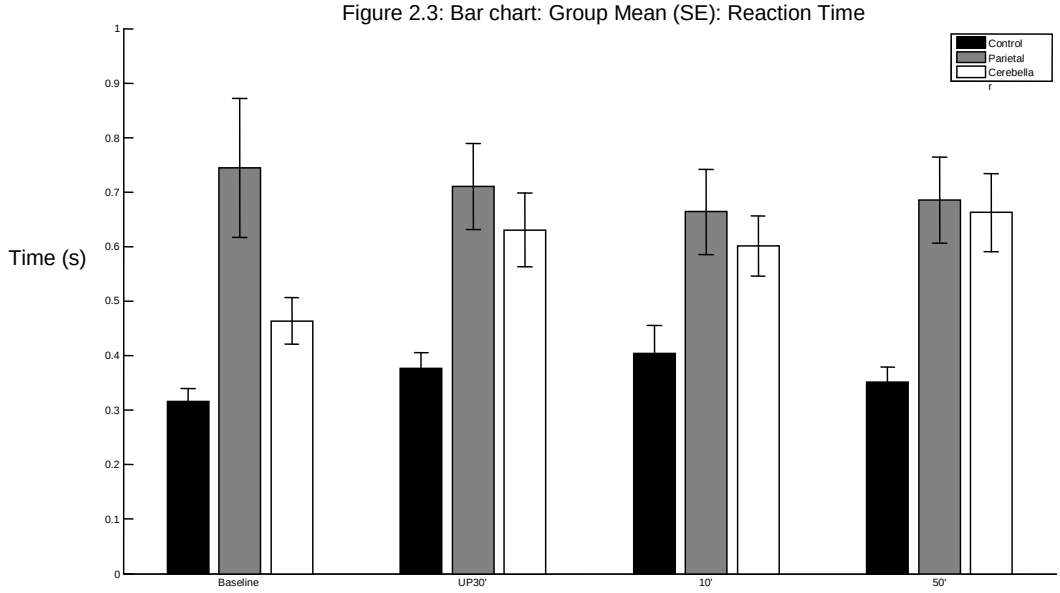


Figure 2.4: Bar chart: Group Mean (SE): Movement Time

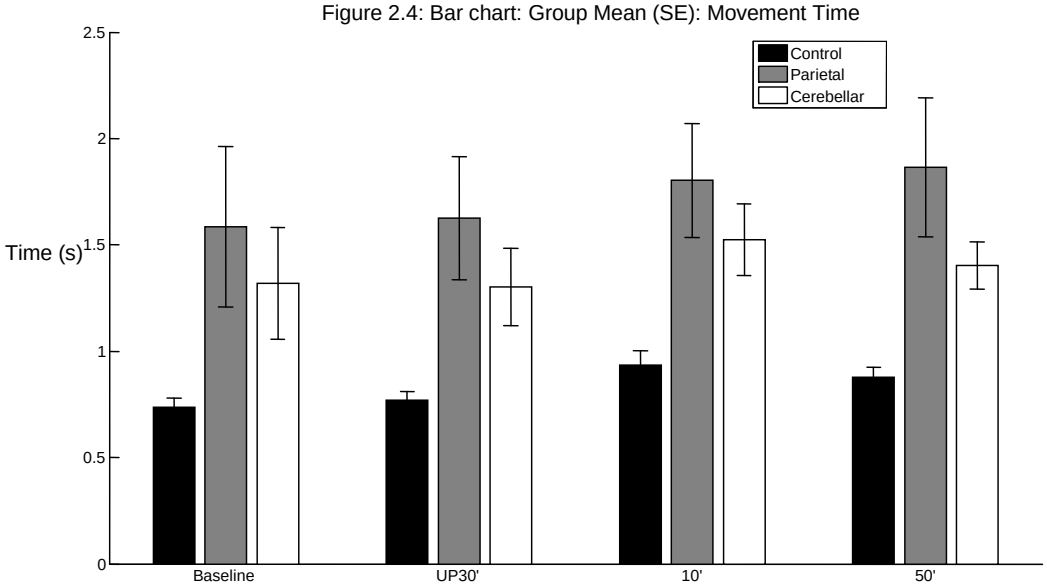


Figure 2.5: Bar chart: Group Mean (SE): Peak velocity

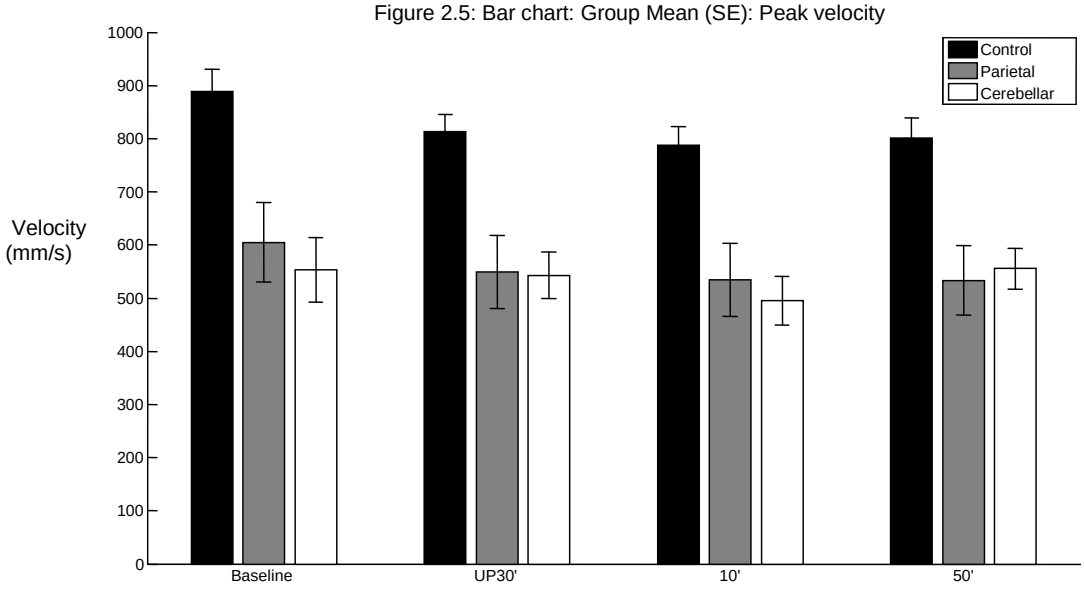


Figure 2.6: Bar chart: Group Mean (SE): Wrist path trajectory

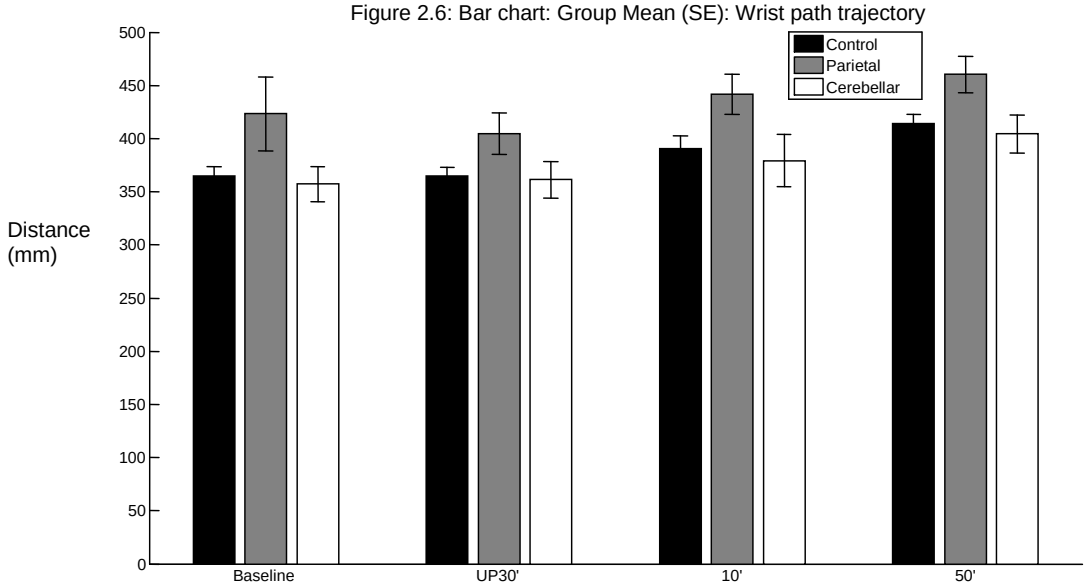


Figure 2.7: Bar chart: Group Mean (SE): Normalised Time to Peak Velocity

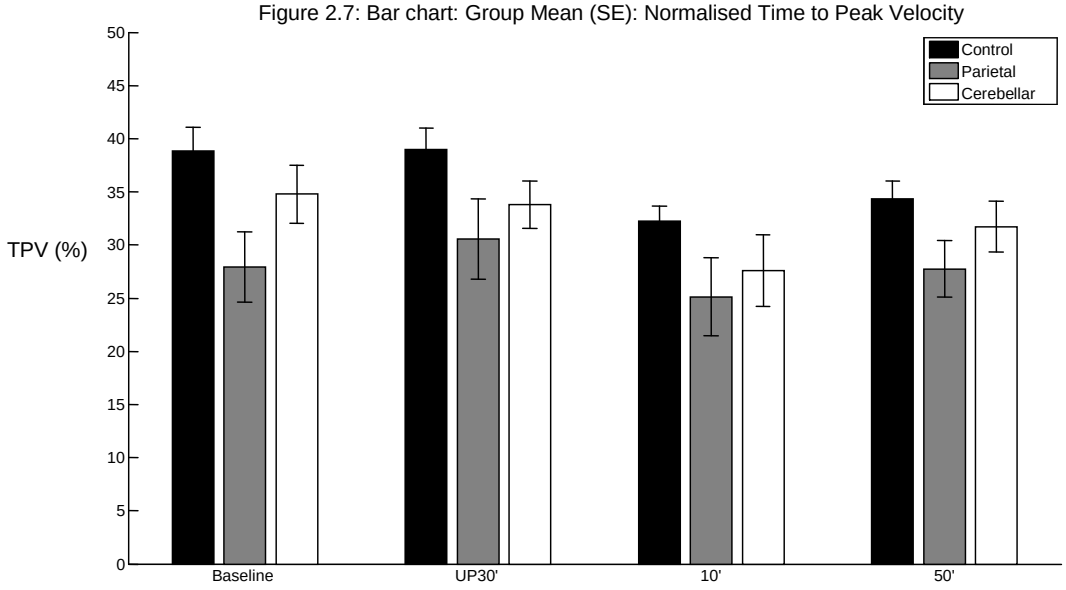


Figure 2.8: Bar chart: Group Mean (SE): Number of wrist peaks

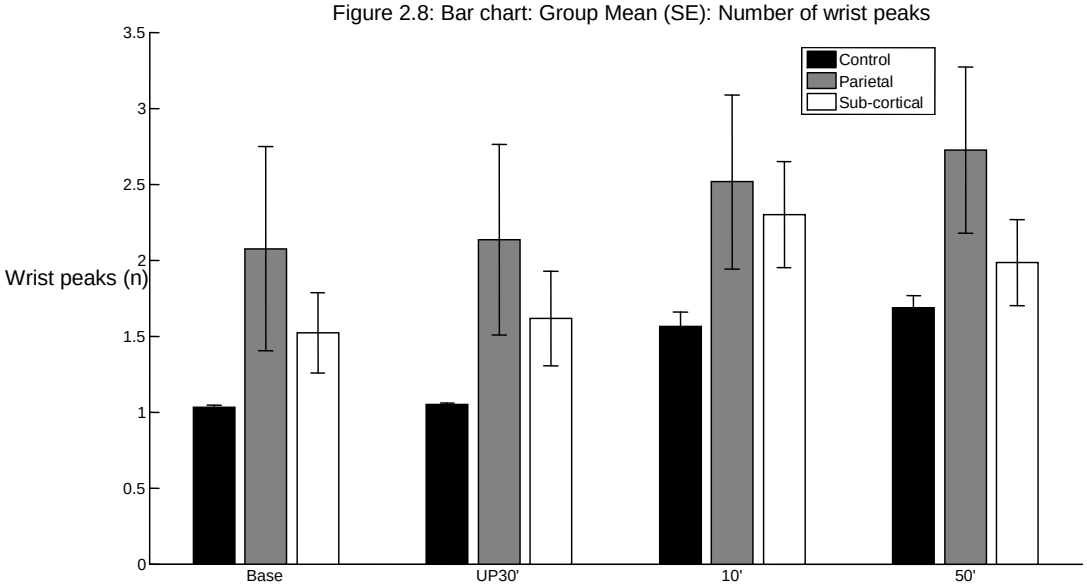


Figure 2.9: Bar chart: Group Mean (SE): Aperture onset relative to wrist onset

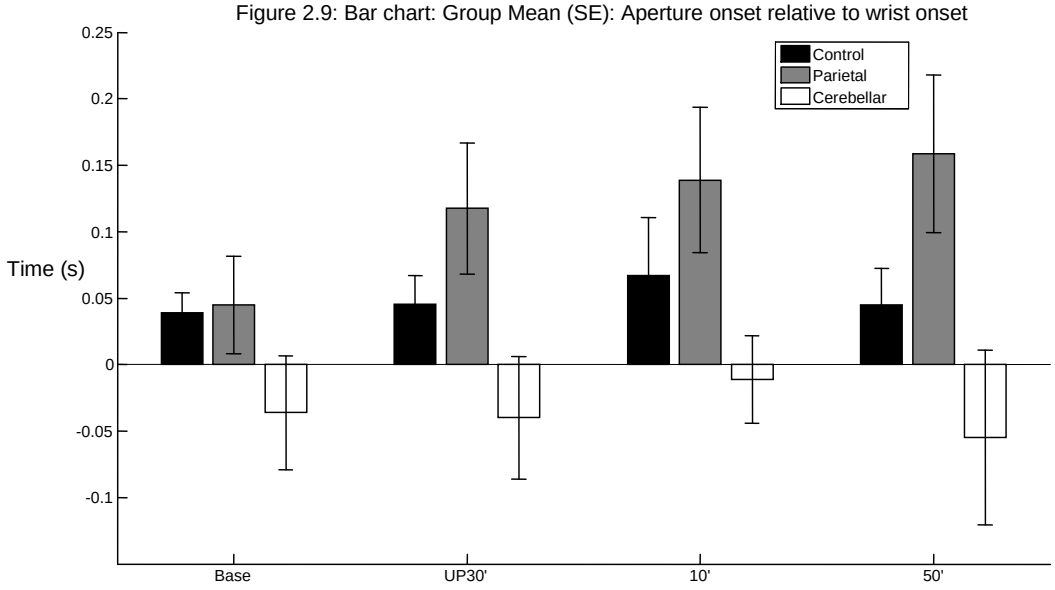


Figure 2.10: Bar chart: Group Mean (SE): Maximum aperture

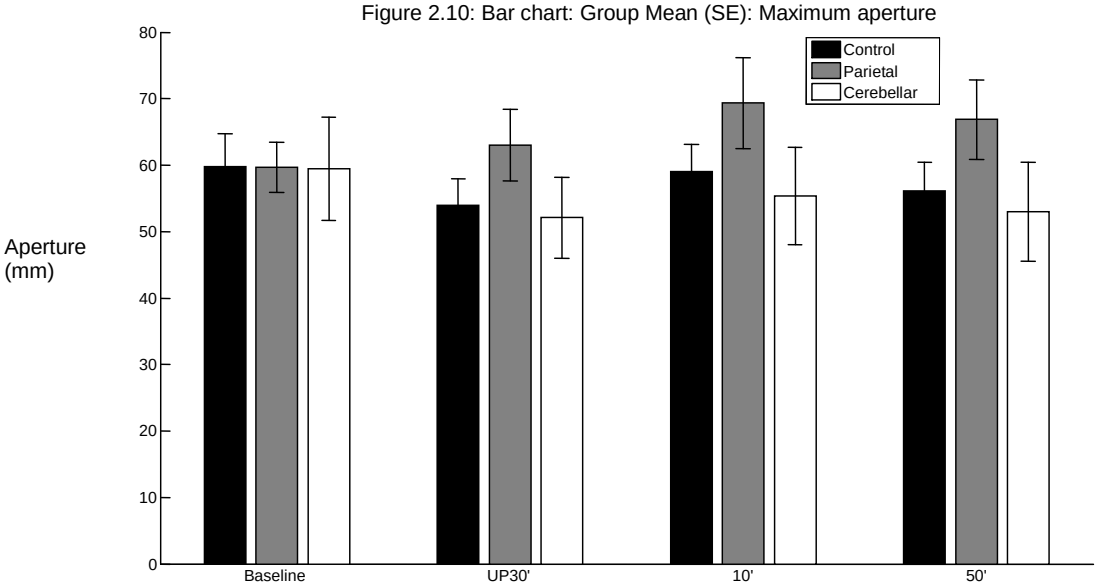


Figure 2.11: Bar chart: Group Mean (SE): Normalised time to max aperture

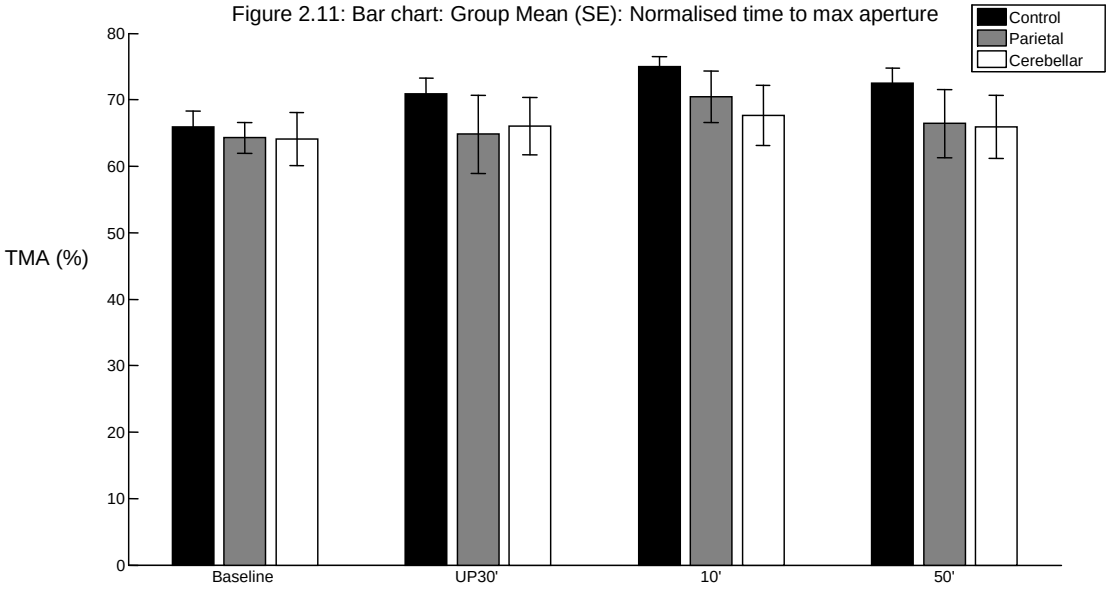


Figure 2.12: Bar chart: Group Mean (SE): Number of aperture peaks

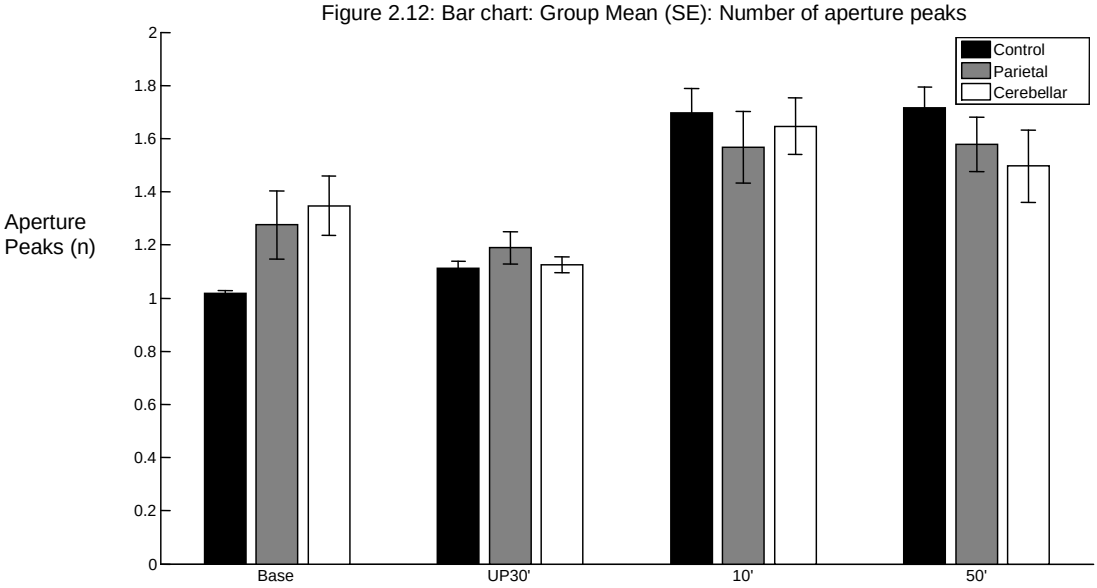


Figure 2.13: Bar chart: Group Mean (SE): Anterior trunk displacement

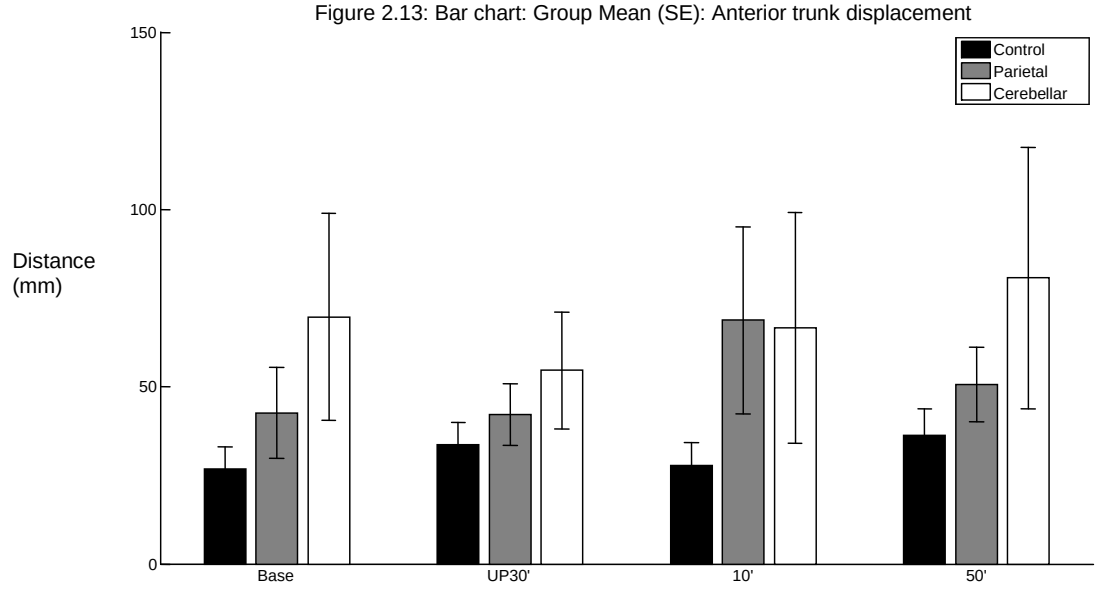


Figure 2.14: Bar chart: Group Mean (SE): Absolute closure distance

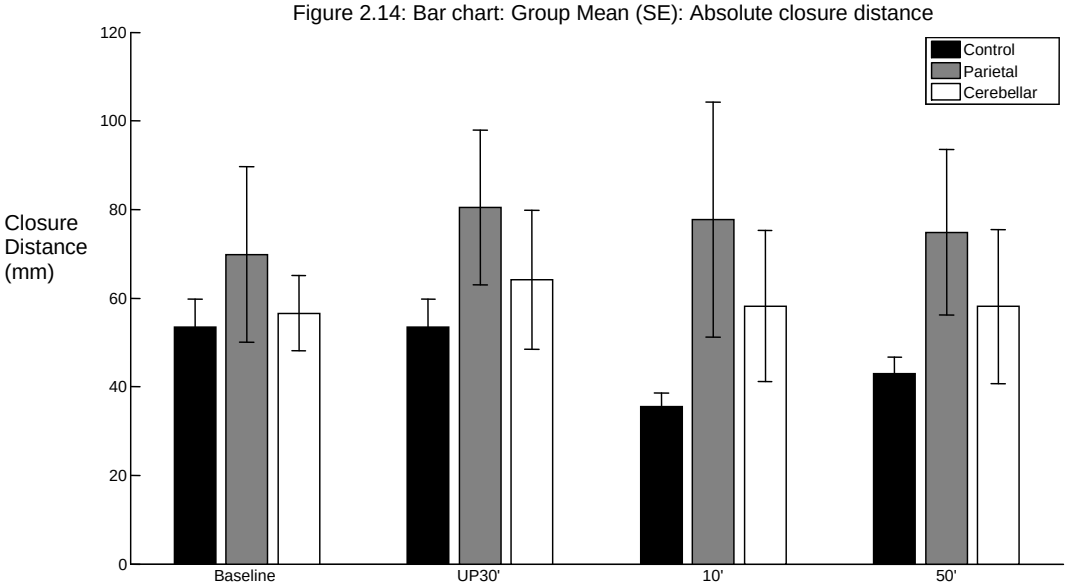
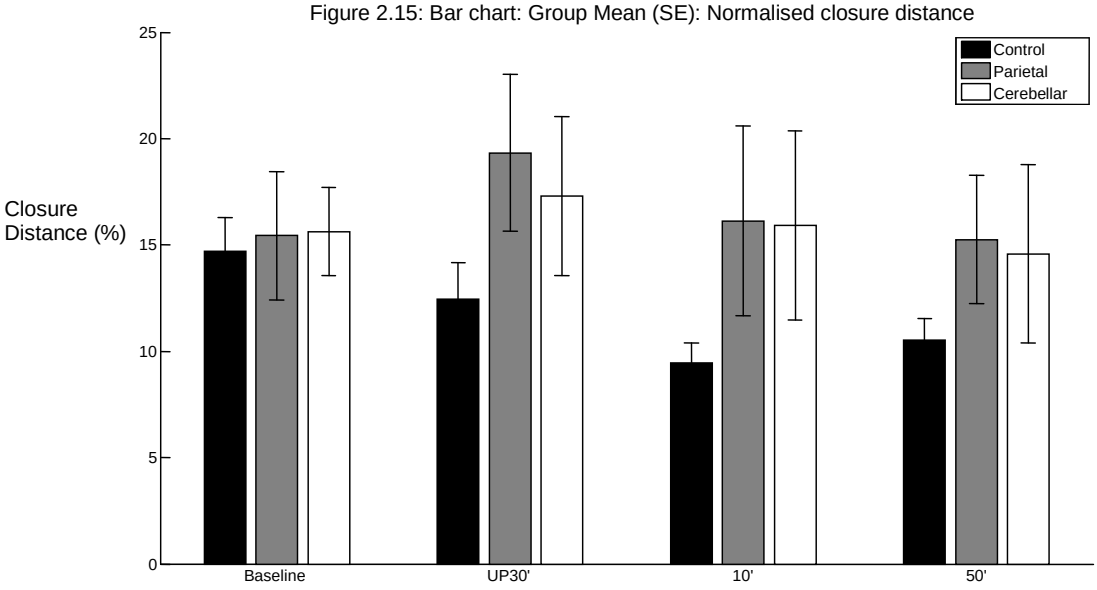


Figure 2.15: Bar chart: Group Mean (SE): Normalised closure distance



Coordination between key events of transport and grasp.

Pearson product correlation coefficients were used to determine if the absolute time to peak velocity or peak deceleration was correlated with the absolute time of maximum grasp aperture. The correlation coefficients were calculated separately within groups for perturbed and non-perturbed trials. We found that both the absolute time of peak velocity (table 2.2) and peak deceleration (table 2.3) correlated significantly ($p<0.01$) with the absolute time of maximum aperture for each group and in all conditions.

Wrist velocity and aperture profiles were often characterised by multiple peaks after stroke. Furthermore perturbations in object location usually elicited more than one peak in wrist velocity and aperture profiles. The peaks detected immediately prior to object lift-off were therefore analysed to determine the relationship between these events. We found significant correlations between the time of the last detected peak wrist velocity and the time of the last detected peak aperture (table 2.4).

Table 2.2 Pearson product correlation r values – absolute times of peak velocity and maximum aperture

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	0.83	0.63	0.78
Parietal N=8	0.52	0.65	0.78
Cerebellar N=8	0.84	0.72	0.61

For unperturbed trials a significant correlation ($p<0.01$) between the time of the peak velocity and the time of maximum aperture was demonstrated by 88% of the control participants, 75% of the parietal group and 63% of the cerebellar group. Whereas for perturbed trials this correlation was observed in only 31% of the control group, 38% of the parietal group and 25% of the cerebellar group.

Table 2.3 Pearson product correlation r values – absolute times of peak deceleration and maximum aperture

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	0.85	0.65	0.77
Parietal N=8	0.81	0.82	0.83
Cerebellar N=8	0.69	0.49	0.47

Table 2.4 Pearson product correlation r values – absolute times of last peak velocity and last peak aperture

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	0.47	0.62	0.86
Parietal N=8	0.94	0.86	0.86
Cerebellar N=8	0.81	0.69	0.63

Significant correlations ($p<0.01$) between the absolute times of the last peak velocity and the last maximum aperture was demonstrated by 69% of the control group, 75% of the parietal group and

63% of the cerebellar group during unperturbed trials. For perturbed trials this correlation was observed in 75% in each of the three groups.

For between group comparisons r values were transformed to Fisher z values. The significance of the difference between z values was tested using two-way mixed ANOVAs with repeated measures and post hoc analysis.

Coordination between the time to peak velocity and time of maximum aperture - Fisher z scores (Table 2.5)

Interestingly results suggest that the stroke patients with parietal and cerebellar lesions maintained coordination between the timing of the peak velocity and maximum aperture similar to controls. There was no significant group effect (Controls M=0.8, SE=0.1; Parietal M=0.7, SE=0.1; Cerebellar M=0.7, SE=0.1). The relationship between the peak velocity and maximum aperture was weaker for the perturbed trials although we found no significant effect of condition and no interaction.

Table 2.5 Mean (SE) z scores (TPV & TMA)

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	1.02 (0.2)	0.97 (0.2)	0.53 (0.2)
Parietal N=8	0.55 (0.2)	0.86 (0.2)	0.80 (0.2)
Cerebellar N=8	1.02 (0.2)	0.65 (0.2)	0.40 (0.2)
Total N=32	0.86 (0.1)	0.83 (0.1)	0.58 (0.1)

Coordination between the time of peak deceleration and time of maximum aperture -Fisher z scores (Table 2.6)

There was a significant effect of condition ($F_{2, 58}$=3.216, $p<0.05$) upon the coordination between peak deceleration and maximum aperture timing, with baseline scores reliably higher than unperturbed and perturbed trials. We found no significant group and condition interaction. Whilst there was no main group effect (Controls M=0.8, SE=0.1; Parietal M=0.7, SE=0.1; Cerebellar M=0.5,

0.1) coordination between peak deceleration and the time of maximum aperture was weakest for the cerebellar group and with marginal significance for the unperturbed trials (t_{22}=1.989, p=0.06).

Table 2.6. Mean (SE) z scores (TPD & TMA)

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	1.06 (0.2)	0.93 (0.1)	0.54 (0.1)
Parietal N=8	0.74 (0.2)	0.75 (0.2)	0.68 (0.2)
Cerebellar N=8	0.67 (0.2)	0.55 (0.2)	0.32 (0.2)
Total N=32	0.82 (0.1)	0.74 (0.1)	0.51 (0.1)

Coordination between the time of the last peak velocity and time of last peak aperture - Fisher z scores (Table 2.7)

Fisher z scores, which reflected the correlation between the last velocity peak (TLPV) and the last aperture peak (TLPA) were highest for perturbed scores, and a main condition effect ($F_{2, 58}$=5.748, P<0.001) was observed. Pairwise comparisons of the Fisher z scores for TLPV and TLPA showed a significant difference (p<0.05) between perturbed trials and both the baseline and unperturbed trials.

We found no main group effect (Controls M=0.87, SE=0.1; Parietal M=0.82, SE=0.1; Cerebellar M=0.82, SE=0.1).

Table 2.7 Mean (SE) z scores (TLPV & TLPA)

	Baseline	***Unperturbed***	***Perturbed***
Controls N=16	0.76 (0.1)	0.67 (0.1)	1.16 (0.2)
Parietal N=8	0.47 (0.2)	0.80 (0.1)	1.19 (0.2)
Cerebellar N=8	0.87 (0.2)	0.64 (0.1)	0.95 (0.2)
Total N=32	0.70 (0.1)	0.70 (0.1)	1.10 (0.1)

Correlation between clinical impairment and reach to grasp movement variables.

The level of function (FMUL) was significantly correlated (Spearman's rho) with MT (r=-0.73, p<0.01) and TPV (r= 0.61, p<0.01). MT was shorter and TPV occurred later in patients with least impairment. FMUL was not correlated with wrist trajectory distance, TMA, amplitude of maximum

aperture, or trunk movement distance. Age did not correlate with any of the movement variables. FMUL scales for patients were significantly negatively correlated to the time taken to complete 10HPT ($r=-0.76$, $p<0.01$).

The 10HPT time was correlated with Movement time ($p<0.01$, $r=0.795$); the wrist trajectory distance ($p<0.01$, $r=0.772$); TPV ($p<0.01$, $r= -0.474$). No correlation was found between 10HPT and TMA; MA; Trunk movement distance or coordination (Pearson's r between TPV and TMA) or age.

Relationship between multiple kinematic relations

Stepwise Multiple Regression analysis was used to describe the relative contributions of each of the 5 kinematic variables (MA, TMA, TPV, Wrist trajectory distance & Trunk movement) to the Movement time.

Controls Stepwise Multiple Regression (Table 2.8).

The stepwise multiple regression analysis suggested that for healthy controls there is a negative relation between the MT and both the maximum aperture amplitude which explained 40% of the variance and ($F_{1,14}=9.426$, $p<0.01$) and the TMA which explained a further 17% ($F_{1,13}=4.954$,$p<0.05$). That is to say those participants with a longer movement time had a smaller maximum grasp aperture and reached maximum aperture earlier than participants with a shorter movement time. The TPV, WPT, and trunk movement distance did not explain any further significant contribution to the variability in MT for healthy controls. This is in contrast to a previous study (Cirstea and Levin 2000) which found that in healthy subjects MT was related to the trunk displacement.

Table 2.8 Stepwise multiple regression of predictors of movement time in Healthy subjects (only significant predictors are included).

Variable	*Multiple R*	*B*	*Standard error b*	*Beta*	*t*	*Significance of t*
MA	0.63	-0.005	0.002	-0.604	-	0.006

TMA	0.75	-0.007	0.003	-0.407	-3.301 - 2.226	0.044

Stroke Participants Stepwise Multiple Regression (Table 2.9)

Whereas for the patient group the wrist trajectory distance explained 49% of the variance in MT ($F_{1,14}$=13.462, p=0.003). A positive relation here between MT and wrist trajectory distance suggests that increased movement time was associated with increased wrist trajectory distance. Time to maximum aperture was entered second and explained a further 19% ($F_{1,13}$=8.160,p=0.013). Thus similar to the healthy participants a longer movement time was associated with earlier TMA. In contrast to the healthy participants there was no relationship between the size of the maximum aperture and the movement time, which suggests that the patient groups were less able to adjust grasp aperture according to the speed (Wing, Turton et al. 1986). For the patient group TPV, MA, and trunk movement distance did not explain any further significant contribution to the variability in MT.

Table 2.9. Stepwise multiple regression of predictors of movement time in Patients (only significant predictors are included).

Variable	*Multiple R*	*B*	*Standard error b*	*Beta*	*t*	*Significance of t*
Distance	0.70	0.008	0.002	0.695	4.478	0.001
TMA	0.83	-0.045	0.016	-0.443	-2.857	0.013

Parietal group Stepwise Multiple Regression (Table 2.10)

Wrist trajectory distance accounted for 74% of the variability in MT in the parietal group, whilst TMA, TPV, MA, and trunk movement distance did not explain any further significant contribution.

Table 2.10 Stepwise multiple regression of predictors of movement time in Parietal subjects (only significant predictors are included).

Variable	*Multiple R*	*B*	*Standard error b*	*Beta*	*t*	*Significance of t*
Distance	0.88	0.009	0.002	0.879	4.526	0.004

Cerebellar group Stepwise Multiple Regression (Table 2.11)

TMA explained 59% of the variance in MT within the sub-cortical group and wrist trajectory distance TPV, MA, and trunk movement distance did not explain any further significant contribution.

Table 2.11. Stepwise multiple regression of predictors of movement time in Sub-cortical subjects (only significant predictors are included).

Variable	*Multiple R*	*β*	*Standard error b*	*Beta*	*t*	*Significance of t*
TMA	0.805	-0.053	0.016	-0.805	-3.319	0.016

Discussion

The study, which contrasted controls and patients with either right parietal or cerebellar lesions, aimed firstly to identify lesion specific RTG coordination impairments and secondly to compare the movement response to perturbation of the object location.

Unperturbed movements

In the absence of perturbation, RTG movements of control subjects were comparable to previous research (Jeannerod 1984; Paulignan, Mackenzie et al. 1991). The wrist velocity profiles for controls generally appeared as asymmetrical bell shaped curves with a single peak and the ballistic pre-planned phase lasted on average 40% of the total movement duration. Scaling of MA for the object size was observed. The average MA (6cm in diameter) was slightly smaller than the 8.5cm previously reported (Paulignan, Mackenzie et al. 1991) although the objects were of the same size. The difference may be due to the fact that in the present study MA was calculated relative to the starting aperture distance. Control subjects demonstrated coordinated control of transport by the arm and grasp by the hand. Specifically the time of maximum hand aperture was correlated with both the time of peak velocity and the time of transport. For unperturbed trials a significant correlation between the time of the peak velocity and the time of maximum aperture was demonstrated by 88% of the control participants. By comparison (Paulignan, Mackenzie et al. 1991) these correlation coefficients were significant in only about 40% of the trials.

The study found similarity between the two patient groups in terms of delayed movement onset, prolonged movement time and reduced velocity of unperturbed RTG movements. In accordance with previous research in heterogeneous stroke (Michaelsen, Jacobs et al. 2004; Thielman, Dean et al. 2004; Lang, Wagner et al. 2005; Vliet and Sheridan 2007) and cerebellar lesions (Haggard, Jenner et al. 1994; Rand, Shimansky et al. 2000) movement duration was longer for parietal and cerebellar participants. As anticipated and in keeping with previous findings (Trombly 1993; Haggard, Jenner et al. 1994; Bastian and Thach 1995; Rand, Shimansky et al. 2000; Zackowski, Thach et al. 2002;

Michaelsen, Jacobs et al. 2004; Vliet and Sheridan 2007; Brandauer, Hermsdorfer et al. 2008; Konczak, Pierscianek et al. 2010) peak velocity was reduced after stroke.

Both patient groups demonstrated decreased movement smoothness as defined by the number of wrist velocity peaks, which is suggestive of corrective movement for spatial errors or dysynergia. In accordance with previous work (Bastian and Thach 1995; Zackowski, Thach et al. 2002) the number of wrist peaks was significantly higher for the cerebellar group in comparison to controls. We found the overall WPT was longer and more variable after parietal stroke. Based upon previous research (Zackowski, Thach et al. 2002) we had anticipated greater WPT variability and a greater number of velocity peaks in the cerebellar group when compared to controls, however WPT in the cerebellar group was similar to the controls. The contrasting findings may partly reflect differences between the patients in terms of the symptom severity, the pathology or time since onset. The 10 patients reported in the previous study (Zackowski, Thach et al. 2002), consisted of 6 patients with cerebellar atrophy and two patients within one month of cerebellar stroke and 8/10 demonstrated moderate or severe ataxia. Whereas the group here consisted of all stroke patients with average time since stroke ranging from 3-24mths. Only 1 of the 6 cerebellar patients presented with severe coordination /speed deficits (Fugl-Meyer, Jaasko et al. 1975), the remainder having more mild to moderate impairments.

A prolonged deceleration phase was observed after stroke and particularly for patients with parietal lesions, suggestive of increased reliance upon corrective motor control. Whereas the normalised time of maximum aperture was more similar between groups, effectively lengthening the time between the two events for parietal patients. For the cerebellar group it had been anticipated that MA% would be early but this was not the case. As predicted however the onset of grip aperture was early in the cerebellar group, perhaps as a result of abnormal velocity control as speculated by previous authors (Haggard, Jenner et al. 1994; Rand, Shimansky et al. 2000) or movement sequencing and difficulty preparing the two movements simultaneously. The aperture onset generally occurred

prior to wrist onset for the cerebellar group whilst it occurred after wrist onset for the parietal group. After parietal stroke the timing of both these events was more variable.

The normalised time to peak velocity (M=33%, SD= 9) was consistent with previous studies where the peak is transported at 30-40% of the total movement time(Jeannerod 1981; Jeannerod 1984; Jeannerod 1986; Kudoh, Hattori et al. 1997). In support of previous work in stroke (Jeannerod 1986; VanVliet and Sheridan 2007) the peak was transported earlier than control ($p<0.05$) for the parietal subjects, this was a reliable observation in each condition. The cerebellar group also transported peak velocity earlier than controls but the difference was not significant and there was no statistical difference between the two stroke groups.

In support of previous research (Trombly 1992; Roby-Brami, Feydy et al. 2003; Michaelsen, Jacobs et al. 2004) it appeared that a strategy of trunk recruitment was used as an additional degree of freedom in compensation for limited arm use. Anterior trunk displacement (M=45.3, SD=51.6) was higher for stroke participants however the difference in the amplitude was not significant between groups and there were no differences in the coefficient of variation. Cirstea & Levin (Cirstea, Ptito et al. 2003) found that level of motor impairment FM scale was correlated with trunk displacement. Whilst we found that the degree of anterior trunk displacement was higher for patients, there was no correlation with clinical impairment.

With respect to the spatial aspect of grasp function, the scaling for size of maximum aperture in stroke participants was statistically no different to controls. We expected poor control for aperture scaling after stroke as a result of dysynergia or impaired visual mapping and difficulties processing this information during the deceleration phase. The relative difference in peak velocity between stroke participants and controls (peak velocity nearly 300mm/s lower for patient groups) may reflect compensation for poor scaling of grip aperture. It is unsurprising that control participants with the higher peak amplitudes displayed comparable aperture size, since faster movements are associated with larger grasp aperture (Wing, Turton et al. 1986). A greater number of aperture peaks during baseline trials supports initial difficulty with grip aperture scaling for the patient groups. The

normalised closure distance was statistically similar for each group but again more variable in the parietal stroke group.

Previous studies involving a heterogeneous group of stroke participants (van Vliet and Sheridan 2007; Michaelsen, Magdalon et al. 2009) do not show problems with grip aperture scaling, whereas in another (Lang, Wagner et al. 2005) grasp apertures were larger in the hemiparetic group when compared to controls. In all three studies (Lang, Wagner et al. 2005; van Vliet and Sheridan 2007; Michaelsen, Magdalon et al. 2009) within group variability was high. In studies involving specific lesion types both cerebellar participants (Haggard, Jenner et al. 1994; Rand, Shimansky et al. 2000; Zackowski, Thach et al. 2002) and parietal participants (Binkofsky F 1998) have demonstrated impairments in terms of increased absolute maximum aperture size.

In terms of the temporal aspect of grasp TMA% (M=69%, SD=11) was consistent with previous studies in control subjects (Jeannerod 1984; Wallace SA 1990) and for stroke (Vliet and Sheridan 2007) and was statistically similar between groups. Previous research suggested that the TMA would occur early for parietal stroke patients (Lang, Wagner et al. 2005; Nowak, Grefkes et al. 2007) and cerebellar participants (Haggard, Jenner et al. 1994; Rand, Shimansky et al. 2000) in comparison to controls, but this was not the case here.

Group comparison of the correlations between the TMA and both the TPV and TPD suggested that for unperturbed trials coordination between transport and grasp was comparable to controls. A significant correlation between the time of the peak velocity and the time of maximum aperture was demonstrated by 88% of control group, however only 75% of the parietal group and 63% of the cerebellar group had a significant correlation. Thus supporting previous suggestion that the correlation was weaker after stroke (van Vliet and Sheridan 2007).

Coordination between the hand and arm was controlled in these patients even though normally it might be controlled by the parietal lobe and or cerebellum. One explanation is that coordination between transport and grasp for RTG may be controlled by another area of the brain such as the Basal

Ganglia. The Basal Ganglia have already been implicated within the control of RTG for managing the sequencing of movements (Fagg and Arbib 1998), so this is one plausible explanation. Alternatively, specific coordinating structures within the parietal lobe such as the PPC were perhaps undamaged in this small sample of participants, more rigorous testing reporting of the lesion size and location would be needed in a future study to verify this account. Another alternative explanation is that impaired coordination was compensated for with more cortical control of slower movements, which require greater attention. As a result of functional reorganization and control by higher centres coordination which was previously impaired may have recovered by the time of testing. Further research to determine time dependent changes in RTG behaviour combined with fMRI is needed to provide further insight into the mechanism for coordination in patients with specific lesions.

Perturbed movements

The second aim of the study was to quantify how patients with right parietal or cerebellar lesions adjust transport-to-grasp when hand transport is perturbed and to verify whether the online adjustments necessary for good coordination are intact. The control group demonstrated rapid movement modification with perturbed trials lasting in the region of just (0.13s) 17% longer than unperturbed trials, which as reported previously (Paulignan, MacKenzie et al. 1990; Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991) is small enough to likely be below the threshold for conscious awareness. Similarly here the movement duration increased during perturbation trials by (0.21s) 13% and (0.16s) 12% for parietal and cerebellar patients respectively. Peak wrist velocity occurred earlier for perturbed movements and with lower amplitude, which is likely due to interruption in initial movement or movement re-organization (Paulignan, MacKenzie et al. 1990; Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991). Controls mainly responded to the perturbation of object location both with a double peak of grasp aperture as in previous research (Paulignan, MacKenzie et al. 1990; Paulignan, Mackenzie et al. 1991) and with a second wrist velocity peak (Paulignan, Mackenzie et al. 1991).

The relationship between peak wrist velocity and maximum aperture was largely preserved for perturbed trials, with maximum aperture occurring later. Temporal rescaling was supported by the significant correlations identified between the timing of both the peak wrist velocity and peak deceleration with maximum aperture. The last peak velocity also correlated significantly with the last aperture peak. The two perturbed conditions were comparable in terms of movement duration and smoothness. Patient groups demonstrated more velocity peaks in general as a result of segmented movements and therefore a direct group comparison is difficult. However both patient groups appeared to respond similarly to controls in response to the perturbation with an increased number of peaks during these trials. With respect to the number of aperture peaks, the majority of unperturbed trials elicited a single peak whereas a second peak in the grasp aperture profile was often observed in response to the perturbed trials. Both patient groups exhibited similar behaviour in terms of the grasp aperture.

The first sub-movement was interrupted early after perturbation and the second sub-movement was executed more rapidly than normal movement. Time for correction to the 10° was longer than to the 50° perhaps due to the greater complexity of motor organization required to revert agonist-antagonist pattern of activation from extension to flexion at the elbow and wrist. Perturbation of object location influenced both transport and grasp components. Finally, group comparisons showed that the correlations between the last TMA and both the last TPV and last TPD for both patient groups, were similar to that of controls during perturbed trials. For perturbed trials this correlation was observed in 75% of the cases in each of the three groups. Overall the results suggest that these patients responded similarly to controls in response to the perturbation of the object location.

Correlation between clinical impairment and reach to grasp movement variables.

Fugl-Meyer (Fugl-Meyer, Jaasko et al. 1975) measure of motor impairment provides a good indication of the prognosis for recovery (Prabhakaran, Zarahn et al. 2008). Here we found that on average Fugl-Meyer Upper limb scores were similar across the two patient groups. Correlation between patient Fugl-Meyer upper limb scores (Fugl-Meyer, Jaasko et al. 1975) and RTG movement

variables indicated that MT was reliably shorter and TPV occurred later in patients with least impairment. A prolonged deceleration phase was observed in the more impaired patients supporting the notion of faulty pre-programming and increased reliance upon corrective motor control. Stepwise multiple regression analysis was undertaken to determine the relationship between the multiple variables. For controls, quicker movements were associated with later and larger MA, supporting the ability to adjust the aperture size according to speed (Prabhakaran, Zarahn et al. 2008). The TPV, wrist trajectory distance, and trunk movement distance did not explain any further significant contribution to the variability in MT for healthy controls. This is in contrast to a previous study (Cirstea and Levin 2000) which found that in healthy subjects MT was related to trunk displacement.

For the patient group a positive relation between MT and WPT suggested that increased movement time that was seen in more impaired patients was related to an increased WPT. In contrast to the healthy participants there was no relationship between the size of the maximum aperture and the movement time, suggesting that the patient groups were less able to adjust grasp aperture according to the speed (Wing, Turton et al. 1986). For the patient group TPV, MA, and trunk movement distance did not explain any further significant contribution to the variability in MT.

With reference to the parietal group WPT accounted the majority of the variability in MT, whilst TMA, TPV, MA, and trunk movement distance did not explain any further significant contribution. This is consistent with the prolonged movement time anticipated for this group, as a result of impaired sensory perception and or integration that would contribute to spatial errors and reduced movement smoothness. For the cerebellar group, TMA explained much of the variance in MT possibly as a result of the faulty internal state estimation and impaired coordination between transport and grasp.

Conclusion

Mild to moderate clinical impairments were observed in the parietal and cerebellar participants together with general effects on transport and grasp. However there was no evidence of altered coordination between transport and grasp in either patient group during the movement. Thus we found significant correlations between the timing of maximum aperture with both the absolute timing of peak velocity and the timing of peak deceleration. The correlations were comparable to age matched controls, which suggested that either coordination between the hand and arm remained relatively intact in these participants, perhaps because the areas of the brain responsible for coordination remained undamaged or that impaired coordination was compensated for by other surviving neural tissue and/ or with slowed movements.

Whilst online adjustments in both patient groups were adequate to maintain coordination between the transport and grasp component, targeted treatment may promote the coupling between the transport and grasp components. Delayed movement onset and prolonged movement duration were identified in both patient groups. It was therefore proposed that patients with either a cerebellar or a parietal lesion would benefit from training, which would progress speed whilst promoting temporal and spatial stability of the hand and arm.

The proposed treatment was tested in a phase 1 proof of principle study in Chapter 4. Prior to which, a systematic review was carried out to establish a profile of existing treatments used to correct coordination deficits in the arm after stroke and to determine their effectiveness.

CHAPTER 3 INTERVENTIONS FOR IMPROVING COORDINATION OF REACH TO GRASP FOLLOWING STROKE: A SYSTEMATIC REVIEW

This chapter is drawn from the paper recently published in the International Journal of Evidence-Based Healthcare (Pelton, van Vliet et al. 2011). T. Pelton was the lead author and was responsible for the majority of the work. Prof. P. Van Vliet was second reviewer and K. Hollands acted as third reviewer and contributed advice where necessary.

In chapter 2 specific RTG movement deficits were identified in patients with lesions involving brain areas thought to be to be highly relevant to RTG coordination. The present chapter provides a profile of evidence-based interventions that have been targeted towards improving hand and arm coordination after stroke. The quality of the evidence and effectiveness of these interventions is described. The combined findings of the preceding chapters were considered for the design of a targeted intervention. In the subsequent chapter a proof of principle study examined the effectiveness of the intervention to ameliorate deficits in RTG coordination in patients with lesions involving the right parietal lobe or cerebellum/pontine region.

Abstract

Objectives: To identify and determine the effectiveness of all existing interventions targeted at coordination of arm and hand segments for reach to grasp following stroke.

Data Sources: The search spanned from 1950 to April 2010 and included English language papers from The Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; CINAHL; AMED; ProQuest Dissertations and Theses (International) and ISI Proceedings (Conference), PEDro, CSP Research and REHABDATA databases. A grey literature search included Mednar, Dissertation International, Conference Proceedings, National Institute of Health (NIH) Clinical Trials and the National Institute of Clinical Studies.

Study Selection: We included studies with a specific design objective related to coordination of the hand and arm during reach to grasp, involving participants with a clinical diagnosis of stroke and was inclusive with regard to study design. To determine effectiveness of interventions we analysed studies with coordination measures that exist within impairment measurement scales or specific kinematic measures of coordination.

Data extraction: Two review authors independently extracted data from the studies using standardised JBI-MAStARI data extraction forms.

Data synthesis: Pooling of results was not appropriate so the findings were summarized in tables and in narrative form.

Conclusions: The review identified three categories of potential interventions for improving hand and arm coordination after stroke; functional therapy, biofeedback or electrical stimulation and robot or computerised training. No definitive conclusion was drawn for the second question regarding the effectiveness of interventions aimed at improving hand and arm coordination after stroke.

Introduction

Studies suggest that although the arm and hand are normally controlled separately during reach to grasp, they are coordinated as one unit for skilled movement according to key temporal and spatial events (Jeannerod 1981; Jeannerod 1984; Hoff and Arbib 1993; Rosenbaum, Meulenbroek et al. 1999). Following stroke people demonstrate deficits of accuracy and efficiency (Lang, Wagner et al. 2005) in both aspects of reach and grasp. Upper extremity function can be directly affected by motor and sensory impairments as well as adaptive changes in response to stroke. Common problems with anticipatory hand shaping, premature hand closure, inadequate aperture, dysmetria, segmented and slowed movements all contribute to clumsy function or disuse after stroke. In comparison to healthy controls coordination of key spatiotemporal events, such as the correlation between the time of maximum aperture and peak deceleration, are not as tightly coupled in patients with moderate recovery after stroke (VanVliet and Sheridan 2007).

A growing body of evidence (Whitall, McCombe Waller et al. 2000; Cunningham, Stoykov et al. 2002; Hesse, Schulte-Tigges et al. 2003; Taub, Lum et al. 2005) highlights the potential for rehabilitation to improve upper extremity function after stroke, even in the chronic phase when patients were previously thought to plateau (Page, Gater et al. 2004). Improved coordination of reach to grasp may depend upon task specific practice which involves the use of grasp and transport together with emphasis on planning and executing the 2 components together (VanVliet and Sheridan 2007). Whereas, conventional therapy has perhaps failed to appreciate the importance of spatiotemporal links between the hand and arm, focusing instead upon more general aspects of upper limb function.

Upper limb motor deficit is the most common symptom following acute stroke with approximately 77% of patients demonstrating symptoms (Lawrence, Coshall et al. 2001). An initial scoping review revealed a small number of published reviews of treatment interventions for the upper limb following stroke (Coote and Stokes 2001; Hiraoke 2001; van der Lee, Snels et al. 2001; Barreca, Wolf et al. 2003) The most recent of these (Barreca, Wolf et al. 2003) identified potentially effective

treatment interventions for the overall management of the paretic upper limb. The present study aimed to build upon previous reviews and to provide more detailed analysis by focusing specifically upon treatments targeted at coordination of reach to grasp. To our knowledge there are no published articles that provide a detailed review of interventions, which are specifically aimed at improving coordination of the reach to grasp following stroke. A systematic review with considered synthesis of results provides a valuable tool for therapists, which will help to steer guidelines for retraining coordination of the upper limb following stroke.

The purpose of this systematic review was two-fold. Firstly, to provide a comprehensive account of the existing interventions targeted at coordination of arm and hand segments for reach to grasp following stroke and secondly, to determine the effectiveness of current treatments for improving coordination of reach to grasp after stroke.

Method

Search strategy

The initial search was undertaken in MEDLINE and identified studies containing the specified keywords (Appendix A3.1) in the title, abstract, or the index terms used to describe the article. A full search was performed with the strategy modified according to the relevant electronic database. Finally, the reference lists of identified articles were searched for additional studies. The search spanned from 1950 to April 2010 and was limited to English language papers only.

The following databases were searched: - Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library), MEDLINE (1950 to April 2010), EMBASE (1980 to April 2010), CINAHL (1982 to April 2010); AMED (1985 to April 2010), ProQuest Dissertations and Theses (International) and ISI Proceedings (Conference).

The grey literature search included Mednar, Dissertation International, Conference Proceedings, National Institutes of Health (NIH) Clinical Trials Database host: NIH

(http://clinicaltrials.gov/ct) and National Institute of Clinical Studies (http://www.med.monash.edu.au/healthservices/cce/index.html.

We also searched the following therapy databases:-Physiotherapy Evidence database (PEDro, http://www.pedro.fhs.usyd.edu.au/index.html), Chartered Society of Physiotherapy Research Database and REHABDATA (http://www.naric.com/research/rehab/default.cfm)

We used the search strategy found in Appendix A3.1, using a combination of controlled vocabulary (MeSH) and free text terms, for MEDLINE and modified it to suit other databases.

Inclusion criteria

Participants had to be adults (18 years and older) with a clinical diagnosis of stroke. Inclusion was regardless of lesion site, time since onset, co-morbidities, previous strokes, where intervention was carried out, initial motor impairment, or ability to follow instructions. We included studies that also recruited participants with other neurological disorders if the data on stroke subjects could be extracted from the data of non-stroke subjects. Subjects had to have a movement deficit in the upper limb. We included subjects with other additional movement deficits (e.g. of the lower limb or aphasia). Data on these participants was collected, documented and used to describe subgroups, such as time since lesion, lesion site and severity of stroke.

Studies could occur in any setting and had to include an intervention or manipulation aimed at improving coordination of the upper limb during reach and grasp. Coordination is a state-dependent control process in which motor commands to one effector depend on the predicted state of another effector (Diedrichsen, Criscimagna-Hemminger et al. 2007). Studies had to have a specific design objective related to coordination of the upper limb. We included studies, which used a single intervention, and also studies that delivered a treatment for coordination as part of a more complex package. The intervention could occur in reach and grasp, or could be delivered as a treatment separate from reach and grasp, if the aim is to improve coordination of hand and arm segments for reach and grasp. The intervention therefore normally involved the hand either grasping an object or

opening and closing. Treatments were prescribed, supervised or delivered by an allied health care professional, or delivered as part of a manipulation in an experimental study investigating the degree or extent of a physiological condition. Studies of bilateral arm training were only included if they involved measures of intra-limb coordination on the affected side. Any duration or intensity of programme was included and subgroups described.

Outcome measures

To provide a comprehensive account of the range of interventions, the review included studies with an intervention aimed at improving upper limb coordination, regardless of whether they incorporated an outcome measure. To determine effectiveness of interventions, studies with any measurement of upper limb coordination were included. These included:

i. Coordination measures that exist within impairment measurement scales such as the Fugl-Meyer Motor Assessment Scale (Fugl-Meyer, Jaasko et al. 1975).

ii. Specific measures of coordination such as movement velocity, acceleration, deceleration and movement duration, maximum hand aperture and reaction time.

Types of studies

For the purpose of answering the first question, the review was inclusive with regard to study design, in order to source all the existing and potential interventions for upper limb coordination. We included experimental studies including randomised, quasi-randomised and non-randomised controlled trials, cross over trials, and observational studies including case-control studies and cohort studies. Studies had to include an intervention or experimental manipulation targeted to improve coordination of the hand and arm following stroke. Studies concerned with the coordination of the shoulder and elbow were excluded if the hand was not involved in some aspect of the task, such as holding an object. Only studies written in the English language were included. For the second question, to determine effectiveness of interventions, the review included studies with any measurement of upper limb coordination.

Identification of relevant trials

Two review authors (PVV and TP) independently read the titles of the identified references and eliminated obviously irrelevant studies. Abstracts were obtained for the remaining studies and, based on the inclusion criteria (types of studies, types of participants, type of interventions), two review authors independently ranked these as 'possibly relevant', or definitely irrelevant'. If both review authors identified a study as 'definitely irrelevant' we excluded this study at this point. We retrieved the full text of studies categorised as 'possibly relevant', reviewed them, and classified them independently as 'include', 'exclude' or 'unsure'. We excluded studies classified as 'exclude' by both review authors. If there was disagreement between review authors, or a decision could not be reached, consensus was made through discussion, including a third review author as necessary.

Assessment of the methodological quality

Two review authors independently assessed the methodological quality of the studies using standardised critical appraisal assessment forms (see Appendix A3.2) from the JBI-MAStARI (Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review instrument). For case control and cohort studies the JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control was used. The JBI Critical Appraisal Checklist for Experimental Studies was used to assess experimental studies. In addition to the assessment of a particular bias associated with each experimental design we wished to assess features common to all of the included studies. Therefore for more rigour and details, we added the following additional questions about quality from the checklist for assessment of the methodological quality described by Downs and Black (Downs and Black 1998).

1) Is the hypothesis/aim/objective of the study clearly described?
2) Is there a sound theoretical basis on which the hypothesis is based?
3) Are the characteristics of the people included in the study clearly described?
4) Is the experimental design reliable & valid?

a. Randomization or counterbalance of intervention or experimental manipulation

b. Baseline comparisons between groups or conditions

c. Control condition/group comparisons or Pre-post comparisons

d. Blinding (where applicable)

5) Were the main findings of the study clearly described?

Each question was answered as either 'yes', 'no', or 'unclear'. Where insufficient information was provided, we attempted to contact the authors for further information.

Data extraction

Two review authors independently extracted data from the studies using a standard data extraction form the JBI-MAStARI and details regarding participants and intervention (see Appendix A3.2).

Data was organised in tables according to the type of intervention/manipulation. If a study included an experimental manipulation or condition as opposed to a direct intervention it was categorised under the appropriate heading. For example, repeated trials of reach to grasp was categorised under task specific practice.

If possible we also documented:

1) participant details (including age, gender, type of stroke, time since stroke, initial upper limb impairment, co-morbid conditions, pre-morbid disability)
2) sample size for each outcome for the intervention group and for any comparison groups.
3) the inclusion and exclusion criteria for recruitment of patients, and sampling frame for participant selection
4) a description of the coordination/reach to grasp intervention (including whether delivered as part of a package of treatment or as a specific intervention.)

5) the duration/intensity/frequency of intervention
6) setting in which the intervention was delivered
7) the comparison intervention, if there was one or pre and post comparisons in non-control condition studies
8) person delivering the intervention and their qualifications and experience
9) the outcome measurement(s) used to describe coordination
10) the outcome measurement(s) used to describe reach to grasp function

for each outcome, the mean and standard deviation for the intervention group and comparison groups

Data synthesis

Coordination interventions were described in detail. Theoretical bases for the interventions provided in the included studies, were extracted and recorded. Studies with and without a sound theoretical basis were identified. A sound theoretical basis may include either experimental evidence from studies with stroke subjects, extrapolation of research findings from studies on the healthy population, or excellent theoretical reasoning. The stated aims of each of the intervention types were documented.

Descriptive statistics were used to summarise the findings. Frequencies of items of interest were recorded, such as number of studies with coordination interventions for upper limb or reach to grasp, number of studies that found a difference in outcome between the coordination intervention and another group (no treatment, placebo, or alternative intervention). Means and standard deviations were reported where available, e.g. mean age of subjects, mean time since stroke and mean duration of treatment.

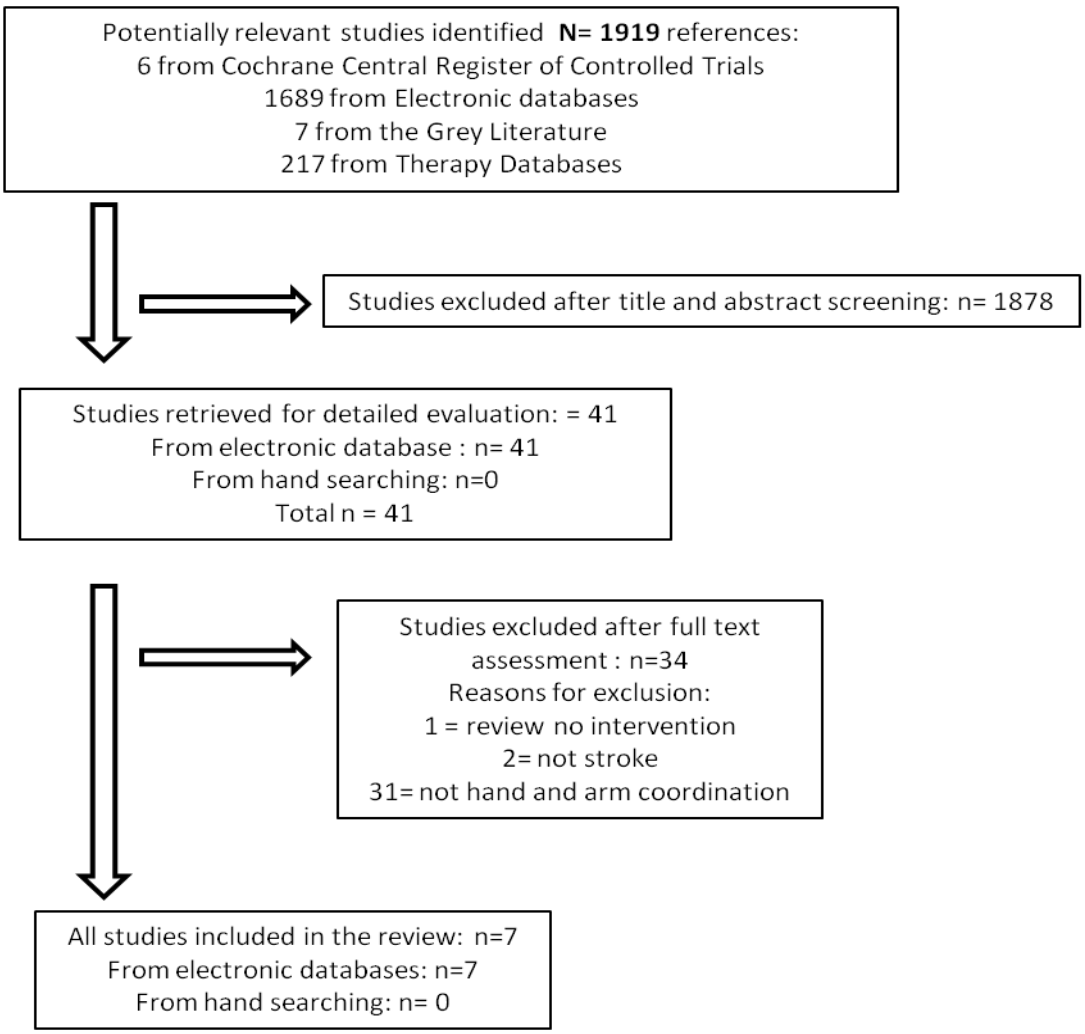
Comparative statistical analyses were only performed if a sufficient number of studies within each intervention type category employed the same measures. Studies to be included in meta-analysis

were to be analysed using JBI-MAStARI software. The approach used to summarise the main effects would be determined by the type of data. Either weighted mean difference or standardised mean differences were to be used for continuous data as appropriate. Confidence intervals (95%) were to be calculated for all data. If statistical pooling of results was not appropriate the findings were to be summarized in a narrative form.

Review Results

The search yielded 1919 non-duplicate titles of potential relevance (see Figure 3.1 Study selection process). In all, agreement was made to include 7 relevant studies.

Figure 3.1 Systematic Review Study Selection Process



Design

The included studies consisted of 1 randomized controlled trial (RCT) (Lin, Wu et al. 2007) which was assigned JBI evidence level 2 (JBI Hierarchy of evidence see Appendix A3.3). Two experimental case-control studies (VanVliet and Sheridan 2007; Krebs, Mernoff et al. 2008) were assigned JBI evidence level 3b. Krebs (Krebs, Mernoff et al. 2008) compared the treatment effects of two types of intervention, whereas van Vliet & Sheridan (VanVliet and Sheridan 2007) compared experimental manipulations in a within-subject design, and then compared stroke participants to age matched healthy controls. The remaining 4 experimental studies without controls were assigned JBI evidence level 3c. Two of these studies (Merians, Poizner et al. 2006) (Qiu, Fluet et al. 2009) employed a simple pretest-posttest design to observe treatment effects. One study (Koesler, Dafotakis et al. 2009) compared treatment and sham treatment effects with participants acting as their own controls. Lum and colleagues (Lum, Mulroy et al. 2009) observed the effects of treatment in 3 stroke participants and made comparisons with one other stroke patient who received usual care. For the purpose of this review comparison within stroke groups is considered, and healthy participant contrasts are omitted from the analysis.

Definition of hand and arm coordination

Hand and arm coordination was defined differently by the various authors. Three studies characterized hand and arm coordination using the percentage of total movement time to peak aperture (%TPGA) (Lin, Wu et al. 2007; VanVliet and Sheridan 2007; Koesler, Dafotakis et al. 2009). The timing of the peak aperture normally occurs at around 50-70% of the movement duration (Jeannerod 1984). After stroke peak grasp aperture might occur earlier in the movement (Lang, Wagner et al. 2005; Nowak, Grefkes et al. 2007), due to an increased reliance upon on-line feedback control. Similarly Qiu et al (Qiu, Fluet et al. 2009) employed the time after peak finger extension velocity. Hand and arm coordination has also been defined by an invariant significant relationship between the two components for reach and grasp (Jeannerod 1984; Castiello, Bennett et al. 1993) with

Pearsons' correlation coefficient values in the region of 0.8 for healthy controls. Correlations between the timing of key events of the hand and the arm movements were reported in two of the included studies(Merians, Poizner et al. 2006; VanVliet and Sheridan 2007). The key events being: i. timing of the onset for aperture opening and wrist onset (Merians, Poizner et al. 2006; VanVliet and Sheridan 2007) ii. timing of onset of arm movement and forearm pronation (Merians, Poizner et al. 2006) iii. timing of maximum grip aperture in relation to peak deceleration(VanVliet and Sheridan 2007). Lum et al (Lum, Mulroy et al. 2009) described the spatial coordination between hand and arm by calculating the correlation coefficient of the phase plot of aperture /elbow extension over the entire movement.

Table 3.1 Patient demographics

Study	Sample size	Male: Female	Age yrs Mean [Range] (SD)	Lesion Location R:L Hemisphere Cortical or subcortical	Type of stroke Ischemic : hemorrhage	Time since stroke months Mean [Range] (SD)	Final sample analysed
(Lin, Wu et al. 2007)	17 Exp 15 Ctrl	11:6 10:5	57.1 (18.3) 58.8 (15.2)	9:8 9:6	Unspecified	16.3mths (13-26mths) Chronic	16 Exp 14 Ctrl
(Koesler, Dafotakis et al. 2009)	12	10:2	67(7)	Subcortical	12:0	16(4) Chronic	12
(Krebs, Mernoff et al. 2008)	15 Exp 32 Ctrl	Unspecified	57.5 [27-79] (4.8)	27:2	Unspecified	29.1 (4.8) Chronic	15 Exp 32 Ctrl
(Lum, Mulroy et al. 2009)	3Exp 1Ctrl	Unspecified	Unspecified	Unspecified	Unspecified	[1-3] Sub acute	3 Exp 1 Ctrl
(Merians, Poizner et al. 2006)	8	6:2	64.3(10.7)	7:1	7:1	2.5 (1) Sub acute	8
(Qiu, Fluet et al. 2009)	8	5:3	56.38 (14.2)	Cortical	7:1 hemorrhage	54.7 (51.7) Chronic	8
(VanVliet and Sheridan 2007)	12	5:7	66.9	Unspecified	12:0	5.3 (6.7) Sub acute / chronic	12

Methodological quality

The methodological quality of each study was assessed using JBI standardised critical appraisal assessment tools and additional questions of quality (Downs and Black 1998) (see Appendix A3.2) . An overview is provided in Tables 3.2; 3.3 & 3.4

The included studies involved small sample sizes ranging from just 3 to 17. Most studies had some design limitations concerning participant sampling, failure to control for confounding factors and a lack of follow up. Five studies (Merians, Poizner et al. 2006; Lin, Wu et al. 2007; VanVliet and Sheridan 2007; Krebs, Mernoff et al. 2008; Koesler, Dafotakis et al. 2009) were judged to be of good methodological quality meeting the criteria in over 65% of all cases of the quality assessment. The remaining two studies (Lum, Mulroy et al. 2009; Qiu, Fluet et al. 2009) met the criteria in less than 60% of cases of the quality assessment.

Intervention Information

The first aim of the review was to provide a comprehensive account of the existing interventions targeted at coordination of arm and hand segments for reach-to-grasp following stroke.

In terms of answering the first question the review has identified three categories of potential intervention for improving hand and arm coordination after stroke; functional therapy, biofeedback or electrical stimulation and computerised or robot training; each with a different but not exclusive theoretical underpinning. Details of the interventions used by each of the studies to improve hand and arm coordination are summarized in Table 3.5.

Table 3.2 Patient characteristics JBI evidence level 2 M (SD) [Range]

Study	Sample size	Modified Ashworth Scale	Bruunstrom Proximal [1-5]	Bruunstrom Distal [1-5]	Motor Activity Log (MAL) [0-5]
(Lin, Wu et al. 2007)	17 Exp 15 Ctrl	0.41 (0.40) 0.32 (0.41)	4.5 [III-V] 4.5 [III-V]	4.5 [III-V] 4.5 [III-V]	0.64 (0.71) 0.69 (0.91)

Table 3.3 Patient characteristics JBI evidence level 3b & 3c M [SD] [Range]

Study	Sample size	Wolf Motor Function Test WMFT (Wolf, Catlin et al. 2001) (seconds)	Action Research Arm Test (Lyle 1981) [0-57]	Fugl-Meyer (Fugl-Meyer, Jaasko et al. 1975) [0-66]	Stroke Impact Scale (Duncan, Bode et al. 2003) (UE) [0-25]	Rivermead Upper Limb (Lincoln and Leadbitter 1979) [0-11]	Modified Rankin score (Bonita and Beaglehole 1988) [0-6]	JTHFT (Jebsen, Taylor et al. 1969) (Seconds)	Box& Block Test BBT (Mathiowetz, Volland et al. 1985) (Seconds|)	9 hole peg test 9HPT (Wade 1989) (Seconds)	NIHSS (Brott, Adams et al. 1989) [25]
(Koesler, Dafotakis et al. 2009)	12		51 (2)				2 (1)				4 (2.3)
(Krebs, Mernoff et al. 2008)	15 Exp 32 Ctrl			27.6 (13.9) 25 (9.6)							
(Lum, Mulroy et al. 2009)	3Exp 1Ctrl	8.4 (3) 1.55		37 (6) 58	9 (3) 16						
(Merians, Poizner et al. 2006)	8							196 (27)			16 (10)
(Qiu, Fluet et al. 2009)	8	57 (12)						117 (34)	35 (9)	92 (92)	
(VanVliet and Sheridan 2007)	12					9 (2)					

Table 3.4 Methodological quality summary – Randomized controlled trial (JBI Level 2 evidence)

Study	Impartial randomization *	Participants blinded to treatment allocation	Allocation concealment	Intention to treat analysis **	Blinding of outcome assessor	Baseline similarity	Groups treated identically other than intervention	Outcomes measured same for all groups	Outcome measures reliable	Appropriate statistics
(Lin, Wu et al. 2007)	Yes	No	Yes	Unclear	Yes	Yes	Unclear	Yes	Yes	Yes

Table 3.5 Methodological quality summary –case-control studies (JBI Level 3b evidence)

Study	Study Design	Representative sample of the population	Patients at a similar time course	Cases and controls - selection bias minimized	Confounding factors acknowledged & control strategy stated	Outcomes objective criteria	Follow-up over a significant time period	Intention to treat analysis **	Reliable Measurement of Outcomes	Appropriate statistics
(Krebs, Mernoff et al. 2008)	Case - control study	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
(VanVliet and Sheridan 2007)	Case-control study	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 3.6 Methodological quality summary – experimental studies without controls (JBI Level 3c evidence)

N.B. Lum et al 2009 was included in this group as only 1 control subject was used.

	Study Design	Random or pseudo-random sample	Clearly defined inclusion criteria	Confounding factors acknowledged & control strategy stated	Outcomes Objective criteria	Characteristics of the people included in the study clearly described	Follow-up over a sufficient time period	Intention to treat analysis **	Reliable Measurement of Outcomes	Appropriate statistics
(Koesler, Dafotakis et al. 2009)	Experimental study without control	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
(Lum, Mulroy et al. 2009)	Experimental study with 1 control	No	Yes	No	Yes	Yes	No	No	Yes	Yes
(Merians, Poizner et al. 2006)	Experimental study without control	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
(Qiu, Fluet et al. 2009)	Experimental study without control	No	No	No	Yes	Yes	No	Yes	Yes	Unclear

* Impartial – randomization using appropriate sequence generation, e.g. coin tossing, throwing dice, minimization. As opposed to non-random approach e.g. date of admission, hospital number or by availability.

** Intention to treat analysis – Either no missing outcome data or missing data balanced across groups, deemed unlikely to introduce bias or input using appropriate method.

Types of intervention

Three main treatment categories were identified:

1. Functional training - Lin et al (Lin, Wu et al. 2007) compared mCIMT with traditional therapy. mCIMT consisted of restriction of movement of the unaffected arm and intensive training of the affected arm. Activities included a range of object manipulations similar to daily life actions. These authors proposed that mCIMT may induce changes in motor control which would help to explain previously evidenced functional improvements. By comparison the traditional therapy concentrated on strength, balance and fine motor dexterity training, stretching and weight bearing by the affected arm and functional task practice. Using pre-post case study reports Lum and colleagues (Lum, Mulroy et al. 2009) evaluated a program of functional training in three stroke subjects and compared the results with one stroke subject who received no intervention, described as usual care. The functional treatment intervention involved collaborative goal setting real-world task practice, patient problem solving, confidence building and home practice. Impairment reduction coupled with repetitive task specific training in the form of ASAP Functional training was used to promote recovery in terms of restoration of normal movement kinematics and muscle activation patterns. Van Vliet & Sheridan (VanVliet and Sheridan 2007) examined temporal coupling adjustments for manipulation of transport speed and grasp size by comparing fast and preferred movements to large and small objects. These interventions combined some element of hand opening and closing with arm movements during task specific practice using actual objects.

2. Robot therapy or computerised training - Three studies (Merians, Poizner et al. 2006; Krebs, Mernoff et al. 2008; Qiu, Fluet et al. 2009) examined robot therapy or computerised training. For each of these studies the experimental intervention involved opening and closing of the hand during assisted arm movements. The first (Krebs, Mernoff et al. 2008) compared functional based robot training with impairment based robot training. The impairment based, control Group A subjects practiced reaching movements of the arm between targets on a computer screen without opening and closing the hand. The functional based, experimental robot therapy (Groups B & C) involved reach

together with active grasp. Group B practiced robot-assisted therapy with the hand free to interact with actual objects, whereas Group C practiced reach and grasp to a virtual object with the hand attached to a grasp sensor. It was speculated (Krebs, Mernoff et al. 2008) that 'functional robotic technology may assist task specific recovery at the capacity level (e.g. strength, isolated movement) whilst providing task specific, intensive therapy for impaired abilities (e.g. speed or coordination of limb movement)'. Merians et al (Merians, Poizner et al. 2006) and Qiu et al (Qiu, Fluet et al. 2009) both used a computerized virtual reality exercise system (VE) with instrumented gloves. Range of motion, speed of movement and fractionation exercises were performed with a glove for hand tracking; whilst strengthening exercises were performed with a force-feedback glove providing resisted finger flexion or assisted extension. With the exception of Group B participants in the Krebs et al (Krebs, Mernoff et al. 2008) study who manipulated an actual object during task specific reach to grasp training, subjects receiving robot therapy generally interacted with a virtual object. Qiu et al (Qiu, Fluet et al. 2009) employed robot-assisted VE rehabilitation for training hand and arm coordination based upon previous evidence of training induced improvements in patterns of shoulder and elbow coordination during reaching (Cirstea, Ptito et al. 2003; Woodbury, Howland et al. 2009) and during reaching and grasping (Caimmi, Carda et al. 2008). The theoretical underpinning for the study by Merians et al (Merians, Poizner et al. 2006) was that 'virtual rehabilitation provides an appropriate interactive, challenging and encouraging environment where stroke subjects can practice repetitively, execute tasks and be guided and rewarded through systematic feedback'.

3. Biofeedback or electrical stimulation - One study evaluated the effect of electrical somatosensory stimulation (ESS) compared with sham ESS (Koesler, Dafotakis et al. 2009). The intensity of stimulation to the median nerve was set to stimulate paraesthesia in the absence of pain or muscle activation so treatment in this study did not involve opening or closing of the hand. Participants were treated exactly the same for the sham control except for zero intensity of stimulation. The intervention did not include task specific practice. Koesler and colleagues (Koesler, Dafotakis et al. 2009) proposed that ESS had the potential to aid relearning of motor skills such as reach to grasp, based

upon enhanced neural excitability within the motor cortical areas. Effectiveness of current treatments for improving coordination of reach-to-grasp after stroke

The second aim of the review was to determine the effectiveness of current treatments for improving coordination of reach-to-grasp after stroke. Where possible study results should be pooled in statistical meta-analysis (Joanna Briggs Institute Review Manual), however when effects are diverse, or the number of methodologically adequate and relevant articles is small, pooling should not be done (Slavin 1995). In this review pooling of evidence for meta-analysis was inappropriate due to the heterogeneity of the population, diversity in terms of study design, treatment intervention and outcome measure and a prevalent risk of bias. Extraction of data which could be used to calculate effect sizes (the mean of the experimental group minus that of the control group divided by the control group's standard deviation) was impracticable due to insufficient data presentation. Instead, the reported results and authors conclusions are summarized in Table 4. A positive result in favor of the experimental group is denoted by '+', whereas 'O' indicates no reported difference, as used by van der Lee et al (van der Lee, Snels et al. 2001) .

Hand and arm coordination during reach to grasp

A summary of the training effects upon hand and arm coordination is presented in table 3.7. Four studies (1 RCT and 3 experimental studies without controls) report a result in favor of the experimental intervention for improved hand and arm coordination, whereas one experimental study without controls found no benefit. Two experimental studies with controls did not report specific training effects for hand and arm coordination after stroke.

There were two studies that indicated benefits to hand and arm coordination after functional therapy (Lin, Wu et al. 2007; Lum, Mulroy et al. 2009). In the first, (JBI evidence level 2) study (Lin, Wu et al. 2007) a RCT, mCIMT had a positive effect on the timing of peak grip aperture: time to peak grip aperture occurred later in the movement post intervention but the improvement was comparable with the traditional therapy group. These authors discussed the potential for these stroke patients with

mild to moderate impairments to have preserved ability to grasp a familiar target with little on-line correction of hand posture during enclosure. Here a possible ceiling effect for the percentage of movement time at which maximum aperture occurs might explain the comparable results for the two groups. The second study (Lum, Mulroy et al. 2009), an experimental study without controls suggested some benefit to distal inter-joint coordination in the 3 patients that received functional training; whereas no improvement was seen in the usual care subject. In this study participants were in the sub-acute phase and the experimental group was more severely impaired than the usual care comparison. van Vliet & Sheridan (VanVliet and Sheridan 2007) in a case-control study provide further support for preserved ability to adapt the temporal coupling to changes in cup size and speed of movement in a heterogeneous group of moderately impaired stroke participants. Correlations between the normalized timing of maximum aperture and peak deceleration which were lower for fast trials to the smaller object, suggest potential for experimental manipulation of task variables in the treatment of reach to grasp coordination.

Support for ESS was provided by Koesler et al (Koesler, Dafotakis et al. 2009), an experimental study without controls in which peak aperture occurred significantly ($p<0.05$) later after 2 hours of ESS. This involved 12 chronic subcortical stroke participants, mean age 67 years, with mild to moderate impairments. Support for robot therapy or computerised training came from Merians et al (Merians, Poizner et al. 2006) (JBI evidence level 3c). This experimental study without controls found more appropriate integration between hand shaping and arm transport after VE based sensorimotor rehabilitation. Subject specific benefits to hand and arm coordination during reach to grasp were reported following the experimental intervention. These sub-acute participants (mean age, 64 years) ranged widely in the level of stroke severity. In this experimental study without controls two subjects failed to improve but they were more significantly impaired than the remaining 6 who showed positive changes to arm and hand coordination. In contrast in an experimental study without controls Qui et al (Qiu, Fluet et al. 2009) found no clinically significant improvements after robot-assisted VE therapy to the time(s) after peak finger extension velocity with robot-assisted therapy. This study (JBI evidence level 3c) involved a group of 8 chronic stroke participants (mean age, 56

years) with moderate to severe impairments. The authors found the benefit of robot, VE therapy to improvements in hand and arm coordination to be inconclusive but emphasized the importance of intervention design with regards to task specific training and impairment level. Qiu et al (Qiu, Fluet et al. 2009) based a lack of improvement to hand and arm coordination during reach to grasp on the lack of task specific training distally. No specific coordination measure was reported by Krebs and colleagues (Krebs, Mernoff et al. 2008) in their case-control study although the robot therapy was aimed at improving hand and arm coordination. Improvement in Fugl-Meyer scores however supported task specific training in this study.

Table 3.7 Results hand and arm coordination during reach to grasp

+ Refers to a positive difference in favor of the experimental group; 0 no difference; - difference in favor of control group.

SS=statistically significant; NS=Not statistically significant.

Study	Sample size	Comparison interventions	Long Term FU	Relevant outcome measure	Reported Effect + 0 -	JBI Evidence Level	Theoretical basis. Author's conclusion.
Lin et al 2007 (Lin, Wu et al. 2007)	Exp16 Ctrls14	3 Different hospitals 3 Different Occupational therapist's **CIMT** Mitt 6 hours per day +training 2 hrs per day, 5 days per week 3 consecutive weeks = 30hrs Level of challenge based on ability and progression. Activities included a range of object manipulations similar to daily life actions. **Traditional therapy** Training 2 hrs per day, 5 days per week 3 consecutive weeks = 30 hrs Controlled for duration and intensity of patient-therapist interaction. Strength, balance and fine motor dexterity training, stretching and weight bearing activities and functional task practice.	None	% of MT to maximum grip aperture. Pre Rx Mean 67.89 [14.66] Mean 58.46[13.04] Mean change +6.44% Mean change + 3.69%	+ NS Comparable improvements	2	CIMT may induce changes in motor control which would help to explain previously evidenced functional improvements. Comparable improvement in grasping strategy for both groups.
(Koesler, Dafotakis et al. 2009)	Exp12	Unspecified location Unspecified therapist **Electrical somatosensory stimulation (ESS)** 2 hours Trains of ESS consisting of five pulses at 10Hz (1ms duration each) delivered every second. 60% above individual somatosensory threshold	None	% of MT to maximum grip aperture. No mean results reported, figure data and statistics only.	+ $p<0.05$ SS	3c	Relearning of motor skills such as reach to grasp, based upon enhanced neural excitability within the motor cortical areas Maximum aperture occurred later for movements of the

		The intensity of stimulation to the median nerve was set to stimulate paraesthesia in the absence of pain or muscle activation. Treatment did not involve opening or closing of the hand. **Sham ESS** 2 hours Zero intensity					unaffected hand and after ESS to affected hand. 2h ESS applied to the median nerve improved kinematics of reach to grasp movements performed with the affected hand.
(Krebs, Mernoff et al. 2008)	0	2 rehab hospitals Physiotherapist or Occupational therapist **Functional MIT-MANUS robot therapy** 1 hour 3 x per week for 6 weeks= 18hrs **Group B 9,000reps** Robot assisted therapy with the hand free to interact with actual objects. **Group C 12,000 reps** Reach and grasp to a virtual object with the hand attached to a grasp sensor. **Impairment reduction MIT-MANUS robot therapy** 1 hour 3 x per week for 6 weeks= 18hrs **Group A 18,000 reps** Reaching movements of the arm between targets on a computer screen without opening and closing the hand	None	Not reported	Not reported	3b	Functional robotic technology may assist task specific recovery at the capacity level (e.g. strength, isolated movement) whilst providing task specific, intensive therapy for impaired abilities (e.g. speed or coordination of limb movement). Until a minimum set of abilities are present, robotic training might serve a patient best if it focuses on impairment reduction, leaving it to integrate motor gains into function during a later phase of treatment.
(Lum, Mulroy et al. 2009)	03 Exp 01 Ctrl	2 rehab centres and 1 University Unspecified therapist **Accelerated skill acquisition Program (ASAP) Functional training** 2 to 3 hours / session 3 days per week for	None	Distal inter-joint coordination Aperture/elbow extension, r value.	+ NS	3c	Impairment reduction coupled with repetitive task specific training used to promote recovery in terms of restoration of normal movement

		4 to 5 weeks. Total of 30 hours training plus home practice= 24-45 hours Classic physiologic overload parameters were used to drive progress. Collaborative goal setting real-world task practice, patient problem solving, confidence building and home practice **Usual care** – no actual treatment of the arm **Healthy Comparison group** – nil intervention					kinematics and muscle activation patterns. Improvements in inter-joint coordination of RTG in ASAP group which in most cases were not seen in UCC group.
(Merians, Poizner et al. 2006)	Individual reports 8 participants	University lab setting Unspecified therapist **Virtual reality sensorimotor training.** A 3 week program consisting of 13 days training with weekend breaks – 2 to 2.5 h per session = 26-32.5hrs Total 3250 to 3900 trials Range of motion, speed of movement and fractionation exercises were performed with a glove for hand tracking; whilst strengthening exercises were performed with a force-feedback glove providing resisted finger flexion or assisted extension.	6 mths (n=2)	Timing of hand opening relative to hand displacement. Coordination between timing of onset of arm movement and forearm pronation.	+ (N=6/8) NS	3c	Virtual rehabilitation provides an appropriate interactive, challenging and encouraging environment where stroke participants can practice repetitively, execute tasks and be guided and rewarded through systematic feedback More appropriate integration between hand shaping and arm transport. Some retention of positive gains at 6 months.
(Qiu, Fluet et al. 2009)	Exp 01	Unspecified location Unspecified therapist **NJIT-RAVR Robot assisted virtual rehabilitation** 2-3 hours over 8 days= 16-24hrs Intensity unspecified Range of motion, speed of movement and fractionation exercises were performed with a	None	Time(s) after maximum finger extension velocity	0 NS	3c	Robot assisted VE rehabilitation for training hand and arm coordination based upon previous evidence of training induced improvements in patterns of shoulder and elbow coordination during

		glove for hand tracking; whilst strengthening exercises were performed with a force-feedback glove providing resisted finger flexion or assisted extension.					reaching (Cirstea, Ptito et al. 2003; Woodbury, Howland et al. 2009) and during reaching and grasping (Caimmi, Carda et al. 2008). No clinically significant improvements. Suggests that hand function may require task specific training more than the proximal upper extremity.
(VanVliet and Sheridan 2007)	Exp 08	University lab setting Physiotherapist **Experimental manipulation of object size and movement speed during task specific reach to grasp** I session 3-5 practice trials 5 min rest between practice and start of data collection. Total 32 trials - 8 trials per condition 5 mins rest half way - after preferred speed trials Compared fast and preferred movements to large and small objects.	None	Relation between wrist onset and start time of aperture Relation between TMA and TPD	NA	3b	Examined temporal coupling adjustments for manipulation of transport speed and grasp size Although stroke participants behave similarly the events are not as tightly coupled in stroke participants as they are in controls.

Discussion

Previous reviews of upper extremity rehabilitation

More general reviews of upper extremity rehabilitation following stroke suggest that a broad scope of physiotherapeutic methods exist for improving motor impairment but there is diversity in the methodological quality, stroke populations and the design of primary studies (Coote and Stokes 2001; Hiraoke 2001; van der Lee, Snels et al. 2001; Barreca, Wolf et al. 2003). There is support for treatments which involve repetitive, task-orientated movements (Coote and Stokes 2001) and more intensive exercise therapy may be beneficial (van der Lee, Snels et al. 2001). Positive treatment effects have been identified for sensorimotor training, electrical stimulation, biofeedback and imagery (Barreca, Wolf et al. 2003). One meta-analysis found medium effect sizes for conventional physical therapy and neurodevelopmental training whereas a large effect size was found for EMG biofeedback (Hiraoke 2001). Previous reviews of robot-assisted therapy after stroke (Prange, Jannink et al. 2006; Kwakkel, Kollen et al. 2008) have shown a significant improvement in upper limb motor control. Interestingly, Kwakkel et al (Kwakkel, Kollen et al. 2008) indicate the need for future research to 'concentrate on kinematical analysis to differentiate between genuine upper limb motor recovery and functional recovery due to compensation strategies by proximal control of the trunk and upper limb'. Research involving behavioural changes detected by motion analysis was in its infancy when Nowak (Nowak 2008) published an overview of the application of kinematic analysis in evaluating hand function after stroke. At that time Nowak (Nowak 2008) reported a limited number of studies which investigated the effects of treatment strategies on the kinematics of grasping, despite its reliability and sensitivity beyond conventional clinical tests and rating scales.

Aims of the review

With its focus upon studies aiming to improve hand and arm coordination this review builds on the conclusions of previous reviews and highlights the lack targeted treatments for improving hand and arm coordination after stroke. Despite this clear focus and the involvement of studies with a

similar objective, the studies employed different measures of hand and arm coordination; these being correlations between temporal and spatial aspects of the two components (Merians, Poizner et al. 2006; VanVliet and Sheridan 2007; Qiu, Fluet et al. 2009), percentage time to peak aperture (Koesler, Dafotakis et al. 2009) and Fugl-Meyer (VanVliet and Sheridan 2007; Krebs, Mernoff et al. 2008). There was heterogeneity of the population within and between studies, diversity in terms of study design, treatment intervention and a prevalent risk of bias. Pooling of evidence for meta-analysis was therefore inappropriate and the analysis was limited to a narrative review.

Existing interventions targeted at coordination of arm and hand segments for reach to grasp following stroke

We aimed firstly to provide a comprehensive account of the existing interventions targeted at coordination of arm and hand segments for reach to grasp following stroke. In contrast to the broad scope of physiotherapeutic interventions for improving upper extremity motor impairment (Coote and Stokes 2001; Hiraoke 2001; van der Lee, Snels et al. 2001; Barreca, Wolf et al. 2003) this review has identified a limited choice of studies with interventions currently targeted at improving hand and arm coordination. In terms of answering the first question the review has identified three categories of potential intervention for improving hand and arm coordination after stroke; functional therapy, biofeedback or electrical stimulation and robot or computerised training; each with a different but not exclusive theoretical underpinning.

As in previous reviews there was diversity in the methodological quality, stroke populations and experimental design. Hand and arm coordination was assessed using a variety of outcome measures. The intervention took place in rehabilitation hospitals, university laboratories or unspecified settings. In three studies the intervention was delivered or supervised by a therapist, the remaining studies did not specify the person's qualification. The duration of the exercise programmes ranged from 1 session to 5 weeks, the most frequent being 3 weeks. The frequency of the individual sessions ranged from 1 session to everyday, typically three times per week for two to three hours.

Effectiveness of interventions aimed at improving hand and arm coordination after stroke

Secondly, we aimed to determine the effectiveness of current treatments for improving coordination of reach to grasp after stroke. In view of the limited availability of good quality evidence and lack of empirical data this review does not draw a definitive conclusion for the second question regarding the effectiveness of interventions aimed at improving hand and arm coordination after stroke. The review identified seven studies involving interventions; 1 RCT, two experimental studies with controls and 4 experimental studies without controls for improving hand and arm coordination after stroke. Specific hand and arm coordination improvements during reach to grasp were noted in 1 RCT (Lin, Wu et al. 2007) and 3 experimental studies without controls, (Merians, Poizner et al. 2006; Koesler, Dafotakis et al. 2009; Lum, Mulroy et al. 2009) whereas one experimental study without controls (Qiu, Fluet et al. 2009) found no benefit. An intervention effect for hand and arm coordination was not reported in the two experimental studies which were case controlled (VanVliet and Sheridan 2007; Krebs, Mernoff et al. 2008). In the main, where differences were observed immediately post intervention there was limited evidence to suggest that these effects were maintained over longer periods of time. In one experimental manipulation study (VanVliet and Sheridan 2007) moderately impaired stroke participants showed temporal coupling similarities to healthy controls. Despite slower movements and greater reliance upon online feedback stroke participants were able to respond to changes in cup size and speed.

Quality of the evidence

The quality of current evidence for interventions designed to improve hand and arm coordination is only moderate. Overall the review involved a total of 75 participants at entry; all studies were small, with a maximum of 17 experimental stroke participants. Studies suffered from the lack of a control group, blinding of assessors and inadequate reporting of results. There was also limited follow-up data to demonstrate the extent to which the effects of interventions were maintained.

Lum et al (Lum, Mulroy et al. 2009) observed that both the extent and the type of improvement in reach and grasp were dependent upon the severity of the UL impairment. In that study improvements in distal interjoint coordination were more evident in the participant with the highest initial UL function, whereas proximal changes were more apparent in the two more severely impaired participants. Krebs et al (Krebs, Mernoff et al. 2008) also speculated that more impaired patients may benefit more from training focused upon impairment reduction before progressing onto integrating the motor gains into function. Similarly Lin et al (Lin, Wu et al. 2007) raised the possibility that high-functioning patients who are able to actively extend both the wrist and the fingers may respond better to mCIMT than patients less activity. Likewise, Merians et al (Merians, Poizner et al. 2006) observed that impairments of coordination and reduced range of movement which interfered with functional movements responded well to VE training The authors speculated that patients with more impaired hand function may benefit from haptic assistance and guidance as these patients were not as successful in this study.

Questions remain regarding the efficacy of interventions for improving hand and arm coordination after stroke and the review identifies implications for designing such interventions. Firstly the intensity of training required for clinically significant improvements in hand and arm coordination remains uncertain. Benefits were observed following 2 hours of electrical stimulation, whereas functional training and robot therapy ranged from 16 to 45 hours. More intensive exercise therapy may be beneficial for upper limb function after stroke (van der Lee, Snels et al. 2001) but commissioners of stroke services will want to see more intelligent forecasting of expenditure in the future and more intelligently designed interventions based upon further research.

The specificity of training is also an important variable for improving hand and arm coordination. Van Vliet & Sheridan (VanVliet and Sheridan 2007) have considered the importance of training the hand and arm together in order to activate temporally linked central commands for the two components, as opposed to treating the hand and arm separately. In support of this notion both Krebs (Krebs, Mernoff et al. 2008) and Qui et al (Qiu, Fluet et al. 2009) identified the need for task

specific training. Similarly Merians et al (Merians, Poizner et al. 2006) speculated that training which combines simple, isolated movements and more complex functional movements may provide higher task demand and has the potential for stronger training effects than exercising discrete movements alone. Those authors conclude that due to the interdependence between the transport and grasp components training the upper extremity as a unit may lead to improved outcomes. Contrary evidence from Koesler et al (Koesler, Dafotakis et al. 2009) however, showed improvements in hand and arm coordination after ESS despite the intervention involving no hand opening or closing movements, thus highlighting the importance of somatosensory input to motor learning. The persistence of ESS alone or as an adjunct to motor training together with its impact upon ADL remains to be tested. Van Vliet and Sheridan (VanVliet and Sheridan 2007) suggest that both the object size and speed of movement may be relevant to training. Similarly, Lin et al (Lin, Wu et al. 2007) identified the need for future research to investigate the benefits of incorporating task demands e.g. emphasis on speed and accuracy during goal directed actions into modified CIMT for task specific training.

Finally the quantity and quality of feedback is another important aspect of motor learning after stroke (Winstein, Merians et al. 1999). Merians et al (Merians, Poizner et al. 2006) highlight the capacity of the virtual environment system to provide augmented feedback in the form of knowledge of performance and knowledge of results. Equally, Krebs et al (Krebs, Mernoff et al. 2008) emphasize the importance of attention for rehabilitation of voluntary arm movement visually-guided attention-demanding interactive characteristic of their robot training system. The ASAP intervention (Lum, Mulroy et al. 2009) was also designed to include elements of interactive problem-solving.

Coordination deficits may arise from problems with anticipatory movement planning, execution and on-line control or both. These problems can be associated with specific impairments for example muscle weakness, abnormal muscle co-activation, proprioceptive loss, impairment in tactile sensation or sensory integration. Each of which may be affected to a lesser or greater degree by a specific lesion. Merians et al (Merians, Poizner et al. 2006) acknowledged variable and divergent

levels of recovery in their heterogeneous sample, and emphasised the need to discriminate the type of patient that would benefit most from VE-based therapy.

Limitations of the Review

We identified only 1 RCT, two case-control studies and 4 experimental studies without controls for inclusion in this review. The search was limited to published studies in English language. The literature search employed a thorough and systematic strategy during April 2010, however there are several potential sources of bias. Firstly additional studies were potentially not identified at the time or may have since been published. Secondly, in our attempt to identify all treatments used to improve hand and arm coordination we decided to include studies, which evaluated performance in a single session. It is argued that experimental manipulations of object size and location (VanVliet and Sheridan 2007) also have the potential to be used as interventions and are therefore important consideration for intervention design. Finally a subjective decision was made regarding the inclusion of studies based upon whether they involved an intervention or experimental manipulation targeted to improve coordination of the hand and arm following stroke. Some studies did not explicitly state this objective but used terminology such as motor control of reach to grasp or movement kinematics during reach to grasp within their aims. In such cases the two independent reviewers confirmed the objective for improving coordination of the hand and arm with the employment of relevant coordination measures e.g. percentage time to peak aperture or Fugl-Meyer as previously listed.

Conclusions

Although there is insufficient evidence to determine effectiveness of interventions for improving hand and arm coordination after stroke, this systematic review does indicate potential benefits. This review has attempted to provide a thorough and unbiased synthesis of research. It incorporates systematic literature search methods together with a detailed analysis of study characteristics. Meta-analysis was impracticable for reasons of insufficient data and risk of bias. Instead the methodological quality, study characteristics and presented results have been summarized

to allow readers to assess the conclusions drawn from individual studies. The authors have made every effort to provide clear review procedures and report sufficient information from the primary research findings to allow readers to reach independent conclusions. The strength of evidence contained within this review is limited, however it provides a valuable account of the existing data for the treatment of hand and arm coordination after stroke, which may help to refine hypotheses for treatment design and prioritise and shape future research agendas.

There is currently a lack of evidence to indicate which patients may benefit from rehabilitation of hand and arm coordination. Only a few studies have explored temporal coupling between the hand and arm after stroke. Heterogeneous stroke participant studies (Michaelsen, Dannenbaum et al. 2006; Lin, Wu et al. 2007; VanVliet and Sheridan 2007; Wu, Chen et al. 2007; Sangole and Levin 2009) suggest some abnormalities in the timing of grasp despite some preservation of temporal coordination. Recently studies have begun to identify specific impairments associated with different types of lesions. Specific grasp deficits have been related to lesions of the posterior parietal cortex, (Binkofsky F 1998) whereas lesions of the superior parietal lobe appear to disrupt the reaching component (Jakobson, Archibald et al. 1991). Impairments in the coupling of reach to grasp movements have also been demonstrated in cerebellar subjects who show variability in the timing of maximum aperture (Zackowski, Thach et al. 2002).

Implications for practice

There is currently insufficient evidence to provide strong recommendations about the effect of interventions for improving hand and arm coordination during reach to grasp after stroke. Preliminary research suggests that functional training, ESS and robot or computerised training may induce positive changes to the spatiotemporal coupling of the hand and arm. Furthermore this improvement appears to translate into upper limb functional gains. The review concurs with previous evidence for continued improvements in motor abilities in chronic stroke patients and specifically adds that improvements in hand and arm coordination can still be made. Notably no side effects were reported

and attrition was not a problem in any of these studies. More importantly the review highlights some theoretical implications for clinical practice, gaps in the research and directions for future research.

Implications for research

Future research should consider improvements in study design and reporting. Power calculations should be performed to ensure future studies have sufficient samples to determine if there are significant differences between groups. A consensus of reliable outcome measures for evaluating the effects of interventions on hand and arm coordination should also be established. RCTs with impartial randomization, adequate blinding and allocation concealment, group similarity at baseline, comparable intervention experiences and appropriate statistics with intention to treat analysis would enable meta-analysis comparison in the future.

Studies which monitor functional performance together with detailed kinematic measures of hand and arm coordination over time would help evaluate levels of recovery and compensation after stroke. Future studies incorporating functional imaging also have the potential to improve our understanding of the neural processes involved in recovery and compensation.

Further studies may help to link specific kinematic abnormalities with infarct location and to identify particular groups of patients who might be more likely to benefit from training. More detailed quantitative analysis in the future will enable therapists to direct therapy for hand and arm coordination more effectively to specific stroke deficits (Krakauer 2005). Further research could establish whether training benefits to hand and arm coordination are dependent on the initial level of impairment. Research is indicated to further establish the implications of attention and feedback for hand and arm coordination.

The present chapter has systematically established that currently a lack of clear evidence for therapists regarding the rehabilitation of hand and arm coordination. There is moderate evidence from three small to medium studies that functional training, may induce positive changes to the spatiotemporal coupling of the hand and arm, even in chronic stroke patients. This intervention poses

minimum risk and has shown good compliance. It was speculated that stroke patients with lesions affecting brain areas thought to be integral for RTG coordination, namely the parietal lobe or cerebellum would benefit from repetitive functional task training with auditory rhythmic cues (ARC). This treatment was designed to enhance the spatial and temporal relationship between the hand and arm. Despite similarities between the kinematic abnormalities of the two patient groups, the mechanism behind these deficits differs and as such it was anticipated that the two patient groups may respond similarly but for different reasons. The following proof of principle study aimed to evaluate patient tolerance to and potential effectiveness of ARC. In 6 case studies involving patients with parietal or cerebellar/pontine lesions the following chapter reports the response to ARC using detailed quantitative analysis of RTG movements.

CHAPTER 4: AUDITORY RHYTHMIC SENSORY CUES COMBINED WITH REPETITIVE TASK PRACTICE TO PROMOTE SPEED AND SPATIOTEMPORAL STABILITY OF HAND AND ARM COORDINATION DURING REACH TO GRASP.

Abstract

BACKGROUND: Earlier work in this thesis showed slowed reach to grasp (RTG) movements with spatial and temporal instability in both parietal and cerebellar patients although these two areas are held to have different functions in RTG coordination. It was suggested that patients with either parietal or cerebellar lesions would benefit from training that would progress speed of RTG whilst promoting temporal and spatial stability of the hand and arm. OBJECTIVE: Patient tolerance and potential effectiveness of combined Auditory Rhythmic Cueing with Repetitive Task Practice (ARC) of RTG was assessed in chronic stroke participants with specific parietal or cerebellar lesions. METHODS: A case study ABA design with multiple baselines was used for this proof of principle study. Training involved more than 3000 RTG movements during 6 practice sessions within a two-week period. A convenience sample of six chronic stroke survivors (mean age=58years, standard deviation=7) with either right parietal (N=3) or cerebellar (N=3) lesions participated in the study which was carried out in a University laboratory setting. OUTCOME MEASURES: RTG at both self-selected (SS) or fast as possible (FAST) pace was assessed using kinematic analysis for which performance indicators included wrist path trajectory (WPT) and normalized time to peak velocity (TPV%). The Ten Hole Peg Test (10HPT) was used as a clinical measure of dexterity. Grip strength served as a control outcome. RESULTS: High intensity practice was well tolerated. A significant reduction in WPT (n=3) and prolonged acceleration (n=2) indicated that RTG movements were shorter and that patients were less reliant upon feedback control after ARC. Improvements were maintained to some degree at 4-week follow up. Overall the absolute WPT and the TPV% were similar for the SS and FAST trials. There was a small overall training related improvement to the number of pegs moved per second in the 10HPT, whereas the control outcome, grip strength remained approximately constant. CONCLUSION: ARC showed some potential for improved motor control of

reach to grasp. For clinicians, no firm conclusion regarding effectiveness can be drawn at this point but the protocol was well tolerated. The relatively small changes suggest a need for more challenging practice and higher dosage.

Introduction

The importance of lesion location in helping to maximise treatment effects has recently been highlighted (Riley, Le et al. 2011). The study showed that tract specific injury is stronger at predicting treatment gains from robot therapy than infarct volume or baseline clinical status measures including Fugl-Meyer and Box and Blocks. The present study aims to provide early indications of how people with specific lesions to the parietal lobe and cerebellum respond to targeted treatment.

Support for functional task practice was presented in Chapter 3. The recent systematic literature review (Pelton, van Vliet et al. 2011) identified three main treatment categories used to improve hand and arm coordination after stroke: functional training, robot & computerised training and electrical somatosensory stimulation (ESS). There was insufficient evidence to draw conclusions about the effect of these interventions, although the review suggests that all three may induce positive changes to the spatiotemporal coupling of the hand and arm which appear to translate into upper limb functional gains. For example (Lin, Wu et al. 2007), a significant increase in the percentage movement time to peak velocity indicates a move towards greater dependency upon feedforward control after Constraint Induced Movement (involving 15 hours of intensive training and 3 weeks of daily restriction of the unaffected hand) in comparison to traditional rehabilitation.

Another study (Thielman, Dean et al. 2004) has indicated that functional task related training (TRT) may induce positive changes to the spatial coordination of reaching movements in low level functioning patients after stroke. These patients performed approximately 2000 repetitions of reaching to objects placed across the work-space over 12 sessions with progressions in speed. Low functioning patients demonstrated straightened hand paths, which suggested better coordination of elbow-shoulder motion following TRT. Except for slight differences in compensatory trunk movement, kinematics for the high-level subjects, with relatively normal movement organization were comparable after either TRT or progressive resistance training (which involved whole-arm pulling in planes and distances similar to that in TRT). Whilst this study does not support TRT over progressive resistance training in high-level subjects, it provides an indication of the dosage needed to obtain improvement.

There is also increasing evidence (Prassas, Thaut et al. 1997; Thaut, McIntosh et al. 1997; Whitall, McCombe Waller et al. 2000; Roerdink, Lamoth et al. 2007; Thaut, Leins et al. 2007; Pelton, Johannsen et al. 2010) to suggest that auditory rhythmic cues (ARC) may enhance motor control after stroke, as observed by decreased temporal and spatial variability and increased speed of movement. Previous research has utilized ARC to promote the temporal stability of movement in gait (Prassas, Thaut et al. 1997; Thaut, McIntosh et al. 1997; Roerdink, Lamoth et al. 2007; Thaut, Leins et al. 2007; Pelton, Johannsen et al. 2010) and reaching (Whitall, McCombe Waller et al. 2000; Thaut, Kenyon et al. 2002; Malcolm, Massie et al. 2009). The latter study (Thaut, Kenyon et al. 2002) showed that cued movements are associated with improvements to the kinematic stability of hemiparetic repetitive arm reaching motion (in terms of smoothness of the velocity curve).

Rhythmic auditory cues provide a fixed reference interval for a given movement and are thought to aid movement planning and execution through entrainment and synchronization with the predictable sensory cues (Thaut and McIntosh 1999; Molinari, Leggio et al. 2003; Thaut 2003; Malcolm, Massie et al. 2009). Auditory-motor entrainment enables the brain to map and scale smoother time parameters for position change throughout the movement, thus regulating the entire movement trajectory (Thaut, Kenyon et al. 1999). In this way ARC which provides a temporal constraint to movements may influence feed-forward mechanisms (Malcolm, Massie et al. 2009) and as such can facilitate planning. Early evidence (Paltsev and Elner 1967) has also suggested a priming effect by which sound can influence the threshold excitability of spinal motor neurons in preparation for movement. As such, it is therefore a potentially useful adjunct to promote the recovery of motor control after stroke.

It maybe that the cyclic nature of the rhythmically cued movement promotes the tuning spatiotemporal features with each repetition, over and above discrete, stop and restart movements (Thaut, Kenyon et al. 2002), because it activates additional brain areas (Thaut 2003). Neuroimaging studies which have involved synchronization of finger tapping movements to an auditory rhythm have shown additional activation of the ipsilateral prefrontal cortex, contralateral primary sensorimotor

areas, bilateral SII, bilateral premotor areas, contralateral insula, putamen and thalamus, with consistent involvement of the cerebellum (Thaut 2003). Interestingly one study has shown that motor entrainment to rhythmic stimuli after cerebellar pathology is comparable to healthy controls, suggesting a direct link between auditory and motor structure which may be utilised in rehabilitation (Molinari, Leggio et al. 2005). Further support for auditory –motor interactions comes from another imaging study (Chen, Zatorre et al. 2006), which demonstrated functional coupling between the Superior temporal gyrus and the dorsal premotor cortex during finger tapping.

Lesions resulting from stroke reduce the neural activation available for action, so for recovery to take place there is a need to facilitate activation of surviving brain areas. Performance of higher level tasks such as RTG with additional sensory cues might achieve more activation than practicing the individual components of elbow extension or finger extension alone. Since movements are planned and executed as coordinated units or schemas, and the brain is wired for function, training should be as task based as possible rather than strengthening muscles in isolation (VanVliet and Sheridan 2007). In fact previous recommendations suggest that RTG training should involve practice of reach and grasp together to activate temporally linked commands (Michaelsen, Jacobs et al. 2004; van Vliet and Sheridan 2007).

Hemiparetic RTG movements have previously been identified with spatiotemporal changes which include increased movement time (Lang, Wagner et al. 2005; Vliet and Sheridan 2007), increased deceleration phase (Vliet and Sheridan 2007), increased variability of timing of peak velocity (vanVliet, Kerwin et al. 1995) and decreased movement smoothness (Lang, Wagner et al. 2005). Disruptions to the normal spatiotemporal relationship between transport and grasp are anticipated in patients with lesions involving brain areas thought to be critical for coordination of RTG. Indeed, kinematic results from our laboratory suggest that RTG movements are impaired in patients with mild to moderate clinical signs following stroke involving the right parietal lobe or cerebellum. Specifically, both patient groups suffer from delayed movement onset, prolonged movement time, reduced velocity amplitude, decreased movement smoothness (as defined by the

number of wrist velocity peaks) and initial difficulty with parameterization. For patients with right parietal lesions the wrist movement trajectory is significantly longer and more variable, the normalised closure distance is more variable in the parietal stroke group and the timing of the normalised peak velocity is reliably early and more variable. Aperture onset generally occurs early after cerebellar lesions and late in the parietal group.

Since movement time is prolonged after parietal or cerebellar stroke it is anticipated that both these patient groups will benefit from training to progress the speed. Whilst movement duration is an important performance indicator, it is most likely to reflect muscle strength, whereas measures of movement coordination appear to be more informative for recovery (Hogan, Krebs et al. 2006). It has been suggested previously that the timing of peak velocity may be indicative of skilled motor control (vanVliet, Kerwin et al. 1995) and that it is normally adjusted according to task constraints with earlier execution for precision tasks (Marteniuk, MacKenzie et al. 1987) such as rapidly grasping a small object. Parietal and cerebellar stoke patients both have a greater dependency upon feedback control during RTG. Increased feedback control after stroke is thought perhaps to compensate for increased variability (van Vliet and Sheridan 2007). Practice which encourages increased speed of movement may help to normalise movement durations, promote greater use of feedforward motor control and improve programming of the movement. For good recovery of RTG it is considered important for these patients to maintain the normal temporal and spatial stability of the hand and arm when movements are performed at faster paces. Here, a short wrist path trajectory with a smooth velocity profile and temporal invariance in terms of TPV% indicates good spatiotemporal stability. Practice of slow errorless movement may help to compensate for obvious impairment, but may not challenge the system for improvement therefore training should allow sufficient functional practice with progressing speed to increase consistency of movement performance (Stergiou, Harbourne et al. 2006).

This study was motivated by wanting to know whether ARC is tolerated and helpful for patients with lesions to the areas generally accepted to be involved in coordination and who moved slower in RTG. Assuming parietal and cerebellar involvement roles in coordination are not identical,

ARC may possibly help with differential improvement. Furthermore fast (FAST) and self-selected (SS) paced conditions are examined before and after training to explore the effect of speed upon the hand and arm coordination during RTG. Both temporal (Newell, Carlton et al. 1982) and spatial (Wing, Turton et al. 1986) variability are liable to increase with faster movements. Fast movements place a greater demand on accuracy (Fitts 1954), with less time available to make fine adjustments. Increasing speeds produce higher passive torques that contribute to greater spatial variability unless they are counterbalanced by appropriate muscle activation. The increased variability, which may uncouple reach and grasp components in both spatial and temporal domains is more profound in fast and accurate movements (Erickson and van Kan 2005; van Vliet and Sheridan 2007) and stronger muscle forces are needed to counteract interaction torques with increasing speed. The cerebellar failure might be in prediction, specification of compensation needed, or implementation of appropriate forces (Bastian, Martin et al. 1996; Topka, Konczak et al. 1998; Topka, Konczak et al. 1998), whereas impaired sensory input could explain parietal deficits. Incoordination of the shoulder and the elbow joints, a curved trajectory, and overshooting are particularly evident during fast-accurate reaches, which may be partly compensated for by using a decomposition strategy to simplify the movement during slower reaches (Bastian, Martin et al. 1996). Accordingly it is suggested (Bastian 1997) that patients with cerebellar lesions may be best treated with strategies to stabilize movements by minimizing the number of joints and slowing of movements to overcome the inability to coordinate the relative activity of multiple muscles and adjust movements for interaction torques caused by other moving joints. This strategic approach however teaches the patient to avoid the problem rather than regain the skills to handle it.

Conversely, another direction for treatment would be to progress the speed of movements with training. Here good reaching performance is considered to be that which consists of a direct wrist trajectory path with few sub-movements, which can be performed under various speeds, different load conditions and from many locations in the reaching space. This view follows from development research (Thelen, Corbetta et al. 1996) in which reaching was observed in infants during the first year. It was reported that during developmental periods, increasing speed was associated with reduced path

straightness but which occurred prior to periods of stability. It is suggested that for stroke patients coordinated control may be comparable to controls within a restricted speed range; however for adaptive movement it is necessary to parameterise movements more flexibly. Therefore it is speculated that training which promotes speed will ultimately contribute to more stable movement patterns with more flexible control over a greater range of velocities. Indeed it has previously been suggested that patients with cerebellar ataxia should practice repetitions with fast movements (Topka, Konczak et al. 1998).

Given the above considerations it is proposed here that in comparison to self-selected (SS) trials, fast (FAST) paced trials would be performed with more variability and time to peak velocity would be early in order to compensate for spatial variability. Furthermore progressive ARC will increase SS speed of movement and promote the spatiotemporal stability of the hand and arm during reach to grasp after stroke affecting either the right parietal lobe or cerebellum.

Accordingly a proof of principle study was run to determine if this novel treatment approach is safe and well tolerated by hemiparetic stroke participants with mild to moderate impairments. It also examined whether ARC has any effect upon the performance of RTG movements, which should warrant potential further investigation. The treatment was directed at 6 chronic stroke participants with mild to moderate impairments. This phase I study aimed to determine if such moderately high-level participants would show any measurable evidence of the intended effect. This group of patients already have many opportunities to practice within their activities of daily living (Dobkin 2009) and as such may be the most challenging patients to demonstrate a treatment related change. The study examined whether intensive ARC involving approximately 3600 repetitions of reach, grasp and lift movements over the course of 6 training days was sufficient to augment RTG performance.

It was anticipated that ability to transfer pegs using a pinch grip during the 10 Hole peg test would increase after task specific practice, whereas grip strength would show no significant training effect. These two tests together represent a check on specificity of intervention effects. Additionally, for RTG movements reaction time was expected to be quicker; the movement duration shorter; the

amplitude of peak velocity higher; time to peak velocity later; the wrist path trajectory shorter; with fewer peaks in the aperture distance and wrist velocity after training. Follow up assessment was made at 4 weeks to determine retention.

Methods

A proof of principle, pilot single case ABA design involving 6 stroke participants was used to determine whether ARC training can improve coordination of reach and grasp. A phased approach is considered important in the development of a new intervention (Craig, Dieppe et al. 2008) beginning with a series of pilot studies to test the concept, assess safety and feasibility and establish protocol. At a later stage in the process a group design is preferable, moving towards a more exploratory and then a definitive evaluation with a randomized controlled trial.

Setting

Data collection, treatment and analysis were based at the School of Psychology, University of Birmingham. Patients were brought to the University using pre-arranged and prepaid taxi transport. Both the training and the assessments were conducted by the author (a physiotherapist) or a Masters Research Student who was trained by the author. Data analysis was performed by the author.

Participants (Table 4.1)

A convenience sample of three right parietal and 3 cerebellar chronic stroke participants were identified from experiment 1 as eligible and were asked to participate in the study. Inclusion criteria were as follows: (i) cerebellar (or pontine) or right parietal stroke of ischaemic or haemorrhagic origin, confirmed by CT scan but not restricted to these areas (ii) a score of 6 or more on the arm section of the Rivermead Motor Assessment (RMA), i.e. ability to reach forward, pick up tennis ball, release at mid thigh on affected side x 5 (iii) Informed consent. Recruitment was inclusive in terms of time since stroke. Exclusion criteria comprised of (i) cognitive dysfunction preventing understanding

of the task, (ii) concurrent medical problems which would prevent repetitive reaching (e.g. shoulder pain).

Clinical measures of impairment and function

Clinical examination included Fugl-Meyer Upper Extremity Motor Function (Fugl-Meyer, Jaasko et al. 1975); Revised Nottingham Sensory Assessment (NSA)(Lincoln, Jackson et al. 1998); Nottingham Extended Activities of Daily Living (NEADL) (Nouri and Lincoln 1987); standard clinical testing procedures for tactile extinction (light touch with fingers to the subjects hand) (Tucker and Bigler 1989) and visual extinction (in which the patient fixates the examiner's nose, the examiner's arms are outstretched, and the patient has to detect movements of the examiner's index finger on either or both sides) (Baylis, Driver et al. 1993), Modified Ashworth Scale (MAS) (Bohannon R 1987) and the Medical Research Council scale (Compston 2010) muscle strength test of the more involved upper limb. Upper limb range of movement (ROM) was recorded as either full or reduced relative to the less impaired side.

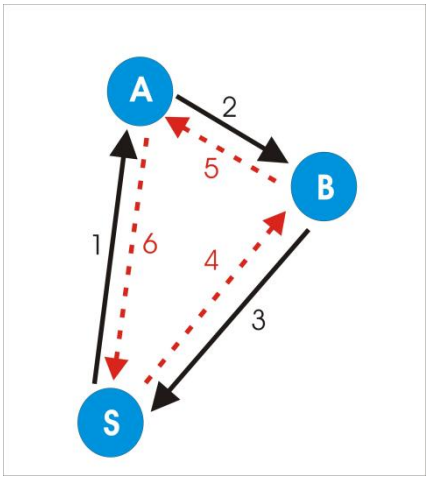
Intervention

Participants were receiving no other forms of rehabilitation throughout the experimental period. The intervention combined repetitive task practice with a rhythmic auditory metronome beat and was conducted in six 1hour sessions over a period of two weeks. The practice task involved reach, grasp, lift and transfer movements. Participants were seated in a comfortable position, close to a table edge, the sternum in line with the start position (see fig 4.1. 'S') and with the pads of the index finger and thumb resting together on the start button. Reaches were to a perspex cylinder, 8cm tall * 1.5 cm in diameter (with a 4cm diameter base 1cm in height). During rhythmic training trials, patients were asked to reach, grasp, lift and transport the object in time with the metronome beat. The metronome beat was controlled with 'Audacity' version 1.2.6 (a free on-line computer based Digital Auditory Editor) and presented with one speaker to each side of the participant. The sequence began with the participant grasping the object from position A on the first beat, moving it to position B on the next beat, and returning the hand to start button on the following beat. On the next beat the patient was

required to grasp the object from position B, transport it back to position A on the next beat and return the hand to the start position on the next beat. The sequence continued with participants moving the object between the two alternate positions until the 40-second period was complete. After a 20 second rest period the participant began another training period of 40 seconds. Rhythmic cue frequency was matched to the patient's self-selected-paced movement frequency, assessed in one 5 minute practice session before the start of treatment. The frequency of rhythm was increased incrementally by 5 to 10% per session depending on the patient's ability and experimenter judgement.

It was anticipated that participants would complete an average number of RTG repetitions of approximately 600 per day and in total 3600 reps would be completed over the course of 6 days training. This was based upon 5 treatment sessions, each consisting of 4 blocks of 15 minutes practice. Participants were required to train for 30 seconds and then rest for 30 seconds repeatedly within each 15 minute block. It was estimated for each 30 seconds training that stroke participants could complete approximately 10 repetitions. Previous work in this laboratory (Johannsen, Wing et al. 2010) has demonstrated that stroke participants are able to perform repetitive lower limb movements at a similar intensity without negative side effects. In that previous study a total of 10 hours training over the course of 5 week resulted in improvements in step length and number of cycles of a foot placement task. In the current study a similar dose of treatment was completed in a more intense 2 week period. Previous researchers (Birkenmeier, Prager et al. 2010) have also demonstrated that stroke participants are able to perform over 300 repetitions (not auditory cued) of a functional upper limb task per session without negative side effects.

Figure 4.1.Diagram to show six sub-movements of the Reach to Grasp (RTG) training task. Each cycle consists of six sub-movements. Each sub-movement is completed at the same time as one metronome beat as follows: 1. reaching and grasping the object from position A; 2. moving object to position B; 3. returning the hand to start button; 4. reaching and grasping object from position B; 5. moving object to position A; 6. return hand to start button. Black arrows illustrate first three movements (1-3), red, dashed arrows highlight three, return movements (4-6). The distance between the start (S) and position A (A) or position B (B) =35cm, the distance between position A and B =25cm.



Outcome measures

The following outcome measures were used to assess tolerance of intervention:-

Training Logs were completed during each session to determine adherence to the treatment protocol.

The Borg Rate of Perceived Exertion (RPE) (Borg 1982). The scale (where 0 is perceived as no exertion at all and 10 is perceived as very, very hard) was used to determine the participants perceived level of exertion after each 15minute session (4 on each of the training days).

Training Satisfaction Questionnaire. A satisfaction questionnaire was used as an additional subjective rating scale to determine the value of the training experience and to report experienced side effects including pain, muscle stiffness and fatigue. This was a take home questionnaire, which was given to participants after the final training session. A scale of 1 to 7 was used with instructions to 'please tick the box that most accurately describes your experience'.

The following outcome measures were used to assess motor control:-

Motor performance outcome measures were recorded at Baseline on 3 separate days (B1, B2, B3) during the week prior to the start of training. Post training assessment (Post) was taken one to two days after training was completed and follow-up (FU) assessment one month later.

10 Hole peg test - Hand dexterity was measured using the 10hole peg test as the primary clinical outcome measure. In a seated position at a table participants were asked to take 10 dowels from a board on the table top and place them into 10 holes on the opposite side of the board. The time to complete all 10 pegs was recorded, with a cut-off at 1 minute (when the number placed was recorded). The number of pegs placed per second was then calculated (Heller, Wade et al. 1987). Participants performed 5 practice trials with each arm in session 1. The mean of 8 test measurements per session was used for analysis. The mean of 8 trials with the non-paretic side was also recorded during session 1 for the purpose of descriptive comparison.

Grip strength - Grip strength was measured using a Smedley digital hand dynamometer (model 12-0286) as a control outcome variable; it was anticipated that the Grip strength would not be influenced by training which did not incorporate strengthening exercises. Participants performed 5 practice trials with each hand during the first session followed by a 5 minute rest. The mean of 8 test measurements in each assessment session was used for analysis. The mean of 8 trials for the non-paretic side was also taken during session 1 only for descriptive comparison.

Kinematic analysis of motor control of reach to grasp - Kinematic analysis was used to detect specific changes in reach to grasp motor control. Data was captured using a Qualysis ProReflex MCU240 3D (Qualysis 2006) motion analysis system with four infrared cameras and a sample rate of 200Hz. Data from reflective markers positioned on the wrist, finger and thumb was analysed using custom written programs in Matlab version R2010a (see Appendix 2.1). Each trial consisted of one movement involving reach, grasp and lift of the target object which was located 30° off midline, in the hemispace ipsilateral to the parietal lesion or contralateral to the cerebellar/pontine lesion. Using the paretic limb

participants were required to complete 5 practice trials followed by 2 blocks of 10 assessment trials each separated by a 1 minute rest interval. During block1 participants performed reach, grasp and lift movements at a self-selected pace (SS). In block 2 participants performed the same movements at a FAST pace. Performance indicators were as follows:

Kinematic variable definitions

Wrist path trajectory (WPT mm): The wrist path trajectory (spatial path) was defined as the sum of the distance of the wrist between each frame of the movement duration.

TPV (%): The time at which peak velocity occurred was expressed as percentage of the total movement duration). This value was used as an indication of the proportion of the movement which was either pre-planned or reliant upon on-line feedback.

Movement duration (s): The time between wrist movement onset (time at which the velocity of the wrist marker exceeded 25mm/s for 5 consecutive frames) and object lift-off (the time at which the velocity of the object exceeded 25mm/s for 5 consecutive frames in the vertical dimension.

Reaction time (s): The time between the object illumination and the wrist movement onset.

Peak velocity amplitude mm(s): The maximum amplitude in the tangential wrist velocity between wrist movement onset and object lift-off.

Movement smoothness: Quantified by the number of peaks in the tangential wrist velocity and the aperture size. Peaks were detected using a library M-script 'Peakdet' for Matlab version R2010a (delta 0.5) and counted if the difference between the peak and the preceding 'valley' (minimum value) exceeded 15% of the global maximum amplitude (Kahn, Zygman et al. 2001). The number of identified wrist velocity and aperture size peaks was recorded. For each component the time of the last peak prior to object lift-off was also recorded.

Statistical Analysis

Paired sample t-tests were employed to compare Baseline, Post-test and Follow Up mean scores for the 10HPT and GS measures. Two-way repeated ANOVA were used to compare the means

of the kinematic variables with condition (SS and FAST pace) and time (Baseline, Post-test and Follow Up) as the two independent variables. Analyses included Bonferonni correction and $p<0.05$ was classed as significant.

Results

Participant characteristics

Table 4.1 Participant characteristics

	Lesion	Time since stroke (mths)	Age (yrs)	Dom hand	NSA (9)	FMUL (66)	Extinction		FROM (y/n)	Elbow MAS (5)	MRC Muscle Strength (5)
							Tactile (y/n)	Visual (y/n)			
A.	R P	32	56	R	5	51	n	n	y	0	4
B.	R P	77	56	R	6	64	y	y	y	0	5
C.	R P	72	58	R	4	53	y	n	y	1	4
		60	57		5	56					
D.	Pontine	25	66	R	9	50	n	n	y	2	4
E.	R Cb	20	63	L	9	54	n	n	y	0	3
F.	L Cb	6	47	R	9	54	n	n	y	0	5
		17	59		9	53					

DOM hand = dominant hand
10HPT (s) (Turton and Fraser 1986)= 10-hole peg test is the time taken to transfer of pegs using a pinch grip, from one side of a block of wood to holes on the opposite side of the block.
NSA(Lincoln, Jackson et al. 1998) =Nottingham sensory assessment score for the hand consisting of – Light touch, pin prick and stereognosis (0= absent, 1 impaired, 2 normal); and proprioception (0- absent, 1 appreciation of movement (wrong direction), 2 Direction of movement (<10 degrees), 3 Joint position sense (<10 degrees)).
NEADL (Nouri and Lincoln 1987)= Nottingham Extended Activities of Daily Living. Group average from a maximum of 63 = 21 activities (0=Not at all, 1with help, 2 alone with difficulty, 3 alone easily)
FMUL (Fugl-Meyer, Jaasko et al. 1975)= Fugl-Meyer Assessment upper limb section.
Visual and tactile Extinction (Vallar, Rusconi et al. 1994) (Bisiach, Vallar et al. 1986). Participants were classified as showing positive signs of extinction (Y), if after double stimulation they failed to perceive the stimulus on the left, in more than 30% of the trials, but correctly reported more than 80% of single left and 100% of single right stimuli.
FROM = Full active range of movement, y=yes, n=no.
MAS (Bohannon R 1987)(Modified Ashworth Scale) - 0=No increase in muscle tone; 1=min resistance at end of range; 2=slight increase min resistance in second half of movement; 3=increase in muscle tone through most of range; 4=passive movement difficult; 5=rigid
MRC Muscle strength (Compston 2010)- The Medical Research Council grading system for the evaluation of muscle strength - 1=Flicker of movement; 2=Movement through full range but not against gravity; 3=movement through full range against gravity; 4=movement through full range with some resistance; 5=movement through range with full resistance.

Prior to the start of training one participant E reported newly acquired medical problems, which precluded them from involvement in the intensive training sessions. 5 participants completed the protocol. It was thus decided that data for participant E would be used as a control comparison. Unfortunately due to researcher error, follow up data for the 10HPT and Grip strength was lost in 3 participants therefore only pre and post comparisons could be made for these outcomes. Kinematic reach to grasp data was captured for the 5 participants at Baseline, Post-test and follow up sessions.

Table 4.2. Descriptive comparison between Non-paretic and Paretic Upper Limb scores for 10 Hole Peg Test and Grip strength. A percentage of the non-paretic score is presented in brackets for the paretic side. The physical status of paretic upper limb in terms of the visual-motor accuracy and strength is summarised in the final column. Below normal peg test scores refer to scores below the 2 SD cut off mean scores as reported by Turton & Fraser 1986 (Turton and Fraser 1986)

	Stroke details	**Dominant hand**	**Gender**	**Age (yrs)**	**10 Hole peg test Mean (s)**		**Grip strength Mean (kg)**		**Physical status of paretic upper limb**
					Non-paretic	Paretic	Non-paretic	Paretic	**Peg test score** **Strength**
A	Right parietal	Right	Male	56	10.9	25.0 (229%)	54.4	27.2 (50%)	Below normal Weak
B	Right parietal	Right	Male	56	9.8	11.4 (116%)	45.6	40.0 (87%)	Normal Normal
C	Right parietal	Right	Male	58	11.3	14.0 (124%)	25.4	16.2 (64%)	Below normal Weak
D	Pontine	Right	Male	66	12.1	16.5 (136%)	32.4	13.7 (42%)	Normal Weak
E	Right cerebellar	Left	Male	63	14.1	18.7 (132%)	27.6	24.5 (89%)	Below normal Weak
F	Right cerebellar	Left	Female	47	10.3	41.7 (405%	27.3	19.9 (73%)	Below normal Normal

Training dosage and patient satisfaction

Training Logs: Each of the five training participants completed the prescribed number of sessions over the course of the planned duration. On average training participants completed 3,934 (SD=709) reach to grasp movements of which details are provided in Table 4.3. Over the course of the training sessions the Borg RPE (Borg 1982) ranged from between 1 to 4 indicating that the intensity of exercise was perceived as fairly light to moderate level of exertion.

The mean score for the *Training Satisfaction Questionnaire* (Table 4.4) was 54 (SD=9) out of a maximum of 63. The lowest score (40) was recorded by Participant B who was least satisfied of the ability of ARC to treat upper limb reach to grasp function.

Table 4.3. Average number of repetitions completed during training

Participant	A	B	C	D	E	F	Total Mean (SD)
Total number of movements	11,230	15,300	10,545	12,090		9,840	11,801 (2,126)
Number of RTG movements	3,743	5,100	3,515	4,030		3,280	3,934 (709)

Table 4.4.Training Satisfaction Questionnaire Scores

* Training satisfaction questionnaire not applicable as E was prevented from taking part in the training due to a newly acquired medical condition.

Participant **Satisfaction Question**	**A**	**B**	**C**	**D**	**E**	**F**	**Total Mean (SD) [Range]**
How satisfied or dissatisfied are you with the ability of the intervention to treat your upper limb reach to grasp function 1. Extremely dissatisfied 7.Extremely satisfied	7	2	7	6		6	**6 (2)**
How severe was any pain you experienced as a result of this training 1= Extremely severe pain 7 = No pain	7	6	6	7		7	**7 (1)**
How severe was any fatigue you experienced as a result of this training 1= Extremely severe fatigue 7 = No fatigue	7	5	6	6		6	**6 (1)**
How severe was any muscle stiffness you experienced as a result of this training 1= Extremely severe muscle stiffness 7 =No muscle stiffness	7	6	6	7		6	**6 (1)**
To what extent did the side effects interfere with your physical health and ability to function 1 = A great deal 7 = Not at all	7	6	6	7		7	**7 (1)**
To what degree have the side effects affected your overall satisfaction with the treatment 1= A great deal 7 = Not at all	7	7	6	7		7	**7 (0)**
How satisfied or dissatisfied are you that the training was enjoyable 1= Strongly disagree 7 = Strongly agree	7	2	6	7		6	**6 (2)**
How satisfied or dissatisfied are you that the training was challenging 1= Strongly disagree 7 = Strongly agree	6	2	2	7		6	**5 (2)**
How satisfied or dissatisfied are you that the training was beneficial 1= Strongly disagree 7 = Strongly agree	7	4	6	6		7	**6 (1)**
Total score (63)	62	40	51	60	*	58	**54 (9)** [40-62]

Figure 4.2. Training Satisfaction Questionnaire mean category scores

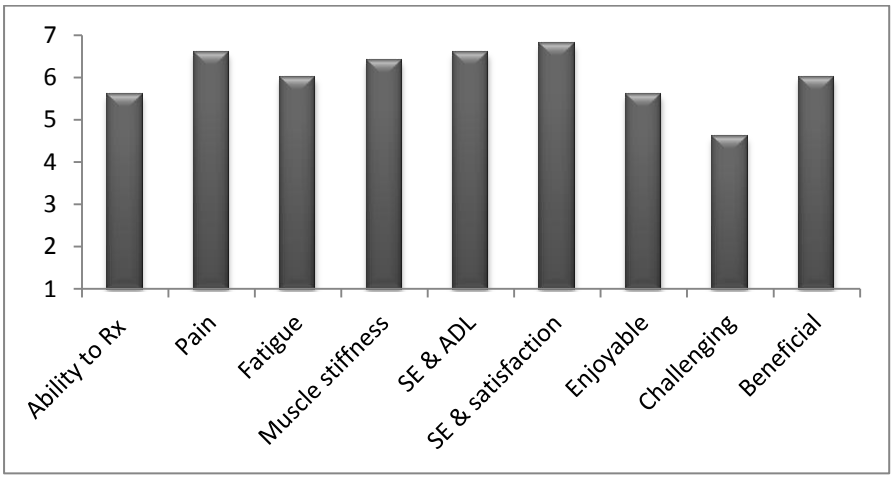


Table 4.5. Training satisfaction questionnaire comments:

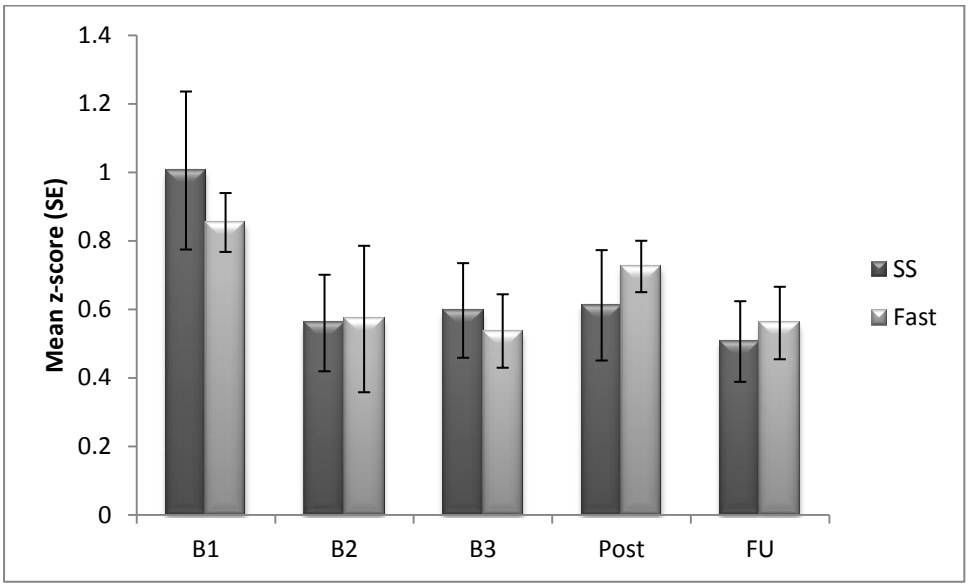
"The training helped me to further develop my grip when picking up objects by using the pincer grip more".
"I would suggest multi-purpose tasks while completing grasping exercise and grasping exercises to the right as well as to the left".
"The experience was enjoyable and interesting".
"Very pleased with the way I was treated and the care shown for my well being. Have noticed the improvement in the use of my left hand".
"Improved movement".

Group Results

Coordination of hand and arm (Figure 4.3)

Pearson's Correlations between TPV and TMA were transformed to Fisher z scores (Figure 4.) There was no significant effect of condition (SS or FAST) or time (Baseline, Post-test or Follow Up) upon the coordination between the timing of these components and no interaction between Conditions or Time. The speed of movement therefore did not appear to disrupt the relationship between the timing of transport and grasp and there did not appear to be changes to the relationship with training. In fact correlations were highest at Baseline assessment 1.

Figure 4.3. Correlation between TPV and TMA Fisher z scores at each assessment B1, B2, B3, Post-test training and Follow up for both the SS and FAST paced conditions.



Group results: RTG Kinematics: Condition (Table 4.6)

Overall movement time (M=1.11s, SD=0.41) and reaction time (M=0.46s, SD=0.09) were significantly shorter for FAST trials and peak velocity amplitude (M=700mm/s, SD=157) significantly ($p<0.05$) higher. Whereas the WPT, TPV%, TMA% the number of wrist velocity peaks and the number of aperture amplitude peaks were statistically similar for the SS and FAST paced conditions.

Table 4.6 Group average comparisons of kinematic parameters for reach to grasp between the SS (Self Selected) and FAST paced trials.

Kinematic parameter of RTG	SS Mean (SD)	FAST Mean (SD)	F(1,16)	P value
WPT mm	*404 (58)*	*399 (57)*	*345.671*	*0.30*
TPV%	*30 (11)*	*38 (15)*	*1.552*	*0.30*
TMA%	*47 (16)*	*52 (16)*	*3.273*	*0.15*
MT s	*1.3 (0.5)*	*0.9 (0.3)*	10.283	0.03 *
RT s	*0.5 (0.1)*	*0.4 (0.1)*	11.169	0.03 *
Peak Velocity mm/s	654 (146)	765 (152)	17.304	0.01 *
Wrist velocity peaks n	1.6 (0.5)	1.3 (0.3)	2.081	0.22

Group results: Training (Table 4.7)

With respect to the clinical measures a significant training effect ($p<0.05$) was observed for the 10HPT (M=0.61, SD=0.2), whereas the average grip strength (M=23, SD=7) was statistically similar at pre and post-test. In terms of the RTG kinematics, average WPT (M=392mm, SD=55) was

significantly ($p<0.05$) smaller after training. The TPV% and TMA% occurred later, MT and RT were quicker, PV was higher and wrist velocity peaks were fewer after training but the differences were not significant.

Table 4.7 Group average Pre (B1, B2 & B3) and post training comparisons of a. clinical measures and b. kinematic parameters for RTG.

	Pre (SD)	**Post (SD)**		
Clinical measures			**t (4)**	**P value**
10HPT pps	*0.58 (0.23)*	*0.64 (0.21)*	*-3.252*	*0.031**
Grip strength kg	*22 (7)*	*24 (7)*	*-0.849*	*0.444*
Kinematic parameters for RTG			**F(1,4)**	**P value**
WPT mm	*416 (63)*	*368 (46)*	*10.601*	*0.03 **
TPV%	*31.0 (11)*	*39.4 (14)*	*2.648*	*0.18*
TMA%	*49.8 (15)*	*51.2 (14)*	*0.165*	*0.70*
MT s	*1.2 (0.5)*	*1.1 (0.3)*	*2.628*	0.18
RT s	*0.5 (0.1)*	*0.4 (0.0)*	*2.455*	0.19
Peak Velocity mm/s	*686 (146)*	*735 (177)*	0.597	0.48
Wrist velocity peaks n	1.5 (0.4)	1.3 (0.3)	*2.006*	*0.23*

Individual Results

Individual case results are presented in the following section. (See also Tables in Appendix A4.6 and A4.7) with a summary of the individual pre-post training improvements in Table 4.8

Table 4.8 Summary of Cases with significant pre-post improvements

	A	B	C	D	E	F	Total
10 HPT			*	*		*	3
Grip strength			*				1
WPT			*	*		*	3
TPV		*		*			2
MT			*	*		*	3
RT			*			*	2
Ap peaks		*				*	2
Velocity peaks				*		*	2

Case study Participant A results

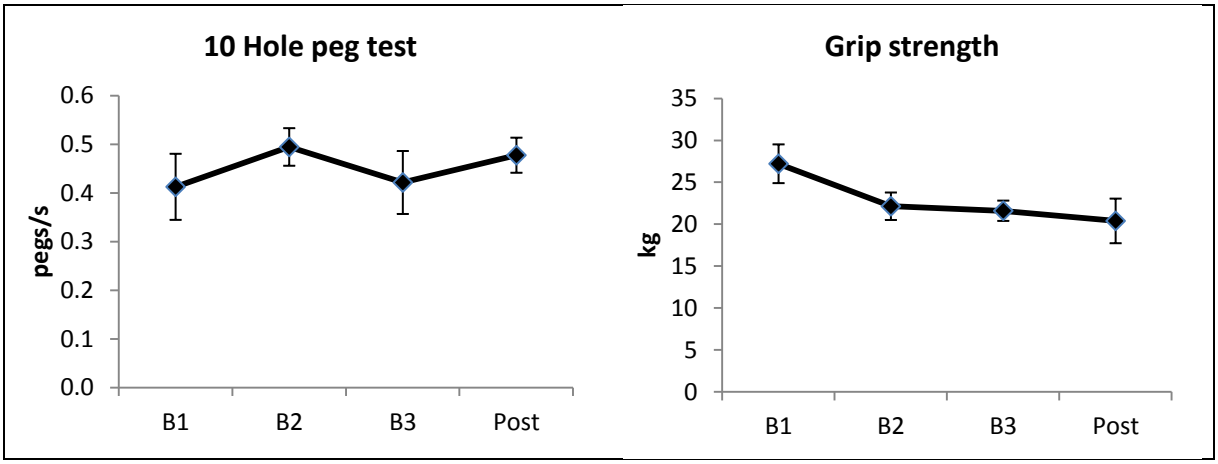
Participant A presented as a 56 year old male who 32 months prior to examination suffered a right parietal lesion affecting his non-dominant upper limb. 'A' had signs of both moderate sensory impairments (NSA 5/9) without visual or tactile extinction, and motor impairments (FMUL 51/66). Active range of upper limb movement was full and there were no signs of increased tone. Visual motor accuracy according to the 10HPT score at baseline was below normal and grip strength was weak. Despite performing 3,743 RTG movements during training A showed no clear improvements as a result of training.

10HPT and Grip strength Participant A (figures 4.4)

On average Participant A moved 0.46pps, (SD= 0.04) for the 10 HPT. The difference in the number of pegs moved per second before and after training (Baseline M=0.44pps, SD= 0.03; Post-test M=0.48pps, SD= 0.04) was significant ($t(15)=-3.684$, $p<0.01$). However paired t-tests revealed Baseline variability (B1toB2 $t(15)=-4.270$, $p=<0.01$; B2toB3 $t_{15}=4.175$, $p<0.01$) which appeared to account for the change and the difference was not attributed to the effects of training. The average grip strength for Participant A was 22.05kg (SD=1.85). A significant ($t(7)=3.455$, $p<0.011$) change in

grip strength was observed across time (Baseline M=23.7kg, SD=1.0 and M=20.4, SD=2.7), however the change occurred within the baseline period (B1toB2 t(7)=4.116, p<0.01).

Figure 4.4. Particpant A a. 10 Hole Peg test and b. Grip strength Mean (SD)



RTG Kinematics Participant A

For Participant A the average WPT was 389mm (SD=66). The wrist path trajectory was statistically unchanged across time (Baseline M=398mm SD=51; Post-test M=380mm, SD=30 and Follow Up M=374.5mm, SD=41). On average TPV% occurred at 31% (SD=8) of the movement duration and a main effect of was observed across time ($F_{4,16}$=9.135, p<0.01). Paired t-test analysis revealed that the differences (Baseline M=29.9%, SD=9; Post-test M=31.2%, SD=6; Follow Up M=32.75, SD=9) were due to variability at Baseline (B2 SS to B3 SS t(13)=-2.373, p=<0.05; B1 FAST to B2 FAST t(14)=6.027, p<0.01; B2 FAST to B3 FAST t(14)=-4.588, p<0.01) and not the result of training. The average movement duration (M=1.22s, SD=0.4) was statistically unchanged across time (Baseline M=1.14s SD=0.5; Post-test M=1.30s, SD=0.6; Follow Up M=1.17s, SD=0.2). The average reaction time for Participant A (M=0.40s, SD=0.1) showed a main effect of Time ($F_{1,11}$=6.362, p<0.01), which paired t-tests revealed was due to slower reaction times after training (Baseline SS to Post-test SS t(11)=-2.803, p<0.05 and Baseline SS to Follow Up t(11)=-3089, p<0.05) within SS paced trials only (Baseline M=0.35s, SD= 0.15; Post-test M=0.43s, SD=0.10; Follow Up M=0.48s, SD=0.20). There was no statistical evidence of training improvements in terms of the number of aperture peaks

(Baseline M=1.2, SD=0.4; Post-test M=1.0, SD=0.0; Follow Up M=1.3, SD=0.45). Similarly the number of velocity peaks identified during Baseline, Post-test and Follow Up trials was statistically comparable (Baseline M=1.6, SD=0.7; Post-test M=1.7, SD=0.7; Follow Up M=1.5, SD=0.7). No significant interactions were found between the time (Baseline, Post-test and Follow Up) and speed of trials (SS and FAST) for any of the kinematic variables.

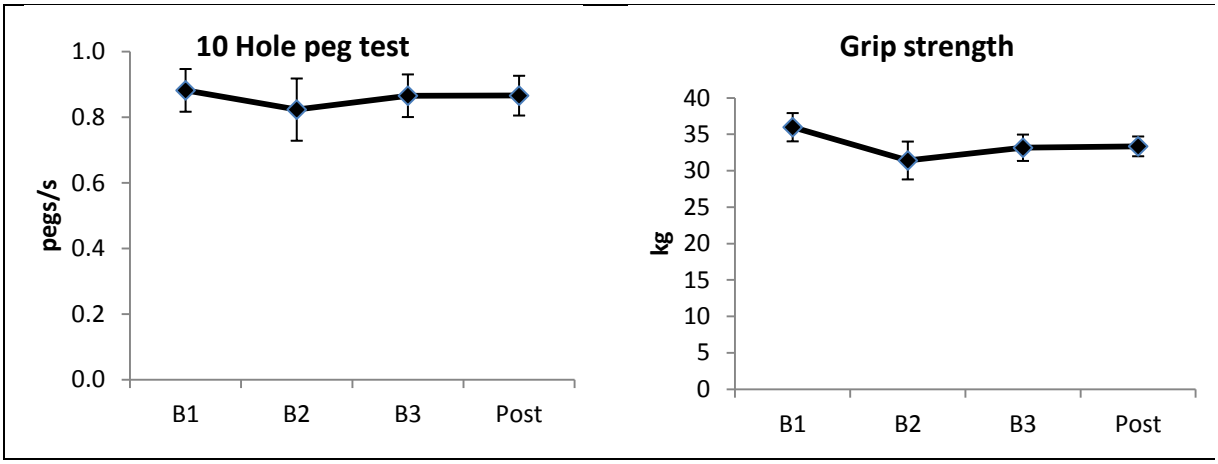
Case study Participant B results

Participant B was a 56-year-old male who suffered from a right parietal stroke 77 months prior to testing which affected his non-dominant upper limb. B suffered from moderate sensory deficits (NSA 6/9) together with signs of both visual and tactile extinction. Motor impairments were mild (64/66 FMUL) and B had full range of movement, muscle strength with some resistance (4/5 Oxford) and no sign of increased tone (0/5 MAS). Baseline scores for the 10HPT and Grip strength were both classed as normal. Participant B was the least satisfied with the ability of ARC to treat his upper limb reach to grasp function. Despite performing 5,100 RTG movements during training B showed no benefit to clinical measures for dexterity and grip strength. There was a training related change to TPV% for SS trials only. Baseline scores for the 10HPT and Grip strength were both classed as normal.

10HPT and Grip strength Participant B (Figure 4.5)

For Participant B there was no significant change to the number of pegs moved per second across time (Baseline M=0.86s, SD=0.1; Post-test M=0.87s, SD=0.1). Grip strength was also statistically similar between Baseline (M=33.5kg, SD=1.2) and Post-test (M=33.4kg, SD=1.4).

Figure 4.5 Participant B a. 10 Hole Peg test and b. Grip strength Mean (SD)



RTG Kinematics Participant B

For Participant B the average WPT was 351mm (SD=14.7) There was a main effect across time ($F_{1,4}$=117.190, p<0.01) upon the WPT (Baseline M=391mm, SD=14; Post-test M=312mm, SD=14; Follow Up M=366mm, SD=16). Paired t-test comparisons revealed variability during Baseline (B1 SS to B2 SS t(14)=18.366, p<0.01; B2 SS to B3 SS t(14)=-18.326, p<0.01; B1 FAST to B2 FAST t(14)=15.039, p<0.01; B2 FAST to B3 FAST t(14)=-19.761, p<0.01) as well as differences for pre-post comparisons (Baseline SS t(4)=20.697, p<0.01 and Baseline FAST t(4)=7.925, p<0.01). TPV% (M=29.8%, SD=11) showed a main effect of time ($F_{4,16}$= 6.686, p<0.01). Paired t-test comparisons (Baseline M=29.2%, SD=10; Post-test M=30.5%, SD=17; Follow Up M=40.5%, SD=5) revealed variability at Baseline (B1 SS to B2 SS t(14)=-2.702, p<0.05; B1 FAST to B2 FAST t(14)=-4.808, p<0.01; B2 FAST to B3 FAST t(14)=3.741, p<0.01). There was also change following training (B3 SS to Post-test SS t(14)=-3.450, p<0.05) for the condition only. There were significant differences ($F_{1,4}$=41.346, p<0.01) in the average movement duration (M=0.78s, SD=0.1) across time (Baseline M=0.87s, SD=0.1; Post-test M=0.69s, SD=0.1; Follow Up M=0.77 s, SD=0.0). Paired t-tests showed Baseline variability (B1 SS to B2 SS t(14)=7.854, p<0.01; B1 FAST to B2 FAST t(14)=6.274, p<0.01 and B2 FAST to B3 FAST t(14)=-9.388, p<0.01) as well as Baseline to Post-test

differences in the SS paced trials (Baseline SS to Post-test SS t(4)=12.169, p<0.01). The average reaction time (M=0.48s, SD=0.1) was similar across time (Baseline M=0.57s, SD=0.1; Post-test M=0.39, SD=0.1; Follow Up M=0.45, SD=0.1). The average the number of aperture peaks detected during trials (M=1.1, SD=0.1) was statistically reduced ($F_{1,4}$=12.667, p<0.01) across time (Baseline M=1.3, SD=0.3; Post-test M=1.0, SD=0.0; Follow Up M=1.0, SD=0.0). Paired t-test revealed differences at Baseline (B2 SS to B3 SS t(14)=-5.292, p<0.01; B2 FAST to B3 FAST t(14)=-6.205) as well as before and after training (Baseline FAST to Post FAST t(4)=165.667, p<0.01). The number of detected velocity peaks was statistically unchanged (Baseline M=1.1, SD=0.2; Post-test M=1.0, SD=0.0; Follow Up M=1.1, SD=0.2) across time.

There was a significant ($F_{4,16}$= 15.902, p<0.01) interaction for WPT between time (Baseline, Post-test & Follow Up) and pace (SS & FAST) caused by differences between the SS and FAST paced trials at Follow Up only. A significant interaction between Condition and time ($F_{4,16}$= 5.210, p<0.01) was also observed for TPV%. The interaction between TPV% qualified the difference between the Baseline and Post t-test for SS trials only, as the result of differences in movement time, which was comparable between SS and FAST trials at Post-test. There were no other significant interactions.

Case study Participant C results

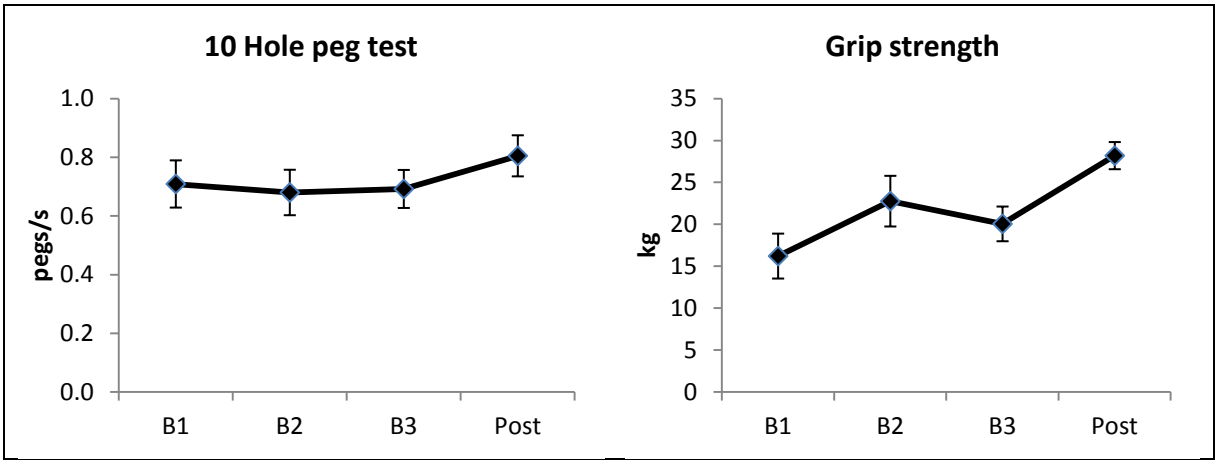
Participant C was a 58-year-old male who suffered a right parietal stroke affecting his non-dominant hand 72 months prior to testing. Participant C presented with moderate sensory impairments (4/9) with tactile extinction but no visual extinction and moderate motor impairment (FMUL 53/66). Both visual motor accuracy in terms of the 10HPT and grip strength were impaired. Participant C completed a total of 3,515 RTG movements during training. Improvements in dexterity and grip strength were observed which were attributed to the training. A gradual reduction in wrist path trajectory, movement time and reaction time was seen across Time but no specific training effect was observed. A narrowed difference between TPV% in SS and FAST paced trials at for Post-test training

measures was reflected by a narrowed difference in movement time between SS and FAST at this point.

10HPT and Grip strength Participant C (figures 4.6)

Paired sample t-tests showed that whilst the average number of pegs moved per second (M=0.75pps, SD=0.1) was comparable during Baseline (M=0.70pps, SD=0.1), there was a significant (t(15)=-5.989, p<0.01) increase in the number of pegs moved after training (Post-test M=0.80pps, SD=0.1). There was a significant ($F_{3,21}$=32.406, p<0.01) increase in the average grip strength across time (M=24kg, SD=2.15). Paired tests showed a significant gain during Baseline (B1 to B2 (t(7)=-4.608, p<0.01) which continued after training (B3 to Post-test t(7)=8.135, p<0.01).

Figure 4.6. Participant C a. Ten Hole Peg test and b. Grip strength Mean (SD)



RTG Kinematics Participant C

For participant C the average WPT was 370mm (SD=11). A significant ($F_{1,13}$=88.232, p<0.01) change across time, reflected a gradual reduction in the WPT (Baseline M=376mm, SD=9; Post-test M=348.5mm, SD=12; Follow Up M=360mm, SD=6). There was a reduction in the WPT at Baseline§ (B2 SS to B3 SS (t(13)=5.531, p<0.01; B2 FAST to B3 FAST t(13)=4.694, p<0.01) which continued after training (Baseline SS to Post-test SS t(13)=7.771, p<0.01 and Baseline FAST to Post-

test FAST t(13)=4.728, p<0.01) and which was partially maintained at Follow Up (Baseline SS to Follow Up SS t(13)=8.340, p<0.01 and Baseline FAST to Follow Up FAST t(13)=6.764, p<0.01). There was no apparent training effect upon the average TPV% (Baseline M=34%, SD=10; Post-test M=34%, SD=7; Follow Up M=36%, SD=3). A significant ($F_{1,13}$=164.7, p<0.01) reduction in movement time (M=0.88s, SD=0.2) was seen across time (Baseline M=1.05s, SD=0.3; Post-test M=0.70s, SD=0.2; Follow Up M=, SD=). Paired t-test comparisons confirmed a reduction in movement time for the SS trials only (B1 SS to B2 SS t(13)=3.010, p=0.01; B2 SS to B3 SS t(13)=2.158, p=0.05). The reduction in movement time for SS trials continued after training (B3 SS to Post-test SS t(13)=7.287, p<0.01) and were maintained at follow up (B3 SS to Follow Up SS t(13)=9.960, p<0.01). There was a significant ($F_{1,13}$=10.146, p<0.01) effect of time upon the reaction time (M=0.50s, SD=0.4). The average RT was quicker after training (Baseline M=0.58s, SD=0.5; Post-test M=0.41s, SD=0.3). Paired t-tests showed a significant difference (B2 FAST to B3 FAST t(13)=-2.664, p<0.05; Baseline FAST to Post-test FAST t(13)=3.860, p<0.01 and Baseline FAST to Follow UP FAST t(13)=3.280, p<0.01). There was no significant training effect upon the number of aperture peaks (Baseline M=1.08, SD= 0.38; Post M=1.10, SD=0.31). There was also no significant effect of training upon the number of velocity peaks across time (Baseline M=1.1, SD=0.2; Post-test M=1.0, SD=0.1).

There was a significant ($F_{4,52}$=5.181, p<0.01) interaction effect between time (Baseline, Post-test & Follow Up) and condition (SS and FAST) for TPV% which reflected a narrowed difference in TPV% between the FAST and SS trials after training. There was also a significant interaction between Condition and Time ($F_{1,13}$=14.365, p<0.01) for movement duration as the gap between SS and FAST paced trials narrowed across time. This suggested a ceiling effect to the movement duration of the FAST paced trials for Participant C.

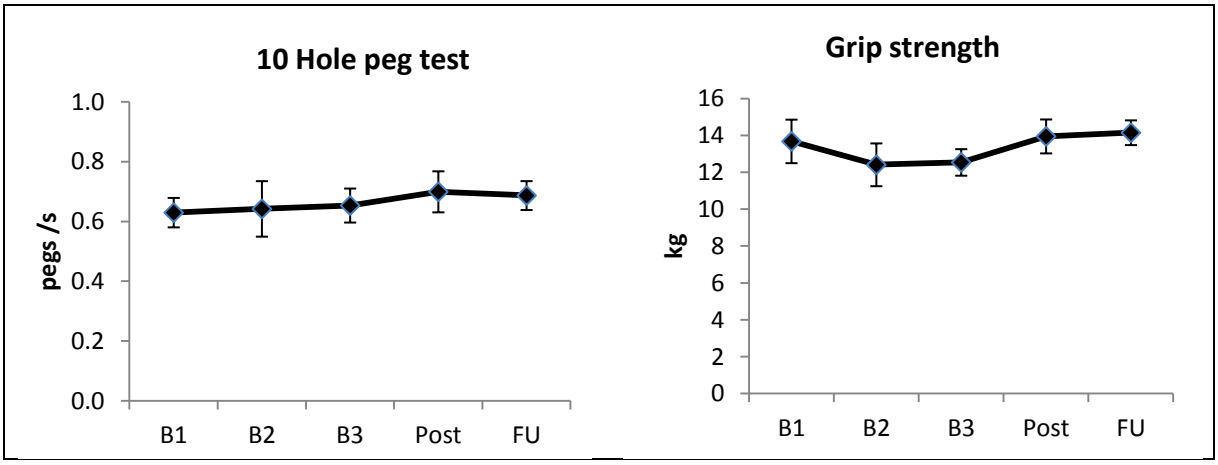
Case study Participant D results

Participant D was a 66-year-old male who suffered a pontine infarct 25 months prior to testing affecting his dominant right upper limb. D suffered from moderate upper limb motor impairment (FMUL 50/66), and some increased tone (MAS 2/5) without any sensory deficit. Visual motor accuracy in terms of the 10HPT at Baseline was classed as normal but grip strength was weak. Participant D performed 4,030 RTG movements during training and demonstrated training related improvement in dexterity, shortened wrist path trajectory and prolonged acceleration phase.

10HPT and Grip strength Participant D (Figure 4.7)

For the 10 HPT (M=0.67pps, SD=0.1) Baseline measures (M=0.64pps, SD= 0.1) were statistically stable. Comparisons between Baseline and Post-test (M=0.70pps, SD=0.1) showed a significant ($t(15)=-3.153$, $p<0.01$) improvement, which was partly maintained at follow up (Baseline to Follow Up $t(15)=-2.756$, $p<0.5$). Grip strength measures (M=13.5kg, SD=0.95) were statistically unchanged across time (Baseline M=12.9kg, SD=1.0; Post-test M=14.0kg, SD=0.9).

Figure 4.7 Participant D a. Ten Hole Peg test and b. Grip strength Mean (SD)



RTG Kinematics Participant D

The wrist path trajectory (M=383mm, SD=27) changed significantly ($F_{4,16}$=27.401, p<0.01) across time. Paired t-tests revealed statistical variance (B1 SS to B2 SS t(5)=-4.921, p<0.01; B2 FAST to B3 FAST t(6)=3.424, p<0.01) during Baseline (M=400mm, SD=25). The post-test WPT (M=366mm, SD=35) was significantly shorter (Baseline SS to Post-test SS t(9)=p<0.01; Baseline FAST to Pos-test FAST t(9)=8.614, p<0.01). The reduction in WPT was partly maintained (Baseline FAST to Follow Up t(9)=3.158, p<0.05) at Follow Up (M=390mm, SD=16). There was a main effect of time ($F_{4,16}$=27.159, p<0.01) upon the average TPV% (M=26%, SD=10). The acceleration phase during the Baseline period (M=23.5%, SD=18) was variable (B1 SS to B2 SS t(5)=-2.798, p<0.05; B2 SS to B3 SS t(5)=3.435, p<0.05; B2 FAST to B3 FAST t(6)=3.464, p<0.05). TPV% increased significantly (Baseline SS to Post-test SS t(9)=-3.164, p=0.01; Baseline FAST to Post-test FAST t(9)=-3.745, p<0.01) after training (post-test M=33%, SD=23). The change was maintained (Baseline SS to Follow Up SS t(10)=-4.269, p<0.01; Baseline FAST to Post-test FAST t(9)=-4.226, p<0.01) at Follow up (M=33%, SD=9). For participant D the average movement duration (M=0.87s, SD=0.2) showed an overall effect of time ($F_{1,4}$=25.573, p<0.01). The Baseline phase (M=0.88s, SD=0.2) was statistically variable (B1 SS to B2 SS t(5)=5.566, p<0.01; B2 SS to B3 SS t(5)=-4.002, p<0.01; B1 FAST to B2 FAST t(4)=4.627, p<0.01; B2 FAST to B3 FAST t(6)=-5.058, p<0.01). The average movement duration after training (Post-test M=0.87s, SD=0.2) was quicker for the SS paced trials (Baseline SS to Post test SS t(9)2.342, p<0.05) but slower for the FAST paced trials (t(9)=-5.634, p<0.01). The average reaction time (M=0.38s, SD=0.1) for participant D was similar between Baseline (M=0.40s, SD=0.3) and Post-test (M=0.36s, SD=0.1). The average number of aperture peaks (M=1.8, SD=0.5) detected during Baseline (M=1.7, SD=0.6) was statistically similar at Post-test (M=1.8, SD=1.2). Whereas, the number of wrist velocity peaks (M=1.6, SD=0.1) which was stable during Baseline (M=1.9, SD=1.4) was significantly reduced after training Post-test (1.4, SD=0.5) (Baseline SS to Post-test SS t(9)=3.103, p<0.05; Baseline SS to Follow UP t(9)=5.111, p<0.01; Baseline FAST to Post-test FAST t(8)=2.984, p<0.05).

For movement duration there was an interaction effect ($F_{4,4}$=6.724, p<0.01) between time (Baseline, Post-test & Follow Up) and pace (SS & FAST). MD was faster for the FAST condition during the Baseline period but the SS and FAST paced trials were more similar at Post-test.

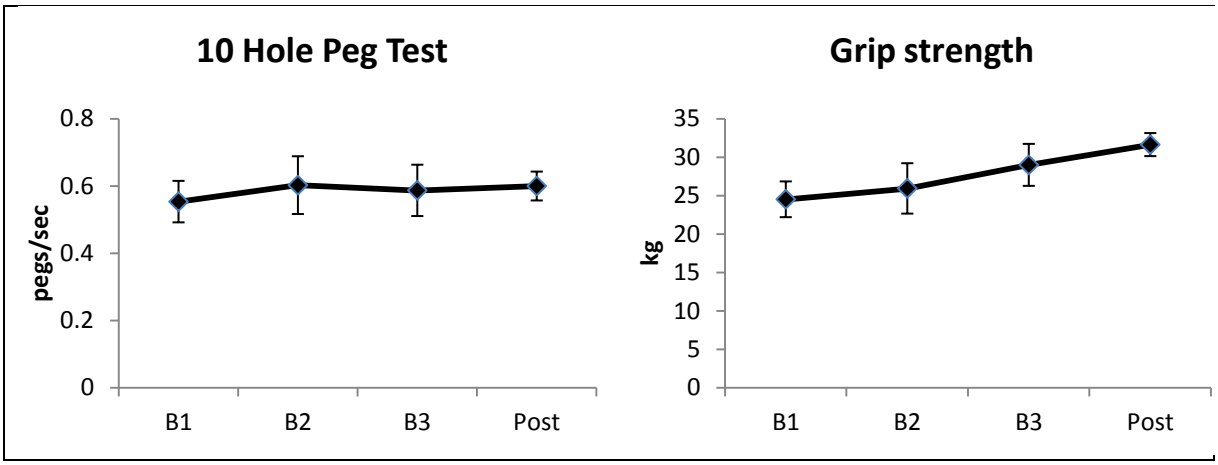
Case study Participant E results * No training

Participant E was a 63year old male who suffered a right cerebellar stroke 20 months prior to entering the study which affected his non-dominant right upper limb. Clinical examination revealed weakness (Oxford Grade 3/5) and moderate motor impairment (FMUL 54/66) but he was without sensory deficits or increased tone. Both the 10HPT and grip strength scores were below normal at Baseline. Participant E did not take part in any training due the onset of a medical condition after Baseline. E showed no change across time for the 10HPT, general improvements across time in Grip Strength. Between Baseline phase 2& 3 there was a significant reduction in WPT and prolonged acceleration phase.

10HPT and Grip strength Participant E (Figure 4.8)

For participant E the average number of pegs moved per second (M=0.59pps, SD=0.07) was comparable during Baseline (M=0.58, SD=0.07) and after training (Post test M=0.60, SD=0.04). There was a significant ($F_{3,21}$=24.296, p<0.01) main effect of grip strength across time (B2 to B3 t(7)=-10.130, p<0.01; B3 to Post-test t (7) -2.414, p<0.05).

Figure 4.8 Participant E a.Ten Hole Peg test and b. Grip strength Mean (SD)



RTG Kinematics Participant E

There was a significant ($F_{3,18}$=34.664, p<0.01) main effect of time upon the average WPT (M=359mm, SD=8.6). Overall the WPT was statistically comparable between Baseline (M=360mm, SD=7.6) and Post-test (M=357mm, SD=9.6). Paired t-tests showed a significant reduction in the wrist path trajectory between (B2 SS to B3 SS t(7)=3.363,p=0.01; B2 FAST to B3 FAST t(6)=9.965, p<0.01), which was lost at Post-test (B3 FAST to Post-test FAST t(6)=-2.950, p<0.05). The average TPV% (M=40%, SD=8) changed significantly ($F_{3,18}$=215.947, p<0.01) across time. Paired t-test comparisons revealed differences with Baseline only (B2 SS to B3 SS t(7)=-4.303, p<0.01; B2 FAST to B3 FAST t(7)=-4.248, p<0.01). Movement time (M=0.90, SD=0.07) was also statistically variable ($F_{3,18}$=52.053, p<0.01) across time (B1 SS to B2 SS t(7)=8.192, p<0.01; B1 FAST to B2 FAST t(7)=4.666, p<0.01; B2 FAST to B3 FAST t(7)= -5.803, p<0.01). The average reaction time for Participant E (M=0.38, SD=0.06) was unchanged across time. A main effect ($F_{1,18}$=13.425, p<0.01) of time was observed for the number of velocity peaks (M=1.16, SD=0.22). Paired t-tests showed that improvement occurred trials between the first and second visits (B1 SS to B2 SS t(7)=2.646, p<0.05 and B1 FAST to B2 FAST t(7)=2.828, p<0.05). The number of aperture peaks (M=1.07, SD=0.46) was statistically unchanged across time.

There was a significant interaction effect observed for TPV% ($F_{3, 21}$=22.869, p<0.01) only for Participant E.

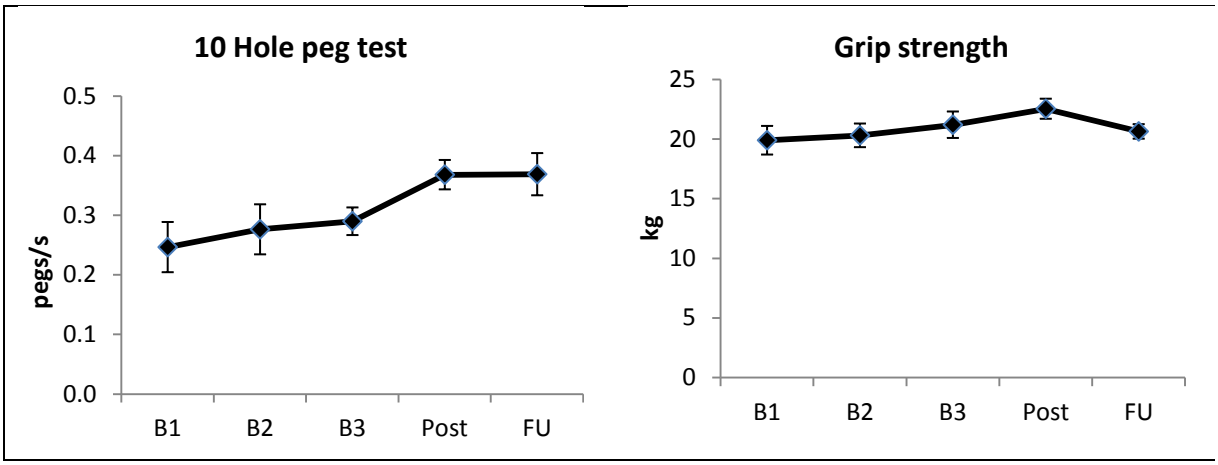
Case study Participant F results

Participant F was a right-handed female aged 47years, with a left cerebellar infarct (Figure 4.10 structural MRI scan) affecting the non-dominant upper limb. F showed no sensory deficit, but moderate motor impairment (FMUL 54/66) and ataxia (SARA 5.5). For Participant F the visual motor accuracy (10HPT) was below normal, whereas grip strength was within the normal range. During the first training session F had difficulty stabilising the object with a firm grasp between locations A&B due to the severity of tremor. The therapist assisted in the initial session by supporting the object between the two locations. In total F completed approximately 9,840 movements during the course of the training of which 3,280 were reach to grasp. The findings from this case study are promising. Data suggest that when reach and grasp movement training was combined with a predictable, rhythmical beat, it significantly improved dexterity for the 10HPT, reduced the wrist path trajectory and reduced the overall movement time.

10HPT and Grip strength Participant F (Figure 4.9)

For the 10HPT Participant F moved on average 0.34pps (0.0). Baseline measures were comparable, whereas there was a significant (t(15)=10.70, p<0.01) improvement between Baseline (M=0.27pps, SD=0.0) and Post-test (M=0.37pps, SD=0.0), which was maintained (t(15)=9.088, p<0.01). at follow up (M=0.37pps, SD=0.0). There was a gradual increase in grip strength over time but the differences between Baseline (M=20.5kg, SD=1.1), Post-test (M=22.5kg, SD=0.8) and follow up (M=20.6kg, SD=0.6) were not significant.

Figure 4.9 Participant F a.Ten Hole Peg test and b. Grip strength Mean (SD)



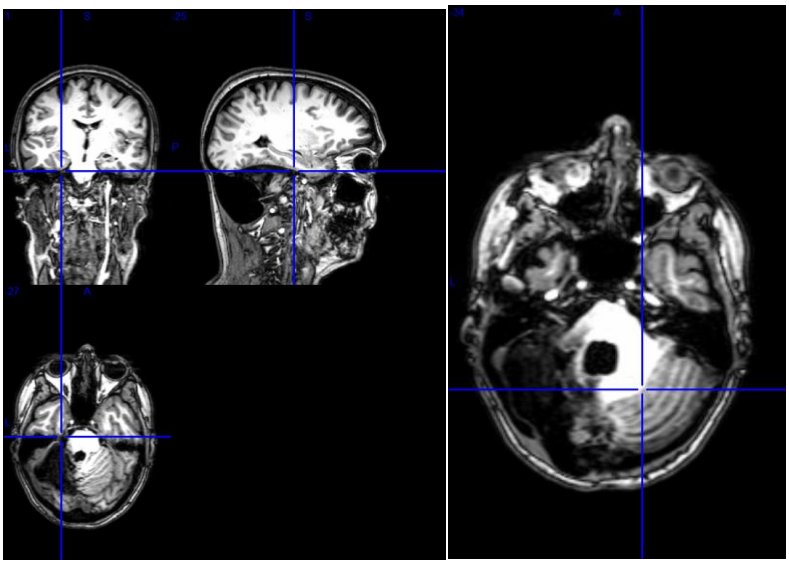
RTG Kinematics Participant F

The average WPT for Participant F was 480 mm (SD=49). ANOVA revealed a main change effect across time ($F_{4,28}$ =22.868, p<0.01). There was some variability in WPT at Baseline (B1 SS to B2 SS t(7)=3.896, p<0.01; B2 SS to B3 SS t(7)=-6.615, p<0.01) for the SS paced trials. There was an overall reduction in the WPT between Baseline (M=526.9mm, SD=7.0) and Post-test (M=430.8mm, SD=14.1). Paired t-tests confirmed that WPT for the SS paced trials was reduced after training (B3 SS to Post SS t(7)=11.642, p<0.01) and this was maintained at Follow Up (t(7)=5.948, p<0.01) (M=450mm, SD=47). The average TPV% for Participant F (M=24%, SD=5) showed no main change across time. There was a significant ($F_{4,28}$ =32.223, p<0.01) effect of time upon the average movement Time (M=1.77s, SD=0.06). Paired t-test analysis showed variability at Baseline (B1 SS to B2 SS t(7)=5.500, p<0.01; B2 SS to B3 SS t(7)=-6.739, p<0.01; B1 FAST to B2 FAST t(7)=6.191, p<0.01). There was also a reduction in movement time between Baseline (M=1.99s, SD=0.03) and Post-test (M=1.56s, SD=0.11) which was significant (Baseline SS to Post-test SS t(7)=5.918, p<0.01; Baseline FAST to Post-test FAST t(7)=2.739, p<0.05). This was maintained at Follow Up (M=1.46s, SD=0.15) according to Paired t-test comparisons (Baseline SS to Follow Up SS t(7)=12.784, p<0.01; Baseline FAST to Follow Up FAST t(7)=2.556, p<0.05). The average reaction time for Participant F improved across time but was statistically similar between Baseline (M=0.55s, SD=0.09) and Post-test

(M=0.36s, SD=0.03). There was a significant change to the average number of wrist velocity peaks (M=1.4, SD=0.1) between Baseline (M=1.5, SD=0.07) and Post-test (M=1.3, SD=0.2). Paired t-test showed a reduction in the number of wrist velocity peaks (Baseline SS to Post-test SS t(8)=2.393, p<0.01); which continued at Follow Up t(8)=5.831, p<0.01). There was a significant effect of time ($F_{4,24}$=8.838, p<0.01) upon the average number of aperture peaks (M=1.6, SD=0.1). The number of aperture peaks detected was significantly variable during Baseline, after training and at Follow Up (Baseline SS to FU SS (t(8)=4.743, p<0.01; B2 FAST to B3 FAST t(6)=-4.260, p<0.01; Baseline FAST to Post-test FAST t(8)=4.225, p<0.01). For participant F the average number of aperture peaks was reduced across time (Baseline M=1.84, SD=0.5; Post-test M=1.25, SD=0.5; Follow Up M=1.1, SD=0.2).

A significant ($F_{4,28}$ =22.868, p<0.01) interaction between Condition and Time was revealed for WPT. The trajectory, which was longer for the SS trials during Baseline, was shorter than FAST paced trials after training.

Figure 4.10 Structural MRI participant F.

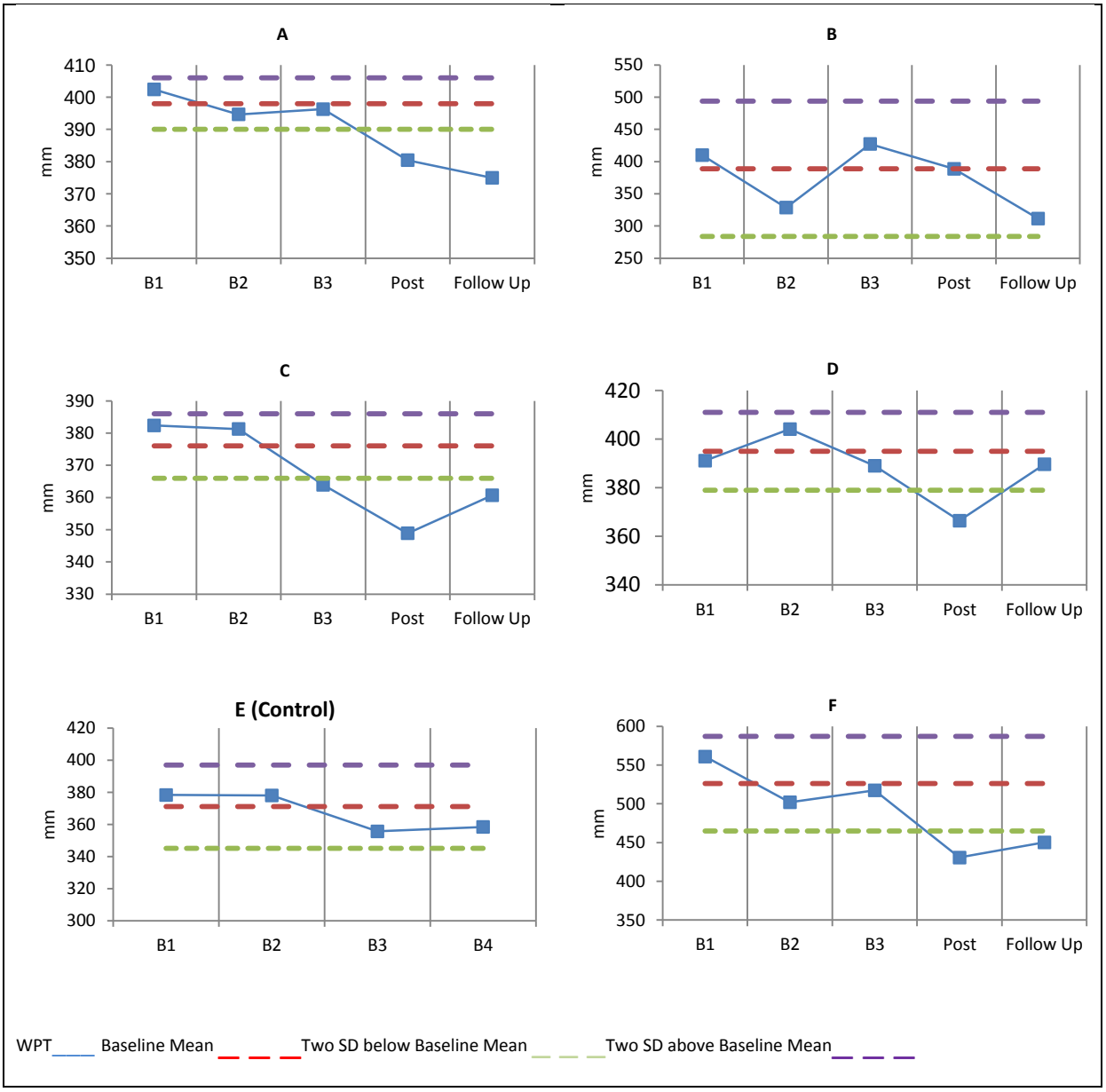


Further exploratory group analysis

Overall there was no statistical difference between SS and FAST paced trials so the WPT data for the two conditions was combined for exploratory purposes and plotted graphically for each individual

(Figure 4.11A-F). Visual inspection of the graphs indicates post training improvement in participants A,D and F, where the mean WPT falls below 2 standard deviations from the Baseline mean. Improvement after training was also observed in participant C, although at the same rate as was observed between B2 and B3. Whereas, the mean WPT for participant B and Control participant (E) remained within ± two-standard deviations. Similarly the data was plotted for TPV% and included in the Appendix A4.14.

Figure 4.11 Wrist path trajectory distance for participants A-F. Wrist path trajectory distance is shown in mm on the vertical axis. The assessment phase is shown on the horizontal axis (Baseline1, 2 & 3 (Phase A), post test (Phase B) and Follow Up). The Baseline Mean is shown with a red dashed line. The dotted green line represents two standard deviations below the Baseline mean. Participant E did not take part in training and did not have a follow up assessment.



Discussion

There has been increasing evidence to support the use of both task specific functional practice and repetitive movements with rhythmic auditory cues for the reacquisition of skilled motor control. Here we combined the two forms of treatment and targeted them towards moderately high-level patients with either parietal or cerebellar or pontine lesions, to promote both the speed and spatiotemporal stability of reach to grasp movements. Firstly the study has shown that ARC can produce high intensities of RTG movement repetitions in the order of 655 movements per session. Secondly the intervention was well tolerated by moderately high level, chronic stroke patients and participants were largely satisfied. Additionally there was some indication of training related improvements to motor control of reach to grasp.

Training related improvements

Good reaching performance was previously defined as that which consists of a direct wrist trajectory path with few sub-movements, which can be performed under various speeds, different load conditions and from many locations in the reaching space. Overall, the group showed asignificant improvement in the number of pegs moved per second, which was attributed to ARC training. Three individuals demonstrated significant training related improvements in the 10HPT. This was an expected finding as the training involved a pinch grip and transfer of objects, which was similar to the 10Hole peg test. Nonetheless, it was positive to see that the training outcome could be translated to higher performance in a slightly different task, and involving different locations in the reaching space. As predicted there was no training related change to grip strength, although there was improvement for one participant. This unexpected improvement in grip strength in participant C with tactile extinction was perhaps the result of increased awareness of the affected limb, which translated into increased use of temporarily redundant motor pathways.

Similar to previous research (Thielman, Dean et al. 2004) an overall significant reduction in the wrist path trajectory was observed. Individually three participants (1 parietal, 1 pontine and 1

cerebellar lesion) showed significant training related improvements to the WPT and 1 (Parietal lesion) showed improvement according to visual inspection. This finding supported auditory-motor entrainment and improved scaling of position change through the entire movement trajectory (Thaut, Kenyon et al. 1999). Two individuals (1 pontine and 1 cerebellar lesion) showed significantly fewer wrist velocity peaks after training lending further support to smoother movements with fewer sub-movements. There was a tendency for a more prolonged acceleration phase after training, although only one individual (Pontine lesion) demonstrated a reliable increase in TPV% as a result of training. This was indicative of better feedforward control and reduced reliance upon sensory feedback for this individual. Comparable improvements in the planning and execution of movements have been reported following 30hours functional training with CIMT (Lin, Wu et al. 2007) and ARC (Malcolm, Massie et al. 2009) in reaching. Overall there is some evidence to suggest that ARC training may help patients learn strategies to coordinate more efficient movements to effectively perform RTG tasks.

Self selected pace and fast movements

Here we found that slower paced trials were characterized by a protracted reaction time, increased movement duration and lower peak velocities than FAST trials. Both TPV% and TMA% occurred later in the FAST paced trials but overall the difference between the SS and FAST trials was not significant. Another study, (VanVliet and Sheridan 2007) also found that both the percentage time of peak velocity and maximum aperture was later for faster movements, although the adjustment of both reach and grasp components to the faster condition was not as evident after stroke as it was for healthy subjects. Normally to meet the demands of increased speeds these fast movements are largely centrally programmed with a smaller proportion of time used to make on-line adjustments. The timing of maximum grasp is consequently delayed to maintain the coordination between the two components. For stroke there is greater reliance on the feedback control phase, which remains prolonged and perhaps limits the overall movement time and peak velocity. Indeed ARC training resulted in a smaller difference in movement time between the SS and the FAST paced trials. It was the SS trials for which movement time was reduced whereas for the FAST paced condition movement

time was similar to Baseline. Increases to peak velocity were more noticeable for the SS trials than for the FAST paced trials.

Movement smoothness in terms of the number of peaks detected and wrist path trajectory was statistically similar between FAST and SS trials. These results are in contrast to previous findings in healthy subjects which indicate that transport was spatially less accurate (Wing, Turton et al. 1986) when movements were performed faster than normal. One reason for this may be the limited difference in speed between the two conditions for stroke participants. In fact, at Baseline when the average movement time was reduced during faster trials the wrist path trajectory was longer and more velocity peaks were observed, supporting greater spatial variability during faster movements.

Measuring performance for RTG coordination

There appeared to be no clear effect upon the relationship between the normalised timing of peak velocity and maximum aperture for either the speed of movement or the acquisition of skill development with practice. Similar to previous findings (Marteniuk, Leavitt et al. 1990) there were some trials which exhibited reliable positive correlations between the TPV% and TMA%, but there were also a considerable number of trials where non-significant correlations indicated no relationship between the transport and grasp components. Correlation in some but not all cases supports the idea that the two components may be loosely coordinated rather than control based upon an invariant relationship between certain temporal events. One view (Wing, Turton et al. 1986) is that the two components are not strictly independent since the hand must always open before contact with the object. The current findings support a functional link between transport and grasp (Marteniuk, Leavitt et al. 1990), involving a central planning process that imposes the same influence on the two components but is task specific. It is suggested that the link is also context dependent and takes into account the impairments associated with the stroke.

An alternative performance indicator is the timing of peak velocity which appears indicative of skilled motor control (van Vliet and Sheridan 2007). Indeed in Chapter 2, healthy controls

exhibited a later TPV% in comparison to stroke participants. Additionally TPV% is normally adjusted according to task constraints with earlier execution for precision tasks (Marteniuk, MacKenzie et al. 1987). Where the task becomes more demanding TPV% and TMA% both occur earlier within the MT (Marteniuk, Leavitt et al. 1990). The current study provides some support for this notion with a trend for a more prolonged acceleration phase after training, suggesting that participants were less reliant upon ongoing feedback to correct for spatial errors after training. A higher treatment dose may be indicated for more significant changes in TPV%. The findings here suggest that WPT may be more sensitive to change.

Treatment dose

In comparison to conventional therapy the intensity of training was high for all participants with an average number of active RTG repetitions in excess of 600 for each of the 6 sessions. This number of active repetitions exceeds that in previous research (Birkenmeier, Prager et al. 2010) in which stroke participants were able to perform in excess of 300 movements without negative side effects. Whilst high intensity of training was well tolerated, there appeared to be no relationship between the number of movements performed in training and the degree of improvement in motor control. Higher functioning participants performed the most movements since the metronome was set at a smaller interval at the beginning of training and progression in speed was relatively prescribed in 10% increments. The treatment dose was therefore not controlled for across participants and treatment was not the controlling parameter for improvement. That is to say that higher repetition did not translate into greater improvement.

In a comparable study (Lin, Wu et al. 2007) chronic stroke participants achieved a +6% mean change to the time of peak grip aperture following 30hours CIMT training during the course of 3 weeks, with additional home practice. The participants in that study were of a similar age and were a heterogenous group in terms of lesion location and with mild to moderate impairments. Similarly improvements in the timing of hand opening relative to hand displacement were achieved (Merians, Poizner et al. 2006) after 3000-4000 trials during 30 hours of sensorimotor training with virtual

reality. The present study has demonstrated a comparable mean change (TPV% +8.4% and TMA%+1.4%) with 3000-5000 repetitions, over the course of just 6 hours of ARC training. ARC is a low cost form of treatment and with simple modifications could be challenging for the patient. Modifications might include varying the object size and location and the metronome interval during practice.

Rhythmic and discrete movements

Another important consideration is the difference between the rhythmic nature of the practice movements and RTG movements, which are usually, performed as discrete movements as per the assessment. Rhythmic and discrete movements may involve different motor control strategies and involve different areas of the brain (Schaal et al 2004). Schaal et al 2004 identified that rhythmic reaching movements included unilateral M1, S1, PMDc, SMA and pre-SMA, the Anterior Cingulate Cortex and the cerebellum; whereas discrete arm movement activated a variety of contralateral non-primary motor areas and showed bilateral activity in both the cerebrum and the cerebellum. The distinction may be related to the different types of control. Cognitive control of movements for tasks involving elaborate timing and movement planning requires more involvement of memory and attention systems, which may not be activated during more simple or automatic movements (Lewis and Miall 2003). Different types of control for single and repetitive RTG may limit the transfer effects of each type of practice. Training programs involving ARC to promote speed and spatiotemporal aspects of RTG, may also include some elements of single RTG practice with cognitive control. ARC in the present form would not be suitable for patients with more severe motor impairment who can manage only practice of separate components of RTG. However with assistive robot training, ARC may help to activate additional brain areas than would be otherwise activated by practicing separate components of RTG.

Participant characteristics and training improvements.

With the exception of participant D all training participants suffered from lesions, which most affected the non-dominant hand. Motor control improvements (in terms of the wrist path trajectory for reach to grasp, prolonged acceleration, MT and 10HPT) were most evident in three participants (1 with a Parietal lesion, 1 with a Pontine lesion and 1 with a Cerebellar lesion.

Two participants with parietal lesions showed the least noticeable training induced changes. One of these demonstrated signs of tactile extinction and all parietal patients demonstrated some sensory deficit. There is only weak evidence here to suggest that auditory cues assist in the recovery of RTG after damage to the parietal cortex, perhaps because these particpants demonstrated only moderate signs of imapirment and as such may be the most challenging patients to demonstrate a treatment related change (Dobkin 2009). It is also speculated that spatial cues may be more effective than temporal cues for improving motor planning in patients with impairments to visuospatial transformations. Indeed, gait in healthy elderly participants is more strongly influenced by stepping stones than metronome beeps (Bank, Roerdink et al. 2011). Similarly motor planning and execution of RTG movements may be influenced more by spatial cues that guide the wrist trajectory and negate spatial errors.

These findings lend some support to the idea that the degree of motor impairment (Fugl-Meyer) is indicative of those participants more likely to improve (Prabhakaran, Zarahn et al. 2008). Four out of the training group (which consisted of 5 participants) had a moderate level of motor impairment according to the Fugl-Meyer. The exception was Participant B whose motor impairment was very mild and was deemed normal in terms of visual motor accuracy (in terms of the 10HPT) and grip strength. Participant B showed the least detectable changes and was also least satisfied that the training could improve upper limb function. The level of motor impairment in this participant may have indicted the need for more challenging training. However increasing knowledge of the effects upon RTG of damage to particular brain areas may help to define more targeted lesion-based interventions in the future.

Limitations to the study

The results of this proof of principle study are of course limited by confounding factors, including the small sample size, potential for participant selection bias, risk of bias due to unblinded assessments and limited detail regarding the lesion location and tract involvement. Multiple baselines were used to establish a stable within subject performance but this was subject to substantial variability. Future research would consider one or more additional baseline assessments and more detailed information regarding damaged areas. The inclusion of a control group allocated to repetitive task training without cues would help to determine the potential benefit of rhythmic auditory cues. A simple ABA design was chosen for practical reasons with repeated measures used to establish trends. An ABAC design (where B = ARC and C=repetititive task training without auditory cues) was also considered and it is acknowledged that this design might reveal more about the benefit of auditory cueing over and above repetitive task practice.

The potential for peripheral changes, for example increased muscle strength to contribute to improved motor control should also be acknowledged. Future research might also consider measuring peripheral response to training such as muscle fiber hypertrophy (due to an increase in actin and myosin protein filaments), muscle fiber composition (proportion of fast twitch and slow twitch), decreased hypertonicity or improved connective tissue flexibility.

Conclusion

The current study focused upon high-intensity therapy specifically for the treatment of upper limb coordination after parietal, cerebellar or pontine stroke, using quantitative measurement to assess recovery. Importantly high intensity ARC training is well tolerated although there is no definitive conclusion regarding efficacy. For clinicians the study has provided early indications that spatial variability of RTG may be reduced by repetitive task practice with entrainment to predictable timing cues. This was particularly notable for one patient with a cerebellar lesion and another with a Pontine lesion and for these patients there is potential for more effective training with different sized objects

and varying speeds. For parietal patients the use of visual cues during training may have a stronger influence upon recovery of RTG due the spatial impairments associated with damage to this brain area. The potential for adjuncts such as auditory cues to drive additional specific neural networks for improved RTG function over and above standard repetitive practice requires further investigation.

CHAPTER 5 CONCLUDING REMARKS

Healthy adults repeatedly perform reach to grasp movements throughout the day without error or conscious attention to the task and without appreciating the complexity of this function. Spatial and temporal coordination between the proximal and distal musculature normally ensures that the hand will reach the object to coincide with enclosure by the fingers. The way in which the brain controls this multisegmental coordination is not yet fully understood, although parietal and cerebellar regions are almost certainly involved. During the course of this research a new question has arisen of whether a control law (Rand, Squire et al. 2006) (whereby aperture closure distance is determined by the hand velocity, peak aperture and hand acceleration) is universally valid and can explain the current data. Future research, designed specifically for this purpose might further explore this potential. In this thesis the author has focused upon the specific aim of comparing the effects of parietal and cerebellar lesions upon reach and grasp coordination in terms of the correlation between temporal events which is taken as indicative of coupling in previous research (Jeannerod 1984; Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991; vanVliet and Sheridan 2007).

Impairment to visual and proprioceptive mapping is expected to cause spatial errors to RTG after parietal stroke; whereas impaired sensory predictions and abnormal velocity control may contribute to spatiotemporal variability after cerebellar stroke. Damage to either region has the capacity to disrupt the normal coordination between the hand and arm components. Brain imaging is likely to play an increasingly important role in neurorehabilitation, contributing to the design of improved interventions and helping clinicians to predict which patients are most likely to benefit from specific treatments (Krakauer 2005; Stinear and Ward 2013). One recent study (Riley, Le et al. 2011) has shown that tract-specific injury is stronger than infarct volume or baseline clinical status for predicting treatment gains. Another (Nouri and Cramer 2011) demonstrates that participants with clinically meaningful improvements in Fugl-Meyer and Motor Ability Arm Test typically have a relatively intact corticospinal tract and a preserved motor system determined by Motor Evoked Response (MER). Participants with subcortical stroke and without significant damage to the primary

motor and sensory cortex are also more likely to elicit a MER. Together these studies indicate that restorative therapies may be optimal for individuals with sufficient biological substrate remaining.

Lesion location also determines specific mechanisms for reorganization which may indicate different strategies for optimal restoration (Luft, Waller et al. 2004). Using fMRI Luft and colleagues showed differences in activation patterns for paretic and non-paretic limb movements. Activation patterns of subcortical stroke patients are characterised by involvement relative to the moving limb of the contralateral motor cortex, ipsilateral cerebellum, bilateral cingulate gyrus, SMA and perisylvian regions, similarly to controls. Cortical stroke patients with lesions affecting the sensorimotor cortex recruited alternative networks involving ipsilateral postcentral mesial hemisphere regions, and areas at the rim of the stroke cavity. It is hoped that the present work will contribute to developments within neurorehabilitation which may include topographic matching of interventions to promote activity within distinct networks. A greater understanding of the specific impairments associated with particular brain regions and of the response to treatment can further develop the scientific rational behind future studies. Adjuncts such as auditory, visual and haptic cues, electrical stimulation and dual tasking could help to drive additional specific networks to standard impairment based treatment.

This final chapter provides a summary of the progress made with respect to the original research aims. Limitations of the work are acknowledged and suggestions made to help direct future research. Based upon the overall findings clinical recommendations are offered to promote the recovery of reach to grasp after stroke, particularly for treating patients with either parietal or cerebellar lesions.

Progress made with respect to the research aims:

The first empirical study (Chapter 2) involved two patient groups and a control group to ascertain specific kinematic impairments according to lesion location. The study identified the RTG coordination impairments associated with damage to either the right parietal lobe or cerebellum and quantified how these patients adjust reach-to-grasp when hand transport is perturbed. Object location was perturbed unpredictably to verify whether processes supporting online adjustments necessary for

good coordination are intact and test the ability of these patients to predict and implement appropriate interaction torque compensation**.** With respect to the first aim, both parietal and cerebellar groups exhibited correlations between key events in transport and grasp, which were comparable to healthy age matched controls. This implied that either coordination between the hand and arm remained relatively intact in these chronic stroke participants with mild to moderate impairments; or that impaired coordination was compensated for with slowed movements. The first possibility, i.e intact function, would suggest that coordination between transport and grasp is controlled by another area of the brain such as the parietal lobe where there is cerebellar damage and the ipsilateral cortex or the cerebellum where there is parietal damage. If compensation is an attention demanding process then movement is expected to be slow. A secondary task might reveal latent deficits as a result of competing attentional resources. Alternatively the lesions were not large enough to affect coordination or that the lesioned areas had recovered their function. These possibilities deserve further investigation within future research.

With respect to the second aim, patient groups demonstrated similar behaviour to controls in response to perturbation. It was concluded therefore that the online adjustments necessary for good coordination appeared intact for this particular set of stroke patients (with their respective lesions and stage of recovery). Perhaps also because of compensation, relevant surviving brain regions or prior recovery. As such it was decided that this aspect of RTG coordination did not require specific intervention for these two patient groups at this stage of their recovery.

The review (Chapter 3) attempted to provide a thorough and unbiased synthesis of research from which to establish a profile of existing treatments currently used to correct coordination deficits in the arm after stroke and to determine their effectiveness. It was determined that functional training, electrical sensory stimulation and robot or computerised training may induce positive changes to the spatiotemporal coupling of the hand and arm in chronic stroke patients and that these appeared to translate into upper limb functional gains. There is currently insufficient evidence to provide strong recommendations about the effect of interventions for improving hand and arm coordination during

reach to grasp after stroke. Currently there is also a lack of evidence to indicate which patients might benefit from rehabilitation of hand and arm coordination.

The aim of the second empirical study (Chapter 4) was to assess the effectiveness of a specific intervention for the rehabilitation of reach and grasp after either right parietal or cerebellar lesions. ARC training was utilised to progress speed whilst maintaining spatiotemporal control (in terms of the timing of peak velocity, time of maximum aperture, wrist path trajectory and wrist velocity peaks). Examining the response to ARC training in people with specific lesions has provided some indication that certain individuals with parietal and cerebellar lesions show improvements. High-intensity training was well adhered to, caused no negative side effects. Kinematic analysis provided a sensitive quantitative measurement to assess recovery. No definitive conclusion regarding efficacy was drawn, although the wrist path trajectory of RTG was reduced in 4/5 participants after ARC training.

Limitations of the studies

Recruitment of eligible participants was challenging despite involvement of the West Midlands Stroke Research Network. The overall findings in the first experimental study are constrained by the small sample size. Patients were heterogenous in terms of the time since stroke, but the parietal group was more chronic. However, the patient characteristics are clearly described and the patients were matched with healthy controls in terms of age and handedness. Furthermore baseline comparisons showed that patient groups were matched in terms of age and function. Recruitment took place in both acute and subacute hospital settings where CT scans were used to identify the lesion. Limited resources meant that there was little information regarding the lesion and as such it was impossible to control for the lesion size and the involvement of other areas in the brain, or for the degree of damage to either the white or grey matter.

Correlations between transport and grasp components at key temporal events was observed here in healthy individuals for a high proportion of trials. The small number of cases where correlations were not significant raises the issue of whether correlations at specific time points are the

most appropriate measurement for coupling. There is a whole body of work (Jeannerod 1984; Paulignan, Jeannerod et al. 1991; Paulignan, Mackenzie et al. 1991; vanVliet and Sheridan 2007) for which these correlations have been observed, suggesting value in their continued use. Moreover these correlations are likely to be present according to context, such as higher correlations in fast and challenging movements. However in view of the variable nature of these correlations in this and previous work, future research may consider additional measures of coordination such as correlations between the whole profile for wrist velocity or acceleration and grasp aperture amplitude.

The systematic review in Chapter 3 consisted predominantly of small studies with heterogeneity of stroke and diversity in terms of assessment of hand and arm coordination. The evidence, which was limited to only one RCT plus 6 experimental studies, was considered to be of only moderate quality. The inclusion of studies was based upon a subjective decision regarding whether the intervention or experimental manipulation was targeted to improve coordination of the hand and arm following stroke.

A single subject design experiment (Chapter 4) was used to determine whether ARC was effective for specific individuals and did not set out to determine whether a treatment group average differed in comparison to an alternative intervention. Participants were chronic stroke patients who were all past the stage of spontaneous recovery (Krakauer 2005; Teasell, Bayona et al. 2006). These patients were a convenience sample recruited from the first study and as such the potential for selection bias is acknowledged, however patient characteristics are described in detail and all patients were allocated the same intervention. Single-subject design may accurately reflect actual practice but is more susceptible to bias than a randomised controlled trial (Higgins, Green et al. 2008). Repeated measures during the baseline phase were used to establish a stable within subject performance prior to training and thus control for threats to internal validity such as statistical regression. Both flat line and linear trend variability were observed during the baseline periods and these were considered during the interpretation of the results. The study did not include a control group which would have minimized effects of variables other than the intervention. The results of the one participant who did not participate in training were included for comparison, although it is acknowledged that inclusion of

one control subject will not ensure validity or correct for systematic errors. For practical reasons there was no attempt made to blind the assessors or the participants so knowledge of the intervention received so the outcomes are disposed to bias in terms of patient effort and researcher measurement.

Implications for treatment

Clinical recommendations for improving RTG coordination after stroke are provided in Table 5.1. In terms of the neuroanatomy (Saleh, Takahashi et al. 2012) there is good reason to suggest that for patients with mild to moderate impairments reach and grasp practice should involve planning and execution of the two components together to activate temporally linked central commands (vanVliet and Sheridan 2007). Practice should also incorporate a variety of behavioural goals to help patients to learn to adapt to different environmental conditions in a predictive way. Damage to brain regions such as the parietal cortex or cerebellum have the potential to cause specific problems with RTG coordination and knowledge of the imaging results can help to guide the clinical examination of motor impairments to ensure that deficits are not overlooked and that treatment is targeted appropriately(van Vliet, Carey et al. 2012). Matching interventions according to lesion location in order to promote activity within distinct brain areas could help optimise upper limb rehabilitation after stroke. Promoting feedback from every possible source including proprioceptive, cutaneous, auditory and visual information may help patients to learn strategies to for more efficient coordination. Based upon the observations here specific considerations for RTG training in patients with lesions involving the parietal lobe or cerebellum are provided in Tables 5.2 and 5.3.

With specific respect to the parietal group (Table 5.2) treatment might focus upon improving movement smoothness and reducing the spatial errors caused by impaired sensory perception and or sensory integration. The normal sensory information may be augmented with visual cues or auditory which have been applied to gait rehabilitation (Bank, Roerdink et al. 2011) and paretic arm training (Thaut, Kenyon et al. 2002) and here in Chapter 3. Spatial visual cues and feedback regarding trajectory may help parietal patients to achieve smoother transport. Feedback and cues could be withdrawn and obstacles included as patients begin to demonstrate more effective movement planning

and reduced reliance upon feedback control. Anterior-intraparietal sulcus lesions may affect control for aperture size and timing (Jeannerod 1986; Jeannerod 1994; Binkofski, Dohle et al. 1998). For these patients clinicians are encouraged particularly to promote grasp within reaching practice, which involves grasping objects of different sizes. Posterior parietal cortex lesions are associated with optic ataxia (Jakobson, Archibald et al. 1991; Roy, Stefanini et al. 2004). Patients with lesions involving the PPC may benefit from RTG training with targets located in both the foveal and peripheral visual fields.

Feedback to highlight the timing of grasp onset and grasp closure (van Vliet, Wimperis et al. 2012)may also promote the coordination between transport and grasp. For parietal patients the problem of delayed grasp onset should be examined, whereas for the cerebellar patients early grasp onset might be a problem. Both groups of patients might be encouraged with feedback to coincide the onset of grasp aperture with the timing of the wrist onset to help normalise the relationship between the two components.

Movement smoothness was also a problem for the cerebellar group perhaps because of abnormal velocity control and poor state-estimation (Haggard, Jenner et al. 1994). The present work together with previous research (Thaut, Kenyon et al. 2002) has indicated that entrainment to predictable rhythmic timing cues may help to reduce the wrist path trajectory. Rehabilitation of cerebellar patients should consider ways of decreasing variability (Rand, Shimansky et al. 2000; Zackowski, Thach et al. 2002) of reaching kinematics and movement endpoints. Practice involving repetitions with a variety of fast and slow movements may help cerebellar patients with hypermetria to learn to generate muscular torques of appropriate levels in order to control the mechanical consequences of dynamic interaction forces during multijoint movements, (Topka, Konczak et al. 1998). Indeed the present study lends support for reduced spatial variability of RTG following repetitive task practice with an emphasis upon progressing speed with entrainment to predictable timing cues.

Dual-task training after stroke has been shown to improve spatial and temporal aspects of walking ability including speed and step length after stroke (Yang, Wang et al. 2007). It is speculated here that for RTG to be successful patients with parietal or cerebellar lesions may utilise attentional resources and slower movements to compensate for impaired coordination. With practice (either single-task or dual-task) participants may learn to perform tasks without limited central resources and movements might become more 'automatic' (Ruthruff, Van Selst et al. 2006). Improvements in performance following dual-task training may be associated with a reduction in activity of the right ventral inferior frontal gyrus perhaps because of a reduction in the cognitive resources needed (Erickson, Colcombe et al. 2007). By limiting the attentional resources available for RTG practice, dual-task practice might therefore activate more direct neural pathways to enable the performance of faster, coordinated RTG movements. Specific recommendations for RTG training after cerebellar stroke are summarised in Table 5.3.

Directions for future research

The thesis has unravelled some important issues regarding control processes for RTG coordination but there are still many more questions for future research to answer.

Increased resources MRI and DTI would enable future research to establish more exact detail of the lesion, including the size, location and the involvement of neural pathways. This is important not only to further our understanding the recovery mechanisms for improving RTG coordination but also because it is known from recent research (Riley, Le et al. 2011) that lesion location and tract specific injury is strong for predicting treatment gains. Use of functional imaging would help to establish whether coordination of RTG after parietal or cerebellar stroke is unaffected by small lesions, or if the lesioned areas have recovered their function or perhaps that coordination is controlled by another area of the brain after stroke. Impairments in coordination perhaps compensated for with slowed movements and increased reliance upon attentional resources might be revealed by a dual-task study. Slower walking speed after stroke has previously been associated with greater

cognitive interference upon gait (Yang, Chen et al. 2007; Plummer-D'Amato and Altmann 2012). Future research involving a dual-task might also reveal deficits in RTG coordination after stroke due to competition for shared attentional processes. Potential for dual-task training to promote the recovery of faster, more coordinated movements after stroke should also be investigated in RTG as it has previously been demonstrated in walking (Yang, Wang et al. 2007).

Functional imaging would also help to establish the recovery mechanisms involved after practice of discrete movements or rhythmic automated movements. Particularly as different pathways have been identified (Pollok, Gross et al. 2008) for the two types of movement, namely the cerebello-diencephalic-parietal loop which might be important for anticipatory motor control, and the parietal-cerebellar connections important for the feedback processing.

Future research involving ARC training would consider one or more additional baseline assessments and the addition of a control group for more robust findings. There is also potential for more effective training with different sized objects and varying speeds. Based upon research in gait (Bank, Roerdink et al. 2011) visual cue training may be adapted for parietal patients to facilitate greater recovery of the spatial impairments of prehension. Future research would consider the use of a combination of assessment techniques including kinematic analysis with FMRI and or TMS. Such research may take the form of a further mechanistic phase II study which will serve as an important source of information prior to an expensive randomized controlled trial (Krakauer, Carmichael et al. 2012).

Despite the aforementioned limitations this thesis provides a useful basis for further research and was carried out with sufficient rigour to serve as a useful contribution to the knowledge base. The empirical studies in the thesis were underpinned by current theory and the principle performance indicators were derived from kinematic analysis. This is a quantitative assessment tool, which is both reliable and valid and does not have the propensity for user bias.

Table 5.1 Clinical recommendations for improving RTG coordination after stroke.

Recommendations for clinical practice	Supporting research	Reference
Practice reach and grasp together to activate temporally linked central commands. Concentrate on planning and execution of the two components together.	Both proximal and distal musculature are activated by single neurons according to spatiotemporal patterns of coordinated reach to grasp movements as opposed to single joint movements	(Saleh, Takahashi et al. 2012)
	Overlap between functional regions of reach and grasp in the parietal cortex	(Fattori, Raos et al. 2010; Vesia and Crawford 2012)
	Temporal coordination is more variable after stroke.	(vanVliet and Sheridan 2007)
Encourage person to start arm movement and hand opening together to improve normal temporal links.	Coordination between transport and grasp at the start of the movement improved with feedback on the time lag between the two movements during reach-to-grasp movements.	(Michaelsen, Jacobs et al. 2004; van Vliet and Sheridan 2007; van Vliet, Wimperis et al. 2012)
Progress from smaller to larger object sizes.	For stroke subjects movement duration was longer for a larger cup size, which may be more difficult to grasp because of the weak finger extensors. Practice with different cup sizes will also allow practice of adjusting temporal aspects.	(vanVliet and Sheridan 2007)
Practice with different cup sizes and different speeds to promote relearning of control programs for scaling movement during different tasks. (van Vliet and Sheridan 2007). Large objects require adequate finger extension for grasp and small objects require coordination of fine motor skills, so both pose different challenges for patients to overcome.	Stroke participants may lack ability to adjust the time of maximum aperture according to different sized objects and speed.	(Wu, Chou et al. 2008)

Practice reaching objects at different distances to promote modulation of forces.	There is a tendency for stroke subjects to overshoot near target and undershoot far objects. Stroke subjects have a reduced ability to scale peak velocity for targets of varying distance.	(van Vliet and Sheridan 2009) (Lang, Wagner et al. 2005)
Practice with different end goals for selective finger positioning.	Finger positioning for grasp is related to the presence and the nature of the task to be performed following grasping	(Ansuini, Giosa et al. 2008)
Stabilisation or constraint of the trunk with seat belts placed diagonally across chest and around seat	Additional recruitment of trunk movement both to transport the hand to the target and to achieve a functional hand orientation for grasping when distal impairments are present.	(Michaelsen, Jacobs et al. 2004)
	Trunk restraint can increase reach extent in patients with more severe arm impairment.	(Michaelsen, Dannenbaum et al. 2006)
Constraint induced movement training (CIMT)	Modified constraint-induced movement therapy improved efficiency of pre-planned reaching and grasping and feedforward control of reaching.	(Lin, Wu et al. 2007)
	A combination of forced-use therapy and conventional physiotherapy enhances motor cortex excitability and improves motor performance.	(Liepert, Uhde et al. 2001)
	After CIMT, kinematic data showed improvement in the speed of movement and in measures related to the capacity for coordination	(Caimmi, Carda et al. 2008)
Bilateral arm training	A reduction in multiple peaks in velocity for smoother hand paths was observed after BATRAC training.	(Whitall, McCombe Waller et al. 2000; Waller, Harris-Love et al. 2006; Waller, Liu et al. 2008; Whitall, Waller et al. 2011)

Table 5.2 Training suggestions for RTG practice in Parietal patients with mild to moderate impairments.

Observed problem during RTG	Training suggestion	Supporting literature
Prolonged movement durations Lengthy wrist path trajectory Increased reliance upon feedback control	Allow sufficient repetitive task to increase consistency of performance and thus decrease variability. Practice movements at different speeds with feedback to optimize ballistic contractions. Practice that emphasises reduced movement times may normalise movement and encourage greater use of feedforward movement control, as faster movements most likely rely more upon feedforward control Training which incorporates resisted movements may also help to reduce movement durations	Stroke patients demonstrate a greater dependency upon feedback control to compensate for increased movement variability (van Vliet and Sheridan 2007) The repetitive training of precise but not rapid grasping and transport movements does not further enhance the functional recovery of the affected arm and hand in stroke patients compared with functionally based therapy (Woldag, Waldmann et al. 2003) Practice of ballistic contractions increased peak pinch acceleration amplitude, peak force & increased in motor evoked potentials in healthy participants (Muellbacher, Ziemann et al. 2001) Movements duration likely to reflect muscle strength (Hogan, Krebs et al. 2006).
	Entrainment to predictable rhythmic timing cues	Reduction in variability of arm kinematics during rhythmic entrainment (Thaut, Kenyon et al. 2002) Stroke participants able to compensate for auditory phase shifts with convergence back to pre-phase shift asynchrony(Pelton, Johannsen et al. 2010)
	Improve movement planning by limiting feedback during RTG movement, either by obscuring the target or the hand after movement onset	PPC plays an important role in movement planning and feedback control; firstly by converting sensory information into motor commands and secondly integrating sensory input with previous and ongoing motor commands to maintain a continuous estimate of arm state used to update ongoing and future movement plans (Buneo and Andersen 2006)
	Vary the distance, location and size of target objects to include both the foveal and peripheral visual fields	PPC lesions result in impairments in modulation of transport to changes in object location and size (Roy, Stefanini et al. 2004) Goal for neurological physiotherapy should be to optimize amount of movement variability by incorporating a rich repertoire of movement strategies (Stergiou, Harbourne et al. 2006)

	Visual or auditory cues regarding spatial aspects such as trajectory and key temporal events during RTG may help parietal patients to achieve smoother more coordinated transport and grasp. Feedback and cues could be withdrawn with progress and obstacles included as patients begin to demonstrate more effective movement planning and reduced spatiotemporal errors.	In healthy elderly treadmill walking, visual cues induced gait adjustments more effectively than did the metronome beeps (Bank, Roerdink et al. 2011).
Compensatory slow movements	Dual-task training - limiting the attentional resources available for RTG practice with dual-task practice to help activate more direct neural pathways.	Dual-task training after stroke has been shown to improve spatial and temporal aspects of walking ability including speed and step length after stroke (Yang, Wang et al. 2007) Improvements in performance following dual-task training have been associated with reduced activity of the right ventral inferior frontal gyrus perhaps because of a reduction in the cognitive resources needed (Erickson, Colcombe et al. 2007).
Late onset of grasp	Feedback to encourage patients to start the grasp onset earlier to coincide with the wrist onset	Coordination between transport and grasp at the start of the movement improved with feedback on the time lag between the two movements during reach-to-grasp movements after stroke (van Vliet, Wimperis et al. 2012)
Poor control for aperture size and timing with increasing speed	Promote grasp within reaching practice, which involves grasping objects of different sizes and at different speeds.	Anterior-intraparietal sulcus lesions may affect control for aperture size and timing (Jeannerod 1986; Jeannerod 1994; Binkofski, Dohle et al. 1998).

Table 5.3 Training suggestions for RTG practice in Cerebellar patients with mild to moderate impairments.

Observed problem during RTG	Training suggestion	Supporting literature
Longer movement durations and reduced velocity amplitude	Practice involving fast and resisted movement repetitions to help patients with hypermetria generate muscular torques of appropriate levels to control the mechanical consequences of dynamic interaction forces during multijoint movements	Cerebellar patients have difficulty generating sufficient levels of phasic muscular torques to counteract fast movement torques during fast movements. (Topka, Konczak et al. 1998) The repetitive training of precise but not rapid grasping and transport movements does not further enhance the functional recovery of the affected arm and hand in stroke patients compared with functionally based therapy (Woldag, Waldmann et al. 2003) Practice of ballistic contractions increased peak pinch acceleration amplitude, peak force & increased in motor evoked potentials in healthy participants (Muellbacher, Ziemann et al. 2001)
Temporal variance of TMA	Entrainment to predictable rhythmic timing cues	Impaired internal state-estimation (Haggard, Jenner et al. 1994; Miall and King 2008) Reduction in variability of arm kinematics during rhythmic entrainment (Thaut, Kenyon et al. 2002)
	RTG practice with varied distance, location and size of target objects	Goal for neurological physiotherapy should be to optimize amount of movement variability by incorporating a rich repertoire of movement strategies(Stergiou, Harbourne et al. 2006)
Early onset of grasp	Encourage to start the grasp onset later to coincide with the wrist onset	Coordination between transport and grasp at the start of the movement improved with feedback on the time lag between the two movements during reach-to-grasp movements after stroke (van Vliet, Wimperis et al. 2012)
Prolonged movement duration	Dual-task training - limiting the attentional resources available for RTG practice with dual-task practice might help activate more direct neural pathways.	Dual-task training after stroke has been shown to improve spatial and temporal aspects of walking ability including speed and step length after stroke (Yang, Wang et al. 2007) Improvements in performance following dual-task training have been associated with a reduction in activity of the right ventral inferior frontal gyrus perhaps because of a reduction in the cognitive resources needed (Erickson, Colcombe et al. 2007).

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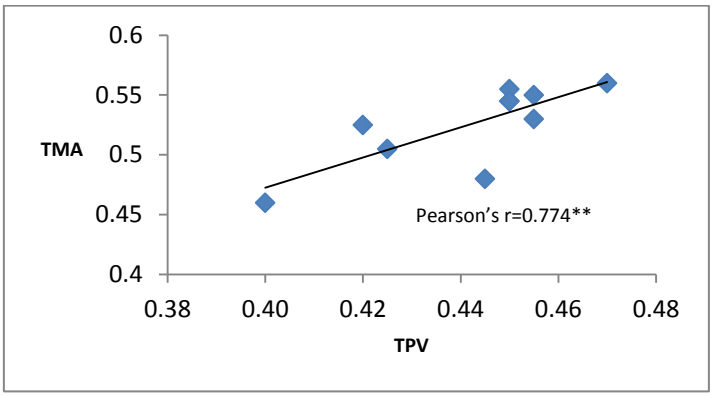
APPENDIX

A1.1 Pilot data example of scatter plot showing temporal coupling between the hand and the arm with significant correlation between the TMA and TPV.



A2.1 MATLAB scripts for empirical studies (Chapter 2 & Chapter 4)

```
%  kinematic data for reach to grasp =21 columns (C 1-3, R 4-6, L 7-9,
sternum1 10-12, sternum2 13-15, sternum3 16-18, shoulder 19-21, elbow 22-24
, 1stmcp 25-27, index 28-30, thumb 31-33)
%find data and call it data%
lose_bad_frames=1;

set(0,'DefaultFigureWindowStyle','docked')

%% DECLARE SOME VARIABLES
% these will allow easy shuffling should your data not align
% note this version requires 12 columns - as column 13 hard coded to be
% time.  It would be eaiser to make it a second variable - then this would
% be robust for less data columns, but hind sight is 20 -20.

% define output variables
f_wrist_start_time =[];
f_peak_wrist_velocity =[];
f_time_wrist_peak_velocity =[];
f_time_peak_wrist_dec =[];
f_max_aperture =[];
f_max_aperture_time =[];
f_max_distance_wrist =[];
f_max_wrist_time =[];
f_max_distance_trunk1 =[];
f_max_trunk1_time =[];
f_dilation_start_time =[ ];
f_object_start_time =[];
f_movement_period = [];
f_wrist_peaks = [];
f_aperture_peaks = [];
f_resultant_max_distance = [];
f_resultant_wrist_maxap = [];
f_resultant_wrist_close = [];
f_time_last_peak_aperture = [];
f_time_last_peak_wrist_velocity = [];

data = [];

%% GET DATA - multiple files may be selected
[filename_load, pathname, filterindex] = uigetfile( ...
    {  '*.mat','MAT-files (*.mat)'; ...
    '*.*',  'All Files (*.*)'}, ...
    'Pick a file', ...
    'MultiSelect', 'on');

%uigetfile behavi  our differs for 1 filename or a set of filenames
if(ischar(filename_load));
    filename_iterations_max = 1;
else %its a cell!
    filename_iterations_max = length(filename_load);
end

% final_plot = figure;
% final_colour = ['k' 'g' 'k'];
% final_line = [ '-' '-' ':' ];
for filename_iterations = 1:filename_iterations_max
```

```
    if(ischar(filename_load));
        load(fullfile(pathname, filename_load));
        disp(['LOADING...',filename_load] );
        %% untested!! this bit here
        data_raw_format = eval([filename_load(1:end-4),
'.Trajectories.Labeled.Data']);
    else %its a cell!
        load(fullfile(pathname, char(filename_load(filename_iterations))));
        disp(['LOADING...',char(filename_load(filename_iterations))] );
        filename_ext = char(filename_load(filename_iterations));
        data_raw_format = eval([filename_ext(1:end-4),
'.Trajectories.Labeled.Data']);
    end

    %% DATA is of shape 12 x 3 x 1000
    %% address the element you want as so

    % data(R,:,:) gives you the data of MARKER R, 1-12, this would be 3 x
1000
    % data(X,1,:) gives you the data of Marker R, and only the first column
X
    % data(X,2,:) gives you the data of Marker R, and only the first column
Y
    % data(X,3,:) gives you the data of Marker R, and only the first column
Y

    data_size = size(data_raw_format); % we expect 12,3,1000

    %% SQUEEZE

    data = [];%zeros(data_size(1)*data_size(2),data_size(3));
    for markers = 1:data_size(1)
        for ordinates = 1:data_size(2)
            data = [data ; squeeze(data_raw_format(markers,ordinates,
:))'];
        end
    end
    %%
    %19/01/10 - HERE + back handed way of resolving problem with
    %calibration not being set at zero therefore added 1000 to xyz
    %coordinates.

    %% right handed hack



    size(data)

    decimation_ = input('"3" FOR THREE "4" FOR FOUR','s');
    %orientation = 'l';
    if decimation_ == '3'
        disp('3 - default');
    else
        disp('4 - deviant')
        [columns_ rows_] = size(data);
        columns_remove = 4:4:columns_;
        columns_final = 1:columns_;
        columns_final(columns_remove) = [];
        data = data(columns_final, :);
```

```
    end
    size(data)
    [columns_ rows_] = size(data);
        %MIRROR - needed!

    orientation = input('"l" FOR LEFT "r" FOR RIGHT','s');
    %orientation = 'l';
    if orientation == 'l'
        disp('LEFT - default')
    else
        disp('RIGHT - deviant')
        data(1:3:columns_, :) = (1000 - data(1:3:columns_, :));
    end

    beep
    data = data + 1000;

    %% LOAD DATA

    if(ischar(filename_load));
        filename_save = filename_load;
    else %its a cell!

        filename_save = char(filename_load(filename_iterations));
    end

    %% CALL
    [   wrist_vel, aperture_pos, wrist_start_time, peak_wrist_velocity, ...
        time_wrist_peak_velocity, time_peak_wrist_dec, max_aperture, ...
        max_aperture_time, max_distance_wrist, max_wrist_time, ...
        max_distance_trunk1, max_trunk1_time, dilation_start_time, ...
        object_start_time, movement_period, wrist_peaks,
aperture_peaks,....
        resultant_max_distance, resultant_wrist_maxap,
resultant_wrist_close,...
        time_last_peak_aperture,time_last_peak_wrist_velocity...
        ] = trudy_GRABIT_analysis_func(data, filename_save,
lose_bad_frames);

    %FINAL PLOT

    %     set(final_plot,'WindowStyle','docked')
    figure;
    subplot (2,1,2), plot((aperture_pos -
(aperture_pos(1))),'LineWidth',2);
    axis([0 200 0 100]);
    title('GRIP APERTURE PROFILE'), xlabel ('TIME(s)'), ylabel('Aperture
size(mm)');
    hold on
    %     [final_colour(filename_iterations)
final_line(filename_iterations)]
    subplot(2,1,1), plot((wrist_vel), 'LineWidth',2);
    axis ([0 200 -50 1000]); %line([0 length(wrist_vel)],[line1 line1]);
    title('WRIST VELOCITY PROFILE'), xlabel ('Time(s))'), ylabel ('Wrist
velocity(mm/s)');

    hold on;

    %% UPDATE
```

```
    f_wrist_start_time          = [ f_wrist_start_time
wrist_start_time ];
    f_peak_wrist_velocity       = [ f_peak_wrist_velocity
peak_wrist_velocity ];
    f_time_wrist_peak_velocity  = [ f_time_wrist_peak_velocity
time_wrist_peak_velocity ];
    f_time_peak_wrist_dec       = [ f_time_peak_wrist_dec
time_peak_wrist_dec ];
    f_max_aperture              = [ f_max_aperture
max_aperture ];
    f_max_aperture_time         = [ f_max_aperture_time
max_aperture_time ];
    f_max_distance_wrist        = [ f_max_distance_wrist
max_distance_wrist ];
    f_max_wrist_time            = [ f_max_wrist_time
max_wrist_time ];
    f_max_distance_trunk1       = [ f_max_distance_trunk1
max_distance_trunk1 ];
    f_max_trunk1_time           = [ f_max_trunk1_time
max_trunk1_time ];
    f_dilation_start_time       = [ f_dilation_start_time
dilation_start_time ];
    f_object_start_time         = [ f_object_start_time
object_start_time ];
    f_movement_period           = [ f_movement_period
movement_period ];
    f_wrist_peaks               = [f_wrist_peaks                wrist_peaks
];
    f_aperture_peaks            = [f_aperture_peaks
aperture_peaks];
    f_resultant_max_distance    = [f_resultant_max_distance
resultant_max_distance];
    f_resultant_wrist_maxap     = [f_resultant_wrist_maxap
resultant_wrist_maxap];
    f_resultant_wrist_close     = [f_resultant_wrist_close
resultant_wrist_close];
    f_time_last_peak_aperture   = [f_time_last_peak_aperture
time_last_peak_aperture];
    f_time_last_peak_wrist_velocity =...
        [f_time_last_peak_wrist_velocity time_last_peak_wrist_velocity];


    %     if (filename_iterations ~= filename_iterations_max)
    %         clf(magicfigure);
    %     else
    %     end
end

%% SAVE COLUMNS
target_cells = {'A1' ;'B1'; 'C1' ; 'D1' ; 'E1' ; ...  %% 20 of them
    'F1' ; 'G1' ; 'H1' ; 'I1' ; 'J1' ; 'K1' ; 'L1' ; 'M1' ; 'N1' ; 'O1' ;
'P1' ; 'Q1' ; 'R1'; 'S1'; 'T1'};

xls_filename = input('UNIQUE NAME FOR SPREADSHEET? ','s');
warning off
for iterations=1:1:filename_iterations_max

    if(ischar(filename_load));
        filename_save = filename_load;
    else %its a cell!
```

```
        filename_save = char(filename_load(iterations));
    end

    save_cell = { filename_save;...
        f_wrist_start_time(:,iterations);...
        f_peak_wrist_velocity(:,iterations);...
        f_time_wrist_peak_velocity(:,iterations);...
        f_time_peak_wrist_dec(:,iterations);...
        f_max_aperture(:,iterations);...
        f_max_aperture_time(:,iterations);...
        f_max_distance_wrist(:,iterations);...
        f_max_wrist_time(:,iterations);...
        f_max_distance_trunk1(:,iterations);...
        f_max_trunk1_time(:,iterations);...
        f_dilation_start_time(:,iterations);...
        f_object_start_time(:,iterations);...
        f_movement_period(:,iterations);...
        f_wrist_peaks(:,iterations);...
        f_aperture_peaks(:,iterations);...
        f_resultant_max_distance(:,iterations);...
        f_resultant_wrist_maxap(:,iterations);...
        f_resultant_wrist_close(:,iterations);...
        f_time_last_peak_aperture(:,iterations);...
        f_time_last_peak_wrist_velocity(:,iterations)};

    confirm_XLS(iterations) =  xlswrite( (fullfile(pathname,[xls_filename,
'.xlsx'])), save_cell, 'sheet', char(target_cells(iterations)));
    pause(0.10);
end
warning on
disp(['Confirm XLS saved [1/0] = ', num2str(confirm_XLS)]);
disp('All 1s All Saved.  Any Zeros indicate a failure.');


%% GRABIT_HAND & ARM COORDINATION AFTER STROKE - function
%% List output variables
function [wrist_vel, ...
    aperture_pos, ...
    wrist_start_time, ...
    peak_wrist_velocity, ...
    time_wrist_peak_velocity, ...
    time_wrist_peak_dec, ...
    max_aperture, ...
    max_aperture_time, ...
    max_distance_wrist, ...
    max_wrist_time, ...
    max_distance_trunk1, ...
    max_trunk1_time, ...
    dilation_start_time, ...
    object_start_time, ....
    movement_period, ...
    wrist_peaks, ...
    aperture_peaks,...
    wrist_path_total,...
    wrist_path_opening,...
    wrist_path_closing,...
    time_last_peak_aperture,...
    time_last_peak_wrist_velocity...
    ] = trudy_GRABIT_analysis_func(data, filename_save, lose_bad_frames)
```

```
set(0,'DefaultFigureWindowStyle','docked')
%% Define step size.
step_size = 3; % dinnae mess
% Current output 3 columns per marker x,y,z
% N.B. LATTER DAY QUALISYS RETURN HAS 4 COLUMNS - revise to step size = 4
% for new software update
% change to 4 for new output version.

%% Define MARKER VALUES
% disp('Does this look right?');
Q_center = 1;
Q_right = 2;
Q_left = 3;
Q_sternum = 4;
Q_shoulderL = 5;
Q_elbow = 6;
Q_wrist = 7;
Q_1stmcp = 8;
Q_index = 9;
Q_thumb= 10;
Q_absolute_time = 11;
% Q_elbow = 5;
% Q_wrist = 6;
% Q_1stmcp = 7;
% Q_index = 8;
% Q_thumb= 9;
% Q_absolute_time = 10;
beep


%% Define end_of_data
% N.B. Lose bad frames used in call program when markers missing in first
few frames- usually for index/thumb.
halfway = max(size(data))- (lose_bad_frames); % obsolete term
end_of_data = halfway;

%% REMOVE BAD FRAMES from DATA for initial missing data (lose bad frames
(generally 1) can be changed in call)
% data is 33 by x - we want to remove lose_bad_frames of x
data = data(:,lose_bad_frames:end);

%% ISNAN - replace this if you want! BELOW
% if anything in the first row is NaN make it 0
if(max(isnan(data(:, 1))));
    find_data =  find(isnan(data(:, 1)));
    data(find_data,1) =0;
end

[rows_of_data columns_of_data] = size(data);

%% Hold previous value NaN filling
for row_iterations = 1:rows_of_data;
    NaN_coords_columns = isnan(data(row_iterations, :));
    for frame_iterations = 2:columns_of_data;
        if(isnan(data(row_iterations, frame_iterations)));
            data(row_iterations, frame_iterations) = data(row_iterations,
frame_iterations-1);
        end;
    end;
```

```
end;

%% FILTER - Butterworth Zero-phase forward and reverse digital filter,
data_size = size(data);
columns_of_data = data_size(2);
rows_of_data = data_size(1);
sample_rate = 200;
framesize = 1/sample_rate;

sample_rate = 200; %define constants before the loop
framesize = 1/sample_rate;
cutoff = 8;
[filt_resp_b,filt_resp_a] = butter(2,(cutoff/(sample_rate*0.5)),'low');

for i = 1:size(data,1)
    data_filt(i,:) = filtfilt(filt_resp_b,filt_resp_a,data(i,:));
end

data_pre_filt = data;
data = data_filt;

%% if


%% CONVERT EACH SET OF XYZ DATA TO VECTOR AND CALL IT data_vector

data_vector = [];
%(data) 33 columns / 3(x,y,z)= 12
%find vectors of x,y,z squared in data-vec column 1,2,3,4, 5,6,7,8,9,10
&11%

for each_xyz = 1:step_size:size(data,1);

    for each_frame = 1:size(data,2)
        data_vector_frames(each_frame) = sqrt(data(each_xyz,  each_frame)^2
...
            + data(each_xyz+1,each_frame)^2 ...
            + data(each_xyz+2,each_frame)^2);
    end
    data_vector = [data_vector ; data_vector_frames];
end




%% CONVERT EACH SET OF XY DATA to VECTOR AND CALLL IT XY_vector
XY_vector = [];
%to get the vector for x y only
for each_xy = 1:step_size:size(data,1);
    for each_frame = 1:size(data,2)
        XY_vector_frames(each_frame) = sqrt(data(each_xy,  each_frame)^2
...
            + data(each_xy+1,each_frame)^2 ...
            );
    end
    XY_vector = [XY_vector ;  XY_vector_frames];
end
```

```
%% CALCULATE VELOCITY & CALL IT data_velocity
data_velocity = diff(data_vector')./framesize;


%% CALCULATE ACCELERATION & CALL IT data_acceleration
data_acceleration = diff(data_velocity);

%% ABSOLUTE TIMING COLUMN
% %make time and frame
frame = 0:(length(data_velocity)-1); %
time = frame.*framesize; %
data_velocity(:,Q_absolute_time)= time; %
%data_velocity(:,end+1)= time;

%% FIND Peak wrist velocity for purpose of threshold value
max_wrist_velocity = abs(max(data_velocity(:,Q_wrist)));  %% Max value for
total recording duration

%% ONSET WRIST > 25mm/s peak velocity - find time when wrist velocity goes
over 15% threshold
%OLD % wrist_detection_threshold = 15; % Based upon Kahn 2001
%NEW 25mm/s
threshold_ =25; %= (max_wrist_velocity/100)* wrist_detection_threshold;
start_time = 0;
start_here = 1;
% 5 contiguous values > threshold
% changed to absolute value of wrist vel to account for backward motion
24/11/09
if (abs(max(data_velocity(:,Q_wrist)))>threshold_);
    while(~start_time)
        wrist_start_five =
find(abs(data_velocity(start_here:end,Q_wrist))>threshold_,5);

        if (wrist_start_five(1)+4 == wrist_start_five(5))
            wrist_start_five = wrist_start_five + start_here;
            start_time = 1;
        else
            start_here = wrist_start_five(2) + start_here;
            disp('WRIST > 25');
        end
    end
    wrist_start_time = wrist_start_five(1) * framesize;
else
    disp('NO WRIST velocity > 25mm/s');
    beep
    wrist_start_time = [-1];
end

%% TIME TO MAX Z-DEVIATION OF A COLUMN MARKER
% 1 2 3
% [ 3 6 9] for 1-2-3 step_size 3
% [ 3 7 11] for 1-2-3 step size 4

% assumption

% if(step_size == 3)
z_columns = [3 6 9];
% else % it equals 4
```

```
%
% z_columns = [4 8 12];
% end
data_z = data(z_columns, :);
%diff(data(data_z))./framesize;

data_z_velocity = diff(data_z')./framesize;

[max_val_z, max_column_z] = max(max(data([z_columns],:)'));
threshold_z = 25;
contigious_ = 5;
start_time = 0;%while we have not found 5 contiguous values above threshold
- this flag is zero-set.
start_here = 1;%start at this point in the data, rather than say after
wrist_start etc.
% 5 contiguous values > 5
if (max(abs(data_z_velocity(:,max_column_z)>threshold_z)));
    while(~start_time)
        object_start_five =
find(data_z_velocity(start_here:end,max_column_z)>threshold_z, contigious_
);
        if (object_start_five(1)+ contigious_ -1 ==
object_start_five(contigious_))
            object_start_five = object_start_five + start_here;
            start_time = 1;
        else
            start_here = object_start_five(2) + start_here;
            %disp('TIME TO MAX Z DEVIATION');
            %filename_save
        end
    end
    object_start_time = object_start_five(1) * framesize;
else
    disp('*DANGER* NO OBJECT_START_TIME');
    beep
    object_start_time = [-1];
end
%% Record peak wrist velocity between onset and object lift off
[peak_wrist_velocity,
peak_wrist_vel_row]=max(abs(data_velocity(wrist_start_five(1):object_start_
five(1),Q_wrist)));
%find time at which peak vel occurs
time_wrist_peak_velocity =  (peak_wrist_vel_row + wrist_start_five(1)) *
framesize ;
%% TIME OF GRASP RELEASE
% MAXIMAL DISTANCE BETWEEN FOREFINGER AND THUMB
%OLD  - FAILS AS THESE ARE DISTANCES FROM THE ORIGIN
%[max_position_value, max_position_grasp] =
max(sum(XY_vector(Q_index:Q_thumb,1:end_of_data)))
% NEW
pdist_argument = [data((Q_index*3)-2:Q_index*3,1:end_of_data)
data((Q_thumb*3)-2:Q_thumb*3,1:end_of_data)];
max_position_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:end_of_data;
comparison_list2 = comparison_list1 +length(comparison_list1);
max_position_value = 0 ; max_position_grasp = 0;
for iterations = 1:end_of_data-1
    max_position_value_check(iterations) =
max_position_square(comparison_list1(iterations),comparison_list2(iteration
s)); %note list is twice as long!
    if (max_position_value_check(iterations) >= max_position_value);
```

```
        max_position_value = max_position_value_check(iterations);
        max_position_grasp = iterations;
    end
end
[max_position_value, max_position_grasp];
time_of_grasp = max_position_grasp * framesize;
% this assumes a vaild wrist_start_time and returns [] if either or both
are []


%% MAX DIST WRIST
%OLD  - FAILS AS THESE ARE DISTANCES FROM THE ORIGIN
% [max_distance_wrist, max_position_wrist] = ...
%     max(abs((data_vector(Q_wrist,2:max_position_grasp) -
data_vector(Q_wrist,1))))
% NEW

pdist_argument = [data((Q_wrist*3)-2:Q_wrist*3,1:end_of_data)];
max_distance_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:end_of_data;
comparison_list2 = 1;
max_distance_wrist = 0 ; max_position_wrist = 0;
for iterations = 1:end_of_data-1
    max_distance_wrist_check(iterations) =
max_distance_square(comparison_list1(iterations),comparison_list2);
    if (max_distance_wrist_check(iterations) >= max_position_wrist);
        max_distance_wrist = max_distance_wrist_check(iterations);
        max_position_wrist = iterations;
    end
end
[max_distance_wrist, max_position_wrist];
max_wrist_time = (max_position_wrist+1) * framesize;

%%% WRIST PATH TRAJECTORY
pdist_argument = [data((Q_wrist*3)-2:Q_wrist*3,1:end_of_data)];
max_distance_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:end_of_data-1;
comparison_list2 = 2:end_of_data;
wrist_path = [];
for iterations = 1:end_of_data-1
    wrist_path(iterations) =
max_distance_square(comparison_list1(iterations),comparison_list2(iteration
s));
end
wrist_path_total = sum( wrist_path);


%% MAX DIST INDEX
% NEW
pdist_argument = [data((Q_index*3)-2:Q_index*3,1:end_of_data)];
max_distance_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:end_of_data;
comparison_list2 = 1;
max_distance_index = 0 ; max_position_index = 0;
for iterations = 1:end_of_data-1
    max_distance_index_check(iterations) =
max_distance_square(comparison_list1(iterations),comparison_list2);
    if (max_distance_index_check(iterations) >= max_position_index);
        max_distance_index = max_distance_index_check(iterations);
        max_position_index = iterations;
```

```
    end
end
[max_distance_index, max_position_index];
max_index_time = (max_position_index+1) * framesize;

%% MAX TRUNK DIST
% NEW
pdist_argument = [data((Q_sternum*3)-2:Q_sternum*3,1:end_of_data)];
max_distance_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:end_of_data;
comparison_list2 = 1;
max_distance_trunk1 = 0 ; max_position_trunk1 = 0;
for iterations = 1:end_of_data-1
    max_distance_trunk1_check(iterations) =
max_distance_square(comparison_list1(iterations),comparison_list2);
    if (max_distance_trunk1_check(iterations) >= max_position_trunk1);
        max_distance_trunk1 = max_distance_trunk1_check(iterations);
        max_position_trunk1 = iterations;
    end
end
[max_distance_trunk1, max_position_trunk1];
max_trunk1_time = (max_position_trunk1+1) * framesize;

%% PEAK DEC
[peak_wrist_deceleration, peak_wrist_dec_row] =
min(data_acceleration((peak_wrist_vel_row+wrist_start_five(1)):
object_start_five(1),Q_wrist));
%find time at which peak dec occurs
time_wrist_peak_dec = (peak_wrist_dec_row + peak_wrist_vel_row +
wrist_start_five(1)) * framesize; %% still this

%% MOVEMENT PERIOD
movement_period = (object_start_time - wrist_start_time);

%% MAX ABSOLUTE APERTURE - THUMB INDEX DISPLACMENT
% NEW
pdist_argument = [data((Q_index*3)-2:Q_index*3,1:object_start_five(1))
data((Q_thumb*3)-2:Q_thumb*3,1:object_start_five(1))];
max_aperture_square = squareform(pdist(pdist_argument', 'euclidean'));
comparison_list1 = 1:object_start_five(1);
comparison_list2 = comparison_list1 +length(comparison_list1);
max_aperture = 0 ; max_position_aperture = 0;
for iterations = 1:object_start_five(1)-1
    max_aperture_check(iterations) =
max_aperture_square(comparison_list1(iterations),comparison_list2(iteration
s)); %note list is twice as long!
    if (max_aperture_check(iterations) >= max_aperture);
        max_aperture = max_aperture_check(iterations);
        max_position_aperture = iterations;
    end
end
[max_aperture, max_position_aperture];
max_aperture_time = (max_position_aperture * framesize);

if max_position_aperture < wrist_start_five(1)

    % NEW
    % NOT YET UPDATED FOR VECTOR COMPARISON - USE MAXIMAL APERTURE OVERALL
    max_aperture = max_position_value;
    max_position_aperture = max_position_grasp;
```

```
    % OLD     [max_aperture, max_position_aperture] = ...
    %
max(abs(data_vector(Q_index,wrist_start_five(1):object_start_five(1)) -
data_vector(Q_thumb,wrist_start_five(1):object_start_five(1))));
    % max_aperture_time = ((max_position_aperture +wrist_start_five(1)) *
framesize);
    disp('*WARNING* - MAX APERTURE OCCURS BEFORE WRIST START - FIDDLING TO
AFTER WRIST START')
    beep
end

%% DISPLAY OPTION
% figure;plot(max_distance_trunk1_check(1:end),'r');
% hold on;plot(max_position_value_check(1:end), 'g');
% plot(max_distance_wrist_check(1:end),'k');
% plot(max_distance_index_check(1:end),'m')
% title('RED TRUNK, GREEN APERTURE, BLACK WRIST, MAGENTA INDEX');hold off
% disp('PRESS SPACE TO CONTINUE - DISPLAYING LOCAL GRAPH')
% pause

%% Max Minus Min dilation calculation added to control for fat fingers
%NEW
min_aperture = min(max_aperture_check);
max_aperture = max_aperture - min_aperture;

%% DILATION BETWEEN THUMB & INDEX GREATER THAN INITIAL VALUE FOR 5 FRAMES
% NEW
dilation = max_position_value_check; % this is aperture for the entire
show!
aperture_vel = diff(dilation)./framesize;
[peak_aperture_vel]=max(  aperture_vel(
wrist_start_five(1):object_start_five(1) )  );


%% APERTURE ONSET aperture_vel > threshold 15% peak aperture velocity
%aperture_vel_threshold = 15;
threshold_ = 25;
%(peak_aperture_vel/100)* aperture_vel_threshold;
start_time = 0;
start_here = 1;
% 5 contiguous values > threshold

if (max(aperture_vel >threshold_));
    while(~start_time)
        dilation_start_five =
find(abs(aperture_vel(start_here:object_start_five))>threshold_, 5);

        if (dilation_start_five(1)+4 == dilation_start_five(5))
            dilation_start_five = dilation_start_five + start_here;
            start_time = 1;
        else
            start_here = dilation_start_five(2) + start_here;

        end
    end
    dilation_start_time = dilation_start_five(1) * framesize;
else
    disp('*DANGER* NO dilation velocity > 25mm/s');
    beep
    dilation_start_time = [-1];
```

```
end



%% Define time for movement
wrist_vector = data_vector(Q_wrist,
wrist_start_five(1):object_start_five(1));
wrist_vel = data_velocity
(wrist_start_five(1):object_start_five(1),Q_wrist);
wrist_acc = data_acceleration
(wrist_start_five(1):object_start_five(1),Q_wrist);

% if(isempty(wrist_vector) || isempty(wrist_vel) || isempty(wrist_acc))
%     disp('ALARM!! EMPTY SETS - object start likely precedes wrist start
5!')
% end
aperture_pos = dilation(wrist_start_five(1):object_start_five(1));
aperture_vel = diff(aperture_pos)./framesize;


%% STANDARDISED PEAK DETECTION
wrist_detection_threshold = 15;
aperture_detection_threshold = 10;
%Various threshold tested with varied results - 15% decided upon ref Kahn
2001.

%% PEAKDET_Wrist 5/11/0
%Counting the number of wrist peaks over 15% of the threshold as Kahn 2001
delta = 0.5;
threshold_peak_wrist_vel = max(wrist_vel)*0.15;
[maxtab_wrist, mintab_wrist] = peakdet(wrist_vel, delta);
figure ;
plot (wrist_vel);
hold on;
plot(maxtab_wrist(:,1), maxtab_wrist(:,2), 'r*');
wrist_plotx = maxtab_wrist(:,1);
wrist_ploty = maxtab_wrist(:,2);

[rows_mintab_wrist, dummy] = size(mintab_wrist)
[rows_maxtab_wrist, dummy] = size(maxtab_wrist)
if ~rows_mintab_wrist;
    mintab_wrist = [0 0];
elseif rows_mintab_wrist < rows_maxtab_wrist;
    mintab_wrist = padarray (mintab_wrist, (1:1), 'post');
else
    disp ('do nowt')
end
wpks = maxtab_wrist(:,2) - mintab_wrist(:,2)>threshold_peak_wrist_vel;
wrist_peaks = sum (wpks)
%% time of last peak vel 5/11/10
% last_peakw = maxtab_wrist - minimum_wrist;
% p = size(last_peakw);
% q = p(1,1);
% for i = 1:q
%  xnumber = last_peakw(i,2);
%     if xnumber >= threshold_peak_wrist_vel
%          last_peakw(1,3) = i;
%          last_peakw1 = last_peakw(i,1);
%
%     end
```

```
% end
% b_last_peak_wrist =last_peakw1 + wrist_start_five(1);
% time_last_peak_wrist = last_peakw1* framesize;
%% commented 5/11/10
% %% Threshold for wrist vel peak detection
% peak_wrist_vel = max(wrist_vel);
% threshold_=(peak_wrist_vel /100)* wrist_detection_threshold;
% %line1 = (peak_wrist_vel / 100) * wrist_detection_threshold;
% wrist_vel_values = wrist_vel(find(wrist_vel>=threshold_));
% wrist_vel_times = find(wrist_vel>=threshold_);
% wrist_vel_count = length(wrist_vel_values);
%
% %Positive going threshold crossings
% if ~isempty(wrist_vel_times)
%     positive_threshold_crossings =
length(find(diff([wrist_vel_times])>1))+1;
% else
%     positive_threshold_crossings = 0;
% end
% wrist_peaks = positive_threshold_crossings;

%% PEAKDET_aperture 5/11/10
%Counting the number of aperture peaks over 15% of the threshold as Kahn
2001
delta = 0.5
threshold_aperture_pos = max(aperture_pos)*0.15;
[maxtab_ap, mintab_ap] = peakdet(aperture_pos, delta);

[rows_mintab_ap, dummy] = size(mintab_ap);
[rows_maxtab_ap, dummy] = size(maxtab_ap);
min_ap = min(aperture_pos);
max_ap = max(aperture_pos);
if ~rows_maxtab_ap;
    maxtab_ap = [0 max_ap];
elseif rows_maxtab_ap < rows_mintab_ap;
    maxtab_ap = padarray (maxtab_ap, (1:1), 'post');
else
    disp ('do nowt')
end

if ~rows_mintab_ap;
    mintab_ap = [0 min_ap];
elseif rows_mintab_ap < rows_maxtab_ap;
    mintab_ap = padarray (mintab_ap, (1:1), 'pre');
else
    disp ('do nowt')
end

mintab_ap(1,2) = min_ap % to account for starting position of aperture ie
not 0
appks = maxtab_ap(:,2) - mintab_ap(:,2)>threshold_aperture_pos;
aperture_peaks = sum (appks)
figure ;
plot (aperture_pos);
hold on;
plot(maxtab_ap(:,1), maxtab_ap(:,2), 'r*');
ap_plotx = maxtab_ap(:,1);
ap_ploty = maxtab_ap(:,2);
hold on
```

```
%% commented 5/11/10 Threshold for aperture vel peak detection
% peak_aperture = max(aperture_vel);
% threshold_=(peak_aperture /100)* aperture_detection_threshold;
% %line2 = (peak_aperture /100)* aperture_detection_threshold;
% aperture_values = aperture_vel(find(aperture_vel>=threshold_));
% aperture_times = find(aperture_vel>=threshold_);
% aperture_count = length(aperture_values);
%
% % Positive going threshold crossings
% if ~isempty(aperture_times);
%     ap_positive_threshold_crossings =
length(find(diff([aperture_times])>1))+1;
% else
%     ap_positive_threshold_crossings = 0;
% end


%% time of last peak ap 5/11/10
last_peaka = maxtab_ap(:,2) - mintab_ap(:,2);
time_peaksa = maxtab_ap(:,1);
ap_matrix=[time_peaksa,last_peaka];

a = size(ap_matrix);
b = a(1,1);
for i = 1:b
    xnumber = ap_matrix(i,2);
    if xnumber >= threshold_aperture_pos
        ap_matrix(1,3) = i;
        last_peaka1 = ap_matrix(i,1);

    end
end
b_last_peak_aperture=last_peaka1 + wrist_start_five(1);
time_last_peak_aperture= last_peaka1* framesize;
%% 5/11/10
last_peak_aperture = b_last_peak_aperture
% %% APERTURE VELOCITY CALCULATION
% aperture_peaks = ap_positive_threshold_crossings;
% delta =5;
% peaks_over_movement = peakdet(aperture_pos, delta);
% % figure;plot(aperture_vel)
% % disp('PRESS ANY KEY')
% % pause
% last_peak_aperture = max(peaks_over_movement(:,1)) +
wrist_start_five(1);%% OFFSET FROM BEGINNING with WS5(1)
% time_last_peak_aperture = (last_peak_aperture - wrist_start_five(1)) *
framesize;  % ADD TO OUTPUT

%% data_velocity(:,Q_wrist)
last_wrist_velocity =
peakdet(data_velocity(wrist_start_five(1):object_start_five(1),Q_wrist),
delta);
time_last_peak_wrist_velocity = (max(last_wrist_velocity(:,1))) *
framesize;

time_last_peak_aperture;
time_last_peak_wrist_velocity;


%% RESULTANT DISTANCE OF WRIST
```

```
% NEW
max_wrist_target1 =
max(max_distance_wrist_check(wrist_start_five(1):object_start_five(1)));
min_wrist_target1 =
min(max_distance_wrist_check(wrist_start_five(1):object_start_five(1)));
resultant_max_distance = max_wrist_target1 - min_wrist_target1;

%NEW
max_wrist_target2 =
max(max_distance_wrist_check(wrist_start_five(1):last_peak_aperture));
min_wrist_target2 =
min(max_distance_wrist_check(wrist_start_five(1):last_peak_aperture));
resultant_wrist_maxap = max_wrist_target2 - min_wrist_target2;

%NEW
max_wrist_target3 =
max(max_distance_wrist_check(last_peak_aperture:object_start_five(1)));
min_wrist_target3 =
min(max_distance_wrist_check(last_peak_aperture:object_start_five(1)));
resultant_wrist_close = max_wrist_target3 - min_wrist_target3;

%% FINAL PLOT
final_plot = figure;
set(final_plot,'WindowStyle','docked')
plot((wrist_vel), 'k', 'LineWidth',4);
Axis ([0 400 -100 900]); %line([0 length(wrist_vel)],[line1 line1]);
title('WRIST VELOCITY'), xlabel ('Frames(200Hz)'), ylabel ('Wrist
velocity(mm/s)');
%subplot(1,4,2), plot(data_acceleration(1:object_start_five(1),Q_wrist),
'k', 'LineWidth',3), line([wrist_start_five(1) wrist_start_five(1)], [-15
30]);
%subplot(1,4,2), title('WRIST ACCELERATION'), xlabel ('Time Hz'), ylabel
('Wrist acceleration mm/s');
%subplot(1,2,2), plot((aperture_pos), 'k', 'LineWidth',4);
%Axis([0 400 0 90]);
%subplot(1,2,2), title('APERTURE'), xlabel ('Frames(200Hz)'), ylabel
('Aperture size(mm)');
hold on;
%subplot(1,3,3),plot((aperture_vel), 'k','LineWidth',4),line([0
length(aperture_vel)],[line2 line2])
%subplot(1,3,3), title('APERTURE VELOCITY'), xlabel ('Frames(200Hz)'),
ylabel ('Aperture velocity (mm/s)');
%% Report absolute values for excel  - wrist_start_time

time_wrist_peak_velocity = time_wrist_peak_velocity - wrist_start_time;
time_wrist_peak_dec = time_wrist_peak_dec - wrist_start_time;
movement_period = movement_period;
max_aperture_time = max_aperture_time - wrist_start_time;
dilation_start_time = dilation_start_time - wrist_start_time;
wrist_start_time = wrist_start_time;
max_wrist_time = max_wrist_time - wrist_start_time;

%% NEW
wrist_path_opening = sum(wrist_path(wrist_start_five(1):last_peak_aperture-
1));%
wrist_path_closing =
sum(wrist_path(last_peak_aperture:object_start_five(1)));%
wrist_path_total =
sum(wrist_path(wrist_start_five(1):object_start_five(1)));%
max_trunk1_time = max_trunk1_time - wrist_start_time;
```

```
% length_wrist_path =
length(wrist_path(wrist_start_five(1):object_start_five(1)));
% wrist_path_section =
wrist_path(wrist_start_five(1):object_start_five(1));
% total_trajectory = zeros(length_wrist_path,1);
% total_trajectory(1) = wrist_path_section((1));
% for iterations = 2 :length(wrist_path_section)
%     total_trajectory(iterations) = total_trajectory(iterations-1) +
wrist_path_section(iterations);
% end

%% END
function [maxtab, mintab]=peakdet(v, delta)
%PEAKDET Detect peaks in a vector
%        [MAXTAB, MINTAB] = PEAKDET(V, DELTA) finds the local
%        maxima and minima ("peaks") in the vector V.
%        A point is considered a maximum peak if it has the maximal
%        value, and was preceded (to the left) by a value lower by
%        DELTA. MAXTAB and MINTAB consists of two columns. Column 1
%        contains indices in V, and column 2 the found values.

% Eli Billauer, 3.4.05 (Explicitly not copyrighted).
% This function is released to the public domain; Any use is allowed.
maxtab = [];
mintab = [];

v = v(:); % Just in case this wasn't a proper vector

if (length(delta(:)))>1
  error('Input argument DELTA must be a scalar');
end

if delta <= 0
  error('Input argument DELTA must be positive');
end

mn = Inf; mx = -Inf;
mnpos = NaN; mxpos = NaN;

lookformax = 1;

for i=1:length(v)
  this = v(i);
  if this > mx, mx = this; mxpos = i; end
  if this < mn, mn = this; mnpos = i; end

  if lookformax
    if this < mx-delta
      maxtab = [maxtab ; mxpos mx];
      mn = this; mnpos = i;
      lookformax = 0;
    end
  else
    if this > mn+delta
      mintab = [mintab ; mnpos mn];
      mx = this; mxpos = i;
      lookformax = 1;
    end
```

```
  end
end
```

A2.2 General movement characteristics - mean (SD). (Base=Baseline; *UP30°=object location 30° from midline & unperturbed; 10° = Perturbed trials to object located at 10° from midline; 50°= Perturbed trials to object located at 50° from midline.*

	Reaction Time (s)				***Movement Duration (s)***			
	Base	**UP30°**	**10°**	**50°**	**Base**	**UP30°**	**10°**	**50°**
Controls	0.32	0.38	0.40	0.35	0.74	0.77	0.92	0.88
N=16	(0.1)	(0.1)	(0.2)	(0.1)	(0.2)	(0.2)	(0.3)	(0.2)
Parietal	0.74	0.71	0.66	0.69	1.58	1.62	1.80	1.86
N=8	(0.4)	(0.2)	(0.2)	(0.2)	(1.1)	(0.8)	(0.8)	(0.9)
Cerebellar	0.46	0.63	0.60	0.66	1.32	1.30	1.52	1.40
N=8	(0.1)	(0.2)	(0.2)	(0.2)	(0.7)	(0.5)	(0.5)	(0.3)
Total	**0.46**	**0.52**	**0.52**	**0.51**	**1.09**	**1.12**	**1.30**	**1.26**
N=32	**(0.3)**	**(0.2)**	**(0.2)**	**(0.2)**	**(0.7)**	**(0.6)**	**(0.6)**	**(0.6)**

A2.3 Characteristics (Mean and SD) of the transport component *(Base= Baseline; UP30^o= Unperturbed trials 30^o from midline; 10^o = Perturbed trials 10^o from midline; 50^o= Perturbed trials 50^o from midline)*

	Peak Wrist Velocity (mm/s)				***Wrist Path Trajectory (mm)***				***Normalised Time to Peak Velocity (%)***			
	Base	**UP30^o**	**10^o**	**50^o**	**Base**	**UP30^o**	**10^o**	**50^o**	**Base**	**UP30^o**	**10^o**	**50^o**
Controls	889	812	787	802	365	365	390	414	38.9	39.0	32.2	34.3
N=16	(168)	(134)	(143)	(148)	(35)	(34)	(50)	(36)	(8.8)	(8.2)	(5.8)	(6.6)
Parietal	605	549	534	533	423	404	442	460	27.9	30.5	25.1	27.7
N=8	(213)	(195)	(194)	(184)	(98)	(55)	(53)	(49)	(9.3)	(10.7)	(10.4)	(7.5)
Cerebellar	553	543	496	556	357	361	379	404	34.8	33.8	27.6	31.7
N=8	(172)	(124)	(129)	(109)	(46)	(49)	(70)	(51)	(7.7)	(6.3)	(9.5)	(6.8)
Total	**734**	**679**	**651**	**673**	**377**	**373**	**400**	**423**	**35.1**	**35.6**	**29.3**	**32.0**
N=32	**(236)**	**(198)**	**(204)**	**(195)**	**(63)**	**(45)**	**(60)**	**(47)**	**(9.5)**	**(9.0)**	**(8.4)**	**(7.2)**

A2.4 Characteristics of the grasp component Mean (SD)*(Base= Baseline; UP30^o= Unperturbed trials 30^o from midline; 10^o = Perturbed trials 10^o from midline; 50^o= Perturbed trials 50^o from midline)*

	Grasp onset time (s)				***Maximum aperture (mm)***				***Normalised Time of maximum aperture (%)***			
	Base	**UP30^o**	**P10^o**	**P50^o**	**Base**	**UP30^o**	**P10^o**	**P50^o**	**Base**	**UP30^o**	**P10^o**	**P50^o**
Control	0.04	0.05	0.07	0.05	59.8	56.3	59.0	56.1	65.9	70.9	75.0	72.5
N=16	(0.06)	(0.08)	(0.17)	(0.11)	(19.8)	(20.0)	(16.4)	(17.5)	(9.8)	(9.5)	(6.4)	(9.0)
Parietal	0.04	0.11	0.14	0.16	59.7	63.0	69.4	66.9	64.2	64.8	70.5	66.4
N=8	(0.10)	(0.14)	(0.15)	(0.17)	(10.7)	(15.3)	(19.4)	(17.0)	(6.6)	(16.6)	(11.0)	(14.6)
Cerebellar	-0.04	-0.04	-0.01	-0.05	59.5	52.1	55.4	53.0	64.1	66.0	67.6	65.9
N=8	(0.1)	(0.13)	(0.09)	(0.19)	(22.0)	(17.3)	(20.7)	(21.0)	(11.3)	(12.1)	(12.8)	(13.4)
Total	**0.02**	**0.04**	**0.06**	**0.05**	**59.7**	**56.9**	**60.7**	**58.0**	**65.0**	**68.2**	**72.0**	**69.3**
N=32	**(0.09)**	**(0.12)**	**(0.16)**	**(0.16)**	**(18.0)**	**(18.2)**	**(18.4)**	**(18.4)**	**(9.3)**	**(12.1)**	**(9.7)**	**(11.7)**

A2.5 Number of detected aperture peaks and velocity peaks *(Base= Baseline; UP30^{o}= Unperturbed trials 30^{o} from midline; 10^{o} = Perturbed trials 10^{o} from midline; 50^{o}= Perturbed trials 50^{o} from midline)*

	Aperture peaks (n)				**Velocity peaks (n)**			
	Base	**UP30^{0}**	**10^{0}**	**50^{0}**	**Base**	**UP30^{0}**	**10^{0}**	**50^{0}**
Control	*1.0*	*1.1*	*1.7*	*1.7*	*1.0*	*1.0*	*1.6*	*1.7*
N=16	*(0.0)*	*(0.1)*	*(0.4)*	*(0.3)*	*(0.0)*	*(0.0)*	*(0.4)*	*(0.3)*
Parietal	*1.3*	*1.2*	*1.6*	*1.6*	*2.1*	*2.1*	*2.5*	*2.7*
N=8	*(0.4)*	*(0.2)*	*(0.4)*	*(0.3)*	*(1.9)*	*(0.8)*	*(1.6)*	*(1.5)*
Cerebellar	*1.4*	*1.1*	*1.6*	*1.5*	*1.5*	*1.6*	*2.3*	*2.0*
N=8	*(0.3)*	*(0.1)*	*(0.3)*	*(0.4)*	*(0.7)*	*(0.9)*	*(1.0)*	*(0.8)*
Total	***1.17***	***1.14***	***1.65***	***1.63***	***1.4***	***1.5***	***2.0***	***2.0***
N=32	***(0.3)***	***(0.1)***	***(0.4)***	***(0.3)***	***(1.1)***	***(1.0)***	***(1.0)***	***(1.0)***

A3.1 Keyword Search Systematic Review

1 ((cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp cerebrovascular trauma/ or exp hypoxia-ischemia, brain/ or exp intracranial arterial diseases/ or intracranial arteriovenous malformations/ or e218xp 'Intracranial Embolism/) and Thrombosis'/) or exp intracranial hemorrhages/ or vasospasm, intracranial/ or vertebral artery dissection/

2 (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.

3 ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.

4 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.

5 hemiplegia/ or exp paresis/

6 (hemipleg$ or hemipar$ or paresis or paretic).tw.

7 1 or 2 or 3 or 4 or 5 or 6

8 rehabilitation/ or 'activities of daily living'/ or exercise therapy/ or occupational therapy/ 9 physiotherapy/ or physical therapy/ or facilitation/ or treatment/ or intervention$/

10 ((motor or movement$ or task$ or skill$ or performance) adj5 (repetit$ or repeat$ or train$ or re?train$ or learn$ or re?learn$ or practic$ or practis$ or rehears$ or rehers$)).tw.

11 ((recovery or regain) adj3 function$).tw.

12 8 or 9 or 10 or 11

13 (upper adj3 (limb or extremity)).tw.

14 (arm or shoulder or elbow or forearm or wrist or finger$).tw.

15 13 or 14

16 (reach$ or transport or grasp or grip or prehen$ or dexterity or grip).tw.

17 (aperture adj1 (hand or grip or finger$)).tw.

18 (coord$ or synchron$ or manipul$ or timing or skill).tw.

19 16 or 17 or 18

20 7 and 12 and 15 and 19

A3.2 Quality Assessment and Data extraction form

Record Number: Reviewer:

Author/s:

Journal:

Country:

Quality Assessment

Item	**Judgement** Y=yes N=no NS=not stated	**Description**
Case control / cohort studies		
Is the hypothesis/aim/objective of the study clearly described?		
Is there a sound theoretical basis on which the hypothesis is based?		
Are the characteristics of the people included in the study clearly described?		.
Is the experimental design reliable & valid? Randomization or counterbalance of intervention or experimental manipulation. Baseline comparisons between groups or conditions. Control condition/group comparisons or Pre-post comparisons. Blinding (where applicable)		
Baseline comparisons between groups or conditions – baseline similarity		
Is the sample representative of patients in the population as a whole?		
Are the patients at a similar point in the course of their condition / illness?		
Has bias been minimized in relation to selection of cases and controls?		
Are confounding factors identified and strategies to deal with them stated?		
Are outcomes assessed using objective criteria?		
Was follow up carried out over a sufficient?		
Were the outcomes of people who withdrew described and included in the analysis?		
Were outcome measures valid and reliable? Y=outcome measures clearly described or reference to other work which demonstrates they are accurate. N= Describe unreliable/ non valid outcome measures. NS= Insufficient information or not addressed.		
Was appropriate statistical analysis used?		
Were the main findings of the study clearly described?		
RCT' s		
Randomization or counterbalance of intervention or experimental manipulation? Was the assignment to treatment groups truly random? – Appropriate sequence generation? Y=Describe a random component e.g. coin tossing, throwing dice, minimization N=Describe non-random approach e.g. date of admission, hospital no. or by availability. NS=Insufficient information about the sequence generation process.		
Were participants blinded to treatment allocation?		

Y=No blinding but outcome and outcome measurement not likely to be influenced by lack of blinding. N=No blinding or incomplete blinding and outcome likely to be influenced by lack of blinding. NS=Insufficient information or not addressed.		
Was allocation to treatment group concealed from the allocator? Y= e.g. central allocation, sealed envelopes. N=e.g. open random allocation schedule, unsealed envelopes, alternation. NS=Method of concealment not described or inadequate information.		
Intention to treat analysis? Were the outcomes of people who withdrew described and included in the analysis? Y=No missing outcome data, missing data balanced across groups, missing data unlikely to introduce bias, missing data input using appropriate method. N= No reasons for missing data and likely to be related to true outcome NS=Issue not addressed or inadequately reported.		
Were those assessing outcomes blind to the treatment allocation? Blinding of outcome assessor? (where applicable) Y=No blinding but outcome and outcome measurement not likely to be influenced by lack of blinding, key personnel blinded. N=No blinding or incomplete blinding and outcome likely to be influenced by lack of blinding. NS=Insufficient information or not addressed.		
Were the control and treatment groups comparable at entry? Control condition/group comparisons or Pre-post comparisons		
Were groups treated identically other than for the named interventions?		
Were outcome measures valid and reliable? Y=outcome measures clearly described or reference to other work which demonstrates they are accurate. N= Describe unreliable/ non valid outcome measures. NS= Insufficient information or not addressed.		
Were outcomes measured in the same way for all groups?		
Was appropriate statistical analysis used?		

Overall comments?

Seek further information?

1. **Data Extraction**

Methods: Type of study	
Participants: Inclusion criteria Exclusion criteria -co-morbid conditions, pre-morbid disability. Sampling frame for participant selection	
Intervention Setting Person delivering the intervention, qualifications and experience.	
Description Intervention group Description of the coordination/reach to grasp intervention (including whether delivered as part of a package of treatment or as a specific intervention.)	

Comparison group	
Duration / intensity / frequency	

Outcome Measures

Outcome Description	**Scale/Measure**

Baseline Measures outcomes clinical

Participant demographics

Group No. of subjects	Age M(SD)	Gender (M/F)	First stroke Y/N/NS	Time since stroke M(SD)	Lesion location R/L hemisphere Subcortical	Type of stroke haemorrhagic/ ischemic	Initial UL function
Intervention N=							
Comparison N=							
Dropouts N=							

Outcomes (All)

Name of outcome	Intervention			Comparison		
	Mean	SD	No of people	Mean	SD	No of people
Kinematic variables RT(s) NMT (s)						

Dichotomous Data

Outcome	Treatment Group Number/total number	Control Group Number/total number

Continuous Data

Outcome	Treatment Group Mean & SD (number)	Control Group Mean & SD (number)

Authors Conclusion

Reviewers Conclusion

A3.3 JBI Hierarchy of evidence

Level 1 (strongest evidence) Meta-analysis (with homogeneity) of experimental studies (e.g. RCT with concealed randomisation) OR One or more large experimental studies with narrow confidence intervals.
Level 2 One or more smaller RCTs with wider confidence intervals OR Quasi-experimental studies (without randomisation).
Level 3a. Cohort studies (with control group).
Level 3b. Case-controlled.
Level 3c. Observational studies (without control group).
Level 4 Expert opinion, or physiology bench research, or consensus.

A4.1 Group reach to grasp kinematic temporal data

Parameter	Condition	Baseline Mean (SD)	Post-test Mean (SD)	Group pre-post mean difference (Effect size) [95% CI]	Follow Up Mean (SD)
%TPV	SS	25.7 (6)	40.8 (18)	15.1	34.8 (14)
	FAST	15.6 (7)	39.4 (14)	23.8	42.9 (15)
	Total	31 (5)	39 (5)	8.4 (1.7) [-28.8 to 12.0]	39 (4)
%TMA	SS	47.3 (16.0)	51.8 (16.5)	4.5	44.4 (18.8)
	FAST	54.0 (12.5)	50.6 (11.0)	3.4	48.7 (15.8)
	Total	49.8 (14.7)	51.2 (13.3)	1.4 (0.1) [-8.9 to 6.2]	46.6 (16.6)
MT (s)	SS	1.42 (0.6)	1.11 (0.5)	0.31	1.09 (0.4)
	FAST	0.95 (0.3)	0.90 (0.2)	0.05	0.92 (0.3)
	Total	1.19s (0.5)	0.99 (0.4)	-0.20 (0.4) [-0.27 to 0.64]	1.00 (0.3)
RT (s)	SS	0.49 (0.1)	0.44 (0.1)	0.05	0.51 (0.1)
	FAST	0.47 (0.1)	0.36 (0.0)	0.11	0.36 (0.1)
	Total	0.48 (0.1)	0.40 (0.1)	-0.08 (0.8) [-0.13 to 0.29]	0.44 (0.1)
PV	SS	654.3 (146.3)	687.9 (183.7)	-33.6	671.9 (141.8)
	FAST	764.9 (152.2)	782.0 (171.6)	-17.1	742.0 (150.4)
	Total	645.5 (146.8)	721.3 (177.7)	-75.7 (33.9) [-210.2 to 58.7]	762.0 (146.1)
WPT	SS	420 (71)	364 (45)	56	395 (33)
	FAST	413 (62)	373 (48)	40	381 (52)
	Total	417 (59)	368 (44)	-49 * (0.8) [-10 to 107]	388 (42)
Ap. peaks	SS	1.4 (0.4)	1.2 (0.2)	-0.2	1.2 (0.2)

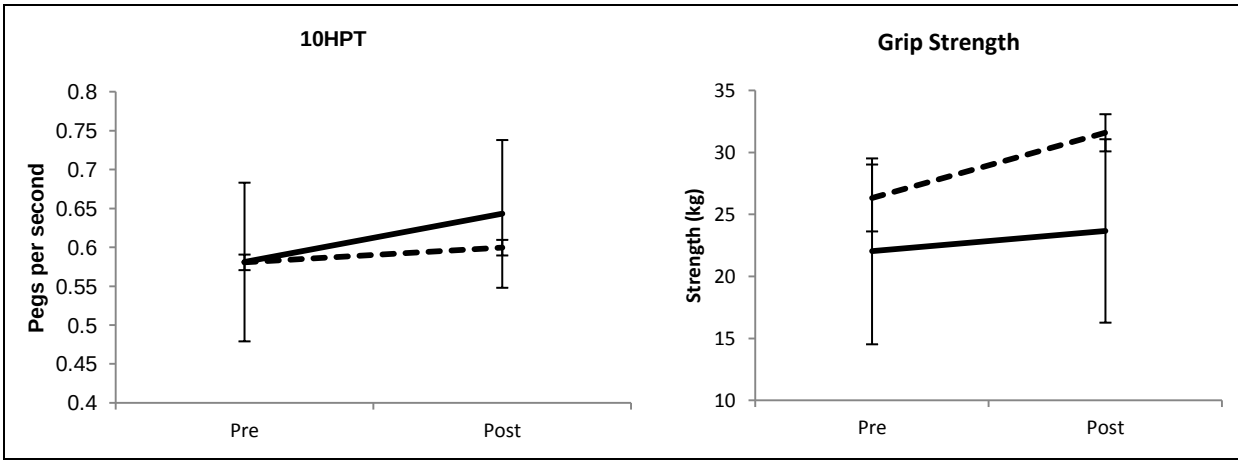
(No.)	FAST	1.5 (0.4)	1.2 (0.4)	-0.3	1.2 (0.3)
	Total	1.45 (0.4)	1.2 (0.3)	-0.25 (0.6)	1.2 (0.25)
Vel. peaks (No.)	SS	1.6 (0.5)	1.3 (0.3)	-0.3	1.2 (0.3)
	FAST	1.3 (0.3)	1.2 (0.4)	-0.1	1.2 (0.2)
	Total	1.45 (0.4)	1.25 (0.35)	-0.2 (0.5)	1.2 (0.25)

A4.2 Motor performance outcome measures Clinical measures Mean and (SD)

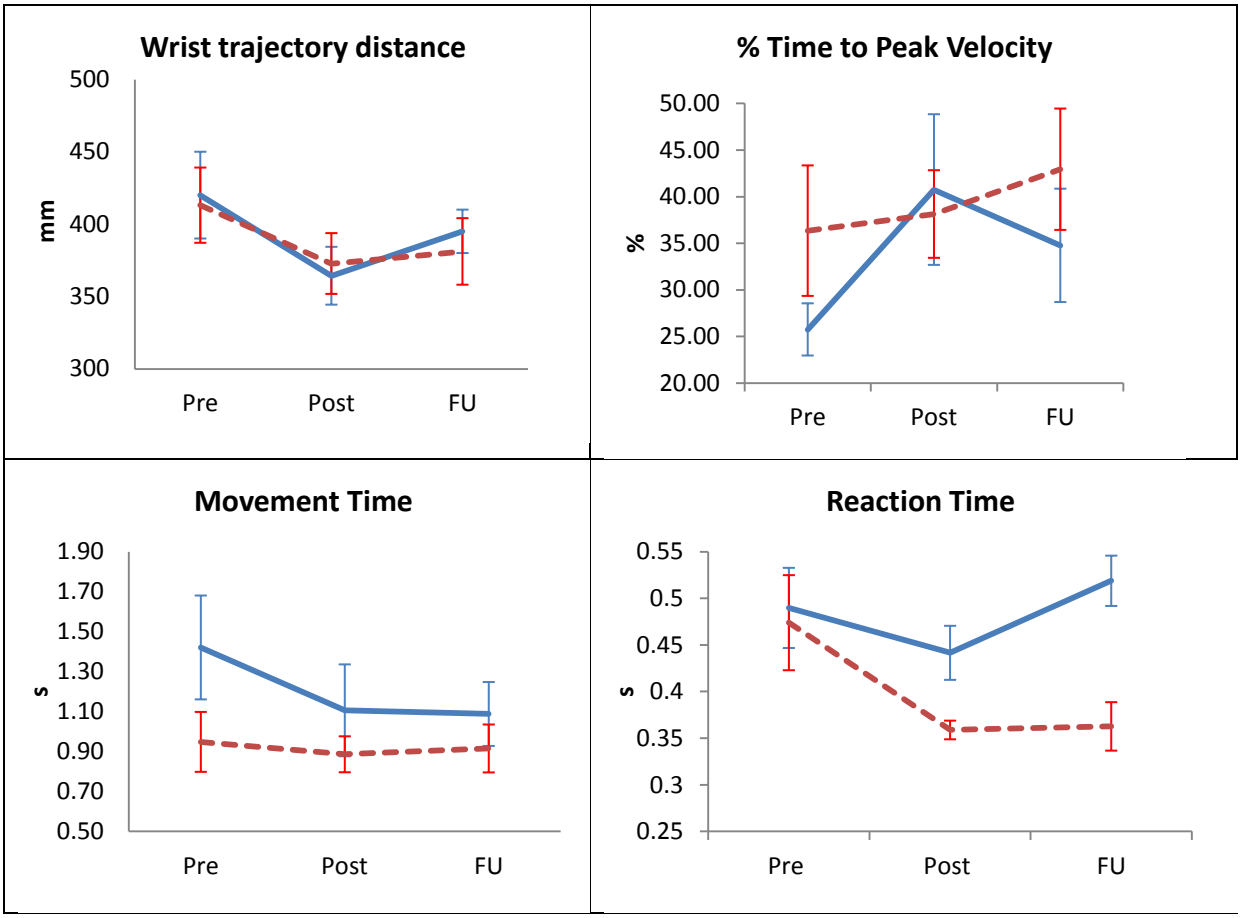
	Baseline	Post	Mean group difference	Effect size
10HPT (Pegs/ sec)	0.58 (0.2)	0.64 (0.2)	0.06 *	0.3
GS (Kg)	22.0 (7.5)	23.7 (7.4)	1.7 (8%)	0.2

*p<0.05

A4.3 Figure Group Mean (SD) a. 10HPT (pegs moved per second) and b. Grip strength (kg) Mean (SD) in solid black line. Control participant in dashed black line.



A4.4. Group Mean Motor Control of reach to grasp a. Wrist path trajectory, b. Normalised Time to Peak Velocity, c. Movement Time, d. Reaction Time. Solid line=SS and dashed line= FAST pace conditions. Error bars show SE.



A4.5 Group Results summary

A4.5a RTG Kinematics: Training

The training group average WPT was (M=401mm, SD=57) and a significant ($F_{4,16}$=4.276, p=0.01) main effect of time was found. Overall, paired t-tests revealed that whilst WPT there were no significant differences during the baseline period (B1 SS M= 433, SD=85; B2 SS M=402, SD=60; B3 SS M=425, SD=67; B1 FAST M=425, SD=67; B2 FAST M=402, SD=66; B3 FAST M=412, SD=54) there was a significant reduction in WPT after training for the SS paced condition (t(4)=2.779, p=0.05) only (Post SS 364, SD=45; Post FAST M=373, SD=48). At follow up the average WPT was shorter than at Baseline but not significantly (Follow Up SS =395, SD=32; Follow Up FAST M=381, SD=52). The CV for WPT was similar across time (Baseline M=0.06, SD=0.04; Post-test 0.06, SD=0.04; Follow Up M=0.06, SD=0.05).

The group average TPV% which at Baseline occurred at (M=31%, SD=5) was later at post-test (M=39%, SD=5), although there was no significant main effect of time for TPV%. Overall the group mean Baseline to Post-test difference was 27% and the effect size was 1.68. There was no statistical interaction effect between condition and time. TPV% CV (Baseline M=0.24, SD=0.09; post-test M=0.22, SD=0.10; Follow Up M=0.19, SD=0.09) was statistically similar between assessments. The group average %TMA was statistically unchanged across time (Baseline M=50%, SD=15; Post-test M=51, SD=13; Follow up M=47%, SD=17).

There was a trend ($F_{4,16}$=2.920, p=0.055) for a main effect of Time for the movement duration (Baseline M=1.18 SD=0.51; Post-test M=1.00, SD=0.38; Follow up M=1.00, SD=0.31). Paired t-test comparisons (B1 SS M=1.58, SD=0.56; B2 SS M=1.24, SD=0.47; B3 SS M=1.44, SD=0.75; Post SS M=1.1, SD=0.51; Follow Up SS M=1.08, SD=0.34; B1 FAST M=0.97, SD=0.42; B2 FAST M=0.91, SD=0.30; B3 FAST M=0.97, SD=0.34; Post FAST M=0.89, SD=0.19; Follow Up FAST M=0.92, SD=0.28) showed a significant difference between B1 SS and B2 SS only (t(4)=7.800, p<0.01). The Mean group difference (0.2ms) between Baseline and Post-test measures was considered to be

clinically meaningful (17%), whilst the effect size was small (0.4). The marginal difference further decreased between baseline and follow up (t_9=1.944, p=0.084).

The group average comparisons between reaction time at Baseline and Post-test were statistically comparable (Baseline M=0.48, SD=0.10; Post-test M=0.40, SD=0.06; Follow up M=0.44, SD=0.10). Peak velocity amplitude was higher after training but pre-post comparisons showed no main effect for time (Baseline M=687mm/s, SD=165; Post-test M=735mm/s, SD=175; follow up M=707mm/s, SD=143). There was no significant difference between either the number of aperture peaks (Baseline M=1.43, SD=0.33; Post-test M=1.24, SD=0.34; Follow up M=1.18, SD=0.16) or the wrist velocity peaks (Baseline M=1.45, SD=0.43; Post-test M=1.27, SD=0.32; Follow up M=1.17, SD=0.20) across time.

A4.5b RTG Kinematics: Condition

The group average WPT was statistically similar for the SS (M=404mm, SD=58) and FAST Paced (M=399mm, SD=57) condition. The WPT CV was also comparable between SS (M=0.05, SD=0.03) and FAST (M=0.07, SD=0.05) paced conditions. The group average TPV% was comparable between the SS (M=30%, SD=11) and the FAST paced conditions (M=38%, SD=15). The TPV% CV Baseline (M=0.24, SD=0.10) and post-test (M=0.20, SD=0.08) was also statistically similar. The group average TMA% (M=49%, SD=14.5) was statistically similar for both the SS (M=47, SD=16) and FAST (M=52, SD=13) pace conditions. The TMA CV% was comparable between SS (M=0.05, SD=0.03) and FAST (M=0.7, SD=0.05) paced conditions. The group average movement time (M=1.11s, SD=0.41) was significantly ($F_{1,16}$=10.283, p<0.05) shorter for FAST trials (M=0.93, SD=0.26) than the SS paced trials (M=1.3s, SD=0.48). The group average reaction time was 0.46s (SD=0.09). FAST paced trials (M=0.43, SD=0.09) were characterised by significantly shorter ($F_{1,16}$=11.169, p<0.05) reaction time than for the SS trials (M=0.49, SD=0.09). The group average peak velocity amplitude (M=700.5, SD=157) was significantly higher ($F_{1,16}$=17.304, p=0.01) for FAST paced trials (M=764.9, SD=152.2) than average peak velocity amplitude for SS trials (M=654, SE=146.3). Overall the number of wrist velocity peaks (M=1.3, SD=0.3) was similar for the SS

(M=1.6, SD=0.5) and FAST (M=1.3, SD=0.3) paced conditions. The overall number of aperture peaks was (M=1.28, SD=0.30). There was no significant difference between the number of aperture peaks in the SS (M=1.3, SD=0.1) and the FAST (M=1.3, SD=0.1) paced conditions.

A4.6 Table Individual 10 HPT and grip strength measures (SD)

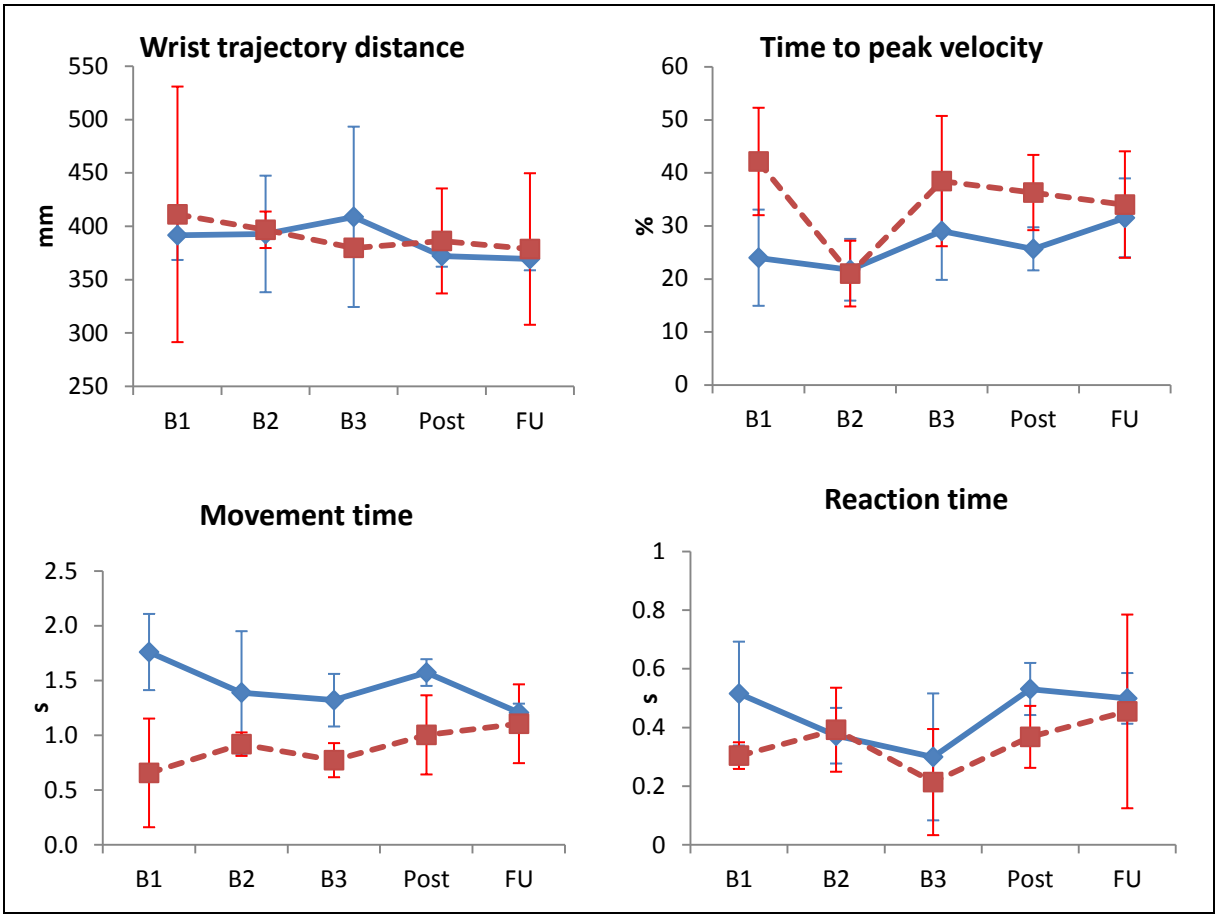
		A	B	C	D	F
10HPT	Pre	0.44 (0.03)	0.86 (0.1)	0.70 (0.1)	0.64 (0.1)	0.27 (0.0)
(Pegs/sec)	Post	0.48 (0.04)	0.87 (0.1)	0.80 (0.1)	0.70 (0.1)	0.37 (0.0)
	Follow Up	-	-	-	0.70 (0.0)	0.37 (0.0)
	Pre-Post Mean Difference	-0.04 (0.04) **	-0.01 (0.06)	-0.1 1 (0.07)**	-0.06 (0.07) **	-0.1 **
	Percentage change	9%	1%	14%	9%	37%
GS (kg)	Pre	23.7 (1.0)	33.5 (1.2)	19.7 (2.6)	12.9 (1.0)	20.5 (1.1)
	Post	20.4 (2.7)	33.4 (1.4)	28.2 (1.7)	14.0 (0.9)	22.5 (0.8)
	Follow Up	-	-	-	14.2 (0.7)	20.6 (0.6)
	Pre-Post Mean Difference	3.3 (2.7) *	0.17 (2.2)	-8.5 (2.3) **	1.1 (0.8) **	2 () *
	Percentage change	14%	6%	43%	8%	10%

A4.7 Table A4.5 Individual kinematic data Mean (SD)

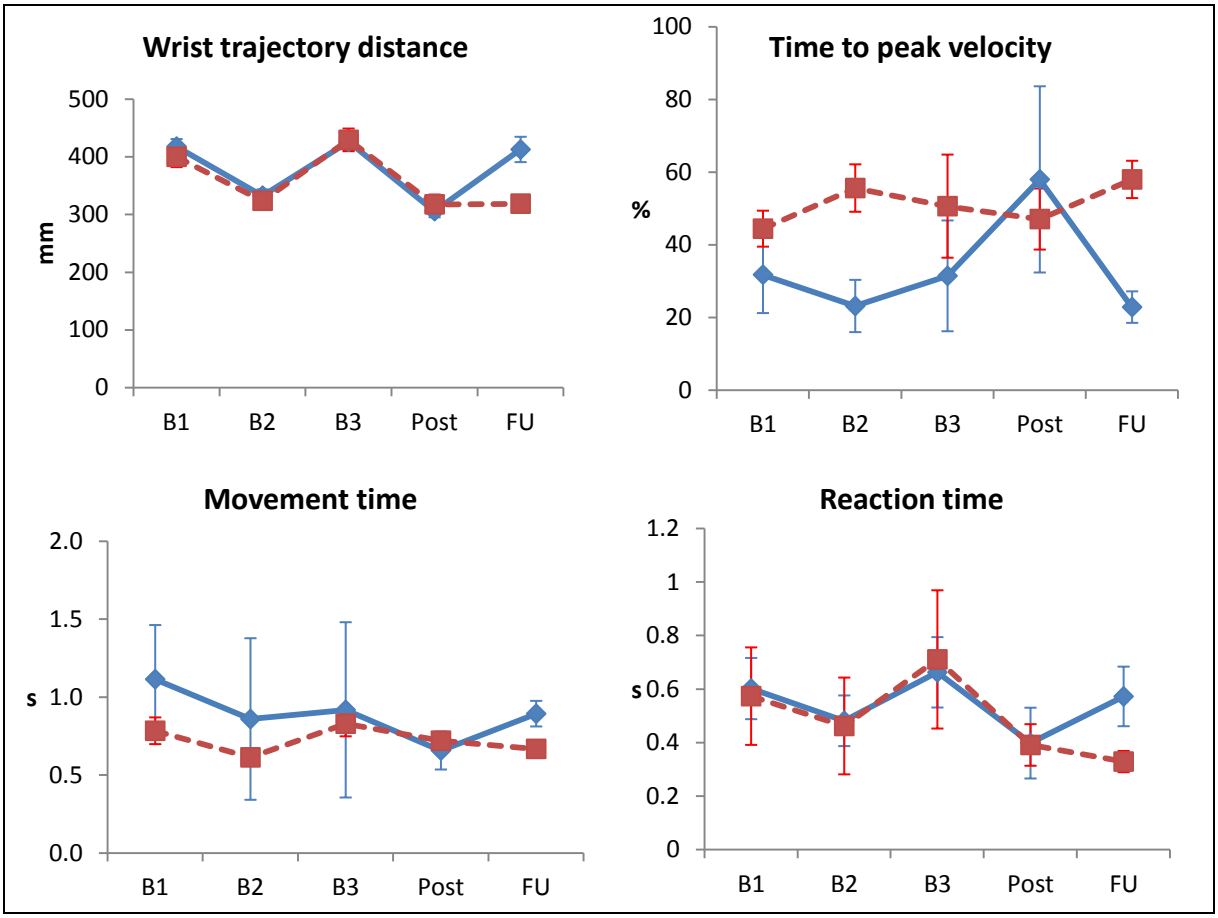
Wrist trajectory distance (mm)	**A**	**B**	**C**	**D**	**F**
Pre					
SS	398 (54) [0.14]	392 (13) [0.03]	375 (10) [0.03]	397 (11) [0.03]	539 (33) [0.06]
FAST	396 (48) [0.12]	384 (15) [0.04]	376 (8) [0.02]	393 (9) [0.02]	516 (37) [0.07]
Post					
SS	372 (10) [0.03]	306 (11) [0.03]	345 (14) [0.04]	371 (22) [0.06]	428 (18) [0.04]
FAST	386 (50) [0.13]	318 (17) [0.05]	352 (20) [0.05]	362 ((6) [0.02]	446 (53) [0.12]
Follow Up					
SS	370 (10) [0.03]	413 (22) [0.05]	359 (5) [0.01]	394 (16) [0.04]	440 (27) [0.06]
FAST	379 (71) [0.19]	319 (10) [0.03]	361 (7) [0.02]	385 (15) [0.04]	462 (43) [0.09]
Grand Mean (SE)	**388.4 (4.3)**	**351.1 (2.0)**	**369.7 (0.89)**	**383.1 (2.7)**	**479.9 (8.5)**
Total SS (SE)	**384.9 (4.0)**	**349 (2.7)**	**365.9 (1.4)**	**386.1 (3.8)**	**480.9 (6.4)**
Total FAST (SE)	**392.0 (8.2)**	**353 (3.4)**	**373.6 (0.9)**	**380.0 (1.9)**	**477.4 (14.7)**
Total SS-FAST Mean difference	**7.1 (9.7)**	**79.35 (3.9) ****	**-7.7 (1.5) ****	**6.1 (2.9)**	**3.94 (15.0)**
(SE)	**397.7 (6.4)**	**390.8 (1.7)**	**375.7 (0.9)**	**399.8 (2.5)**	**526.9 (7.0)**
Total Pre (SD)	**380.1 (6.8)**	**311.5 (3.6)**	**348.5 (3.2)**	**366.4 (3.5)**	**430.8 (14.1)**
Total Post (SD)	**16.6 (10.0)**	**79.3 (3.9) ****	**27.2 (2.9) ****	**33.4 (3.0) ****	**96.15 (14.4) ****
Total Pre-Post Mean difference (SD)	**4.2%**	**20%**	**7%**	**8.4%**	**18%**
Percentage pre-post change					
%TPV	A	B	C	D	F
Pre					
SS	24.9 (8)	28.9 (11)	34.7 (11)	21.8 (5)	18.6 (3)
FAST	33.9 (10)	50.2 (9)	53.7 (9)	16.6 (2)	27.3 (5)
Post					
SS	25.7 (4)	58.0 (26)	35.5 (6)	61.7 (18)	22.9 (3)
FAST	36.3 (7)	47.1 (8)	50.6 (8)	30.0 (11)	26.7 (5)
Follow Up					
SS	31.5 (7)	22.9 (4)	36.0 (3)	57.4 (15)	26.1 (5)
FAST	34.0 (10)	58.0 (5)	59.6 (15)	33.0 (10)	30.1 (7)
Grand Mean (SE)	**30.5 (0.6)**	**29.8 (0.7)**	**35.0 (0.8)**	**25.5 (1.0)**	**24.4 (0.5)**
Total SS	**25.7 (0.7)**	**30.1 (1.2)**	**35.5 (1.1)**	**27.9 (2.0)**	**21.9 (0.5)**
Total FAST	**35.2 (1.0)**	**29.6 (1.4)**	**34.4 (1.0)**	**23.2 (1.8)**	**26.8 (0.5)**
Total SS-FAST Mean difference	**-9.5 (1.2) ****	**0.60 (2.2)**	**1.1 (1.3)**	**4.8 (3.2)**	**-5.0 (0.2) ****
Total Pre	**29.9 (0.7)**	**29.2 (0.65)**	**34.1 (1.0)**	**17.7 (1.8)**	**23.4 (0.7)**
Total Post	**31.2 (1.0)**	**30.5 (1.0)**	**34.5 (1.7)**	**33.4 (2.3)**	**25.3 (0.8)**
Total Pre-Post Mean difference	**-1.41 (1.2)**	**-1.4 (1.0)**	**-0.3 (1.5)**	**-15.8 (3.6)****	**-2.0 (1.1)**
Percentage pre-post change	**5%**	**4.8%**	**0.9%**	**89.2%**	**9%**
Grand Mean (SE)	**1.22 (0.04)**	**0.775 (0.01)**	**0.88 (0.02)**	**0.87 (0.02)**	1.77 (0.06)
Total SS	**1.53 (0.04)**	**0.84 (0.02)**	**0.96 (0.03)**	**0.92 (0.04)**	2.15 (0.05)
Total FAST	**0.91 (0.07)**	**0.71 (0.01)**	**0.80 (0.02)**	**0.82 (0.01)**	1.39 (0.09)
Total SS-FAST Mean difference	**0.62 (0.08) ****	**0.13 (0.02) ****	**0.16 (0.03) ****	**0.10 (0.04) ***	0.77 (0.08) **
Total Pre	**1.14 (0.05)**	**0.87 (0.01)**	**1.05 (0.03)**	**0.88 (0.02)**	1.99 (0.03)
Total Post	**1.30 (0.06)**	**0.69 (0.01)**	**0.70 (0.02)**	**0.87 (0.02)**	1.56 (0.11)
Total Pre-Post Mean difference	**-0.17 (0.08) ***	**0.18 (0.01) ****	**0.35 (0.33) ****	**0.01 (0.03)**	**0.43 (0.03) ****
Percentage Pre-Post change	**-14.5%**	**21%**	**33%**	**1%**	**22%**
RT (s)	**A**	**B**	**C**	**D**	**E**
Pre					
SS	0.39 (0.2)	0.58 (0.1)	0.58 (0.5)	0.38 (0.1)	0.50 (0.2)
FAST	0.30 (0.1)	0.40 (0.1)	0.57 (0.3)	0.43 (0.1)	0.48 (0.3)
Post					
SS	0.53 (0.1)	0.40 (0.1)	0.48 (0.3)	0.37 (0.1)	0.43 (0.1)
FAST	0.37 (0.1)	0.34 (0.1)	0.34 (0.1)	0.36 (0.1)	0.34 (0.1)
Follow Up					
SS	0.50 (0.1)	0.57 (0.1)	0.60 (0.4)	0.48 (0.1)	0.45 (0.2)
FAST	0.45 (0.3)	0.32 (0.0)	0.36 (0.1)	0.39 (0.2)	0.30 (0.2)
Grand Mean (SE)	**0.40 (0.01)**	**0.48 (0.02)**	0.50 (0.04)	**0.38 (0.01)**	0.46 (0.05)
Total SS	**0.46 (0.02)**	**0.50 (0.03)**	**0.53 (0.06)**	**0.38 (0.02)**	0.46 (0.02)
Total FAST	**0.33 (0.02)**	**0.47 (0.03)**	**0.46 (0.03)**	**0.39 (0.02)**	0.45 (0.09)
Total SS-FAST Mean difference	**0.14 (0.03) ****	**0.03 (0.05)**	**0.07 (0.07)**	**0.01 (0.02)**	0.01 (0.09)
Total Pre	**0.35 (0.02)**	**0.57 (0.02)**	**0.58 (0.05)**	**0.40 (0.03)**	0.55 (0.09)
Total Post	**0.43 (0.01)**	**0.39 (0.04)**	**0.41 (0.03)**	**0.36 (0.01)**	0.36 (0.03)
Total Pre-Post Mean difference	**-0.08 (0.03) ****	**0.18 (0.05) ****	**0.17 (0.05) ****	**0.04 (0.04)**	0.19 (0.10)
Percentage pre-post change	**-23%**	**32%**	**29%**	**10%**	**34%**
Ap. peaks (No.)	**A**	**B**	**C**	**D**	**F**
Pre					
SS	1.2 (0.3)	1.3 (0.3)	1.0 (0.2)	1.5 (0.3)	1.8 (0.8)
FAST	1.2 (0.5)	1.4 (0.3)	1.1 (0.2)	1.9 (0.5)	1.9 (0.8)
Post					

SS	1.0 (0.0)	1.0 (0.0)	1.1 (0.3)	1.8 (0.4)	1.4 (0.5)
FAST	1.0 (0.0)	1.0 (0.0)	1.1 (0.4)	1.9 (0.3)	1.1 (0.5)
Follow Up					
SS	1.3 (0.5)	1.0 (0.0)	1.1 (0.2)	1.5 (0.5)	1.0 (0.0)
FAST	1.2 (0.4)	1.0 (0.0)	1.2 (0.4)	1.3 (0.5)	1.2 (0.4)
Grand Mean (SE)	1.1 (0.02)	1.1 (0.02)	1.08 (0.03)	1.8 (0.05)	1.6 (0.1)
Total SS (SE)	1.1 (0.04)	1.1 (0.04)	1.1 (0.03)	1.7 (0.09)	1.7 (0.1)
Total FAST (SE)	1.1 (0.03)	1.2 (0.00)	1.1 (0.05)	1.9 (0.06)	1.5 (0.2)
Total SS-FAST Mean difference	0.04 (0.05)	-0.07 (0.04)	-0.04 (0.07)	-0.19 (0.09)	0.16 (0.25)
(SE)	1.2 (0.04)	1.3 (0.04)	1.1 (0.06)	1.7 (0.06)	1.8 (0.05)
Total Pre (SD)	1.0 (0.00)	1.0 (0.00)	1.1 (0.05)	1.8 (0.12)	1.4 (0.16)
Total Post (SD)	0.2 (0.04) **	0.3 (0.04) **	-0.04 (0.06)	-0.14 (0.15)	0.45 (0.12) **
Total Pre-Post Mean difference (SD)	17%	23%	4%	8%	25%
Percentage pre-post change %					
Wrist Vel. peaks (No.)	**A**	**B**	**C**	**D**	**F**
Pre					
SS	1.6 (0.8)	1.1 (0.2)	1.2 (0.4)	2.1 (0.6)	1.9 (0.8)
FAST	1.5 (0.5)	1.1 (0.2)	1.0 (0.1)	2.0 (0.5)	1.0 (0.1)
Post					
SS	2.0 (0.8)	1.0 (0.0)	1.0 (0.0)	1.3 (0.5)	1.1 (0.5)
FAST	1.4 (0.6)	1.0 (0.0)	1.1 (0.3)	1.6 (0.7)	1.2 (0.5)
Follow Up					
SS	1.5 (0.6)	1.2 (0.4)	1.0 (0.0)	1.1 (0.3)	1.1 (0.3)
FAST	1.5 (0.7)	1.0 (0.0)	1.0 (0.0)	1.3 (0.5)	1.0 (0.0)
Grand Mean (SE)	1.6 (0.1)	1.05 (0.03)	1.07 (0.03)	1.6 (0.1)	1.4 (0.1)
Total SS (SE)	1.7 (0.1)	1.03 (0.03)	1.10 (0.04)	1.5 (0.1)	1.6 (0.1)
Total FAST (SE)	1.4 (0.1)	1.07 (0.04)	1.04 (0.03)	1.7 (0.1)	1.2 (0.1)
Total SS-FAST Mean difference	0.32 (0.1) *	-0.03 (0.03)	0.06 (0.05)	-0.14 (0.15)	0.4 (0.1) **
(SE)	1.5 (0.1)	1.1 (0.1)	1.11 (0.05)	1.9 (0.14)	1.5 (0.07)
Total Pre (SD)	1.6 (0.2)	1.0 (0.0)	1.03 (0.03)	1.3 (0.11)	1.3 (0.2)
Total Post (SD)	-0.04 (0.2)	0.1 (0.1)	0.08 (0.06)	0.6 (0.02) *	0.21 (0.25)
Total Pre-Post Mean difference (SD)	3%	9%	7%	32%	14%
Percentage pre-post change %					

A4.8 Participant A Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.

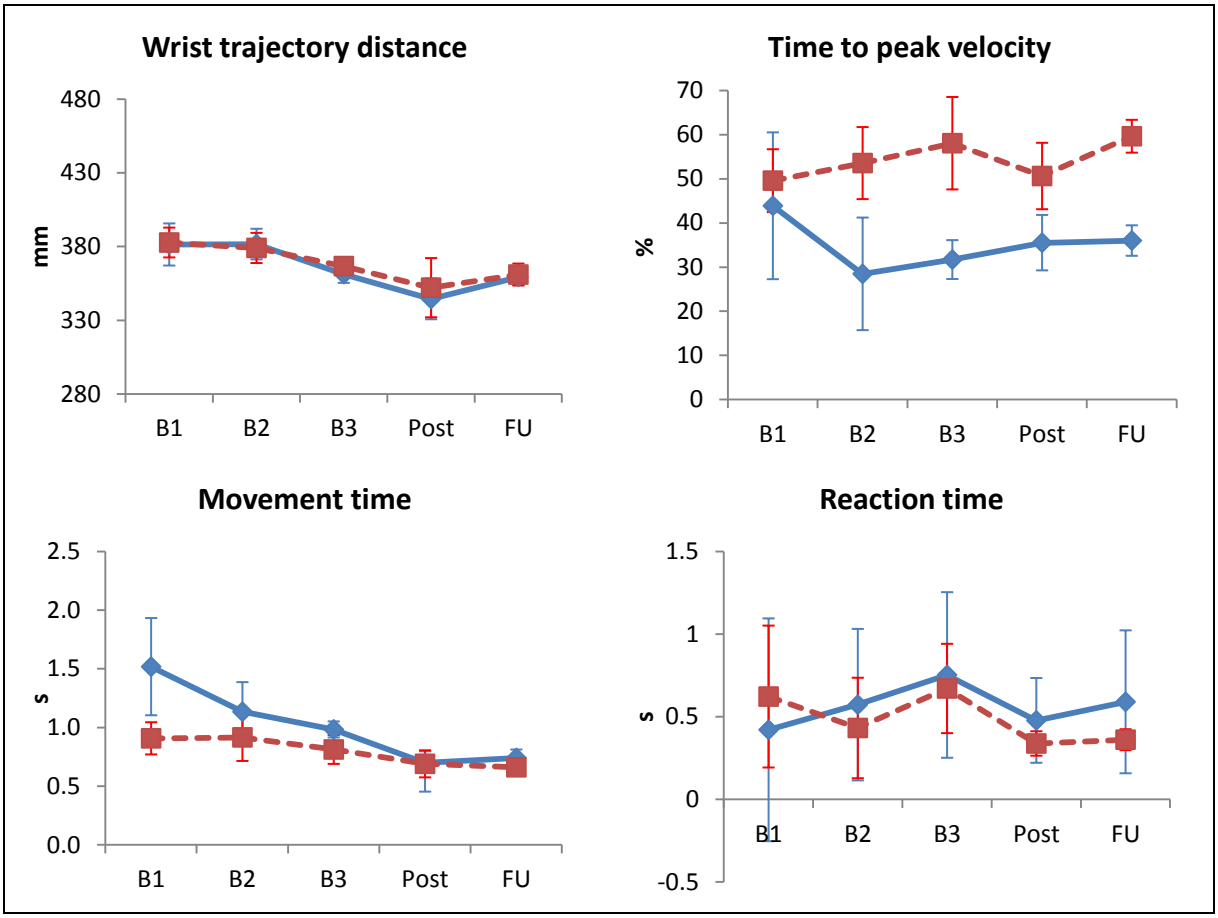


A4.9 Participant B Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.

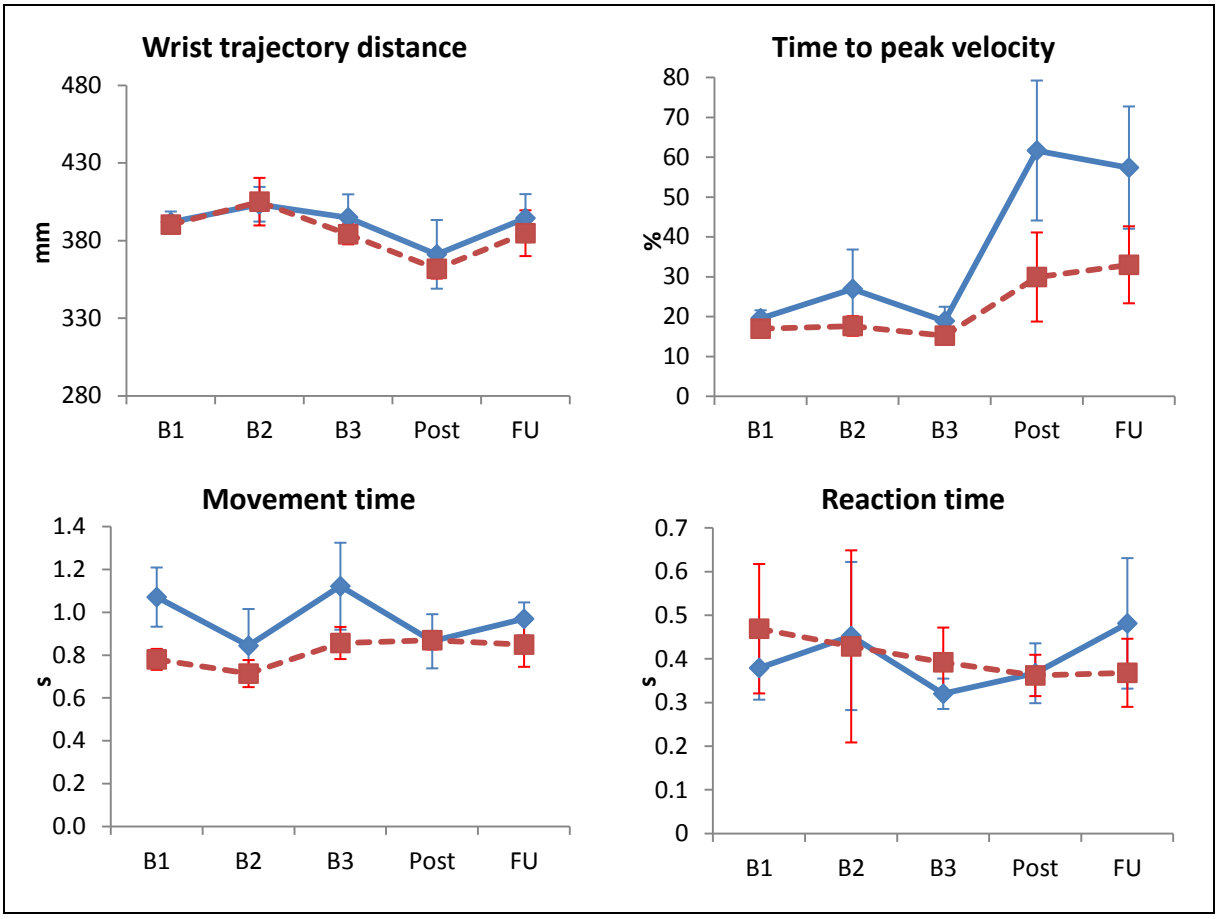


(N.B Only 5 trials in post-test compared to 15 in others- due to loss of markers)

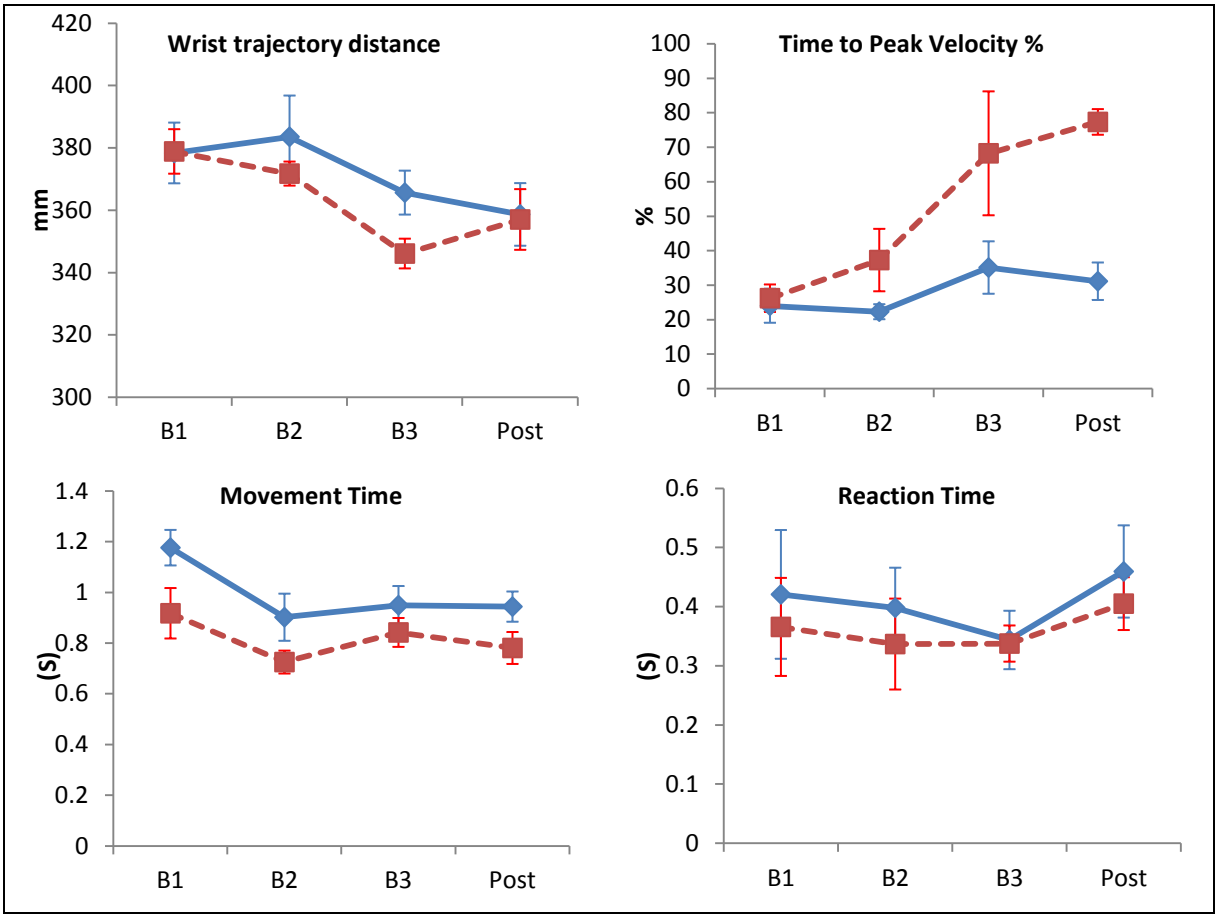
A4.10 Participant C Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.



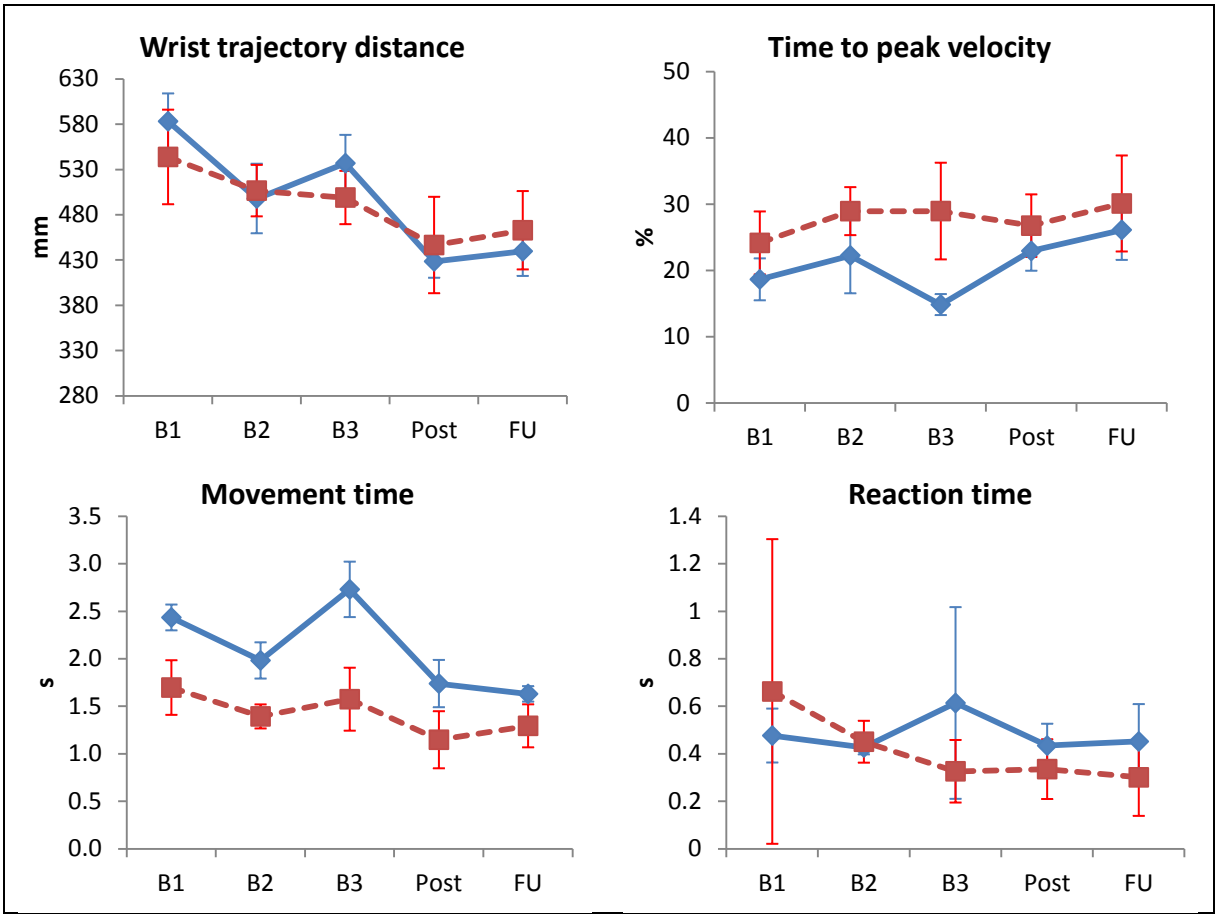
A4.11 Participant D Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.



A4.12 Participant E. Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.



A4.13 Participant F Motor control of reach to grasp (a. Wrist trajectory distance, b. Normalised time to peak velocity, c. Movement time, d. Reaction time). Solid line=SS and dashed line= FAST pace conditions. Error bars show SD.



A4.14 Figure 1 Time to peak Velocity % for participants A-F combined SS and FAST paced trials. TPV is shown in % on the vertical axis. The assessment phase is shown on the horizontal axis (Baseline1, 2 & 3 (Phase A), post test (Phase B) and Follow Up). The Baseline Mean is shown with a red dashed line. The dotted green line represents two standard deviations below the Baseline mean. Participant E did not take part in training and did not have a follow up assessment.