An Investigation of the Neuromuscular Correlates of Upper Limb Movement Recovery after Stroke

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Abstract

Stroke survivors often face neuromuscular impairments and functional limitations in their upper limbs (ULs), significantly affecting their daily lives and independence (1–3). Understanding the relationships between neuromuscular impairments and functional abilities in the UL post-stroke is crucial for developing effective rehabilitation strategies (4–6). This doctoral research contributes to this understanding through three original studies:

A systematic review assessed exercise-based therapies' impact on neuromuscular impairments and functional abilities in stroke survivors. It determined that exercise-based therapies simultaneously enhance both aspects, without significant differences between the improvements. An almost perfect correlation was found between these improvements, suggesting that exercise-based therapies included in the review enhance functional ability without adversely affecting neuromuscular impairment.

A correlational agreement study, using advanced technological methods, identified reference values, test-retest reliability and smallest detectable changes for neuromuscular impairment and functional ability variables in adults without mobility-impairing conditions. The 'Time to Task Completion (TTC)', 'Reach Path Ratio (RPR)', and 'Movement Smoothness (MS)' variables showed high absolute reliability despite overall test-retest reliability being insufficient across the variables assessed.

A longitudinal observational cohort study involving stroke survivors assessed twice post-stroke focused on the relationships and stability of neuromuscular impairments and functional abilities. It revealed that the Fugl-Meyer Assessment (FMA), MS, and RPR consistently demonstrated significant and stable relationships with functional ability.

These findings suggest that targeting neuromuscular impairments in post-stroke rehabilitation can be an effective and efficient approach to improving functional ability. MS, RPR and neuromuscular impairments, as captured by FMA, consistently displaying significant and stable relationships with functional ability, can be effective therapeutic targets for enhancing stroke survivors' functionality. The use of sensitive assessment instruments in stroke research and clinical practice can help to refine the understanding of the relationships between neuromuscular impairments and functional abilities, thereby advancing rehabilitation strategies and supporting the functional recovery of stroke survivors.

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List of Abbreviations and Acronyms

3D: Three Dimensional

ADL: Activities of Daily Living

ARAT: Action Research Arm Test

BB: Biceps Brachii

BBT: Box and Block Test

CAHAI: Chedoke Arm and Hand Activity Inventory

CDH: Contralateral Workspace with Dominant Hand

CI: Confidence Interval (used for statistical values); Control Intervention (used only in participant and outcome measure descriptions in Tables 9 and 10).

CLAH: Contralateral Workspace with the Less Affected Hand

CMAH: Contralateral Workspace with the More Affected Hand

CMSA: Chedoke McMaster Stroke Assessment

CNH: Contralateral Workspace with Non-Dominant Hand

cm: centimetre/s

Coef.: Regression Coefficient

Cohen's d: Effect Size

ECR: Extensor Carpi Radialis

EI: Experimental Intervention

EMD: Electromechanical Delay

EMG: Electromyography

FCR: Flexor Carpi Radialis

FMA: Fugl-Meyer Assessment

FMH: Faculty of Medicine and Health Sciences

FIN: Finger

Haem: Haemorrhagic

HD: Hand Displacement

HSC: School of Health Sciences

ICC: Intraclass Correlation Coefficient

ICF: International Classification of Functioning and Disability

IQR: Interquartile Range

Isch: Ischaemic

ITT: Intention-to-Treat

KD: Kinematics-Derived

LOA: Limits of Agreement

LOA Plot: Bland-Altman Plot

MAOT: Muscle Activity Onset Time

Max: Maximum

MCA: Middle Cerebral Artery

MDH: Midline Workspace with Dominant Hand

Med: Median

MeSH: Medical Subject Headings

MESUPES: Motor Evaluation Scale for Upper Extremity in Stroke Patients

Min: Minimum

MMAH: Midline Workspace with the More Affected Hand

MLAH: Midline Workspace with the Less Affected Hand

mm: millimetre/s

MNH: Midline Workspace with Non-Dominant Hand

MoveExLab: Movement and Exercise Laboratory

MS: Movement Smoothness

ms: millisecond/s

N: Sample Size

NHS: National Health Service

NHPT: Nine Hole Peg Test

P5: 5^{th} Percentile

P95: 95^{th} Percentile

PIS: Participant Information Sheet

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols

PSD: Power Spectral Analyses

RCT: Randomised Controlled Trial

RPR: Reach Path Ratio

RoB 2 Tool: Revised Cochrane Risk of Bias Tool for Randomised Trials

ROM: Range of Motion

s: second/s

SD: Standard Deviation

SDC: Smallest Detectable Change

SEM: Standard Error of Measurement

SEM%: The 'Standard Error of Measurement' Expressed as a Percentage of the Mean

SMD: Standardised Mean Difference

SPARC: Spectral Arc Length

SRRR: Stroke Rehabilitation Research Roundtable

TIA: Transient Ischemic Attack

TD: Trunk Displacement

TEMPA: FR: The Upper-Extremity Performance-Functional Rating Test

THDR: Trunk-Hand Displacement Ratio

TTC: Time to Task Completion

UEA: University of East Anglia

UK: United Kingdom

UL: Upper Limb

WHO: World Health Organisation

WMFT: Wolf Motor Function Test

WMFT-FA: Wolf Motor Function Test – Functional Ability Scale

WMFT-PT: Wolf Motor Function Test – Performance Time

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Dissemination

Manuscripts awaiting editorial review

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Conference Presentations

Oral and Poster Presentation: Yüksel, C., Hancock, N. J., Clark, A. B., Pomeroy, V. M. (2023). "Correlation between Change in Upper Limb Motor Impairment and Activity in Response to Exercise-Based Therapy after Stroke: A Systematic Review with Meta-Analysis." A 15-minute talk presented at the 4th Congress on NeuroRehabilitation and Neural Repair, Poster No. 106. [https://www.neurorehabrepair.eu/resources/media/Congress_2023/NEUROREHAB_ECNR_proceedingsbook_2023_Final_version_30-05-2023.pdf]. Nominated for the Young Scientist Award.

This abstract was also presented at:

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Poster Presentation: C. Yüksel, N. J. Hancock, A. B. Clark, V. M. Pomeroy (2022). "Correlation between Change in Motor Impairment and Functional Ability in Response to Upper Limb Exercise-Based Therapy after Stroke: A Systematic Review with Meta-Analysis." Poster Presentation, P 084. Presented at the World Congress for Neurorehabilitation. Neurorehabilitation and Neural Repair, 2023, 37(5). DOI: 10.1177/15459683231159499. Available from: https://journals.sagepub.com/doi/epub/10.1177/15459683231159499.

Introduction

1. Statement of the Problem

The global population of stroke survivors currently exceeds 101 million, with stroke incidence and prevalence rates expected to rise (7, 8). Stroke frequently leads to neuromuscular impairments in the upper limb (UL), which severely restricts individuals' ability to perform daily activities and increases their dependency on others (1–3). Determining effective rehabilitation strategies for managing neuromuscular impairments and functional limitations in the UL is crucial. Effective strategies not only enhance the quality of life for stroke survivors and reduce their dependency but also alleviate the broader impact of stroke on healthcare systems, social services, caregivers, and the community at large (6).

2. Rationale for Research

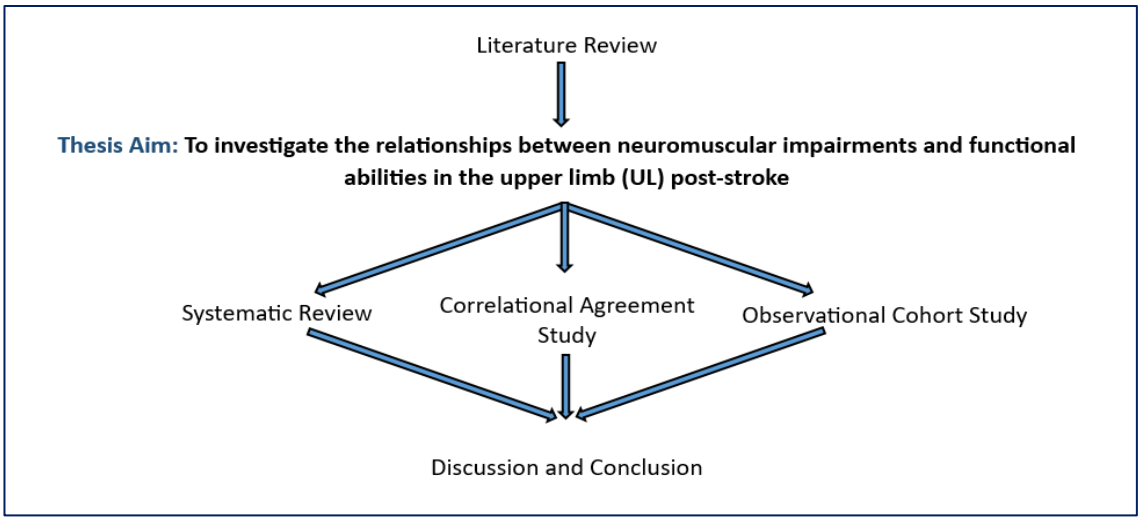
Understanding the relationships between neuromuscular impairments and functional abilities in the UL of stroke survivors can facilitate the identification of effective rehabilitation strategies (4, 5). Elucidating the specific effects of exercise-based therapies on neuromuscular impairments versus functional abilities is needed, as this knowledge can enhance the effectiveness and efficiency of therapy goals (4, 5). However, these effects are not yet sufficiently understood (9–15). The use of kinematics- and electromyography (EMG)-derived variables can enable a comprehensive understanding of these relationships (16–18), yet their use for this aim is limited in the current literature (19–22). Establishing the reference values, test-retest reliability, and 'Smallest Detectable Changes' (SDCs) for these types of variables in adults without mobility-impairing conditions is important for their informed application in stroke research, but such foundational studies are scarce and small-scale (23–28). Due to the dynamic nature of post-stroke improvements, longitudinal, high-quality research examining these relationships using kinematics- and EMG-derived variables can provide a detailed understanding of these relationships, but there is a lack of such studies in the current literature (19, 21, 22, 29–33).

3. Overview of the Thesis Structure

This thesis is structured around a central aim, developed through a comprehensive review of the literature: **To investigate the relationships between neuromuscular impairments and functional abilities in the UL post-stroke.**

Based on the research gaps identified in the literature review (Chapter 1), this thesis is composed of three original studies: Systematic Review (Chapter 3), Correlational Agreement Study (Chapter 5), and Observational Cohort Study (Chapter 6) (Figure 1).

Figure 1. Structure of the Thesis



The thesis comprises seven chapters. The structure is as follows:

Chapter 1: Introduces and evaluates the literature on the impact of stroke on the UL, the relationships between neuromuscular impairments and functional abilities in the UL of stroke survivors, and UL assessment post-stroke.

Chapter 2: Outlines the aims of the studies presented in the thesis.

Chapter 3: Presents the systematic review investigating whether exercise-based therapies are more effective in neuromuscular impairments or functional abilities and whether there is a relationship between these effects.

Chapter 4: Introduces common methods and instruments used in the correlational agreement study and the observational cohort study.

Chapter 5: Presents the study establishing the reference values, test-retest reliability, and SDCs for the selected variables of neuromuscular impairments and functional abilities in adults without mobility-impairing conditions**.**

Chapter 6: Presents the observational repeated measures cohort study investigating the relationships between neuromuscular impairments and functional abilities in the UL of stroke survivors.

Chapter 7: Provides a comprehensive discussion of the presented studies in the thesis in the context of the literature, the strengths and limitations of the thesis, implications for research, and concluding remarks.

4. Impact of COVID-19 Pandemic on Research Progress and Methodology

The COVID-19 pandemic introduced significant challenges to this PhD project, affecting both the research progress and methodology. The pandemic had distinct effects on each of the three studies involved: the systematic review, the correlational agreement study, and the observational cohort study. The specific impacts on each component of the research are detailed below.

Systematic Review Study (Chapter 3)

The initial database searches were completed on December 16, 2020. During the pandemic-related closure of the research laboratory, which lasted approximately seven and a half months, the focus shifted to the systematic review. Once the laboratory reopened, priority was given to the experimental studies to ensure the timely completion of the PhD.

Due to the adjustments required by the pandemic, it was not feasible to update the database searches within the timeframe of the PhD. This decision was made to ensure the overall project remained on track despite the laboratory closures. As a result, the systematic review presented in Chapter 3 includes studies published between 2011 and December 2020. Given the training nature of the PhD and the unprecedented circumstances, this approach was deemed acceptable. An updated review, incorporating more recent studies, is planned for future publication.

Experimental Studies: Correlational Agreement Study (Chapter 5) & Observational Cohort Study (Chapter 6)

The Movement and Exercise Laboratory (MoveExLab) at the University of East Anglia (UEA), where data collection for the experimental studies took place, was closed due to the pandemic from March 18, 2020, to September 1, 2020, and again from January 4, 2021, to March 11, 2021, totalling seven and a half months. These closures, in adherence to university and government guidelines to ensure the safety of students and staff, suspended all in-person research activities and restricted access to the facilities.

Data collection resumed on October 22, 2020, and May 12, 2021, following the first and second closures, respectively. However, recruitment efforts were hampered by individuals' reluctance to engage in activities they deemed non-essential during the pandemic. This required greater efforts than usual to promote the studies and recruit a sufficient number of participants. Additionally, for an extended period, data collection was limited to one participant per day to

allow for thorough sanitation of equipment and laboratory spaces between sessions. This restriction further delayed the completion of data collection for the experimental studies.

Correlational Agreement Study (Chapter 5): The aim of the correlational agreement study was to establish reference values, test-retest reliability, and SDC for selected variables of neuromuscular impairments and functional abilities in adults without mobility-impairing conditions. In response to the challenges posed by the pandemic, no specific age limit was imposed, other than requiring participants to be over 18 years old. This decision was made to prioritise securing a sufficient sample size within the limited timeframe, rather than narrowing the age range, to meet the study's objectives despite recruitment difficulties.

Observational Cohort Study (Chapter 6): The recruitment process for the observational cohort study, which aimed to include stroke survivors, was significantly impacted by the COVID-19 pandemic. Initially, recruitment through the Early Supported Discharge Team was planned, and National Health Service (NHS) ethics approval was being pursued. However, the NHS prioritised COVID-19-related studies and temporarily suspended approvals for other studies not funded by them.

In anticipation of recruitment challenges, the eligibility criteria were intentionally kept broad to maximise the potential participant pool. No specific targets were set for recruiting equal numbers of participants across different impairment levels or stages of stroke recovery, as the primary goal was to secure sufficient participants despite the pandemic's constraints. Ethical approval was obtained from UEA's Faculty of Medicine and Health Sciences (FMH) Research Ethics Committee, and recruitment efforts were redirected to local voluntary stroke support groups and other communication channels such as social media. Recruitment was experienced as quite difficult, and the temporary suspension of these group activities due to virus transmission concerns further validated the decision to broaden the eligibility criteria.

Most participants recruited into the study had mild impairments and were in the chronic stage of stroke recovery. This outcome was likely influenced by the pandemic, as individuals with more severe impairments or those in the acute stage may have been more reluctant to participate due to health concerns and fears related to virus transmission.

In conclusion, the COVID-19 pandemic significantly impacted the progress and methodology of this PhD project, necessitating adjustments to research timelines and recruitment strategies. As a training program, the primary aim was to meet the academic standards required for degree

completion. Despite the disruptions, the project remained focused and adaptable, demonstrating resilience and resourcefulness. These efforts ensured that the research objectives were achieved, contributing valuable insights to the field. This experience underscored the importance of flexibility and perseverance, ultimately strengthening both the research outcomes and preparedness for future academic challenges.

5. Key Definitions

Key definitions are provided below to ensure clarity, and consistency, and to prevent potential misinterpretations in the subsequent chapters of this thesis.

Physical Exercise: Physical exercise refers to any bodily activity that enhances or maintains physical fitness and overall health (34). Certain daily activities, such as walking, housework, or gardening, can also be considered physical exercise when they are intentionally structured to improve fitness or support rehabilitation (35).

Motor Training: Motor training, a form of targeted physical exercise, involves the systematic and repetitive practice of movements aimed at the acquisition or reacquisition of motor skills and the improvement of motor control (36, 37).

Exercise-Based Therapy: Exercise-based therapy is a specialised form of physical exercise, specifically designed and structured as a therapeutic intervention to improve neuromuscular impairments and/or enhance functional abilities (38). These therapies may include advanced techniques such as robotic-assisted therapy, virtual reality, mental practice, and other technology-driven or innovative approaches. Exercise-based therapies can be administered independently by patients, guided by clinical staff, or supported by external devices.

Conventional Therapy: In the context of this thesis, “Conventional Therapy” refers to the standard, routine care typically provided by physiotherapists or performed independently at home. This includes practices such as stretching, passive mobilisation, and range of motion (ROM) exercises (passive, assisted, and active), along with approaches like the Bobath concept.

No Therapy: In the context of this thesis, "No Therapy" refers to the absence of any specific intervention aimed at improving UL neuromuscular impairments and/or functional abilities following a stroke.

Sham Therapy: Sham therapy is a placebo intervention commonly used in clinical research to evaluate the effectiveness of actual treatments. In the context of therapies such as mental practice and mirror therapy, sham therapy involves procedures that simulate the real treatment but lack its active therapeutic components.

Chapter 1. Literature Review

1.1 Introduction

This chapter establishes a solid foundation for the investigative focus of this thesis by identifying and discussing gaps in the current knowledge. It commences with a comprehensive introduction to stroke and its impacts. It then describes the effects of stroke on the UL and continues by introducing key concepts related to neuromuscular and functional recovery. It then presents mechanisms for exercise-driven neuromuscular and functional recovery. After that, it provides a critical assessment of the available evidence on the relationships between UL neuromuscular impairments and functional limitations in stroke survivors. It continues by explaining the limitations of clinical outcome measures and advocating for using kinematics- and EMG-derived variables to enhance understanding of the relationships between UL neuromuscular impairments and functional abilities post-stroke. Following that, the importance of the International Classification of Functioning and Disability (ICF) framework is highlighted for the identification of the relationships between neuromuscular impairments and functional abilities. Lastly, it shows that the framework is inadequately applied in this context and ends by providing a summary of all these.

1.2 Stroke

Stroke is a sudden neurological event caused by a disruption in blood flow to the brain (39). The main types of stroke are (40):

1. **Ischemic stroke**, caused by insufficient blood and oxygen supply to an area of the brain due to a blood clot (39).
2. **Haemorrhagic stroke**, caused by bleeding in the brain due to a ruptured or leaking blood vessel (39).
3. **Transient ischemic attack (TIA)**, caused by a temporary interruption of arterial blood circulation in the brain (40).

Ischemic and haemorrhagic strokes can lead to a range of complications, including neuromuscular and sensory impairments, visual disturbances, and speech difficulties (41). The nature and severity of these complications vary based on the location and extent of the stroke-induced brain damage. The middle cerebral artery (MCA), for example, provides oxygenated blood to the primary motor and somatosensory cortical areas that control the face, trunk, ULs and lower limbs (42). Thus, a stroke impacting the MCA can lead to varying degrees of impairment in these areas, depending on the stroke's severity.

TIAs are neurological events that closely resemble ischemic strokes (43). The primary difference between TIAs and ischemic strokes is the duration of symptoms; TIA symptoms are generally accepted to last less than 24 hours (43). However, TIAs can cause neuromuscular impairments in the ULs, gait, and balance, which may persist beyond the typical 24-hour period of TIA symptoms (44, 45). Due to its potential lasting impacts, TIA is recognised as a main type of stroke, aligning with recent studies (40, 46–48).

According to the latest data from the World Health Organisation (WHO):

- with an annual toll of 6.5 million lives, stroke is the second most prevalent cause of death worldwide (7, 49).
- on a global scale, it is the third most prevalent cause of disability (49).
- currently, over 101 million individuals worldwide have a history of stroke (7).
- each year, 12.2 million individuals experience their first stroke (7).
- approximately one-fourth of individuals aged 25 and up have a stroke at some stage in their lives (7).

Available evidence on the economic consequences of stroke shows a significant challenge to the financial sustainability of healthcare systems in several countries. According to a recent systematic review of 46 studies from 27 countries, the average annual cost of stroke per patient varies from $27,702 in high-income countries to $2,100 in low-income countries (50). In the United Kingdom (UK), the total annual economic burden of stroke is estimated at £26 billion, including £3.4 billion attributed to services provided by the National Health Service (NHS) alone (51).

In addition to the serious financial consequences of stroke, there are serious effects on caregivers and the community at large. Caregivers face a particularly heavy burden; such that there is a reported association between poor quality of life after stroke and the need for more than 60 hours of informal care per week (52). This intensive caregiving often leads to emotional strain, as evidenced by the high rates of anxiety (51.1% in the first month after discharge) and depression (31.1% in the first month after discharge) among caregivers (53, 54). Stroke also leads to an increased demand for social support and resources, including income support, medication subsidies, social housing, benefit programs and disabled transportation services (52, 55).

Between 1990 and 2019, there was a reported increase of 70% in the incidence of stroke and an 85% increase in its prevalence (56). Age is a significant non-modifiable risk factor for stroke, as

the incidence of stroke increases with advancing age (57, 58). Due to the ageing population globally and advances in stroke treatment, which lead to higher survivor rates, these figures are projected to continue to increase (8). Between 2015 and 2035, the annual stroke incidence rate in the UK is predicted to increase by 60%, while the prevalence rate is predicted to increase by 120% (8).

Considering the serious negative impacts of stroke and the expected increase in stroke incidence and prevalence rates, improving the quality of post-stroke rehabilitation is of the utmost importance (59, 60). Effective, well-structured, and evidence-based rehabilitation strategies can support the recovery process of stroke survivors, improve their quality of life, and reduce their dependence on others (6, 61, 62). This can both alleviate the economic effects of stroke by causing reductions in health expenditures and mitigate the social burden by reducing the need for caregivers and social services (6, 61, 62). Therefore, addressing research gaps in stroke rehabilitation and transferring these insights into clinical practice is crucial for providing optimal recovery support to stroke survivors.

1.3 The Impact of Stroke on the Upper Limb

Neuromuscular impairments in the UL resulting from stroke often restrict an individual's ability to perform daily activities, engage in social interactions, and, in some cases, return to paid work. Such that, the devastating impacts of stroke on UL functionality have led to the recognition of UL recovery as one of the top ten research priorities in stroke rehabilitation (63).

1.3.1 Impact of Stroke on the Upper Limb at the Neuromuscular Impairment Level

Commonly reported UL neuromuscular impairments following a stroke include paresis, abnormal muscle tone, loss of active and/or passive ROM, abnormal muscle synergies, and abnormal force production (64–67). The existing longitudinal studies provide valuable insights into the severity of these impairments. For example, a study of 1,259 stroke survivors from various ethnic backgrounds reported that 77.4% had UL neuromuscular impairments after their first stroke (68). Another study involving 102 MCA stroke survivors revealed that 76% of them experienced UL paralysis at the onset of the stroke, and within the entire cohort, 62% did not regain any dexterity within the first six months (3).

1.3.2 Impact of Stroke on the Upper Limb at the Functional Ability Level

Difficulties in routine functional tasks such as manipulating objects, using a telephone and dressing are examples of functional limitations caused by neuromuscular impairments of the UL (69). A cross-sectional survey of 1,725 individuals in France with a history of stroke found that

80.5% reported some degree of functional limitation in their UL activities, with 67.4% of those aged 85 and older reporting severe functional limitations (1). Another cross-sectional study involving 65 stroke survivors with UL impairments reported that a majority experienced difficulties in daily activities, with challenges in various tasks reported by 73.8% to 89.2% of participants (2).

1.4 Neuromuscular and Functional Recovery after Stroke

Effectively facilitating improvements in neuromuscular impairments and functional limitations after stroke requires an accurate understanding of how neuromuscular and functional recovery occurs. Neuromuscular recovery, which corresponds to recovery from neuromuscular impairments, requires repair of neuromuscular systems damaged by brain injury (70–73). Functional recovery, specifically for the UL, necessitates improvements in the ability to perform daily activities such as grasping objects, managing personal care tasks such as dressing, engaging in occupational tasks such as typing, and executing fine motor skills required for a variety of everyday activities (70–73).

In this thesis, 'neuromuscular recovery' is used synonymously with **'behavioural restitution'**, which involves returning to typical motor control patterns using the impaired effector such as the hand and achieving functional goals in the same manner as before the stroke (71, 72). This process requires neural repair, which always occurs to some degree after stroke but is often incomplete (71). Behavioural restitution also includes **'spontaneous neurological recovery,'** which refers to the natural healing process of the brain that progresses independently of active treatment in the weeks to months after stroke (74). The majority of spontaneous neurological recovery typically occurs in the first three months after stroke onset (75).

Neuromuscular recovery can lead to functional recovery (72). However, functional improvements can also result from **behavioural compensation**, which includes **behavioural adaptation**–using the impaired body parts in unusual ways–and **behavioural substitution**–using unimpaired body parts for task execution (72, 73). Behavioural compensation, unlike neuromuscular recovery, does not require neural repair but may require learning new movement strategies (71). For instance, a stroke survivor who has arm paresis and has learned to use increased trunk forward flexion to reach objects has learned to compensate for this condition but has not recovered neuromuscularly (71).

The term 'recovery' is often used vaguely in stroke research; so that it sometimes expresses both neuromuscular recovery and behavioural compensation, which leads to erroneous reporting of

research findings (5, 72, 76). Accurate reporting of research findings in the context of the above-mentioned terms can contribute to an accurate understanding of neuromuscular and functional improvements in stroke survivors and facilitate the identification of effective strategies to promote them (71, 77).

1.5 Exercise-Driven Neuromuscular and Functional Recovery Post-Stroke

While spontaneous neurological recovery typically occurs in the early months of post-stroke (71), additional neuromuscular recovery hinges on motor training (78). This training essentially involves a form of motor relearning, leading to lasting changes in motor behaviour depending on practice or experience (79).

The reacquisition of impaired motor skills by stroke survivors is driven by neuroplasticity—the central nervous system's ability to structurally and functionally adapt to new experiences (80). Physical exercise plays an important role in improving neuroplasticity through mechanisms such as modulating angiogenesis, increasing neurotrophic factor production, enhancing cell signalling, growth, and development, and decreasing infarct volume (80–83). Thus, exercise-based therapies, appropriately planned according to the needs of stroke survivors, can significantly and effectively mitigate their neuromuscular impairments and subsequently improve functional abilities (84, 85).

Stroke survivors' dependence on behavioural adaptations may lead to maladaptive neuroplasticity that impedes neuromuscular recovery (77, 86). Additionally, over-reliance on behavioural substitutions can lead to learned non-use, limiting further neuromuscular recovery by inhibiting experience-dependent plasticity in the brain hemisphere affected by stroke (72). Although compensatory strategies may help stroke survivors complete tasks in the short term, their prolonged use can lead to long-term consequences, such as pain, limited ROM, and excessive muscle shortening (72, 87). Therefore, exercise-based therapies should effectively and efficiently promote neuromuscular and functional recovery after stroke by limiting dependence on compensatory strategies.

However, therapies that allow or promote compensatory strategies have recently received great attention due to their potential to improve stroke survivors' safety and quality of life (71). In current stroke practice, functional recovery after stroke is mostly attributed to the acquisition of compensatory strategies (88, 89). Despite the risk that therapies focusing on functional improvements can induce compensatory strategies in stroke survivors (71), overcoming functional limitations rather than neuromuscular recovery is often prioritised in current practice

(69, 90).

Published guidelines have a substantial impact on the practices of clinical teams. A study with 227 healthcare professionals in a Swedish hospital, for instance, showed that approximately 75% of them use clinical guidelines in treatment planning (91). Current guidelines, such as the 2023 UK National Stroke Guidelines and the 2019 Canadian Stroke Guidelines, recommend the implementation of exercise-based therapies that are centred on practising functional tasks (92, 93). However, while these recommendations are valuable if a strong relationship exists between neuromuscular impairments and functional abilities in response to exercise-based therapies, incorporating a focus on movement quality within functional tasks, rather than simply task completion, could foster improvements in neuromuscular impairments that, in turn, enhance functional abilities. Emphasising movement quality particularly in the early post-stroke period, can optimise therapy outcomes by reducing reliance on compensatory strategies and more effectively leveraging neuroplasticity during this critical window for recovery (94). Understanding the impact of exercise-based therapies, used in current stroke practice, on neuromuscular and functional recovery, is therefore of utmost importance (72, 95, 96).

However, the current state of knowledge regarding the relationship between neuromuscular recovery and functional recovery remains limited due to the ineffective differentiation between compensation and neuromuscular recovery in clinical trials and observational studies (94). Existing reviews of the effects of exercise-based therapies predominantly focused on a single type of exercise-based therapy and/or did not include primary studies measuring both neuromuscular impairments and functional abilities or did not report the effects on neuromuscular impairments and functional abilities individually (9–15). A systematic review of existing research on the correlations between changes in neuromuscular impairments and changes in functional limitations in response to exercise-based therapies is not yet available. Therefore, there is a need to systematically synthesise evidence on the effects of exercise-based therapies, used in current practice, on both neuromuscular impairments and functional abilities and identify the correlates between these effects.

A systematic review of 10 studies assessing the intensity of exercise-based therapy for UL in stroke rehabilitation settings revealed a significant shortfall in the provision of adequate UL therapy after stroke (97). During acute rehabilitation, stroke survivors were found to receive less than four minutes and only 11 minutes of UL therapy per physiotherapy and occupational therapy session, respectively. The duration of UL therapy provided during the subacute rehabilitation process was found to be less than six minutes per physiotherapy session and 12

minutes per occupational therapy session. The emphasis on walking in stroke rehabilitation often overshadows the critical need for UL training (98). For example, an observational cohort study in the United States and Canada demonstrated that per session, the average number of repetitions for UL movements during UL therapy was only 32 (95% [Confidence Interval (CI)] = 20 – 40), while the average number of gait steps was 357 (95% [CI] = 296 – 418) (98).

Considering the limited time dedicated to UL training in rehabilitation programmes and the critical importance of the first three to six months after stroke for recovery (3, 99), understanding the effects of exercise-based therapies on neuromuscular impairments and functional abilities is of great importance. This understanding can greatly contribute to the recovery processes of stroke survivors by ensuring that the limited rehabilitation time is used as effectively as possible and that the critical time window for recovery is utilised as efficiently as possible.

1.6 Relationships between Neuromuscular Impairments and Functional Abilities on the Upper Limb after Stroke

Although it is recognised that there is a relationship between the severity of neuromuscular impairments and functional limitations, there is no comprehensive understanding of the extent of this relationship (33). This is probably due to the complex, multifaceted and dynamic nature of this relationship.

In stroke survivors, various neuromuscular impairments can impact the same functional task/s differently. For instance, Schiefelbein et al. (100) found a strong correlation between functional ability, as assessed by the Box and Block Test (BBT), and the Fugl-Meyer Assessment (FMA)-UL Motor Scale ($r = 0.78$, $p < 0.05$). However, BBT performance showed no significant relationship with grip strength ($r = 0.09$, $p = 0.77$) and had a moderately negative relationship with movement smoothness ($r = -0.56$, $p < 0.05$). Another study by Burridge et al. (33) reported that the relationship between functional ability, measured by the Action Research Arm Test (ARAT), and hypertonia of wrist flexors was weak and negative ($r = -0.36$, $p = 0.16$). In contrast, the relationship of ARAT with active wrist flexion/extension ROM was moderate and positive ($r = 0.54$, $p < 0.05$), as were the relationships with wrist flexor and extensor strength ($r = 0.52$ and 0.58, respectively; $p < 0.05$ for both). There was no significant relationship between ARAT and hyperreflexia ($r = 0.049$, $p = 0.85$).

Additionally, the impact of specific post-stroke neuromuscular impairments on different aspects of functional ability can vary. For example, Massie et al. (19) found that shoulder and elbow

ROM had a strong to moderate relationship with performance on the BBT ($r = 0.7$ and 0.6, sequentially; $p < 0.05$ for both). However, the relationship of these ROMs with the time required to complete a reaching task was either negligible or low ($r = -0.2$ and -0.4, respectively; $p > 0.05$ for both) (19). This suggests that while improvements in shoulder and elbow ROM can enhance BBT performance, they have a lesser effect on reducing task completion time. Similarly, Faria-Fortini et al. (32) reported that lateral pinch strength had varying effects on different functional ability measures, showing a negligible correlation with the Nine Hole Peg Test (NHPT) ($r = 0.15$, $p > 0.05$) and a moderate correlation with the BBT ($r = 0.50$, $p < 0.05$).

This complex and multifaceted nature of the relationships between post-stroke neuromuscular impairments and functional abilities requires comprehensive evaluation for an accurate and detailed understanding of the relationships between them. However, existing studies on these relationships generally have small sample sizes (19,22,33), limiting the generalisability of findings, and mostly assessing the effects of specific neuromuscular impairments on functional abilities, precluding a comprehensive evaluation (29–32).

The relationships between neuromuscular impairments and functional abilities in stroke survivors may vary over time and can be influenced by factors like compensatory strategies, familiarity with the experimental setting, fatigue, and motivation (101–103). Single-session cross-sectional studies provide a snapshot of these relationships, but they fall short of capturing the dynamic and evolving nature of stroke. Longitudinal studies, conducted over multiple sessions, are crucial for assessing the stability of these relationships. Such studies can determine if observed relationships are genuine or influenced by external factors. By identifying neuromuscular impairments that consistently correlate with functional abilities, therapy targets can be more effectively set, potentially enhancing functional recovery outcomes in stroke survivors. However, in the literature, these relationships have mostly been evaluated with single-session cross-sectional studies (19–21, 30, 32, 33, 87). There is no longitudinal study in the literature that investigates these relationships by evaluating whether they are stable.

1.7 Importance of Standardisation and Advanced Technological Instruments in Post-Stroke Evaluation

The diversity of outcome measures used in stroke recovery and rehabilitation trials often complicates the comparison of different studies and poses a substantial challenge to effectively translating research findings into clinical practice (27).

Accurate and timely assessments are crucial for effective rehabilitation (104, 105). However, current clinical guidelines do not provide clear and standardised recommendations on outcome measures (104). Consensus on this matter provides a benchmark for quality in clinical practice because consistent and evidence-based evaluations can provide critical information on the effectiveness of therapy provided, allowing for timely adjustments and improvements in rehabilitation strategies (104, 105).

To address these issues, the Stroke Rehabilitation Research Roundtable (SRRR) recommends using the FMA scale and ARAT in post-stroke UL assessment (106). Similarly, Pohl et al. (105) support their use as core outcome measures in stroke rehabilitation practice, due to their excellent clinimetric properties.

Although the ability to distinguish between neuromuscular recovery and behavioural compensation is critical to tailor therapy programmes more effectively and efficiently for stroke survivors, clinical outcome measures usually lack this ability (71, 106). Recognising this, the SRRR strongly supports the inclusion of kinematics-derived variables in post-stroke assessments, as kinematics-derived variables obtained from advanced technological instruments can make this distinction (106).

Clinical outcome measures are also incapable of capturing electrophysiological factors underlying motor control; however, variables derived from EMG, another advanced technological instrument, can provide data on muscle activation (107, 108). While EMG-derived variables may not directly distinguish between neuromuscular recovery and behavioural compensation, their combined use with kinematics-derived variables can provide detailed information about post-stroke neuromuscular impairments (109).

Kinematics- and EMG-derived variables are superior to clinical outcome measures for post-stroke assessments due to their sensitivity in detecting subtle changes in neuromuscular impairments and functional abilities (16, 17). Therefore, these variables can facilitate a more thorough and precise examination of the relationships between neuromuscular impairments and functional abilities. However, current research mostly uses clinical outcome measures to investigate these relationships (29–32). Studies using kinematics- and EMG-derived variables are limited (19–22), and some suffer from small sample sizes (19, 22).

The diversity of these variables makes it difficult to select the appropriate ones for research (28, 106). Establishing reference values, test-retest reliability, and SDCs of such variables in adults

without mobility-impairing conditions before using them in stroke research can be beneficial (110). This foundational data can guide the selection of appropriate variables for assessing these relationships in stroke survivors. Although they cannot be applied directly to the stroke population, they can provide valuable insights into the precision and potential measurement biases of the variables (110). Reference values serve as a standard for detecting deviations from the norm in stroke survivors, improving understanding of the extent of neuromuscular impairments and functional limitations (110–112). Determining the test-retest reliability of variables in adults without mobility-impairing conditions helps identify their inherent variability, independent of stroke-related factors, such as recovery over time, and cognitive decline (110, 113). By establishing a threshold for meaningful change, the SDCs of these variables in adults without mobility-impairing conditions help distinguish clinically significant improvements in stroke survivors from changes that are within the range of measurement error (110, 114). As a result, these data can contribute to a deeper understanding of the clinical utility and applicability of the variables, laying the groundwork for their standardisation and informing their selection.

However, in the current literature, there is a lack of comprehensive research on reference values, test-retest reliability, and SDCs for UL kinematics- and EMG-derived variables in adults without mobility-impairing conditions (18, 23–25, 28, 115). The existing studies are limited in number and often have small sample sizes, with some kinematics-derived variables being studied in only nine individuals (26) and EMG-derived variables in samples from 10 to 23 individuals (23–25). Therefore, there is a need for further high-quality research with larger samples of adults without mobility-impairing conditions.

1.8 Assessment of Neuromuscular Impairments and Functional Abilities after Stroke

Accurate distinction of whether outcome measures evaluate neuromuscular impairments or functional abilities can be challenging. This challenge often leads to misinterpretations of research findings, affecting their quality and applicability. Therefore, accurate classification of outcome measures based on what they assess is essential for an accurate understanding of the links between neuromuscular impairments and functional abilities in stroke survivors (116).

In this context, the ICF framework, designed by the WHO, offers a helpful structure. It categorises disease consequences into three main dimensions: impairment, activity limitation, and participation restriction (117). These categories correspond to three fundamental domains: body functions/structures, activity, and participation, respectively (117). A comprehensive description of the ICF domains and their associated health-related dimensions, along with contextual examples, is provided in Table 1.

Table 1. ICF Domains: Definitions and Contextual Examples

Domains	Definitions and Contextual Examples
Body Functions/ Structures	• **Body functions** refer to the physiological functions of body systems, such as the force required to grasp an object, while **body structures** are the anatomic parts of the body like muscles and joints (118). • Deviations and/or losses in normal body functions and structures that are indicative of the underlying pathology's direct neuromuscular implications, are called (motor/neuromuscular) **impairments** (117, 119). They represent the extent of abnormality in body integrity compared to individuals of the same age, and gender without mobility-impairing conditions. A subluxed shoulder and contracted elbow joint are examples of impairments in body structures whilst a decrease in muscle strength, changes in muscle tone (either increase or decrease), and loss of dexterity are examples of impairments in body functions.
Activity	• **Activity** refers to the execution of tasks or actions by an individual in a purposeful and intentional manner (117). • **Activity limitations** (functional/behavioural limitations) refer to challenges experienced in performing tasks, often reflecting a reduced level of independence due to pathology and/or impairments, compared to adults of the same age, and gender without neurological or musculoskeletal pathology (117, 119). Difficulties in lifting and carrying objects, as well as challenges in feeding oneself, are examples of activity limitations.
Participation	• **Participation** is an individual's engagement in real-life situations (117). • Challenges experienced in engaging in real-life situations are known as **participation restrictions** (117). Difficulties experienced in returning to a pre-stroke job, participating in community events, or engaging in hobbies like gardening are examples of participation restrictions.

Note: Since the participation level is concerned with involvement in real-world scenarios, differentiating the precise contribution of the UL at this level is challenging. Therefore, this thesis does not evaluate the effects of stroke on this level.

According to the definitions provided by the ICF framework (Table 1), outcome measures quantifying impairments occurring at the body functions/structures level are termed **neuromuscular impairment measures**. Those assessing the activity dimension of the ICF can be referred to as **functional ability measures**. Measures of neuromuscular impairments indicate the underlying causes of activity limitations (Table 2) (117). Measures of functional ability used in stroke rehabilitation assess how an activity is performed compared to pre-stroke, such as whether the task requires more time, effort, or assistance to complete (Table 2) (117).

Table 2. Specific Domains of Interest Assessed by Impairment and Functional Ability Measures

	Neuromuscular Impairment Measures	Functional Ability Measures
Specific Interests	• The neuromuscular signature contributing to difficulty achieving an action, or a task • How similar the movement is to movement patterns of adults without motor impairments	• Which activities or tasks can/cannot be accomplished • How much time achieving an activity takes • How much assistance is needed to achieve an activity or a task • How much difficulty achieving an activity or a task involves

1.9 Challenges in the Classifications of Outcome Measures

Although the ICF framework provides a structured approach for classifying outcome measures, its full potential is not utilised effectively, occasionally leading to inaccurate classifications (119–125).

Efforts to apply the ICF framework in this regard have typically focused on the content of the measure's items (116,126–129). However, this approach can be misleading, particularly when evaluating neuromuscular impairments within the context of functional tasks. For example, the 'Motor Evaluation Scale for Upper Extremity in Stroke Patients (MESUPES)' is categorised as a functional ability (activity level) measure by Demers and Levin (120). Its items include both direct evaluations of body functions, such as shoulder abduction and finger extension, and functional tasks like gripping a plastic bottle (120, 130, 131). Items involving functional tasks can lead to their classifications within the ICF's activity domain based on content. However, MESUPES's arm subscale uses a three-stage scoring system that evaluates **muscle tone**, **normal muscle contraction** and **normal joint movement** (132). Its hand function subscale evaluates the **ROM** of some hand joints and **hand orientation** during functional tasks (132). As a result, MESUPES's

scoring criteria primarily assess body functions, leading to its classification as a measure of neuromuscular impairment. Contrary to common practice (116, 126–129), evaluating the scoring criteria rather than the content of a measure's items using the ICF framework can lead to a more accurate classification of outcome measures by determining what they truly assess.

The scoring criteria of some outcome measures encompass multiple domains of the ICF framework, leading to classification challenges (116). For instance, Fritz et al. (121) categorise the Wolf Motor Function Test (WMFT)-Functional Ability Scale as an impairment measure, although it is commonly classified as a functional ability measure (122–124). This scale's scoring criteria assess both neuromuscular impairment and functional ability. Scores of 0 (no attempt) and 1 (non-functional attempt), along with a score of 2 (task attempted with assistance), primarily assess task engagement capacity, reflecting functional ability. A score of 3, for movements influenced by synergy or performed slowly or with effort, represents a blend of impairment and functional ability. Scores of 4 and 5, assigned for near-normal movements that lack precision, coordination, or fluidity, and for normal movements that mirror pre-stroke patterns predominantly assess the extent of neuromuscular impairments. Therefore, the WMFT-Functional Ability Scale primarily evaluates functional ability but also incorporates elements of neuromuscular impairment, making it a composite measure spanning both domains.

Additionally, contrary to the common perception that all kinematics-derived variables measure neuromuscular impairments (123, 124, 133), some assess functional ability. A systematic review of UL robot-assisted therapy studies classified several kinematics-derived variables as functional ability measures within the ICF activity level. These include the active movement index (measuring the percentage of a functional activity completed independently), movement overlap (assessing bimanual activity engagement), performance index (evaluating task difficulty), robot power (determining support need), and task completion time (measuring time taken to complete tasks) (125). However, the study categorised 'Movement Duration'–the total time from movement onset to offset–under the ICF body functions/structures level, despite its conceptual similarity to 'Task Completion Time'. Apart from this, this study provides important information on the correct classification of variables derived from kinematics.

In summary, classifying outcome measures based solely on the content of their items could be misleading. Scoring criteria often provide a clearer indication of what a measure is truly assessing, as they more comprehensively reflect the underlying domains. Additionally, some outcome measures do not align perfectly with a single domain, as their scoring criteria span

multiple domains of the ICF framework, combining elements of both neuromuscular impairments and functional abilities. In such cases, identifying the primary focus of the scoring criteria–whether it predominantly reflects impairments or functional abilities–can provide essential insights into the measure's intended application and how its results should be interpreted. Such awareness is particularly crucial for ensuring that results are appropriately contextualised in research and clinical practice, guiding their practical application and the conclusions drawn from studies. Given these complexities, careful consideration and scrutiny are essential when selecting outcome measures to ensure they reflect the intended assessment domain. Accurately classifying outcome measures is thus critical for investigating relationships between neuromuscular impairments and functional abilities, enabling more meaningful insights and applications in stroke rehabilitation research.

1.10 Conclusion

In summary, stroke's high prevalence and incidence pose substantial economic and societal burdens. Many stroke survivors suffer from neuromuscular impairments and functional limitations in their ULs, affecting their daily lives and independence. Comprehending how exercise-based therapies, commonly used in stroke practice, influence neuromuscular impairments and functional abilities can inform stroke practice and improve therapy outcomes. However, the full effects of these therapies remain unexplored. Deeper insights into the relationships between neuromuscular impairments and functional abilities, particularly by considering their consistency and susceptibility to external factors, can enable effective goal setting and increase therapy effectiveness and efficiency. However, in the current literature, there is a lack of studies investigating the stability and sensitivity of these relationships. Kinematics- and EMG-derived variables can enable a more in-depth investigation of these relationships but are underutilised in longitudinal research. Additionally, the diversity of these variables poses challenges in selecting the most appropriate ones to investigate these relationships. Establishing their reference values, test-retest reliability, and SDCs in adults without mobility-impairing conditions could inform their selection and application, yet such foundational information is not firmly established. Before researching this topic, an accurate classification of measures of neuromuscular impairment and functional ability is imperative to correctly identify these relationships.

Chapter 2. Statement of Aims

2.1 Introduction

The literature review chapter revealed the need:

To investigate the relationships between neuromuscular impairments and functional abilities in the UL post-stroke.

This need arose from the following gaps in the current literature:

Understanding the Relationships Between Neuromuscular Impairments and Functional Abilities: A critical knowledge gap in stroke rehabilitation research is the lack of understanding of the relationships between neuromuscular impairments and functional abilities after stroke. The extent and dynamics of these relationships, particularly their response to various therapies and progression over time, remain ambiguous. In order to effectively profit from neuroplasticity and develop efficacious therapeutic strategies, it is critical to acquire a comprehensive understanding of this subject.

Challenges in Accurate Assessment of Neuromuscular Impairments and Functional Abilities: Another knowledge gap lies in the reliable and precise identification of the relationships between neuromuscular impairments and functional abilities. While clinical outcome measures have limitations in accurately identifying the links between neuromuscular impairments and functional abilities, variables obtained from kinematics and EMG show promise for a better understanding. However, it is unclear whether these variables allow for precise identification of these interactions and how far their limitations extend. Identifying precise and accurate assessment variables, along with knowledge of what they assess, whether impairment or function, is the first step towards understanding the true nature of these post-stroke relationships.

Based on these knowledge gaps, this thesis aims to address the following research questions and aims:

2.2 Research Question 1

What is the nature of the relationships between UL neuromuscular impairments and functional abilities in response to exercise-based therapies?

To answer the question, the aims were:

Aim 1a. Explore whether there is a greater benefit for UL neuromuscular impairments or functional abilities after stroke in response to exercise-based therapies compared with:

- no therapy;
- sham therapy;
- physical therapy provided as a 'routine' intervention (conventional therapy)

Aim 1b. Estimate the correlation between changes in the UL neuromuscular impairments and functional abilities after stroke in response to exercise-based therapies compared to:

- no therapy;
- sham therapy;
- conventional therapy

This first research question was investigated through a systematic review including meta-analyses and meta-regressions (Chapter 3).

2.3 Research Question 2

What are the reference values, test-retest reliability, and SDC for UL neuromuscular impairment and functional ability variables, as derived using the Vicon motion analysis and Delsys EMG system, in adults without mobility-impairing conditions?

The aims were:

Aim 2a. Identify the reference values for neuromuscular impairment and functional ability variables during a standardised UL task using the Vicon motion analysis and Delsys EMG system in a sample of people representative of the adult population without mobility-impairing conditions.

Aim 2b. Determine the test-retest reliability of neuromuscular impairment and functional ability variables during a standardised UL task using the Vicon motion analysis and Delsys EMG system in a sample of people representative of the adult population without mobility-impairing conditions.

Aim 2c. Ascertain the smallest detectable change of neuromuscular impairment and functional ability variables during a standardised UL task using the Vicon motion analysis and Delsys EMG system in a sample of people representative of the adult population without mobility-impairing conditions.

Aims 2a, 2b and 2c were explored through a prospective correlational test-retest agreement study in adults without mobility-impairing conditions, using a functional, daily UL task (Chapter 5).

2.4 Research Question 3

To what extent do UL neuromuscular impairments in stroke survivors correlate with UL functionality?

The following aims were set:

Aim 3a. Estimate the relationships between measures of neuromuscular impairment and functional ability in people after stroke.

Aim 3b. Explore whether there are stable relationships between measures of neuromuscular impairment and functional ability collected two to four months apart when improvement is not expected in people after stroke.

Aims 3a and 3b were investigated through an observational repeated measures cohort study using kinematics- and EMG-derived variables and two clinical assessment tools. Kinematics- and EMG-derived variables were obtained from Vicon motion analysis and Delsys EMG system and collected from research participants while they were performing a functional, daily UL task (Chapter 6).

These questions and aims are designed to directly address the gaps in understanding the impact of exercise-based therapies on neuromuscular impairments and functional abilities, as well as the long-term dynamics of these relationships in stroke survivors.

Note: In this thesis, outcome measures were carefully examined and classified as measures of neuromuscular impairment or functional ability to ensure that the association between neuromuscular impairments and functional abilities was accurately identified. The lead researcher (the author of this work) executed this procedure, and when necessary, consultation with the supervisory team was sought.

Chapter 3. Correlation between Change in Neuromuscular Impairments and Functional Abilities in Response to Upper Limb Exercise-Based Therapies after Stroke: A Systematic Review with Meta-Analyses and Meta-Regressions

3.1 Introduction

Knowing whether a specific therapy drives neuromuscular recovery to achieve functional recovery is required to contribute to optimum UL recovery after stroke (71). This is because the alternative mechanism is compensation, limiting the opportunities for experience-induced neuroplasticity and potentially fostering maladaptive plasticity (72, 86), which is undesirable.

Post-stroke rehabilitation often targets functional limitations (72, 86, 134). Conventional therapy, largely focusing on compensatory strategies due to functional independence concerns, has shown limited success in post-stroke neuromuscular impairments (134, 135). Exercise-based therapies, aimed at addressing these impairments, may enhance neuromuscular recovery in stroke survivors (134, 136). Therefore, discerning whether such therapies promote neuromuscular recovery or compensation is crucial.

This subject, however, has been underexplored in clinical and observational studies (94). Existing systematic reviews have either concentrated on one type of exercise therapy or have neglected to include statistics regarding the effects of exercise-based therapies on neuromuscular impairments and functional abilities separately (9–13, 137, 138).

To address the thesis's first research question, this systematic review aims to (1) explore whether exercise-based therapies offer greater benefits for UL neuromuscular impairments or functional abilities after stroke compared with no therapy, sham therapy and conventional therapy (**Aim 1a**); and (2) estimate the correlation between changes in the UL neuromuscular impairments and functional abilities after stroke in response to exercise-based therapies versus no therapy, sham therapy and conventional therapy (**Aim 1b**).

3.2 Methods

3.2.1 Design

A systematic review was undertaken in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) (139, 140). The review protocol is registered in the PROSPERO database with the identification number CRD42022322542.

3.2.2 Searching for Studies

Information Sources: Electronic searches were conducted in the following databases:

- MEDLINE (via Ovid),
- EMBASE (via Ovid),
- Cochrane Library – Cochrane Central Register of Controlled Trials (CENTRAL)
- CINAHL

Utilising MEDLINE, EMBASE, and CENTRAL is advised for conducting a thorough search of pertinent studies (141–143). Studies not available in other databases can be accessed using CINAHL, a subject-specific bibliographic database for nursing and allied health (144).

Search Strategy: In collaboration with a medical librarian, a thorough search strategy was established. A preliminary electronic search using the terms: hemiplegia, stroke, paresis, cerebrovascular disorders, upper extremity, arm, hand, rehabilitation, and exercise, was performed to validate the strategy's effectiveness and comprehensiveness. The strategy was adapted for each database, incorporating specific indexing terms: Medical Subject Headings (MeSH) for Cochrane Library, Medline, and CINAHL, Emtree terms for EMBASE, and additional text terms, as necessary. To mitigate the risk of missing studies not yet indexed in databases (145), no database filters, including language, were used. The search focused on studies published from 2011 onwards because of the enhancements in the methodological quality of UL stroke rehabilitation research in the last decade (146). The database search was completed on December 16, 2020.

Table 3 shows the search strategy for MEDLINE; strategies for CENTRAL, EMBASE, and CINAHL are in Appendix 1.

Table 3. The Search Strategy for MEDLINE[1]

ID	Search Term
1	cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial
2	(stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$).tw.
3	((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
4	((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
5	hemiplegia/ or exp paresis
6	(hemipleg* or hemipar* or paresis or paretic).tw.
7	or/1-6
8	exp Upper Extremity/
9	("upper limb$" or "upper extremit$" or arm or arms or shoulder or shoulders or hand or hands or elbow$ or forearm$ or finger$ or wrist$).tw.
10	or/8-9
11	Exercise/
12	exp Exercise Therapy/
13	(physiotherap$ or physicaltherap$ or exercise$).tw.
14	(exercise* adj3 (treat* or program* or train* or therap*)).tw.
15	11 or 12 or 13 or 14
16	7 and 10 and 15
17	randomized controlled trial.pt.
18	randomization/
19	(quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
20	controlled clinical trial.pt.
21	clinical trials as topic.sh.
22	Double-Blind Method/
23	Single-Blind Method/
24	Cross-Over Studies/
25	Placebo Effect/
26	(assign$ or allocat$).tw.
27	((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
28	(randomi?ed controlled adj1 trial*).tw.
29	(RCT or "randomly allocated" or "allocated randomly" or random allocation).tw.
30	(allocated adj2 random).tw.
31	placebo*.tw.
32	or/17-31
33	(((systematic adj review*) or (meta adj analys*)) not (trial or study)).ti,ab.
34	32 not 33
35	16 and 34
36	limit 35 to yr="2011 -Current"
37	exp animals/ not humans.sh.
38	36 not 37
39	(Adolescent/ or exp child/ or exp Infant/) not exp Adult/
40	38 not 39

[1] ID denotes the order number of the search term. The ab = abstract, ti = title, tw = text word, pt = publication type, sh = MeSH (subject headings in MEDLINE).

Additional Search Resources: Reference lists of included studies were manually searched. Grey literature and unpublished studies were not searched. The eligibility criteria prioritised randomised controlled trials (RCTs) with methodological rigour, excluding studies with a high risk of bias. A cross-sectional analysis of 129 meta-analyses reported that grey literature (specifically dissertations) and unpublished studies were rarely included and had minimal impact on findings (147). Grey literature was included in nine meta-analyses, generally with negligible impact, except in one case where its exclusion, representing half of the included studies, significantly changed the point estimate and led to a loss of statistical significance. Excluding unpublished studies caused notable changes in two of eight meta-analyses, likely due to their predominance in these analyses, but statistical significance was unaffected. Given the focus on high-quality evidence and the large number of studies retrieved from databases, excluding grey literature and unpublished studies was deemed a reasonable methodological choice unlikely to significantly affect the findings.

Study Management: Retrieved studies were consolidated and de-duplicated in EndNote X9. Each study was assigned a unique ID and catalogued in Microsoft Excel. Reviewers were given access to full texts, published protocols and analysis plans of all studies through a Mendeley Library.

3.2.3 Identification of Eligible Studies

Two reviewers, working independently, identified eligible studies using the predetermined eligibility criteria (Table 4), structured according to the PICO framework (148):

- **Population (P):** Adult stroke survivors (≥ 18 years) with UL neuromuscular impairments.
- **Intervention (I):** Exercise-based therapy, either as a standalone treatment or combined with conventional therapy, provided the specific effects of exercise-based therapy could be distinguished.
- **Comparison (C):** No therapy, sham therapy, or conventional therapy.
- **Outcome (O):** At least one neuromuscular impairment and one functional ability measure were reported together.

After the title and abstract screening, studies considered possibly eligible underwent full-text screening. Those deemed potentially eligible after full-text screening were then assessed for risk of bias. The title screening was conducted solely by the lead reviewer (the author of this work), while the remainder of the process—including abstract screening, full-text screening, and risk of bias assessments—was conducted independently by two reviewers (the lead reviewer and another reviewer) working in parallel for every study. Disagreements between the two reviewers during these processes were resolved through discussion and referral to the full text.

Table 4. Eligibility Criteria

Categories	Inclusion Criteria	Exclusion Criteria
Types of Studies	• Individually randomised controlled trials	• All other study designs, including cluster-randomised controlled trials • Conference abstracts
Types of Participants	• Adult (≥ 18 years) stroke survivors with UL neuromuscular impairments	• Children and animals
Types of Experimental Interventions	• Exercise-based therapy, delivered alone • Exercise-based therapy, provided along with conventional therapy, provided that the specific effects of exercise-based therapy can be differentiated	• Non-exercise-based intervention • Combined intervention where the specific effects of exercise-based therapy cannot be distinguished
Types of Control Interventions	• No Therapy • Sham Therapy • Conventional Therapy	• Interventions involving stimulation or pharmaceutical agents • Exercise-based therapy, the same as used in the experimental group, but with different doses or alternative forms of feedback
Types of Outcome Measures	• Measures of neuromuscular impairment and functional ability together	• Measure of only neuromuscular impairment or functional ability
Language	• English or Turkish	• Other Languages
Risk of Bias	• Low or Some Concerns	• High

Types of Studies: Only individually RCTs were included in this review because systematic reviews or meta-analyses of methodologically sound RCTs typically provide the most reliable evidence for therapeutic interventions (149). According to the Cochrane Handbook, non-randomised studies should only be included in reviews of intervention efficacy if RCTs are insufficient to address the research questions or if the intervention cannot be evaluated through RCTs (150). Given the availability of numerous RCTs addressing the specific research questions of this review, it was deemed appropriate to exclude non-randomised studies.

Cluster RCTs and conference abstracts were not considered. Clusters, such as hospitals and geographical regions, may possess traits that influence intervention results (151). Even in matched pairs, natural response variations among clusters can still lead to potential confounding, separate from risk-of-bias issues (151). Conference abstracts frequently offer unreliable information with inadequate reporting quality (152, 153). A study found a notable difference between abstracts and their full-text publications, with cost-effectiveness ratios in abstracts differing by an average of ± 24% from their full-texts (153).

Types of Participants: The review included studies with participants aged 18 and older, at any post-stroke stage, and experiencing UL neuromuscular impairments. No limitations were imposed regarding the number of strokes experienced, the location of stroke lesions, or the time elapsed since stroke onset for the participants of the included studies. Although these factors may significantly affect post-stroke recovery (154, 155), inter-individual variation was not the focus of this review.

Studies with children or animals were excluded due to significant differences in brain development benchmarks, including synaptogenesis, myelination, and distinct immune response profiles (156). These processes occur on different timescales and are governed by unique developmental mechanisms in children and animals compared to adults (156). As highlighted in the literature, these differences influence vulnerability to injury and recovery capacities (156), rendering direct comparisons with adult stroke recovery processes unreliable.

Types of Experimental Interventions: Included experimental interventions were any type of exercise-based therapy interventions aimed at improving neuromuscular impairments and/or functional abilities in the affected UL post-stroke. Exercise-based therapy involves physical exercises and activities, prescribed to enhance neuromuscular impairments and/or facilitate daily activities following illness or disability. In this review, it encompassed passive, active, imagined, and observed movements. Exercise-based therapy interventions included were: self-

administered; provided by clinical staff; and/or enabled with the use of external devices, such as mirrors, exoskeletons, orthoses, or virtual reality. Interventions, exploring motor learning principles, such as feedback and repetition, were also considered. These interventions should be administered alone or in conjunction with conventional therapy. When exercise-based therapy is provided along with conventional therapy, its effects should be discernible. For example, in cases where both study arms received conventional therapy, the experimental group also underwent additional exercise-based therapy. There were no restrictions on the therapy setting (e.g., hospital, home).

Experimental exercise-based interventions combined with another exercise-based therapy were excluded due to the inability to isolate their individual effects. Interventions employing stimulation techniques, or pharmaceutical agents were excluded due to their distinct effect mechanisms from those of exercise-based therapy. Exercise-based therapy induces molecular (e.g. changes in protein regulation), morphological (e.g. the growth of dendritic spines), and physiological (e.g. excitation and inhibition among parts of neurons) changes that support neuroplasticity (157, 158). Stimulation techniques primarily target peripheral nerves and muscles, unaffected by central nervous system damage (159), or influence neuronal depolarisation and brain region excitability (160, 161). Pharmaceutical agents, baclofen and botulinum toxin, used in post-stroke rehabilitation influence muscle tone and activity (159). Their inclusion could confound the findings, thereby impacting the review's precision and credibility.

Types of Control Interventions: Control interventions were no therapy, sham therapy, or conventional therapy.

Control interventions involving the provision of stimulation or pharmaceutical agents were excluded for the reasons stated in the 'Types of Experimental Interventions' section. Control interventions employing the same exercise-based therapy as the experimental group, but with different doses or feedback forms were excluded, as they do not assess the effectiveness of the exercise-based intervention itself.

Types of Outcome Measures: Studies measuring both neuromuscular impairments and functional abilities of the affected UL after stroke were included. Those measuring only one were excluded.

The FMA, Motricity Index, and certain kinematics-derived variables such as reaction time and movement smoothness are examples of neuromuscular impairment measures. The ARAT, BBT, and some kinematics-derived variables, such as task completion time, are examples of functional ability measures. The FMA and ARAT were selected as the primary outcome measures, aligning with the international consensus for stroke recovery research consistency (106). Their widespread use in clinical trials and healthcare settings, validated by the detailed literature review and expert consultations, affirms their appropriateness for this review.

Outcome measures deemed outside the scope of this review are listed in Table 5, along with the rationales for exclusion.

Table 5. Excluded Outcome Measures with Their Exclusion Rationales

Outcome Measure	Rationale for Exclusion
Activities of Daily Living (ADL) Measures	• ADL measures, such as the Stroke Impact Scale, assess general daily activities involving multiple body parts, making it difficult to isolate the specific impact of stroke on the UL.
Accelerometer-Derived Measures	• These measures are limited in distinguishing between isolated UL movements and those resulting from overall body acceleration while sitting, standing, walking, or lying down (162, 163), leading to confounded measurements.
Self-Assessment Questionnaires	• The objectivity and precision of self-assessment questionnaires, like the Motor Activity Log, are limited. These depend on individuals' subjective perceptions and understanding of the assessment questions. This dependency can challenge accurate assessments, often leading to over- or under-estimations.
Balance Measures	• The performance of balance is not solely attributed to the UL, but also to the functions of the trunk, pelvis, neck, and lower extremities.
Trunk Displacement as a Kinematics-Derived Measure	• The extent of trunk displacement is influenced not just by neuromuscular impairments in the UL but also by the neuromuscular capacities of the trunk, neck, pelvis, and lower extremities. This multifactorial influence makes it unsuitable for inclusion in this review.
Electromyography (EMG)-Derived Variables	• Significant variability in EMG data measurement, processing, and analysing methods impacts data interpretation and comparability across studies. • Among EMG-derived variables, the maximum voluntary isometric contraction is widely regarded as reliable. However, its application in patients with neurological deficits presents challenges (164, 165), potentially introducing biases that affect findings. Other EMG-derived variables were not included in this review due to similar methodological concerns.

Language: Due to the lack of funds for professional translation, the review included only studies written in English or Turkish. Turkish was included as the lead reviewer's native language, enabling accurate assessment of relevant studies without requiring additional translation resources. While no language filter was applied during the database search, studies in languages other than English and Turkish were excluded during the screening process. This decision aligns with findings from a cross-sectional analysis of 129 meta-analyses, which demonstrated that while the majority searched for non-English studies, these were included in only 12% of cases (147). Substantive changes in results were observed in only four meta-analyses: in two, all included studies were non-English, while in the other two, where most studies were non-English, their inclusion did not cause changes in statistical or clinical significance. These findings suggest that excluding non-English studies generally has minimal impact on meta-analyses' findings, particularly when sufficient evidence is available in English. Given the extensive availability of studies on exercise-based therapies for neuromuscular impairments and functional abilities in English, excluding non-English and non-Turkish studies was deemed acceptable for this review.

Risk of Bias: Studies assessed as having a high risk of bias were excluded to avoid potential systematic errors and methodological flaws that could compromise the robustness of the findings (166). According to the Cochrane Handbook, including all eligible studies in a meta-analysis may improve precision by narrowing confidence intervals, but this approach risks introducing serious bias if some studies have substantial methodological flaws (167). Conversely, restricting the analysis to studies with a low risk of bias can minimise bias but may reduce precision if there are only a few studies at low risk of bias (167). To address this trade-off, this review included studies assessed as having a low risk of bias and those with some concerns, aiming to ensure methodological rigour by excluding studies assessed as having a high risk of bias, while maintaining sufficient comprehensiveness and precision to provide robust findings.

While alternative approaches to managing studies with a high risk of bias were considered, they were ultimately not adopted, in line with guidance from the Cochrane Handbook (167). For example, weighting studies by their risk of bias could theoretically balance bias and precision; however, bias-based weighting is currently underdeveloped and not recommended for Cochrane Reviews (167). Similarly, a stratified analysis, presenting effect estimates by bias level (e.g., for all studies, low-risk, and high-risk studies), was not pursued as it could complicate interpretation for readers seeking a single, unified estimate of effect (167). Another option was to include all studies with a narrative discussion of their risk of bias (167). However, this approach risks diluting clarity in the findings by incorporating studies with a high risk of bias without sufficiently down-weighting their influence (167). Lastly, Bayesian adjustments, while

possible, were not applied here due to the strong assumptions involved and the level of expertise required (167). This review instead prioritised interpretive clarity, methodological rigour, and robustness by including only studies meeting acceptable methodological standards, while acknowledging that this choice, though reducing bias, may limit absolute precision.

3.2.4 Assessment of Risk of Bias

Risk of bias assessments of the studies assessed as potentially eligible were conducted using the 'Revised Cochrane risk of bias tool for randomised trials (RoB 2 tool)' (Appendix 2) (168). Prior to the tool's use, calibration exercises, essential for enhancing reliability by ensuring its proper application, were conducted (169). A pilot risk of bias assessment on ten randomly selected studies was performed by two reviewers independently. They convened to discuss their evaluations of each study, aligning their interpretations with the tool's guidance (170).

The Cochrane RoB 2 tool was chosen for its ability to comprehensively evaluate methodological quality and risk of bias, outperforming alternatives such as the Jadad Scale and the PEDro Scale (171–173). The PEDro Scale is considered more comprehensive than the Jadad Scale in stroke rehabilitation research (171). A meta-epidemiological study on 41 Cochrane reviews and 353 physiotherapy trials, on the other hand, found that the Cochrane RoB 2 outperformed the PEDro in terms of risk of bias assessment (172). The thoroughness of the Cochrane ROB 2 tool in detecting bias is critical for assuring the high quality of the systematic review (174) by contributing to the reliability and validity of the review's conclusions. It also offers a standardised approach, enhancing comparability and consistency in bias evaluation.

The tool includes five domains: (1) randomisation process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, (5) selection of the results (170). Each domain includes several signalling questions, and the digital tool's algorithms assess bias risk at the domain level based on responses to these questions (170). The domain-level judgements are then used to determine the overall risk of bias in a study (170).

The review aimed to assess the intervention assignment effect (intention-to-treat (ITT) effect), which seeks to preserve the original randomisation to avoid selection bias (170). Evaluations in the "Deviations from intended interventions" domain of the tool were conducted with this focus.

For each study, the existence of a pre-specified analysis plan was confirmed by searching sources such as trial register entries (e.g., ClinicalTrials.gov), published protocols, or available statistical

analysis plans, using the trial registration number provided in the study reports. When these plans were electronically accessible, they were compared with the study reports, specifically focusing on outcome measures relevant to this review (170). Assessments in the "Selection of the reported result" domain of the tool were undertaken based on these comparisons.

3.2.5 Data Extraction

Studies that met the eligibility criteria underwent data extraction conducted by the lead reviewer using pre-designed forms. While time and resource constraints precluded the involvement of a second reviewer in the data extraction process, any uncertainties or inquiries that arose were resolved through consultation with the second reviewer, who had been involved in earlier stages of the review, and the supervisory team. Due to frequent dropouts and long-term follow-up issues in research, the review concentrated on the immediate post-intervention effects of exercise-based therapy, and data were extracted accordingly, ensuring that a larger number of stroke survivors was included in the analyses.

The extracted data were sample size (at baseline and outcome), baseline participant characteristics (age, biological sex, more affected side, time after stroke, stroke type), types of experimental and control interventions, intervention dosages (frequency; duration; intensity), a list of neuromuscular impairment and functional ability measures used, and the timing of outcome measures. Appendix 3 contains a list of outcome measures from the eligible studies included in the meta-analyses and meta-regressions. This list was compiled following the principles outlined in Section 1.9 of the literature review to ensure the accurate classification of outcome measures.

Since studies were expected to employ more than one measure of neuromuscular impairment and functional ability, and each study could only be included once in both a meta-analysis and meta-regression, a priority order was established for data extraction of outcome measures.

The priority order for measures of neuromuscular impairment was:

1. Fugl-Meyer Assessment (FMA) as this is an internationally recommended core measure of neuromuscular impairment after stroke (106) with reported substantial clinical utility and widespread use in stroke rehabilitation research and practice (175).
2. Kinematics-Derived Neuromuscular Impairment Variables, internationally recommended alongside the FMA for evaluating post-stroke neuromuscular impairments (106), provide objective assessments (176).

3. Grip Strength is recognised for its sensitivity, reliability, validity, and responsiveness as a measure of neuromuscular impairment (94, 177). Its focus on functional grip ability, a key indicator of patient independence, makes it particularly significant compared to other muscle strength measures.
4. Range of Motion (ROM). Changes in ROM post-stroke are typically observed before improvements in muscle strength and are associated with the ability to perform daily activities (178).
5. Muscle Strength provides a direct and quantifiable neuromuscular assessment (179).

The priority order employed in the selection of a functional ability measure was:

1. Action Research Arm Test (ARAT) is an internationally recommended core measure of functional ability (106).
2. Kinematics-Derived Functional Ability Variables, internationally recommended for use alongside the ARAT in post-stroke functional ability assessments (106), are also recognised for their objectivity (176).
3. Box and Block Test (BBT), a sensitive measure for monitoring functional ability over time in stroke survivors (177), demonstrates excellent test-retest reliability (180), and shows excellent concurrent (181) and convergent validity (182) when compared with the ARAT.
4. Wolf Motor Function Test - Performance Time (WMFT-PT) is a reliable and sensitive measure (121).

In instances where the prioritised outcome measures were not present, data was then extracted for available measures of neuromuscular impairment and functional ability.

When multiple measurements of ROM or muscle strength were provided in studies, a single measurement was selected for data extraction based on pre-defined criteria. These criteria were:

- Prioritised proximal joints' ROMs and proximal muscle groups' strengths measurements over distal ones. This is because movements generated at distal joints may be limited when it is challenging to achieve adequate stability at the proximal end of the limb (183).
- Movements that typically resist gravity, such as shoulder flexion when upright, were prioritised over those usually assisted by gravity, such as shoulder extension when upright, to mitigate gravity's confounding influence on findings.
- Measurements of ROM in the flexion direction and strength assessments of the flexor muscle groups were prioritised over those of their abduction counterparts, due to the greater functional relevance of flexion in UL activities (184).

After the selection of outcome measures for a study, mean and standard deviation (SD) values for changes from baseline to post-intervention were extracted. When the SDs for these changes were not reported, they were estimated using other available data, like p-values and CIs, following the Cochrane Handbook guidelines (185). In cases where SDs could not be estimated, the corresponding authors were contacted for further details.

3.2.6 Data Synthesis

Data were imported into and organised within STATA (version 17.0, StataCorp LLC) for tailored analyses per research aim.

Aim 1a: To evaluate whether exercise-based therapies more effectively improve neuromuscular impairments or functional abilities post-stroke, two separate meta-analyses were performed using STATA's 'Meta-Analysis' interface: one focused on neuromuscular impairments and the other on functional abilities. Effect sizes were calculated using Cohen's d, a standardised mean difference (SMD) approach. This was chosen to account for variations in trial settings, participant characteristics, and outcome measures (186, 187), ensuring consistent comparisons across various study conditions (186, 187). The 95% CIs were computed for each study and aggregated along with the effect sizes to determine overall effect sizes and 95% CIs. Cohen's d effect sizes were interpreted following the established criteria (188) (Table 6). To address potential heterogeneity among studies, a random effects model was employed, utilising the Hedges and Olkin standard error for more precise effect size calculations (189). Results were visualised using the 'Forest Plot' feature of the interface.

A STATA script was used to evaluate the statistical significance of differences in effects on neuromuscular impairments and functional abilities in response to exercise-based therapies versus control conditions, with a significance level set at $p < 0.05$.

Table 6. Interpretation of Cohen's d

Cohen's d Effect Size	Interpretation
d = 0 to 0.19	Trivial Effect
d = 0.2 to 0.5	Small Effect
d = 0.5 to 0.8	Moderate Effect
d = 0.8 or higher	Large Effect

Sensitivity Analyses: When there were studies with extreme effect sizes (outliers), that deviated substantially from the overall pattern of effect sizes in the analyses, sensitivity analyses were performed to test the robustness and stability of the results (190).

Aim 1b: To estimate the correlations between changes in neuromuscular impairments and functional abilities in responses to exercise-based therapies versus control conditions, a meta-regression analysis was performed using STATA's *'meta.regress'* command. Functional ability was used as the predictive variable. The correlations were plotted using STATA's *'estat bubbleplot'* command. The correlation coefficient (r value) and significance level (p-value) were reported. The correlation coefficient was assessed using pre-defined criteria (Table 7) (191). The significance level was set to $p < 0.05$.

Table 7. Interpretation of Correlation Coefficients

Size of Correlation	Interpretation
1 (-1)	Perfect positive (negative) correlation
0.9 to 0.99 (-0.9 to -0.99)	Almost perfect positive (negative) correlation
0.7 to 0.9 (-0.7 to -0.9)	High positive (negative) correlation
0.5 to 0.7 (-0.5 to -0.7)	Moderate positive (negative) correlation
0.3 to 0.5 (-0.3 to -0.5)	Fair positive (negative) correlation
0.1 to 0.3 (-0.1 to -0.3)	Poor positive (negative) correlation
0	None

Subgroup Analyses: For each of these research aims (**Aim 1a** and **Aim 1b**), subgroup analyses were conducted on studies reporting primary outcomes (FMA and ARAT) to limit variability from different outcome measures.

Heterogeneity: Heterogeneity in the data was assessed using the I^2 statistic, with reference values for interpretation based on the Cochrane Handbook (192). These values are as follows:

- 0% to 40%: may not be clinically important heterogeneity
- 30% to 60%: may suggest the presence of moderate heterogeneity
- 50% to 90%: may suggest the presence of substantial heterogeneity
- 75% to 100%: could represent considerable heterogeneity

Publication Bias: Funnel plots were utilised to check for asymmetry in the distribution of study outcomes. Egger's regression tests determined the presence of publication bias, with p-values < 0.05 indicating significant asymmetry and thus suggesting publication bias.

Note: Since the primary focus of this review is the general effects of exercise-based therapies, additional subgroup analyses performed were not reported here to keep it focused. These analyses, including the impact of timing on therapy efficacy and the effects of different exercise-

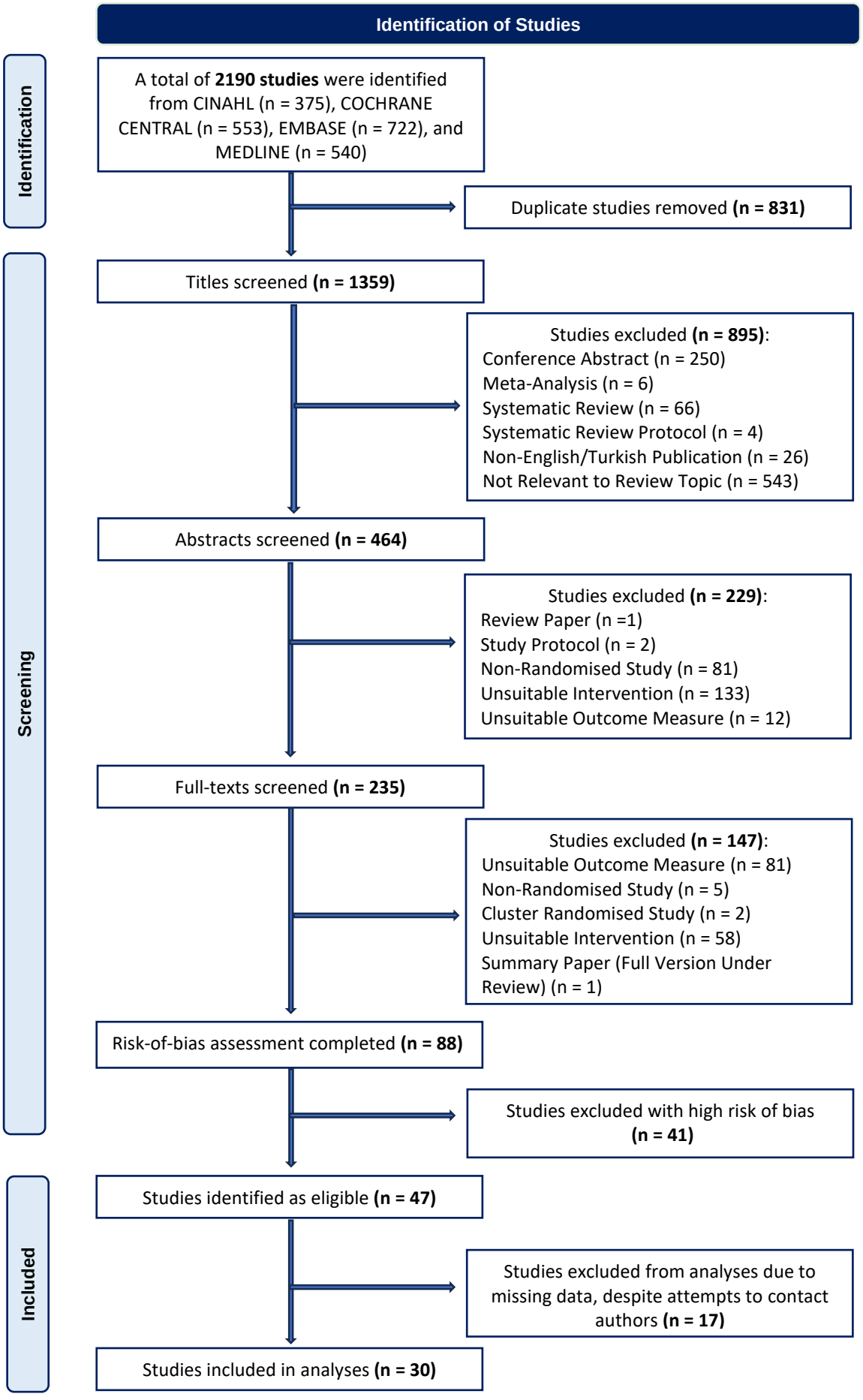
based therapies, as well as meta-regression analyses for subacute and chronic stroke survivors, are provided in Appendix 4.

3.3 Results

3.3.1 Search Results and Identification of Relevant Studies

An overview of the search results and the identification of relevant studies is provided in the PRISMA flow diagram (Figure 2) (193).

Figure 2. PRISMA Flow Diagram

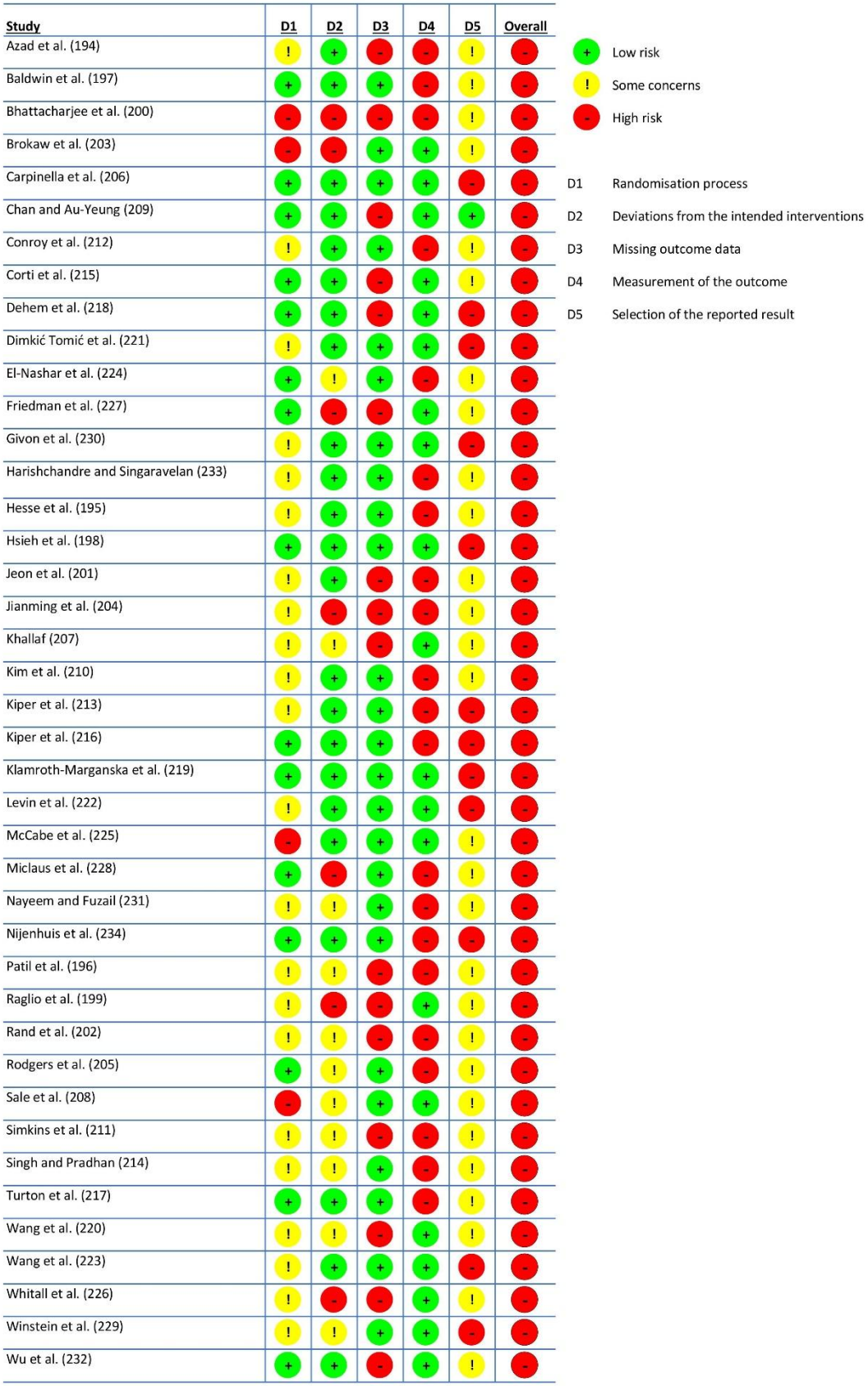


The electronic database search yielded 2190 studies. After removing duplicates, 1359 studies underwent title screening and 464 were taken forward for abstract screening. Of those, the full texts of the 235 studies were read, and 88 were taken to risk of bias assessment. Of those, 41 studies were assessed with a high risk of bias and excluded (Table 8; Figure 3). Of the remaining 47 eligible studies, 17 lacked the statistical data required for analyses, despite attempts to contact the corresponding authors. Consequently, 30 studies were included in the analyses.

Table 8. Studies Assessed as High Risk of Bias

Azad et al. (194)	Hesse et al. (195)	Patil et al. (196)
Baldwin et al. (197)	Hsieh et al. (198)	Raglio et al. (199)
Bhattacharjee et al. (200)	Jeon et al. (201)	Rand et al. (202)
Brokaw et al. (203)	Jianming et al. (204)	Rodgers et al. (205)
Carpinella et al. (206)	Khallaf (207)	Sale et al. (208)
Chan and Au-Yeung (209)	Kim et al. (210)	Simkins et al. (211)
Conroy et al. (212)	Kiper et al. (213)	Singh and Pradhan (214)
Corti et al. (215)	Kiper et al. (216)	Turton et al. (217)
Dehem et al. (218)	Klamroth-Marganska et al. (219)	Wang et al. (220)
Dimkić Tomić et al. (221)	Levin et al. (222)	Wang et al. (223)
El-Nashar et al. (224)	McCabe et al. (225)	Whitall et al. (226)
Friedman et al. (227)	Miclaus et al. (228)	Winstein et al. (229)
Givon et al. (230)	Nayeem and Fuzail (231)	Wu et al. (232)
Harishchandre and Singaravelan (233)	Nijenhuis et al. (234)	

Figure 3. Risk of Bias Assessment in Excluded Studies



3.3.2 Included Studies

The characteristics of the 30 studies included in the analyses are in Table 9. The characteristics of the remaining 17 eligible studies which are included in the review but could not be included in the analyses due to the unavailability of necessary statistical data are in Table 10.

Table 9. Characteristics of Eligible Studies Included in Analyses

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Abdullah et al. (235) RCT EI: 8; CI: 11	Robotic Therapy: 45 minutes/day, 3 days/week, continued until discharge	CT: 45 minutes/day, 3 days/week, continued until discharge	After the Intervention Period	▪ Age (Years) = EI: 75.7 (Range = 65–86); CI: 70.4 (Range = 41–83) ▪ Sex (Male:Female) = EI: 5:3; CI: 3:8 ▪ Time Since Stroke (Weeks) = EI: 4.3 (Range = 2–7); CI: 4.3 (Range = 1–8) ▪ More Affected Side (Left:Right) = EI: 3:5; CI: 6:4, 1 Both Sides ▪ Stroke Type (Isch:Haem) = Not Reported	CMSA – Arm: EI: 2 CI:2.36	CAHAI - 7 EI: 2.27 CI: 2.27
Almhdawi et al. (236) RCT EI: 10; CI: 10	Task-Orientated Training: 1.5 hours/session, twice weekly for 6 weeks + Daily Homework (Functional and Impairment Exercises): averaging 1–1.5 hours/day	No Therapy	Within a Week after the Intervention Period	▪ Age (Years) = EI: 61.1 (9.56); CI: 62.5 (8.54) ▪ Sex (Male:Female) = EI: 6:4; CI: 7:3 ▪ Time Since Stroke (Months) = EI: 62.3 (46.11); CI: 61.9 (45.24) ▪ More Affected Side (Left:Right) = EI: 3:7; CI: 2:8 ▪ Stroke Type (Isch:Haem) = Not Reported	Grip Strength = EI: 35.78 (28.37) CI: 27.02 (23.19)	WMFT-PT = EI: 33.94 (35.08) CI: 43.92 (29.46)
Amasyali and Yaliman (237) RCT EI: 9; CI: 8	Mirror Therapy: 30 minutes/day, 5 days/week for 3 weeks + CT: 2 hours/day, 5 days/week for 3 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 58.78 (10.12); CI: 65.38 (9.07) ▪ Sex (Male:Female) = EI: 4:5; CI: 4:4 ▪ Time Since Stroke (Months) = EI: 4.11 (2.14); CI: 6.50 (1.60) ▪ More Affected Side (Left:Right) = EI: 5:4; CI: 1:7 ▪ Stroke Type (Isch:Haem) = EI: 9:0; CI: 8: 0	FMA = EI: 36.55 (17.80) CI: 39.87 (17.74)	BBT = EI: 11.67 (11.56) CI: 12.50 (12.87)
Antoniotti et al. (238) RCT EI: 16; CI:19	Mirror Therapy: 30 minutes/day, 5 days/week for 30 days + CT: 90 minutes/day, 5 days/week for 30 days	Sham Therapy: 30 minutes/day, 5 days/week for 30 days + CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 68.2 (14.4); CI: 69.5 (14.1) ▪ Sex (Male:Female) = EI: 14:6; CI: 12:8 ▪ Time Since Stroke (Days) = EI: 23.3 (6.57); CI: 22 (9.28) ▪ More Affected Side (Left:Right) = EI: 13:7; CI: 13:7 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 28.5 (21.8) CI: 30.9 (23.9)	ARAT = EI: 23.5 (24.0) CI: 25.1 (25.5)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Askin et al. (239) RCT EI: 18; CI: 20	Virtual Reality Training (Kinect-Based): 1 hour/day, 5 days/week for 4 weeks + CT: 5 days/week for 4 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 53.27 (11.9); CI: 56.55 (9.85) ▪ Sex (Male:Female) = EI: 13:5; CI: 14:6 ▪ Time Since Stroke (Months) = EI: 20.27 (5.47); CI: 19.40 (4.48) ▪ More Affected Side (Left:Right) = EI: 10:8; CI: 10:10 ▪ Stroke Type (Isch:Haem) = EI: 16:2; CI: 19:1	FMA (Med [min;max]) = EI: 39 [22;56] CI: 30.5 [19;58]	BBT (Med [min;max]) = EI: 4 [0;64] CI: 0.5 [0;39]
Carmeli et al. (240) RCT EI: 16; CI: 15	Impairment-Oriented Training with Augmented Feedback (via HandTutor system): 20–30 minutes/day, 5 days/week for 3 weeks	CT: 20-30 minutes/day, 5 days/week for 3 weeks	Immediately after the Intervention Period	▪ Age (Years) = EI: 57.8 (8.9); CI: 62.5 (5) ▪ Sex (Male:Female) = EI: 11:5; CI: 11:4 ▪ Time Since Stroke (Days) = EI: 8.41 (7.54); CI: 11.25 (8.24) ▪ More Affected Side (Left:Right) = EI: 10:6; CI: 5:10 ▪ Stroke Type (Isch:Haem) = EI: 14:2; CI: 13:2	FMA = EI: 46.8 (13.1) CI: 49.3 (9.4)	BBT = EI: 18.1 (10.9) CI: 25.5 (14.3)
Ehrensberger et al. (241) RCT EI:17; CI:15	Mirror Therapy with Unilateral Maximal Isometric Strength Training: 20 minutes/day, 3 times/week for 4 weeks	CT: Unilateral Maximal Isometric Strength Training: 20 minutes/day, 3 times/week for 4 weeks	Between 48 Hours and 7 Days after the Last Intervention Session	▪ Age (Years) = EI: 61.12 (Range = 32–90); CI: 63.53 (Range = 36–80) ▪ Sex (Male:Female) = EI: 10:7; CI: 11: 4 ▪ Time Since Stroke (Months) = EI: 74.76 (74.58); CI: 90.07 (83.33) ▪ More Affected Side (Left:Right) = EI: 10:7; CI: 7:8 ▪ Stroke Type (Isch:Haem) = Not Reported	Muscle Strength – Elbow Extensors (Highest Peak Torque) EI: 24.58 (17.55); n = 16 CI: 24 (13.93); n = 14	CAHAI - 8 EI: 34.53 (21.64); n = 17 CI: 34.57 (21.86); n = 14
Graef et al. (242) RCT EI: 13; CI: 14	Functional Strengthening Training: 30 minutes/day, 3 times/week for 5 weeks	CT: 30 minutes/day, 3 times/week for 5 weeks	Immediately after the Intervention Period	▪ Age (Years) = EI: 72 (12); CI: 63 (11) ▪ Sex (Male:Female) = EI: 6:7; CI: 5:9 ▪ Time Since Stroke (Years) = EI: 2.0 (1.4); CI: 2.8 (1.4) ▪ More Affected Side (Left:Right) = EI: 5:8; CI: 3:11 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 49.3 (11.81) CI: 43.92 (12.25)	TEMPA: FR - Unilateral Tasks EI: - 3.84 (3.38) CI: - 5.78 (4.64)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Hsieh et al. (243) RCT EI: 16; CI: 15	Robotic Therapy (Bilateral Robotic Priming): 40-45 minutes/day, 5 days/week for 4 weeks + CT: 40-45 minutes/day, 5 days/week for 4 weeks	CT: 90 minutes/day, 5 days/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 49.28 (10.90); CI: 52.87 (10.40) ▪ Sex (Male:Female) = EI: 11:5; CI: 7:8 ▪ Time Since Stroke (Months) = EI: 2.56 (1.69); CI: 2.21 (1.11) ▪ More Affected Side (Left:Right) = EI: 8:8; CI: 11:4 ▪ Stroke Type (Isch:Haem) = EI: 8:8; CI: 8:7	FMA = EI: 26.81 (12.13) CI: 29.07 (16.12)	BBT = EI: 5.31 (7.91) CI: 8.6 (12.29)
Hunter et al. (244) RCT EI: 145; CI: 143	Functional Strength Training: 90 minutes/day, 5 days/week for 6 weeks	CT: Movement Performance Therapy: 90 minutes/day, 5 days/week for 6 weeks	Within ± 7 Working Days after the Intervention Period	▪ Age (Years) = EI: 71.9 (12.7); CI: 72.4 (12.3) ▪ Sex (Male:Female) = EI: 96:49; CI: 90:53 ▪ Time Since Stroke Onset (Days) = EI: ≤ 30 = 86 (59.3); ≥ 31 = 59 (40.7); CI: ≤ 30 = 84 (58.7); ≥ 31 = 59 (41.3) ▪ More Affected Side (Left:Right) = EI: 82:63; CI: 85:58 ▪ Stroke Type (Isch:Haem) = EI: 131:14; CI: 132:11	Grip Strength EI: 7.6 (8.72); n = 122 CI: 7.2 (8.19); n = 115	ARAT EI: 24.40 (18.45); n = 126 CI: 26.50 (17.78); n = 114
Huseyinsinoglu, Ozdincler and Krespi (245) RCT EI: 11; CI: 11	Constrained-Induced Movement Therapy: 3 hours/day for 10 consecutive weekdays + Mitt use on the less affected hand for 90% of waking hours over 12 consecutive days.	CT: 1 hour/day for 10 consecutive weekdays	After the Intervention Period	▪ Age (Years) = EI: 49.1 (13.7); CI: 48.2 (15.4) ▪ Sex (Male:Female) = EI: 7:4; CI: 5:6 ▪ Time Since Stroke (Months) = EI: 10.6 (6.1); CI: 13.1 (6.3) ▪ More Affected Side (Left:Right) = Not Reported ▪ Stroke Type (Isch:Haem) = EI: 7:4; CI: 10:1	Motor Evaluation Scale for Arm in Stroke Patients EI: 43 (7.42) CI: 38 (12.2)	WMFT-PT = EI: 25.6 (19) CI: 31.5 (23.7)
Johnson et al. (246) RCT EI: 28; CI: 30	Virtual-Reality Therapy (Juntronix Rehabilitation System with Microsoft Xbox Kinect camera): 45 minutes/day, 2 non-consecutive days/week for 8 weeks	No Therapy	Post-intervention, Exact Timing not Specified	▪ Age (Years) = EI: 64.7 (13.9); CI: 59.3 (15.6) ▪ Sex (Male:Female) = EI: 17:11; CI: 14:16 ▪ Time Since Stroke (Years) = EI: 12.1 (7.6); CI: 15.3 (10.1) ▪ More Affected Side (Left:Right) = EI: 13:15; CI: 12:18 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 36.6 (5.6) CI: 38.2 (5.1)	ARAT = EI: 31.5 (6.3) CI: 29.8 (5.8)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Lee et al. (247) RCT EI: 15; CI: 15	Bilateral Arm Training: 30 minutes/day, 5 days/week for 8 weeks + CT: 30 minutes/day, 5 days/week for 8 weeks	CT: 1 hour/day, 5 days/week for 8 weeks	Post-intervention, Exact Timing not Specified	▪ Age (Years) = EI: 57.33 (9.88); CI: 54.60 (16.03) ▪ Sex (Male:Female) = EI: 9:6; CI: 10:5 ▪ Time Since Stroke = EI: 7-12 Months = 4; 13-24 Months = 3; ≥ 25 Months = 8; CI: 7-12 Months = 5; 13-24 Months = 5; ≥ 25 Months = 5 ▪ More Affected Side (Left:Right) = EI: 5:10; CI: 6:9 ▪ Stroke Type (Isch:Haem) = EI: 7:8; CI: 6:9	FMA = EI: 48.73 (16.42) CI: 46.60 (12.03)	BBT = EI:25.46 (10.41) CI: 20.86 (14.96)
Meng et al. (248) RCT EI: 64; CI: 64	Hand-Arm Bimanual Training: 2 hours/day, 5 days/week for 2 weeks	CT: 2 hours/day, 5 days/week, for 2 weeks	After the Intervention Period	▪ Age (Years) = EI: 55.38 (6.97); CI: 55.19 (7.82) ▪ Sex (Male:Female) = EI: 34:30; CI: 31:33 ▪ Time Since Stroke (Hours) = EI: 8.87 (2.69); CI: 9.08 (2.35) ▪ More Affected Side (Left:Right) = EI: 35:29; CI: 33:31 ▪ Stroke Type (Isch:Haem) = EI: 50:14; CI: 45:19	FMA = EI: 33.25 (5.89) CI: 32.86 (5.11)	ARAT = EI: 30.31 (6.07) CI: 31.48 (5.94)
Michielsen et al. (249) RCT EI: 20; CI: 20	Mirror Therapy: 1 hour/day, 5 days/week for 6 weeks	Sham Therapy: 1 hour/day, 5 days/week for 6 weeks	Immediately after the Intervention Period	▪ Age (Years) = EI: 55.3 (12.0); CI: 58.7 (13.5) ▪ Sex (Male:Female) = EI: 7:13; CI: 13:7 ▪ Time Since Stroke (Years) = EI: 4.7 (3.6); CI: 4.5 (2.6) ▪ More Affected Side (Left:Right) = Not Reported ▪ Stroke Type (Isch:Haem) = EI: 14:6; CI: 14:6	FMA = EI: 39.7 (14.1) CI: 36.4 (14.7)	ARAT = EI: 23.8 (15.8) CI: 20.6 (17.0)
Milot et al. (250) RCT EI: 6; CI: 6	Strength Training: 1 hour/day, 3 days/week for 4 weeks	CT: 1 hour/day, 3 days/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 64 (9); CI: 68 (6) ▪ Sex (Male:Female) = Not Reported ▪ Time Since Stroke (Months) = EI: 47 (18); CI: 58 (79) ▪ More Affected Side (Left:Right) = EI: 5:1; CI: 4:2 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 50 (17) CI: 56 (7)	WMFT-PT = EI: 13.6 (25.6) CI: 3.1 (0.9)
Park et al. (251) RCT EI: 22; CI: 21	Game-Based Hand Resistance Exercises (TPS 100, Cybermedic Inc): 30 minutes/day, 5 days/week for 6 weeks + CT: 30 minutes/day, 5 days/week for 6 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 56.91 (13.31); CI: 61.95 (10.24) ▪ Sex (Male:Female) = EI: 14:8; CI: 12:9 ▪ Time Since Stroke (Months) = EI: 3.86 (1.61); CI: 3.57 (1.12) ▪ More Affected Side (Left:Right) = EI: 10:12; CI: 12:9 ▪ Stroke Type (Isch:Haem) = EI: 10:12; CI: 10:11	Grip Strength = EI: 5.37 (1.85) CI: 6.11 (1.52)	BBT = EI: 15.64 (2.75) CI: 16.38 (2.92)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Park et al. (252) RCT EI: 12; CI: 13	Virtual-Reality Therapy: 30 minutes/day, 5 days/week for 4 weeks + CT: 30 minutes/day, 5 days/week for 4 weeks	CT: 1 hour/day, 5 days/week for 4 weeks	Immediately after the Intervention Period	▪ Age (Years) = EI: 53.5 (13.0); CI: 51.5 (16.7) ▪ Sex (Male:Female) = EI: 7:5; CI: 8:5 ▪ Time Since Stroke (Days) = EI: 982.3 (1473.3); CI: 533.5 (635.3) ▪ More Affected Side (Left:Right) = Not Reported ▪ Stroke Type (Isch:Haem) = EI: 5:7; CI: 8:5	FMA = EI: 17.1 (7.5) CI: 19.9 (9.9)	WMFT-PT = EI: 3.1 (0.1) CI: 3.0 (0.2)
Prange et al. (253) RCT EI: 35; CI: 33	Weight-Supported Arm Training with Video Games: 30 minutes/day, 3 times/week for 6 weeks	CT: 30 minutes/day, 3 times/week for 6 weeks	After the Intervention Period	▪ Age (Years) = EI: 60.3 (9.7); CI: 58 (11.4) ▪ Sex (Male:Female) = EI: 17:18; CI: 24:19 ▪ Time Since Stroke (Weeks) = EI: 7.3 (3.4); CI: 6.8 (3.1) ▪ More Affected Side (Left:Right) = EI: 10:25; CI: 17:16 ▪ Stroke Type (Isch:Haem) = EI: 28:7; CI: 25:8	FMA = EI: 21.6 (14.7) CI: 27.3 (16.4)	Stroke Upper Limb Capacity Scale = EI: 2.5 (1.7) CI: 3.3 (2.7)
Rodrigues et al. (254) RCT EI: 8; CI: 8	Mirror Therapy: 1 hour/day, 3 days/week for 4 weeks	Sham Therapy: 1 hour/day, 3 days/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 58.4 (8.3); CI: 56.6 (5.3) ▪ Sex (Male:Female) = EI: 4:4; CI: 6:2 ▪ Time Since Stroke (Months) = EI: 33.5 (22.6); CI: 36.1 (31.2) ▪ More Affected Side (Left:Right) = EI: 5:3; CI: 6:2 ▪ Stroke Type (Isch:Haem) = EI: 8:0; CI: 8:0	FMA = EI: 36.3 (5.6) CI: 40.6 (6.9)	TEMPA: FR - Unilateral Tasks EI: 7.4 (3.0) CI: 6.1 (3.0)
Shimodozono et al. (255) RCT EI: 26; CI: 23	Repetitive Facilitative Therapy: 40 minutes/day, 5 days/week for 4 weeks + CT: 30 minutes/day, 5 days/week for 4 week	CT: 70 minutes/day, 5 days/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 63.9 (12.4); CI: 67.0 (15.0) ▪ Sex (Male:Female) = EI: 16:10; CI: 10:13 ▪ Time Since Stroke Onset (Weeks) = EI: 6.4 (2.1); CI: 7.4 (3.0) ▪ More Affected Side (Left:Right) = EI: 13:13; CI: 13:10 ▪ Stroke Type (Isch:Haem) = EI: 12:14; CI: 12:11	FMA = EI: 39.2 (20.1) CI: 39.5 (21.5)	ARAT = EI: 19.0 (19.5) CI: 19.8 (22.6)
Thrane et al. (256) RCT EI: 24; CI: 23	Constraint-Induced Movement Therapy: 3 hours/day for 10 consecutive weekdays + Mitt use on the less affected arm for 90% of waking hours	CT: Provided according to Norwegian Stroke Unit Guidelines (Specific Details not Provided).	After the Intervention Period	▪ Age (Years) = EI: 65.3 (8.0); CI: 61 (14.8) ▪ Sex (Male:Female) = EI: 19:5; CI: 17:6 ▪ Time Since Stroke (Days) = EI: 16.6 (7.2); CI: 18.0 (6.5) ▪ More Affected Side (Left:Right) = EI: 14:10; CI: 11:12 ▪ Stroke Type (Isch:Haem) = EI: 23:1; CI: 20:3	FMA = 49.4 (11.8) 50.1 (9.4)	WMFT-PT (LogWMFT Time) EI: 0.69 (0.49) CI: 0.62 (0.50)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Timmermans et al. (257) RCT EI: 20; CI: 19	Mental Practice (Video-Instructed): 10-minute sessions, at least 3 times/day for 6 weeks	CT: 10-minute sessions, at least 3 times/day for 6 weeks	After the Intervention Period	▪ Age (Years) = EI: 59.7 (7.3); CI: 58.7 (9.6) ▪ Sex (Male:Female) = EI: 13:8; CI: 13:8 ▪ Time Since Stroke (Days) = EI: 36.1 (27.4); CI: 32.3 (17.9) ▪ More Affected Side (Left:Right) = EI: 14:7; CI: 10:11 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 41.6 (17.4) CI: 45.4 (15.6)	WMFT-PT EI: 5.8 (3.3) CI: 5.1 (3.3)
Timmermans et al. (258) RCT EI: 11; CI: 11	Robot-Assisted Task-Oriented Therapy (Haptic Master): 1 hour/day, 4 days/week for 8 weeks	CT: 1 hour/day, 4 days/week for 8 weeks	After the Intervention Period	▪ Age (Years) = EI: 61.8 (6.8); CI: 56.8 (6.4) ▪ Sex (Male:Female) = EI: 8:3; CI: 8:3 ▪ Time Since Stroke (Years) = EI: 2.8 (2.9); CI: 3.7 (3.0) ▪ More Affected Side (Left:Right) = EI: 7:4; CI: 8:3 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA Med. [IQR] = EI: 50 [39,58] CI: 53 [47,57]	ARAT Med. [IQR] = EI: 31 [24,40] CI: 39 [28,46]
Turkbey, Kutlay and Gok (259) RCT EI: 10; CI: 9	Upper Limb Therapy with Video Games (Xbox KinectTM): 1 hour/day, 5 times/week for 4 weeks + CT: 1 hour/day, 5 times/week for 4 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 61.70 (Range = 38–79); CI: 62.44 (Range = 47–79) ▪ Sex (Male:Female) = EI: 6:4; CI: 8:1 ▪ Time Since Stroke (Days) = EI: 46.80 (Range = 13–125); CI: 47.67 (Range = 28–116) ▪ More Affected Side (Left:Right) = EI: 8:2; CI: 4:5 ▪ Stroke Type (Isch:Haem) = EI: 9:1; CI: 9:0	Brunnstrom Motor Recovery Stage - UL EI: 5.80 (0.63) CI: 5.33 (1.00)	BBT = EI: 18.8 (12.19) CI: 20 (13.13
Tyson et al. (260) RCT EI: 62; CI: 31	Mirror Therapy: Up to 30 minutes/day for 4 weeks.	No therapy	After the Intervention Period	▪ Age (Years) = EI: 64 (15); CI: 64 (13) ▪ Sex (Male:Female) = EI: 37:25; CI: 23:8 ▪ Time Since Stroke (Days) = EI: 26 (18); CI: 35 (27) ▪ More Affected Side (Left:Right) = EI: 35:27; CI: 20:11 ▪ Stroke Type (Isch:Haem) = EI: 50:12; CI: 26:5	Grip Strength = EI: 4 (7) EI: 2 (3)	ARAT = EI: 13 (18) CI: 10 (15)
Wolf et al. (261) RCT EI: 51; CI: 48	Robotic Therapy (Hand Mentor Pro): 2 hours/day, 5 days/week for 8 weeks + CT: 1 hour/day, 5 days/week for 8 weeks	CT: 3 hours/day, 5 days/week for 8 weeks	After the Intervention Period	▪ Age (Years) = EI: 59.1 (14.1); CI: 54.7 (12.2) ▪ Sex (Male:Female) = EI: 25:26; CI: 31:17 ▪ Time Since Stroke (Days) = EI: 115.5 (53.1); CI: 127.1 (46.2) ▪ More Affected Side (Left:Right) = EI: 31:20; CI: 25:23 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA (Mean [95 CI]) = EI: 34.1 [24.2; 44] CI: 33.3 [23.6; 43]	ARAT (Mean [95% CI]) = EI: 34.4 [24.7; 44.0] CI: 31.1 [22.1; 40.1]

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Wu et al. (262) RCT EI: 20; CI: 18	Constraint-Induced Movement Therapy with Trunk Restraint: 2 hours/day, 5 days/week for 3 weeks + Mitt use on the less affected hand: 6 hours/day for 3 weeks	CT: 2 hours/day, 5 days/week for 3 weeks	After the Intervention Period	▪ Age (Years) = EI: 54.0 (9.7); CI: 58.6 (11.6) ▪ Sex (Male:Female) = EI: 16:4; CI: 14:4 ▪ Time Since Stroke (Months) = EI: 15.7 (13.5); CI: 17.7 (13.4) ▪ More Affected Side (Left:Right) = EI: 8:12; CI: 13:5 ▪ Stroke Type (Isch:Haem) = Not Reported	KD - Normalised Shoulder Flexion EI: 0.14 (0.07) CI: 0.17 (0.07)	ARAT = EI: 35.9 (16.7) CI: 30.1 (19.8)
Wu et al. (263) RCT EI: 16; CI: 17	Mirror Therapy: 1 hour/day, 5 days/week for 4 weeks + CT: 30 minutes/day, 5 days/week for 4 weeks	CT: 1.5 hours/day, 5 days/week for 4 weeks	Immediately after the Intervention Period	▪ Age (Years) = EI: 54.77 (11.66); CI: 53.59 (10.21) ▪ Sex (Male:Female) = EI: 11:5; CI: 12:5 ▪ Time Since Stroke (Months) = EI: 19.31 (12.57); CI: 21.88 (15.55) ▪ More Affected Side (Left:Right) = EI: 8:8; CI: 10:7 ▪ Stroke Type (Isch:Haem) = EI: 10:6; CI: 10:7	FMA = EI: 45.94 (8.91) CI: 44.41 (10.69)	KD - Normalised Movement Time [s/mm] = EI: 0.009 (0.006) CI: 0.006 (0.002)
Zondervan et al. (264) RCT EI: 8; CI: 8	High-Repetition Home Therapy (Mechanical Device: Resonating Arm Exerciser): Participants were instructed to exercise for 3 hours/week, at least 3 times/week for 3 weeks	CT: Participants were instructed to exercise 3 hours/week, at least 3 times/week for 3 weeks	After the Intervention Period	▪ Age (Years) = EI: 61 (17); CI: 54 (14) ▪ Sex (Male:Female) = EI: 6:2; CI: 7:1 ▪ Time Since Stroke (Months) = EI: 39 (46); CI: 19 (9) ▪ More Affected Side (Left:Right) = EI: 5:3; CI: 7:1 ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 19 (9) CI: 24 (8)	BBT = Only changes from baseline were reported; baseline data was unavailable.

Note: EI: Experimental Intervention; **CI:** Control Intervention (applies to participant and outcome measure descriptions in this table); **Isch:** Ischaemic; **Haem:** Haemorrhagic; **FMA:** Fugl-Meyer Assessment; **ARAT:** Action Research Arm Test, **KD:** Kinematics-Derived; **BBT:** Box and Block Test, **WMFT-PT:** Wolf Motor Function Test – Performance Time; **CAHAI:** Chedoke Arm and Hand Activity Inventory; **TEMPA: FR:** The Upper-Extremity Performance-Functional Rating Test; **CMSA:** Chedoke McMaster Stroke Assessment; **Med:** Median; **IQR:** Interquartile Range; **min:** minimum; **max:** maximum; **CI:** Confidence Interval (statistical value); **s/mm:** seconds/millimetres. The 'Sample Size' indicates the number of participants at baseline. Where baseline sample sizes differed for specific outcomes, 'n' denotes these variations. Data are presented as Mean (SD) unless otherwise specified in the table.

Table 10. Characteristics of Eligible Studies Not Included in Analyses

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Coroian et al. (265) RCT EI: 10; CI: 10	Isokinetic Strength Training (using CON-TREX dynamometer): 45 minutes/session, 3 days/week for 6 weeks + CT: 1 hour and 45 minutes/session, 3 days/week for 6 weeks	CT: 2.5 hours/ session, 3 days/week for 6 weeks	After the Intervention Period (Days 45-60 from the first session)	▪ Age (Years) = EI: 63.6 (12.6); CI: 63.6 (10.6) ▪ Sex (Male:Female) = EI: 8:2; CI: 8:2 ▪ Time Since Stroke (Months) = EI: 32.2; CI: 29.1 ▪ More Affected Side (Left:Right) = EI: 1:9; CI: 3:7 ▪ Stroke Type (Isch:Haem) = EI: 9:1; 7:3	FMA = EI: 43.1 (11.0) CI: 46.9 (6.4)	BBT = EI: 14.5 (10.3) CI: 12.1 (12.3)
Crosbie et al. (266) RCT EI: 9; CI: 9	Virtual Reality Therapy: 30-45 minutes/session, 3 sessions/week for 3 weeks	CT: 30-45 minutes/session, 3 sessions/week for 3 weeks	After the Intervention Period	▪ Age (Years) = EI: 56.1 (14.5); CI: 64.6 (7.4) ▪ Sex (Male:Female) = EI: 5:4; CI: 5:4 ▪ Time Since Stroke (Months) = EI: 10 (6.4); CI: 11.7 (7.8) ▪ More Affected Side (Left:Right) = EI: 5:4; CI: 6:3 ▪ Stroke Type (Isch:Haem) = Not Reported	Motricity Index = EI: 81.7 (9.4) CI: 77.4 (19.5)	ARAT = EI: 51.3 (8.2) CI: 47.3 (18.1)
Dodzo et al. (267) RCT EI: 5; CI: 5	Strengthening Therapy (Graded Arm Strengthening Program [GRASP]): Advised self-practice for at least 1 hour/day, 5 days/week for 4 weeks	CT: Advised Self-Practice for at least 1 hour/day, 5 days/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 58 (Range = 30–83); CI: 62 (Range = 52–77) ▪ Sex (Male:Female) = EI: 1:4; CI: 3:2 ▪ Time Since Stroke (Days) = EI: 130 (Range = 56–285); CI: 137 (Range = 24–240) ▪ More Affected Side (Left:Right) = EI: 3:2; CI: 4:1 ▪ Stroke Type (Isch:Haem) = Not Reported	Grip Strength = EI: 11.5 CI: 4.5	WMFT-PT Only changes from the baseline were reported; the baseline mean was unavailable.
Khan et al. (268) RCT EI: 13; CI: 14	Constrained Induced Movement Therapy: 15-20 hours/week + Self-Training: 5 hours/week (duration unspecified likely until discharge)	CT: 15-20 hours/week (duration unspecified likely until discharge)	After the Intervention Period	▪ Age (Years) = EI: 60.4 (16.1); CI: 60.4 (14.8) ▪ Sex (Male:Female) = EI: 10:3; CI: 7:7 ▪ Time Since Stroke (Months) = EI: 5.2 (10.9); CI: 15.7 (40.4) ▪ More Affected Side (Left:Right) = EI: 5:8; CI: 8:6 ▪ Stroke Type (Isch:Haem) = Not Reported	ROM (Shoulder Flexion) = EI: 76.5 (56.6) CI: 68.6 (59.7)	WMFT-PT = EI: 64.5 (38.4) CI: 58.7 (38.6)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Kong et al. (269) RCT EI: 33; CI: 35	Virtual Reality Therapy: 1 hour/session, 4 times/week for 3 weeks + CT: 1 hour/day, 5 times/week for 3 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 58.1 (9.1); CI: 55.8 (11.5) ▪ Sex (Male:Female) = EI: 27:6; CI: 25:10 ▪ Time Since Stroke (Days) = EI: 14.2 (8.9); CI: 13.1 (8.6) ▪ More Affected Side (Left:Right) = EI: 20:13; CI: 24:11 ▪ Stroke Type (Isch:Haem) = EI:25:8; CI: 27:8	FMA = EI: 14.6 (12.6) CI: 18.0 (14.4)	ARAT = EI: 5.1 (9.6) CI: 8.3 (10.4)
Lee et al. (270) RCT EI: 14; CI: 10	Robotic Therapy: 1 hour/session, 2 times/week for 6 weeks	CT: 1 hour/session, 2 times/week for 6 weeks	After the Intervention Period	▪ Age (Years) = EI: 59.56 (8.29); CI: 53.5 (12.33) ▪ Sex (Male:Female) = EI: 9:5; CI: 7:3 ▪ Time Since Stroke (Years) = EI: 2.4; CI 2.4 ▪ More Affected Side (Left:Right) = EI: 9:5; CI: 8:2 ▪ Stroke Type (Isch:Haem) = EI: 9:5; CI: 4:6	FMA = Baseline data for each group separately are unavailable.	BBT = Baseline data for each group separately are unavailable.
Masiero et al. (271) RCT EI: 14; CI: 16	Robotic Therapy (Neurorehabilitation Robot [NeReBot]): 35% of exercise time + CT: 65% of exercise time – 2 hours/day, 5 times/week for 5 weeks	CT: 100% of exercise time – 2 hours/day, 5 times/week for 5 weeks	After the Intervention Period	▪ Age (Years) = EI: 65.6 (9.2); CI: 66.83 (7.9) ▪ Sex (Male:Female) = EI: 10:4; CI: 10:6 ▪ Time Since Stroke (Days) = EI: 8.34 (3.2); CI: 10.23 (2.4) ▪ More Affected Side (Left:Right) = EI: 3:11; CI: 3:13 ▪ Stroke Type (Isch:Haem) = EI: 12:2; CI: 14:2	FMA (Med [IQR]) = EI: 36 [28, 48] CI: 25 [8, 47]	BBT (Median [IQR]) = EI: 13 [2, 16] CI: 3 [0, 15]
Norouzi-Gheidari et al. (272) RCT EI: 9; CI: 9	Virtual Reality Training (using Microsoft Kinect): 30 minutes/session, 2 to 3 times/week for 4 weeks + CT: 2 to 3 times/week for 4 weeks	CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 42.2 (9.5); CI: 57.6 (10.5) ▪ Sex (Male:Female) = EI: 5:4; CI: 5:4 ▪ Time Since Stroke (Months) = EI: 5.7 (3.2); CI: 8.4 (7.8) ▪ More Affected Side (Left:Right) = EI: 5:4; CI: 6:3 ▪ Stroke Type (Isch:Haem) = EI: 7:2; CI: 8:1	FMA = EI: 44.2 (18.8) CI: 48 (11.4)	BBT = EI: 27 (23.5) CI: 33.1 (14.3)
Page et al. (273) RCT EI: 8; CI: 8	Mental Practice: 20 minutes/session, 3 times/week for 10 weeks + CT: 30 minutes/session, 3 times/week for 10 weeks	Sham Therapy: 20 minutes/session, 3 times/week for 10 weeks + CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = EI: 66.4 (6.3); CI: 54.0 (18.5) ▪ Sex (Male:Female) = Not Reported ▪ Time Since Stroke = > 12 months (no further information provided) ▪ More Affected Side (Left:Right) = Not Reported ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = EI: 29.1 (14.2) CI: 32.1 (12.5)	ARAT = EI: 21.9 (20.0) CI: 24.1 (14.0)

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Patten et al. (274) RCT EI: 10; CI: 9	Power Training: 35 minutes/session, 3 times/week for 4 weeks + CT: 40 minutes/session, 3 times/week for 4 weeks	CT: 75 minutes/ session, 3 times/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 72.9 (11.1); CI: 64.7 (9.7) ▪ Sex (Male:Female) = EI: 9:1; CI: 6:3 ▪ Time Since Stroke (Months) = EI: 11.4 (4.3); CI: 14.7 (2.7) ▪ More Affected Side (Left:Right) = EI: 5:5; CI: 5:4 ▪ Stroke Type (Isch:Haem) = EI: 7:2 and 1 Infarct w/haemorrhagic conversion; CI: 7:2	FMA = EI: 43.2 (10.6) CI: 37.3 (13.1)	WMFT-FA = EI: 3.1 (0.8) CI: 2.9 (1.1)
Sale, Ceravolo and Franceschini (275) RCT EI: 33; CI: 34	Action Observation Therapy: 15 minutes/session, 2 times/day, 5 days/week for 4 weeks + CT: At least 2 hours/ day, 5 days/week for 4 weeks	Sham Therapy: 30 minutes/day, 5 days/week for 4 weeks + CT: Same as Exercise-Based Therapy Group	After the Intervention Period	▪ Age (Years) = 66.5 (12.7) in total ▪ Sex (Male:Female) = 41:26 in total ▪ Time Since Stroke (Days) = 29.6 (4.5) in total ▪ More Affected Side (Left:Right) = 37:30 in total ▪ Stroke Type (Isch:Haem) = Not Reported	FMA = Only changes from the baseline were reported; baseline mean values were unavailable.	BBT = Only changes from the baseline were reported; baseline mean values were unavailable.
Sánchez-Sánchez et al. (276) RCT EI: 7; CI:8	Strength Training + Bimanual Exercises: 75 minutes/session for 12 weeks, 33 sessions in total	No Therapy	Immediately after the Intervention Period	▪ Age (Years) (Mean [95% CI]) = EI: 57.6 [46.6; 68.5]; CI: 62.4 [53.0; 71.7] ▪ Sex (Male) = EI: 71.4%; CI: 37.5% ▪ Time Since Stroke (Months) (Mean [95% CI] = EI: 41.3 [9.6; 73.0]; CI: 33.8 [11.8; 55.7] ▪ More Affected Side (Right) = EI: 14.3%; CI: 37.5% ▪ Stroke Type (Isch) = EI: 62.5%; CI: 71.4%	FMA (Mean [95%CI]) = EI: 37.57 (23.46; 51.67) CI: 47 (33.8; 60.19)	WMFT-FA (Mean [95%CI]) = EI: 3.45 (2.17; 4.73) CI: 3.64 (2.44; 4.83)
Saposnik et al. (277) RCT EI: 71; CI: 70	Virtuality Reality Training (using Nintendo Wii gaming system): 1 hour/session, 5 days/week for 2 weeks	CT: 1 hour/session, 5 days/week for 2 weeks	After the Intervention Period	▪ Age (Years) = EI: < 55 = 19, 56-69 = 34, 70 (unclear if exceeding 70) = 18; CI: < 55 = 16, 56-69 = 34, 70 (unclear if exceeding 70) = 20 ▪ Sex (Male:Female) = EI: 46:25; CI: 48:22 ▪ Time Since Stroke (Months) = All participant ≤ 3 months post-stroke ▪ More Affected Side (Left:Right) = EI: 36:35; CI: 39:31 ▪ Stroke Type (Isch:Haem) = All Ischaemic	Grip Strength = Baseline data are not available.	BBT = Baseline data are not available.

Study Study Design Sample Size	Details of Interventions: Duration, Frequency, Intensity		Outcome Measurement Time Points	Participants (Age [Mean (SD)], Sex, Time Since Stroke [Mean (SD)], More Affected Side, Stroke Type)	Prioritised UL Measures at Baseline	
	Exercise-Based Intervention	Control Intervention			Neuromuscular Impairment	Functional Ability
Smania et al. (278) RCT EI: 30; CI: 29	Constrained-Induced Movement Therapy: 2 hours/session, 5 days/week for 2 weeks + Mitt use on the less affected hand for at least 12 hours/day, 5 days/week	CT: 2 hours/session, 5 days/week for 2 weeks	After the Intervention Period	▪ Age (Years) = EI: 63.93 (9.56); CI: 68.25 (12.68) ▪ Sex (Male:Female) = EI: 26:4; CI: 23:6 ▪ Time Since Stroke (Months) = EI: 11.1 (8.91); CI: 9.38 (7.78) ▪ More Affected Side (Left:Right) = EI: 16:14; CI: 16:13 ▪ Stroke Type (Isch:Haem) = EI: 25:5; CI: 25:4	Ashworth Scale (Elbow Score) = EI: 0.73 (1.04) CI: 0.74 (0.66)	WMFT-PT = EI: 11.16 (15.29) CI: 23.27 (29.20)
Thant et al. (279) RCT EI: 14; CI: 14	Task-Oriented Training: 1 hour/session, 5 times/week for 4 weeks	CT: 1 hour/session, 5 times/week for 4 weeks	After the Intervention Period	▪ Age (Years) = EI: 55 (8.43); CI: 55.14 (10.44) ▪ Sex (Male:Female) = EI: 8:6; CI: 6:8 ▪ Time Since Stroke (Weeks) = EI: 10.79 (7.29); CI: 11.43 (6.38) ▪ More Affected Side (Left:Right) = EI: 7:7; CI: 7:7 ▪ Stroke Type (Isch:Haem) = EI: 13:1; CI: 14: 0	FMA = EI: 30.14 (8.25) CI: 30.86 (5.50)	WMFT-PT = EI: 54.86 (22.7) CI: 52.45 (14.47)
Wu et al. (280) RCT EI: 8; CI:9	Constraint-Induced Movement Therapy: 2 hours/day, 5 days/week for 3 weeks + Mitt use on the less affected hand and wrist for 6 hours/day for 3 weeks	CT: 2 hours/day, 5 days/week for 3 weeks	After the Intervention Period	▪ Age (Years) = EI: 65.5 (9.8); CI: 61.33 (11.2) ▪ Sex (Male:Female) = EI: 5:3; CI: 7:2 ▪ Time Since Stroke (Months) = EI: 10.1 (10.4); CI: 13.7 (14.1) ▪ More Affected Side (Left:Right) = Not Reported ▪ Stroke Type (Isch:Haem) = Not Reported	KD: Reaction Time (s) = EI: 0.58 (0.44) CI: 0.48 (0.08)	KD: Normalised Movement Time = EI: 0.03 (0.04) CI: 0.02 (0.01)
Wu et al. (281) RCT EI: 22; CI:22	Constraint-Induced Movement Therapy: 2 hours/day, 5 days/week for 3 weeks + Mitt use on the less affected hand for 6 hours/day	CT: 2 hours/day, 5 days/week for 3 weeks	After the Intervention Period	▪ Age (Years) = EI: 51.91 (11.93); CI: 55.19 (2.50) ▪ Sex (Male:Female) = EI: 15:7; CI: 16:6 ▪ Time Since Stroke (Months) = EI: 14.91 (12.04); CI: 17.77 (12.45) ▪ More Affected Side (Left:Right)= EI: 14:8; CI: 12:10 ▪ Stroke Type (Isch:Haem) = Not Reported	KD: Peak Velocity (cm/s) = EI: 67.33 (15.95) CI: 73.94 (18.92)	KD: Normalised Movement Time (s/cm)= EI: 0.057 (0.029) CI: 0.043 (0.020)

Note: EI: Experimental Intervention; **CI:** Control Intervention (applies to participant and outcome measure descriptions in this table); **Isch:** Ischaemic; **Haem:** Haemorrhagic; **FMA:** Fugl-Meyer Assessment; **ARAT:** Action Research Arm Test, **KD:** Kinematics-Derived; **BBT:** Box and Block Test, **WMFT-PT:** Wolf Motor Function Test – Performance Time; **WMFT-FA:** Wolf Motor Function Test – Functional Ability Scale; **Med:** Median; **IQR:** Interquartile Range; **CI:** Confidence Interval (statistical value); **s/cm:** seconds/centimetres; **cm/s:** centimetres/seconds. The 'Sample Size' indicates the number of participants at baseline. Data are presented as Mean (SD) unless otherwise specified in the table.

Among the eligible studies, those included in the analyses (n = 30) and those excluded (n = 17) shared similar participant characteristics, interventions, and outcome measures (Tables 9 and 10). This similarity suggests that the overall findings are unlikely to be significantly impacted by the exclusion of those 17 studies. However, their exclusion reduced the sample size by approximately 310 participants in the experimental group and 311 in the control group, which may have affected the statistical power of the analyses. These 17 studies were excluded from the meta-analyses and meta-regressions due to missing essential statistical values, specifically the mean and/or SD of changes between pre- and post-therapy. Despite efforts to obtain the missing data from the authors, it could not be retrieved, making their exclusion inevitable.

The design, sample size, participant characteristics, interventions, and outcome measures from the included studies are provided below.

Design: Only one study employed a crossover design, with data collected before the crossover included in the analyses (236).

Sample Size: A total of 1,469 stroke survivors were enrolled in the studies, with 763 in the experimental groups and 706 in the control groups. Due to dropouts during the intervention phase, the meta-analysis on neuromuscular impairment measures included 1,349 participants (694 in the experimental groups, 655 in the control groups), and the analysis on functional ability involved 1,353 participants (699 experimental, 654 control).

Participants: The experimental groups at recruitment included 449 males and 287 females, while the control groups comprised 429 males and 275 females, based on data from 29 studies. One study did not provide gender data on the participants (250). Participants in the experimental groups were aged 49.1 to 75.7 years (mean = 60.31 ± 6.32), while those in the control groups were 48.2 to 72.4 years (mean = 60.05 ± 5.93). Time since stroke onset varied from 8.87 hours to 12.1 years (mean = 22.8 months) in the experimental groups and from 9.08 hours to 15.3 years (mean = 24.9 months) in the control groups, based on data from 28 studies. Two studies reported time since stroke onset in intervals rather than a clear mean (244, 247). Of the studies, 18 reported stroke types: in the experimental groups, there were 411 ischemic and 118 haemorrhagic strokes; in the control groups, there were 383 ischemic and 106 haemorrhagic strokes. Stroke types were not reported in the remaining studies (235, 236, 238, 241, 242, 246, 250, 257, 258, 261, 262, 264). Twenty-seven studies reported more affected body sides: in the experimental groups, 375 individuals were more affected on the left, 324 on the right; in the control groups, 354 individuals had greater left-side impact, 302 on the right, and

one individual was equally affected on both sides. Data on the more affected body side was not provided in three studies (245, 249, 252).

Interventions: Mirror therapy was the most common experimental intervention, used in seven studies (237, 238, 241, 249, 254, 260, 263), followed by robotic therapy in four studies (235, 243, 258, 261). Constraint-induced movement therapy (245, 256, 262), strength training (242, 244, 250), virtual reality (239, 246, 252), and game therapy (251, 253, 259) were each provided in three studies. Bilateral arm training was employed in two studies (247, 248). Mental practice (257), task-oriented therapy (236), impairment-oriented therapy (240), high-repetition home therapy (264), and repetitive facilitative therapy (255) were each used in one study.

Control interventions included no therapy (236, 246, 260) and sham (238, 249, 254) in three studies, each, and conventional therapy in 24 studies (235, 237, 239–245, 247, 248, 250–253, 255–259, 261–264).

In four studies, both the control and experimental groups received the same conventional therapy, while the experimental groups also received an additional exercise-based therapy (237, 239, 251, 259). In one study, both groups received conventional therapy, with the experimental group also receiving mirror therapy and the control group receiving sham therapy (238).

Selected Outcome Measures: The FMA was employed in 21 studies (237–240, 242, 243, 246–250, 252–258, 261, 263, 264). A kinematics-derived neuromuscular impairment variable was used in one study (262), grip strength in four (236, 244, 251, 260), and other measures in individual studies: muscle strength (241), 'Chedoke McMaster Stroke Assessment' (235), 'Motor Evaluation Scale for Arm in Stroke Patients' (245), and 'Brunnstrom Motor Recovery Stage – UL' (259).

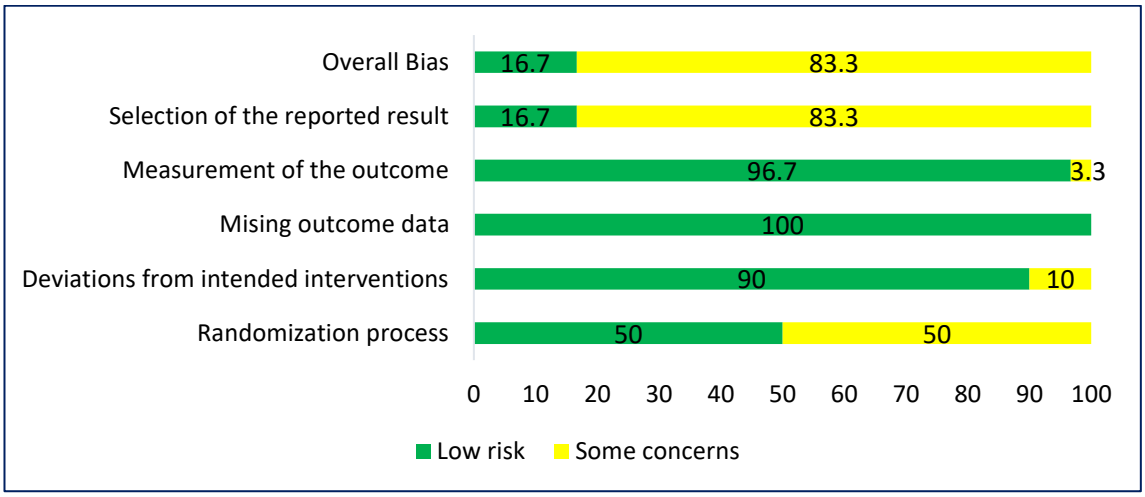
The ARAT was employed in ten studies (238, 244, 246, 248, 249, 255, 258, 260–262). A kinematics-derived functional ability variable was used in one study (263), the BBT in eight (237, 239, 240, 243, 247, 251, 259, 264), and the WMFT-PT in six (236, 245, 250, 252, 256, 257). The 'Chedoke Arm and Hand Activity Inventory' was used in two studies (235, 241), 'The Upper-Extremity Performance-Functional Rating Test' in two (242, 254), and 'Stroke Upper Limb Capacity' in one (253).

Potential Risk of Bias: The risk of bias assessments for eligible studies, whether included in the analyses or not, showed similar results (Figures 4 and 5). This similarity indicates that excluding

studies from which statistical data could not be extracted likely does not impact the overall findings substantially, suggesting that the analyses' results are representative of eligible studies.

Figure 4. Summary Plot of the Risk of Bias Assessments in Eligible Studies (A and B)

A. Bias Risk in Studies Included in Analyses (n = 30)



B. Bias Risk in Studies Not Included in Analyses (n = 17)

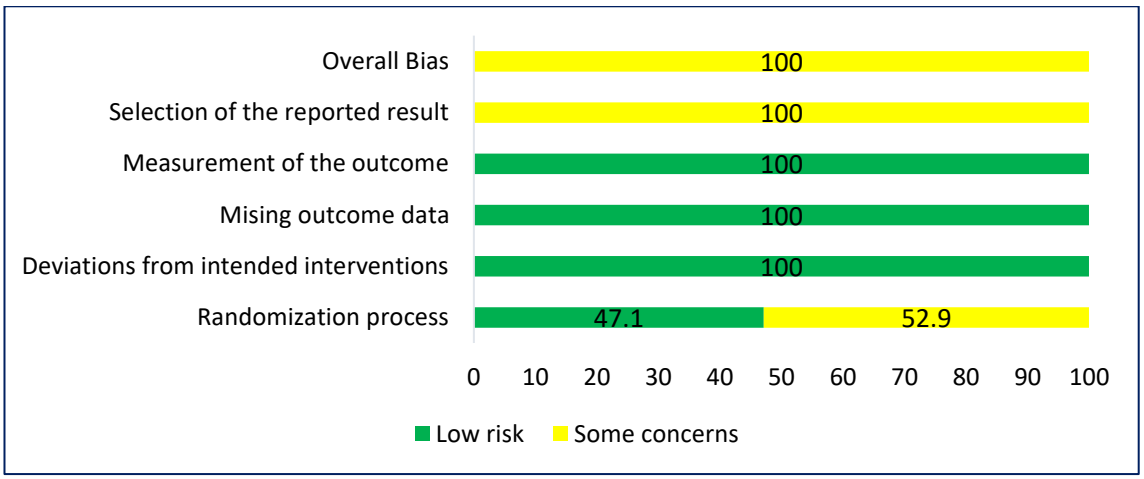
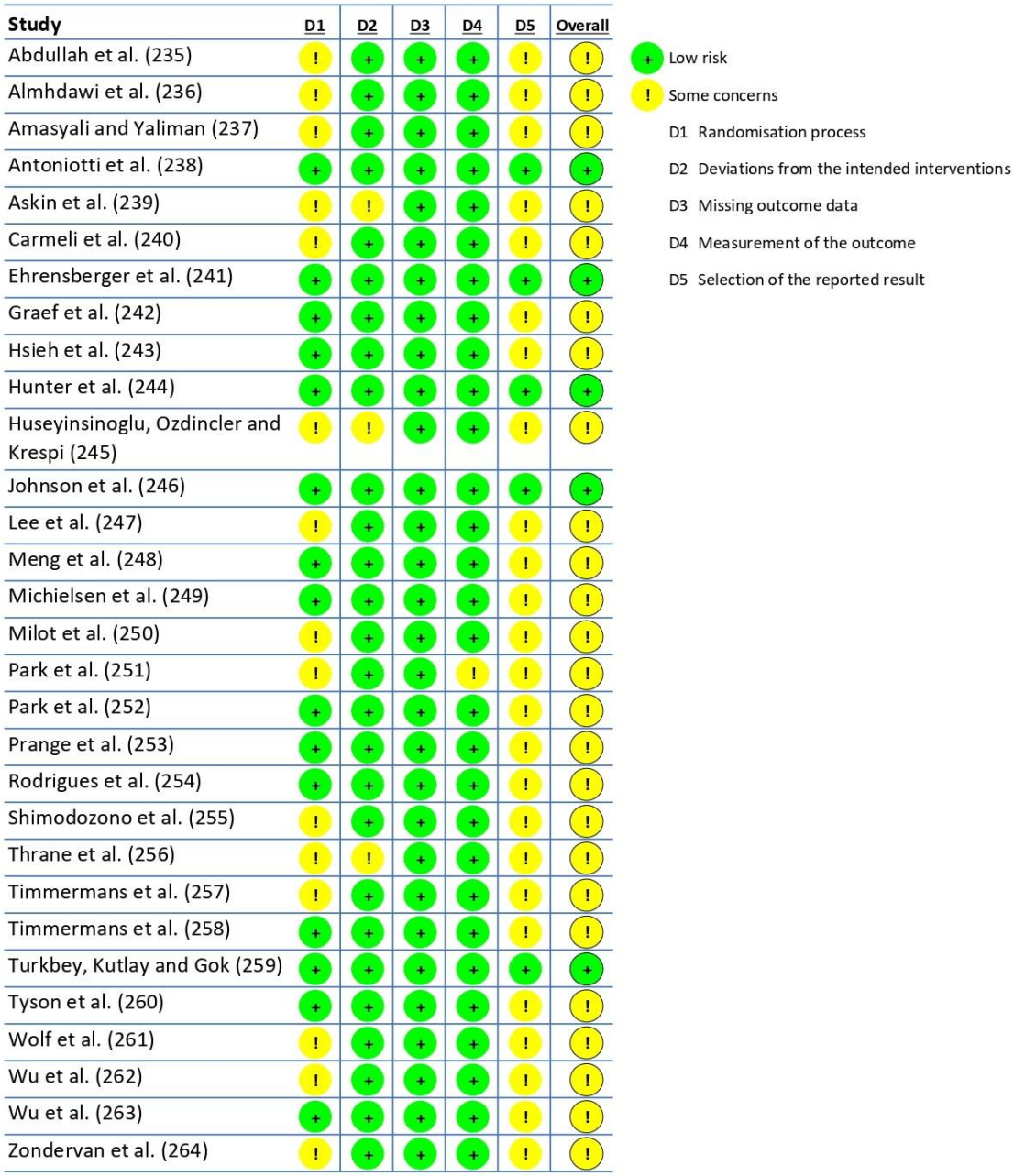
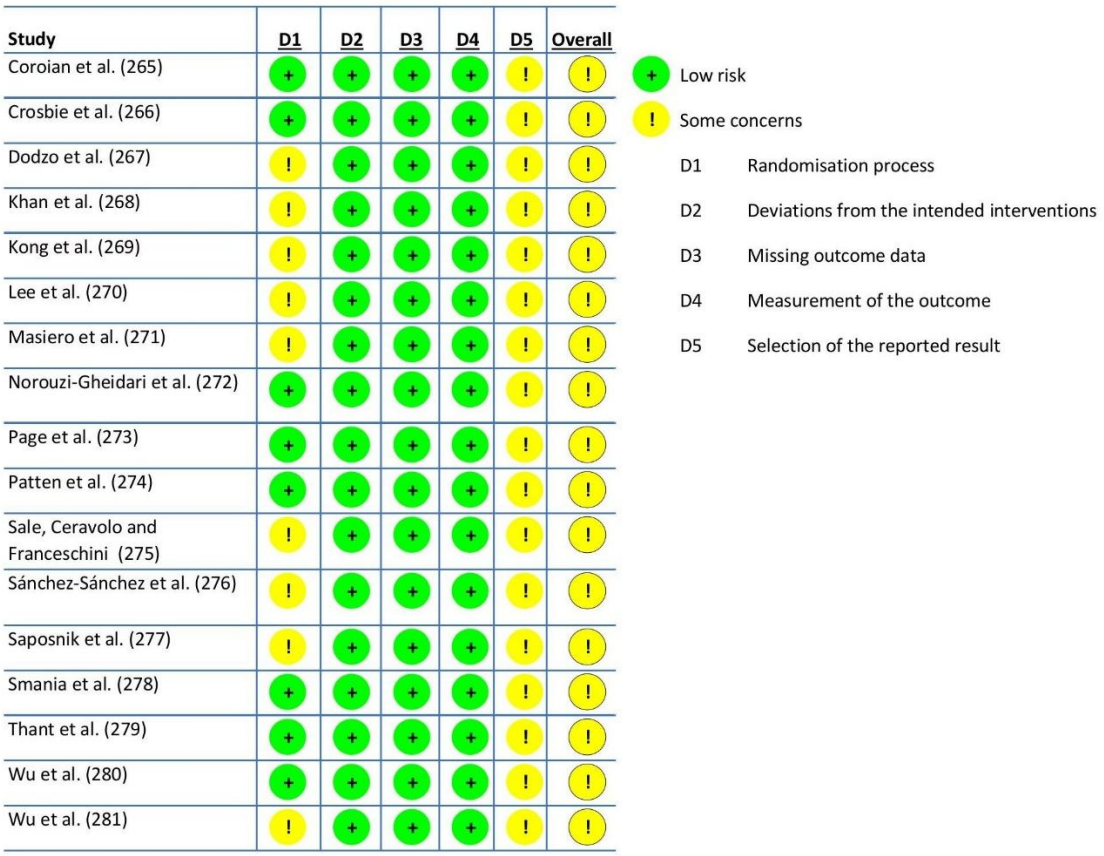


Figure 5. Risk of Bias Assessment in Eligible Studies (A and B)

A. Included in Analyses (n = 30)



B. Not Included in Analyses (n = 17)



In the 30 studies included in the analyses, five were assessed as having a low risk of bias (238, 241, 244, 246, 259), while the remaining 25 were assessed with 'some concerns' regarding the risk of bias (235–237, 239, 240, 242, 243, 245, 247–258, 260–264). In these 25 studies, ‘some concerns’ were noted in the 'selection of the reported result,' often due to the absence of a pre-specified analysis plan. This factor alone led to a 'some concerns' overall rating for 10 studies (242, 243, 248, 249, 252–254, 258, 260, 263). Half of the studies showed 'some concerns' in the 'randomisation process,' mainly due to unclear allocation sequence concealment (235–237, 239, 240, 245, 247, 250, 251, 255–257, 261, 262, 264). Only three studies raised concerns about the 'deviations from intended interventions' (239, 245, 256), and one study about the 'measurement of the outcome' (251). All studies were assessed as having a low risk of bias in the 'missing outcome data' domain, indicating strong data completeness across the studies.

3.3.3 Synthesis

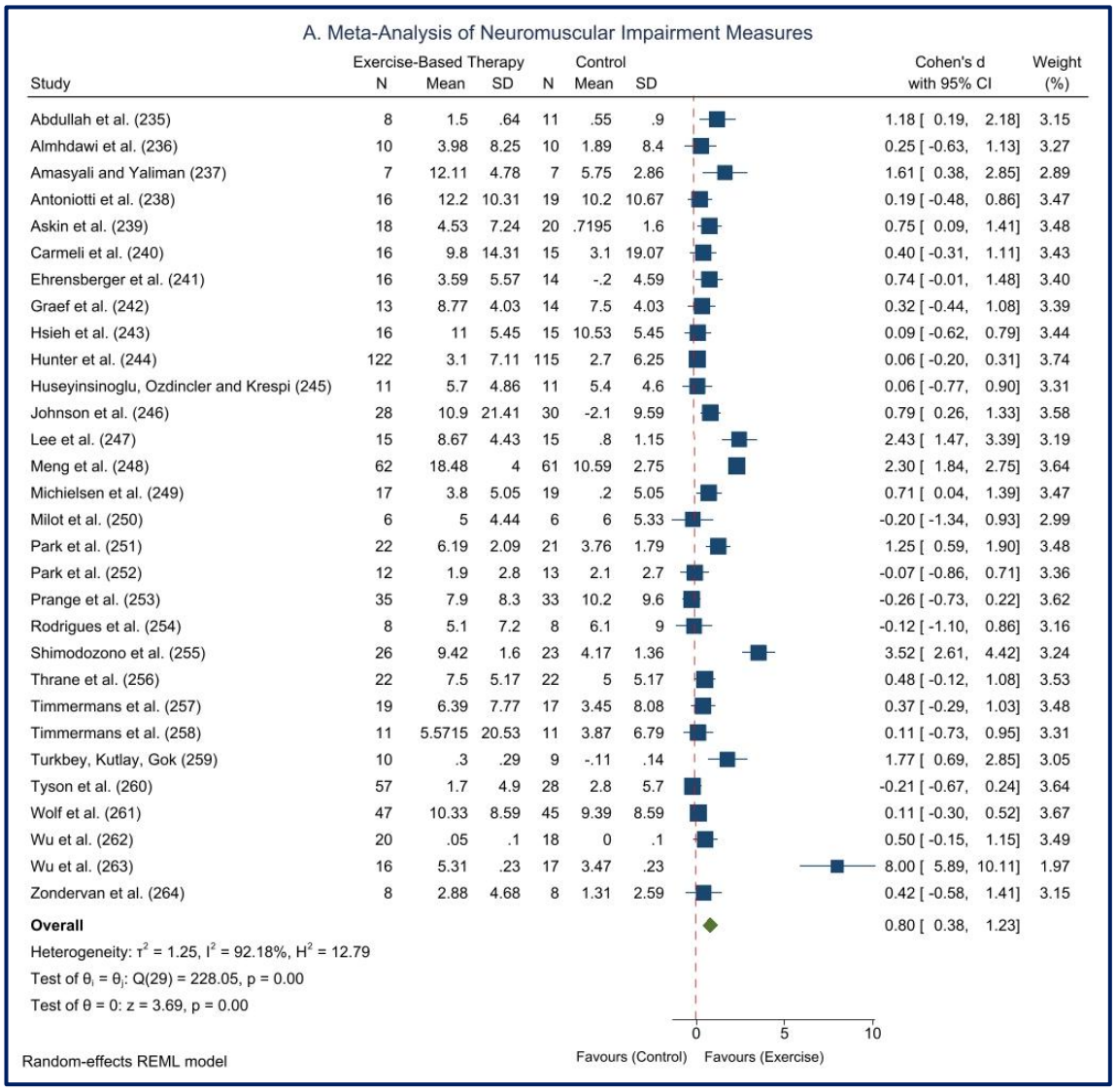
Aim 1a: Explore whether there is a greater benefit for UL neuromuscular impairments or functional abilities after stroke in response to exercise-based therapies compared to control interventions.

The meta-analyses included data from 1,349 individuals for the neuromuscular impairment analysis and 1,353 for the functional ability analysis. In the sensitivity analyses, participant numbers were 1,267 and 1,271, respectively. Subgroup analyses, focusing on studies reporting primary outcome measures (FMA and ARAT), included data from 415 stroke survivors in each analysis.

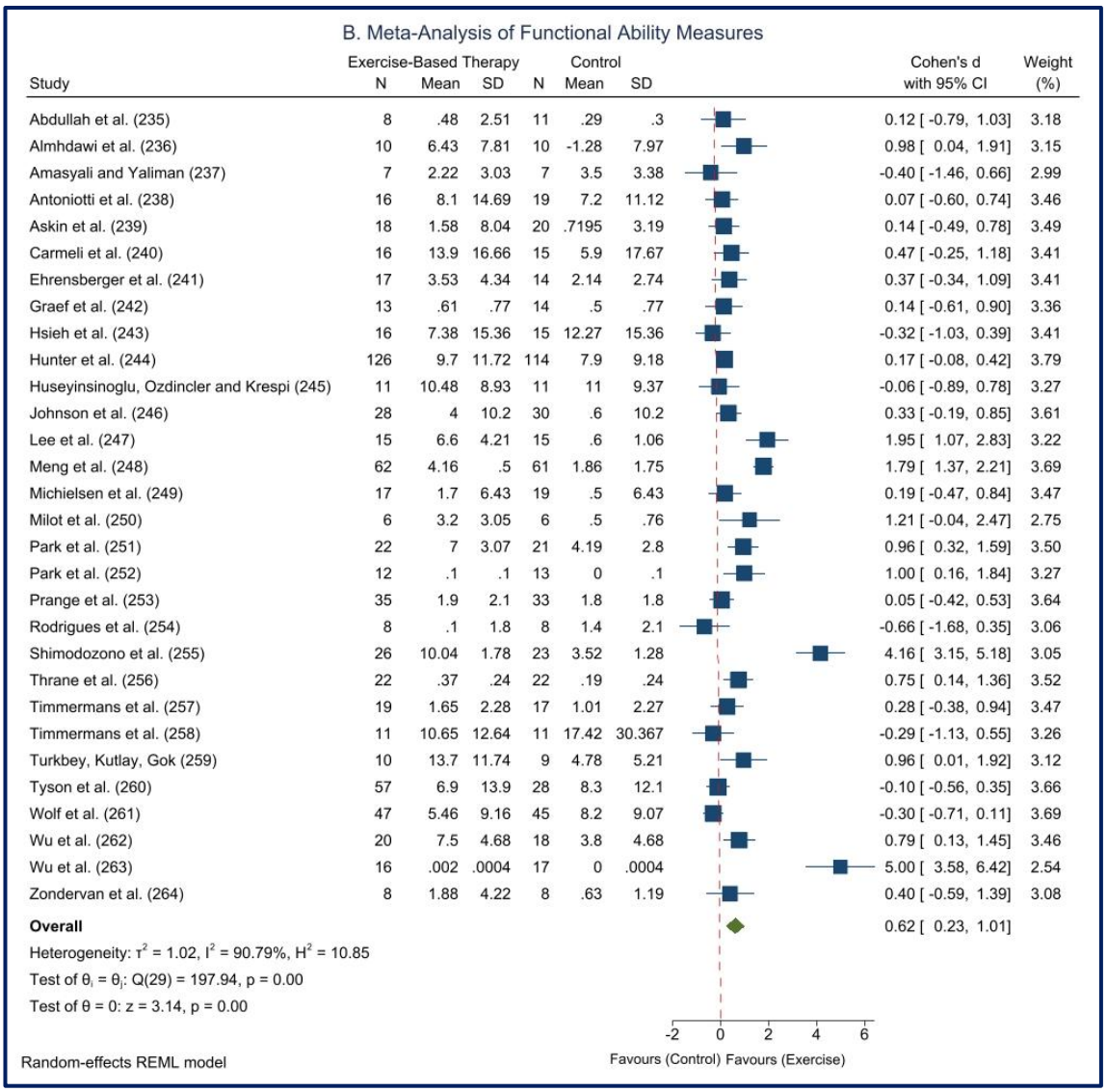
The findings of the meta-analyses and sensitivity analyses, which excluded the studies by Shimodozono et al. (255) and Wu et al. (263) due to their larger effect sizes compared to the overall trend, are visually presented in forest plots in Figures 6 and 7, respectively. The results of the subgroup meta-analyses are presented in the forest plots in Figure 8.

Figure 6. Forest Plots: Meta-Analyses of Comparative Effects of Exercise-Based Therapies (A and B)

A. Neuromuscular Impairment



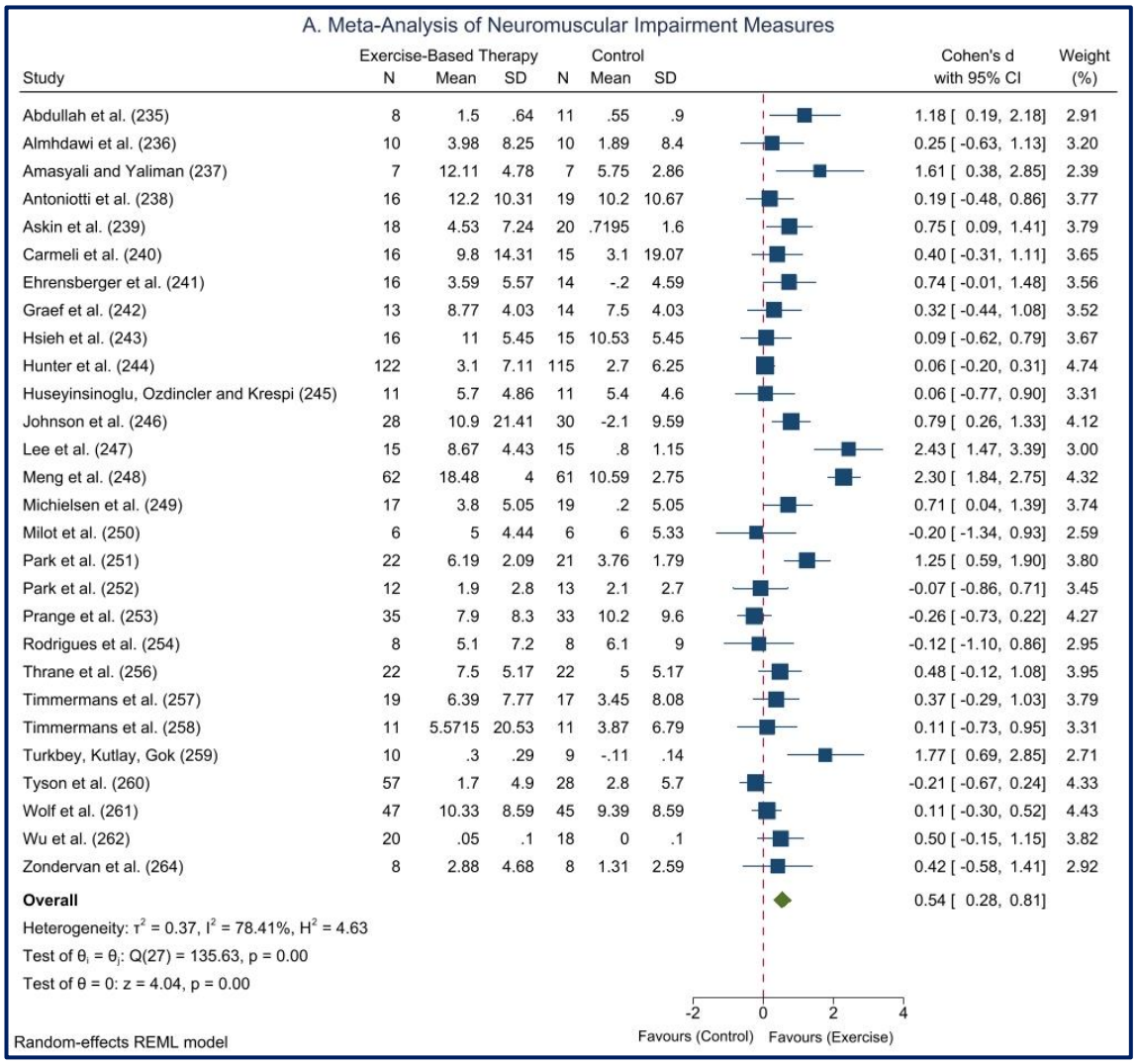
B. Functional Ability



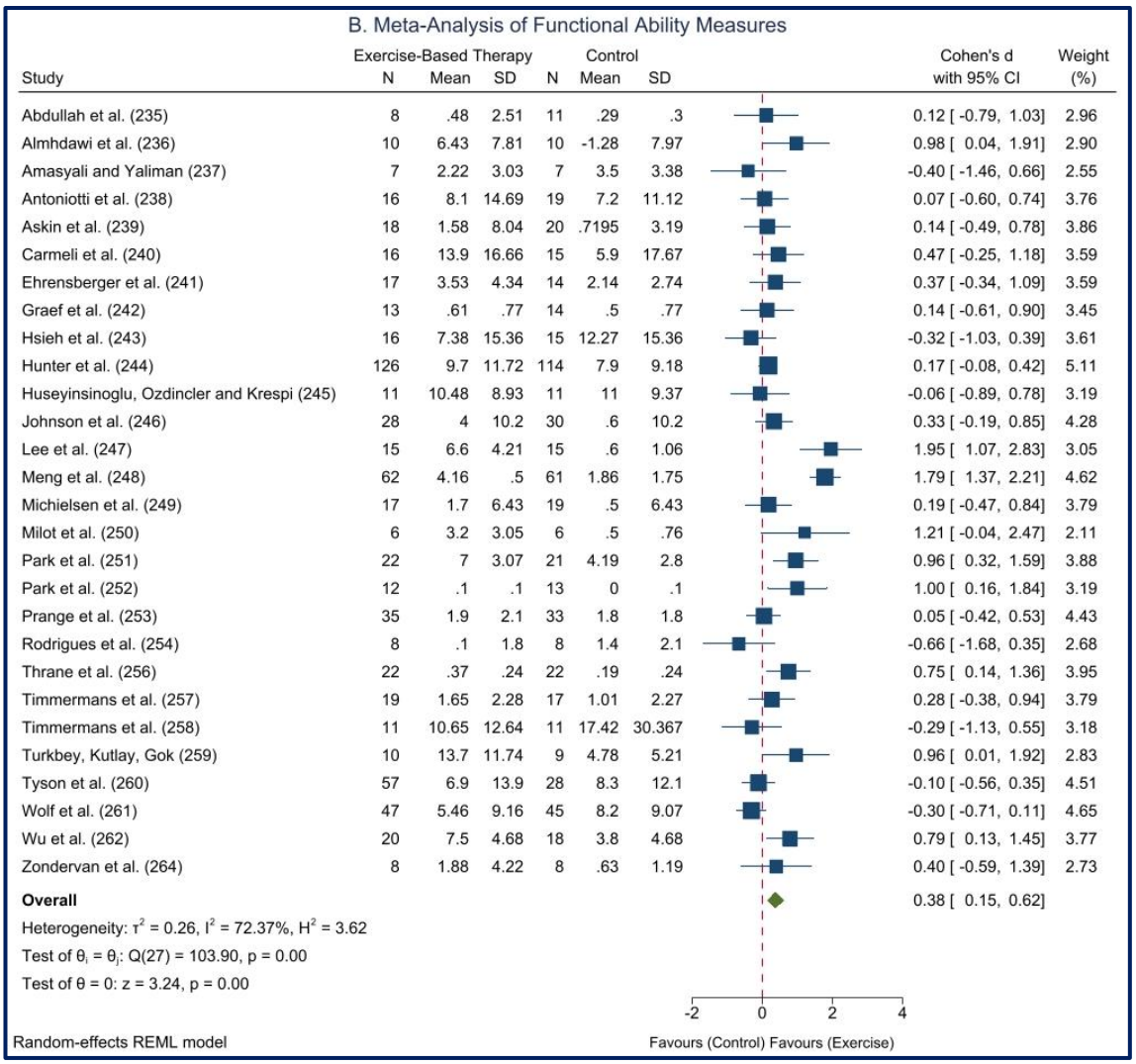
Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Figure 7. Forest Plots: Sensitivity Meta-Analyses of Comparative Effects of Exercise-Based Therapy (A and B)

A. Neuromuscular Impairment



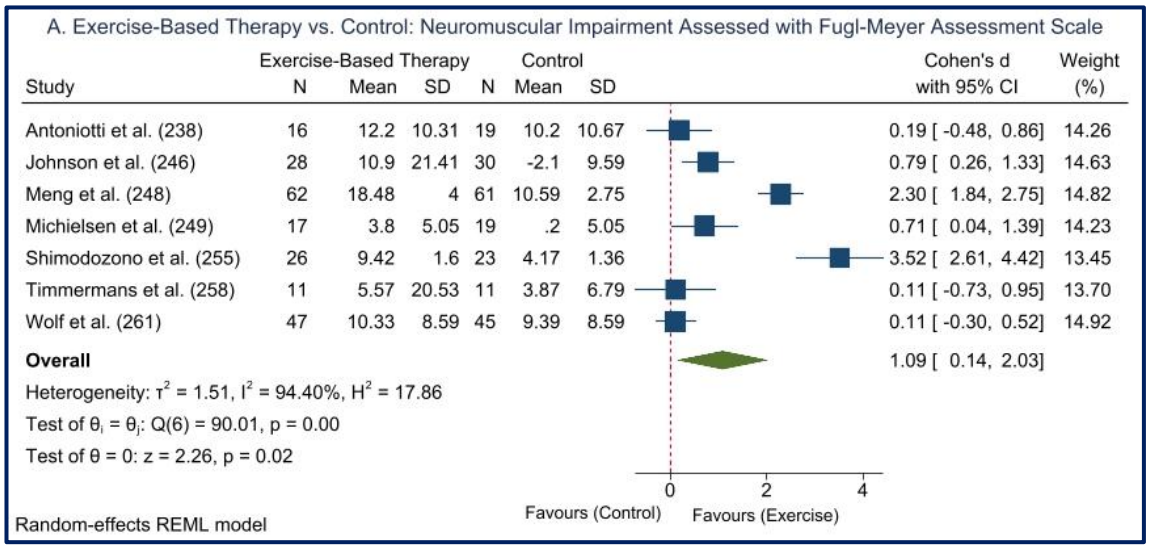
B. Functional Ability



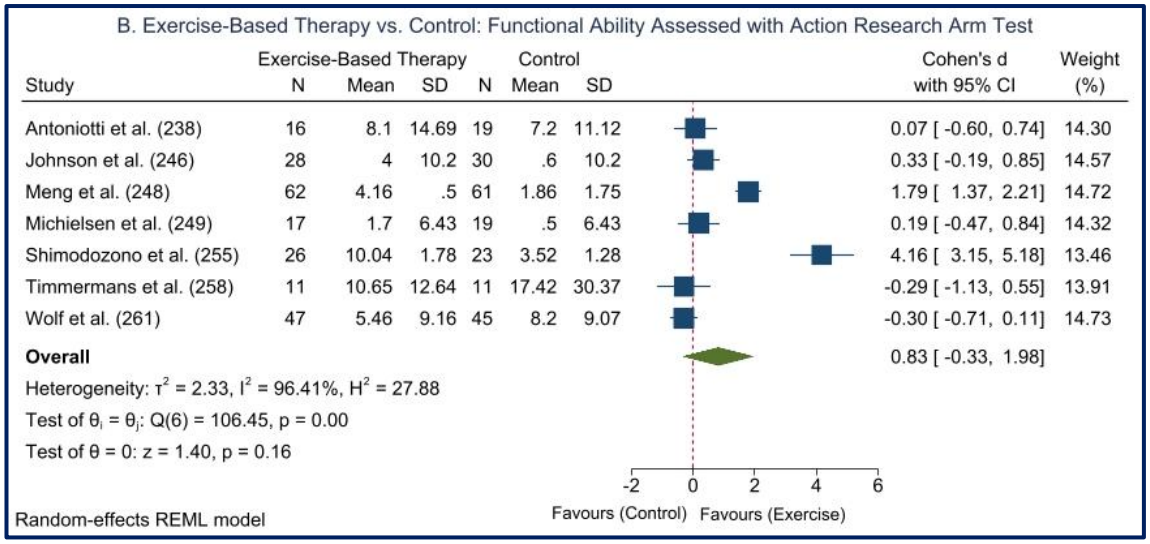
Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Figure 8. Forest Plots: Meta-Analyses of Comparative Effects of Exercise-Based Therapy (A and B)

A. Neuromuscular Impairment Assessed with Fugl-Meyer Assessment Scale



B. Functional Ability Assessed with Action Research Arm Test



Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Meta-analyses (Figure 6) revealed that exercise-based therapies significantly improved neuromuscular impairments (large effect, Cohen's d [95%CI] = 0.80 [0.38, 1.23], $p < 0.05$) and functional abilities (moderate effect, 0.62 [0.23, 1.01], $p < 0.05$), compared to control interventions. There was considerable heterogeneity among the studies (I^2 = 92.18% and 90.79%, respectively). Sensitivity analyses (Figure 7) showed smaller but still significant effects: moderate for neuromuscular impairments (0.54 [0.28, 0.81), $p < 0.05$]) and small for functional abilities (0.38 [0.15, 0.62], $p < 0.005$), with reduced heterogeneity (I^2 = 78.41% and 72.37%, respectively). The 95% CIs not encompassing zero in these analyses support the statistical significance, indicating a spectrum of effects from small to large for neuromuscular impairments and from trivial to large for functional abilities. Comparisons of effects between neuromuscular impairments and functional abilities in both meta-analyses ($p = 0.53$) and sensitivity analyses ($p = 0.37$) showed no significant differences.

Subgroup meta-analyses (Figure 8) showed that exercise-based therapies significantly improved neuromuscular impairments as measured by FMA (1.09 [0.14, 2.03], $p = 0.02$) compared to control interventions, but did not significantly affect functional abilities as measured by ARAT, despite the large effect size (0.83 [-0.33, 1.98], $p = 0.16$). These effects were not significantly different from each other ($p = 0.73$). There was substantial heterogeneity among the studies (I^2 = 94.4% for neuromuscular impairment, 96.41% for functional ability). Their sensitivity analyses, excluding the study by Shimodozono et al. (255), indicated a moderate, significant effect on neuromuscular impairments (0.72 [0.03, 1.42], $p = 0.04$), but a small, non-significant effect on functional abilities (0.32 [-0.33, 0.98], $p = 0.33$) (Appendix 5: Figure 1). Similarly, no significant difference was observed between these effects ($p = 0.41$).

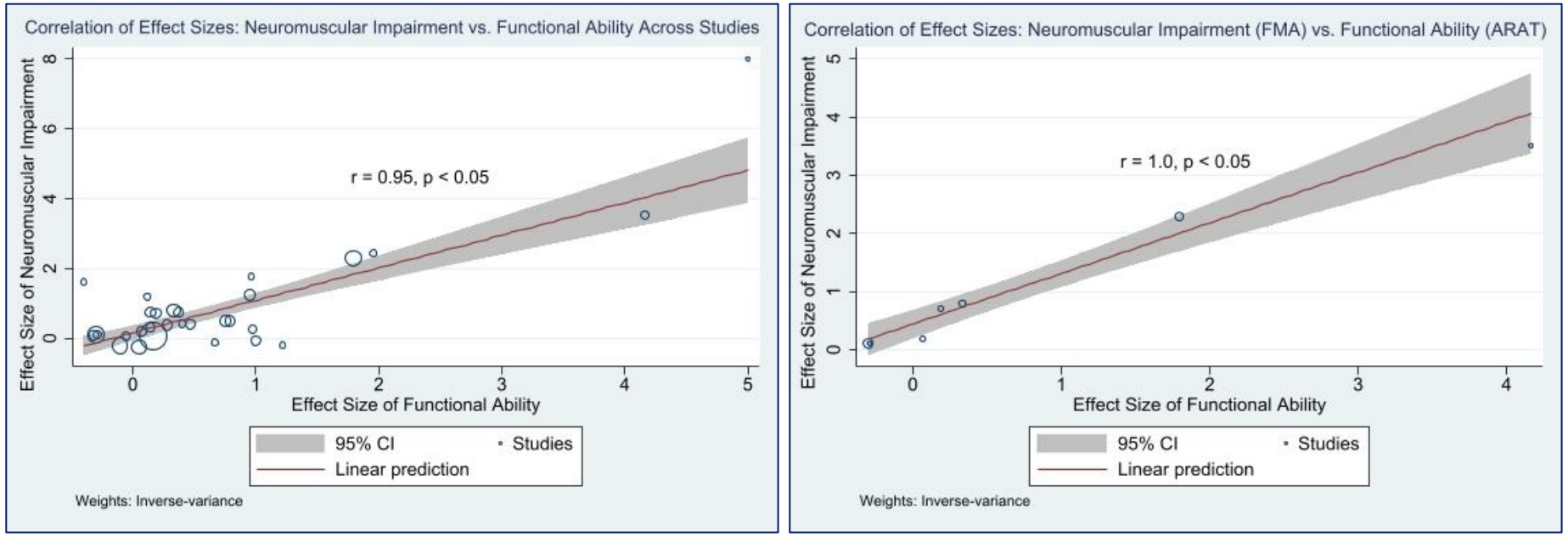
Aim 1b: Estimate the correlation between changes in the UL neuromuscular impairments and functional abilities after stroke in response to exercise-based therapies compared to control interventions.

The meta-regression findings are visually presented in two separate bubble plots in Figure 9. Plot A represents data from all studies included in the analyses (Table 9), while Plot B reflects data from the studies included in the analyses that reported both FMA and ARAT scores.

Figure 9. Meta-Regression Bubble Plots Illustrating the Correlations between Changes in Neuromuscular Impairments versus Changes in Functional Abilities in Response to Exercise-Based Therapies Compared to Control Interventions (A and B)

A. Meta-Regression of All Studies Included in Analyses

B. Subgroup Meta-Regression Focused on FMA and ARAT



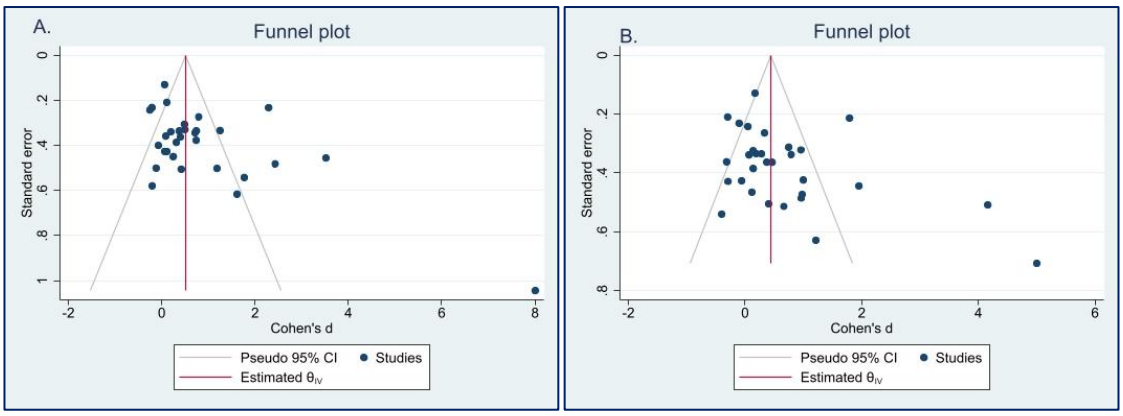
Note: Blue circles reflect the studies' effect sizes. Larger circles correspond to larger effects. The red line represents the regression line of best fit. The grey-shaded area represents the 95% confidence interval for the predicted values of the regression line.

The meta-regression analysis revealed an almost perfect, statistically significant positive correlation between improvements in neuromuscular impairments and functional abilities following exercise-based therapies compared to control interventions ($r = 0.95$, $p < 0.05$) (Figure 9, A). This analysis showed moderate heterogeneity among the studies ($I^2 = 55.74\%$). The subgroup meta-regression analysis showed a perfect and statistically significant positive correlation between changes in FMA-measured neuromuscular impairments and ARAT-measured functional abilities ($r = 1.0$, $p < 0.05$) (Figure 9, B), with no heterogeneity among the studies ($I^2 = 0\%$).

Publication Bias

Figure 10. Funnel Plots of Meta-Analyses (A and B)

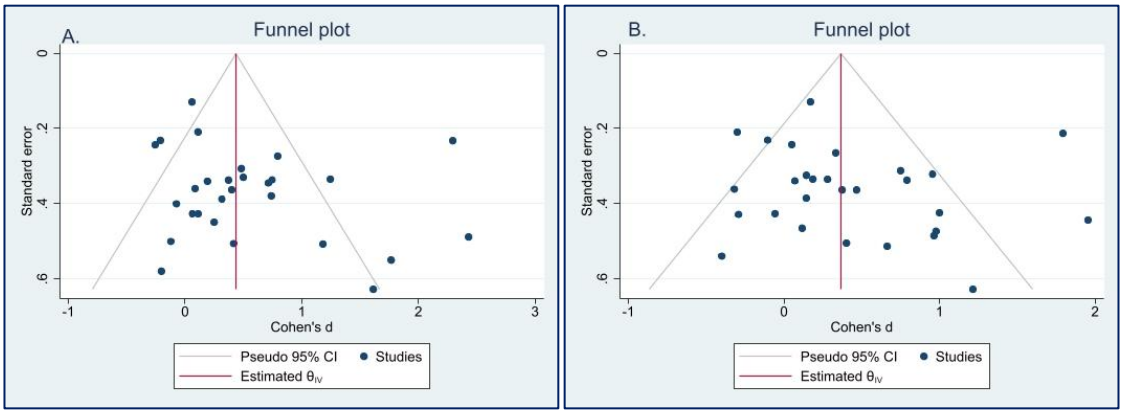
A. Neuromuscular Impairment **B.** Functional Ability



Note: Blue dots present studies. The red vertical line indicates the overall effect size estimated from the meta-analysis. Two grey lines on either side represent the pseudo 95% confidence intervals.

Figure 11. Funnel Plots of Sensitivity Analyses (A and B)

A. Neuromuscular Impairment **B.** Functional Ability



Note: Blue dots present studies. The red vertical line indicates the overall effect size estimated from the meta-analysis. Two grey lines on either side represent the pseudo 95% confidence intervals.

In the meta-analyses, funnel plot asymmetry (Figure 10) suggested the presence of publication bias, which was further supported by significant results from Egger's tests ($p < 0.05$ for both analyses). However, sensitivity analyses, which excluded studies by Shimodozono et al. (255) and Wu et al. (263), presented less asymmetrical funnel plots (Figure 11), and Egger's tests for these analyses showed no evidence of publication bias ($p = 0.27$ for neuromuscular impairment and 0.42 for functional ability analyses). These findings suggest that the initial detection of publication bias in the meta-analyses was primarily due to the inclusion of the aforementioned studies, rather than a systematic issue affecting the entire set of included studies.

3.4 Discussion and Interpretation

This study found that exercise-based therapies improve both UL neuromuscular impairments and functional abilities after stroke compared to control interventions: no therapy, sham therapy, or conventional therapy. The comparative benefits of exercise-based therapies were greater for neuromuscular impairments; however, no statistically significant difference was found between the effects on neuromuscular impairments and functional abilities (**Aim 1a**). A perfect and statistically significant positive correlation was identified between functional ability improvements and improvements in neuromuscular impairments resulting from exercise-based therapies, as compared to control interventions (**Aim 1b**).

The greater effects of exercise-based therapies on neuromuscular impairments found in the current review appear to be consistent with the findings of some earlier reviews (12, 282) while contradicting those from another (14). Nevertheless, existing reviews reported the effects on distinct cohorts of stroke survivors as a result of incorporating different sets of studies into their analyses of neuromuscular impairments and functional abilities, which is different from the current review. It is therefore not possible to conclude, based on these reviews, that exercise is more efficacious in addressing neuromuscular impairments or functional abilities. For example, Shi et al. (14) reported that constrained-induced movement therapy improves functional abilities more than neuromuscular impairments (mean difference [95% CI] = 7.80 [4.21, 11.38] for FMA; 14.15 [10.71, 17.59] for ARAT). However, these results were reported based on five studies examining impairment and six studies examining function, of which four were identical and the remaining were varying. Individual responses to therapy may be substantially impacted by variables including the time since the stroke onset, age, gender, and the type of stroke. Therefore, it is not possible to conclude from the review of Shi et al. (14) that exercise-based therapies have a greater impact on functional abilities than on neuromuscular impairments.

This current review is the first to investigate the correlations between changes in neuromuscular impairments and functional abilities in response to exercise-based therapies compared to control interventions, including no therapy, sham therapy, and conventional therapy. A direct comparison with previous reviews is therefore not possible. Although the existing reviews present the effects of exercise-based therapies on neuromuscular impairments and functional abilities including different cohorts in their analyses, their findings consistently showed that exercise-based therapies improve both neuromuscular impairments and functional abilities (12, 14, 282), which are in alignment with the current review.

Compared to the previous reviews (12, 14, 282), the robust methodology of the current review provides a more nuanced understanding of the impact of exercise-based therapies after stroke. For example, Yang et al. (282) found beneficial effects of robot-assisted therapy on both neuromuscular impairments (SMD [95% CI] = 0.69 [0.34, 1.04] for FMA) and functional abilities (0.27 [-0.73, 1.27] for WMFT). However, their inclusion of studies where conventional therapy involved electrical stimulation applied to both intervention and control groups may have introduced confounding effects, as the working mechanisms of stimulation techniques differ from those of exercise. In contrast, this review, which excludes such interventions, provides a clearer insight into the specific effects of exercise-based therapies, free from this potential confounder. Additionally, by limiting inclusion to studies with a low risk of bias or some concerns for bias, this review enhances methodological rigour and reduces potential biases, offering findings that are more robust than those of reviews that included studies with a broader range of bias risks (12, 14).

This focus on minimising bias in the current review reflects a deliberate trade-off between bias and precision, guided by the Cochrane Handbook (167). Excluding studies with a high risk of bias strengthens the robustness of the findings but may reduce the precision of the estimates by narrowing the pool of included studies. However, the relatively large sample size in this review—30 studies involving 1,349 individuals for neuromuscular impairment measures and 1,353 for functional ability measures—helps mitigate this trade-off, reducing bias and enhancing precision. By addressing this balance, this review delivers robust findings grounded in high-quality evidence, providing valuable insights into the effects of exercise-based therapies.

While the review achieved a large sample size, the methodological quality of the included studies varied, with five assessed as having a low risk of bias (238, 241, 244, 246, 259) and the rest assessed as having some concerns about bias (235–237, 239, 240, 242, 243, 245, 247–258, 260–264). This variability underscores the challenge of ensuring methodological rigour while maintaining sufficient comprehensiveness for robust analyses. Although studies with some concerns were included to preserve the sample size and provide a more comprehensive evidence base, the mixed quality of evidence may have introduced minor imprecision in effect estimates.

In this review, the exclusion of 17 studies from analyses, which was inevitable due to missing data, resulted in the loss of approximately 310 participants in the experimental group and 311 in the control group. Despite this reduction, the remaining sample size was sufficiently large to provide robust estimates, and the results remained statistically significant. Additionally, this

review features a larger sample size compared to previous reviews reporting the effects of exercise-based therapies on both neuromuscular impairments and functional abilities (12, 14, 282).

Additionally, the inclusion of a variety of therapies in the current review expanded the participant pool, improving the representativeness of the clinical stroke population and enhancing the generalisability of the findings. While this approach may have contributed to the observed heterogeneity, it also provided a broader understanding of the effects of exercise-based therapies. Notably, except for one review (14), other previous reviews (12, 282), which assessed only a single type of exercise-based therapy, also reported substantial heterogeneity. This suggests that the variability observed in both previous reviews and this review is more likely driven by individual responses to the interventions rather than by the diversity of therapies included.

Pooling data from several different outcome measures in the current review could have also contributed to the high heterogeneity observed in the analyses. However, this approach provides a comprehensive understanding of the effects of exercise-based therapies on a broader spectrum of neuromuscular impairments and functional abilities. For example, Yang et al. (282) found that robotic therapy had a moderate, statistically significant effect on neuromuscular impairments as assessed with FMA (Cohen's d [95% CI] = 0.69 [0.34, 1.04], p = 0.0001); however no significant effect on neuromuscular impairment as assessed by the 'modified Ashworth Scale' (-1.03 [-2.06, 0.01], p = 0.05). Thus, exercise-based therapies can be effective in some aspects of neuromuscular recovery, but not in others. Therefore, using diverse and targeted assessment tools to fully understand the multifaceted effects of exercise-based therapies is important.

In this review, only one study included in the analyses recruited acute stroke survivors (248), while the remaining studies focused on subacute or chronic stroke survivors at recruitment (Table 9). This study involving acute stroke survivors demonstrated one of the largest effect sizes compared to others (Cohen's d [95% CI] = 2.30 [1.84, 2.75] for neuromuscular impairments; 1.79 [1.37, 2.21] for functional ability (Figure 6)), excluding the two studies identified as outliers (255, 263). This suggests that the effectiveness of exercise-based therapies may vary across different stages of recovery. Although individual variability was beyond the scope of this review, subgroup analyses examining the differential effects of exercise-based therapies across recovery stages could provide valuable insights into their stage-specific impacts. Additionally, different types of exercise-based therapies may yield distinct effects on stroke recovery. While this review focused on the overall effectiveness of exercise-based therapies, future analyses exploring both the

recovery stage and the therapy type could provide a more nuanced understanding. Such insights would support the development of tailored interventions to meet the specific needs of stroke survivors at different recovery stages.

Overall, the meta-analyses of all included studies exhibited considerable heterogeneity and evidence of publication bias (Figures 6 and 10). By contrast, sensitivity analyses revealed acceptable heterogeneity levels and no indication of publication bias and yielded smaller but still significant effect sizes (Figures 7 and 11). Consequently, sensitivity analyses generated more precise and unbiased estimates of exercise effects, reinforcing the conclusion that exercise-based therapies have statistically significant effects on both neuromuscular impairments and functional abilities in stroke survivors.

Limitations of the Review

A major limitation of the review was the absence of an independent second reviewer for data extraction due to time and resource constraints. Data extraction was conducted solely by the lead reviewer, which may have introduced bias. However, this limitation was mitigated through consultation with the other independent reviewer, who had been involved in the earlier stages of the review, to resolve uncertainties encountered during data extraction. Additionally, the entire review process was closely supervised on a monthly basis by experienced third parties.

Another limitation of this review is the inclusion of heterogeneous studies with varied interventions, samples, and outcome measures. While this variability reflects the diversity of current clinical practices and enhances the real-world applicability of the findings, it introduces heterogeneity that can increase variability in pooled effect sizes and reduce precision. However, given the aim of this review to assess the general effects of exercise-based therapies across diverse contexts, this heterogeneity was anticipated. Sensitivity analyses (Figure 7) partially addressed this issue by removing two outlier studies (255, 263), which reduced heterogeneity in the pooled effect sizes and demonstrated that the overall findings remained statistically significant.

A potential limitation of this review is the inclusion of studies published only from 2011 onwards. This decision was based on the substantial volume of studies and evidence of improved methodological quality in UL stroke rehabilitation research over the last decade (146). While this approach supports a focus on up-to-date and methodologically sound studies, it might overlook valuable insights from earlier research.

Excluding grey literature and unpublished studies may have introduced a potential risk of publication bias, as null or negative findings may be underrepresented. However, evidence indicates that such exclusions typically have minimal impact on overall findings (147). Similarly, the decision to include only RCTs in this review was guided by the Cochrane Handbook to enhance methodological rigour (150). However, this approach may have limited the generalisability of the findings by omitting potentially valuable insights from real-world interventions or hard-to-reach populations.

Limiting the included studies to those published in English or Turkish may have introduced a potential language bias. However, this decision was guided by evidence suggesting that excluding non-English studies typically has a minimal impact on the overall findings (147). Additionally, practical constraints, including limited resources for professional translation, necessitated this approach. However, this may have restricted the inclusion of additional perspectives or differing insights from a broader global evidence base.

Excluding studies assessed as having a high risk of bias was a deliberate methodological choice, guided by the Cochrane Handbook, to enhance rigour and minimise bias (167). However, this decision may have limited the scope of the findings by excluding potentially valuable insights from these studies.

Strengths of the Review

A key strength of this review was its exclusive focus on RCTs, as systematic reviews or meta-analyses of methodologically sound RCTs typically provide the most reliable evidence for therapeutic interventions, by minimising design biases and other methodological limitations (149). The exclusion of grey literature and unpublished studies was supported by the availability of a substantial number of high-quality RCTs (150), facilitating a focus on rigorously conducted research. This methodological approach enhances the robustness of the findings by prioritising high-quality evidence and reducing the risk of skewed conclusions.

Another strength of this review was the rigorous process employed throughout the study selection and risk-of-bias assessment stages, both of which were independently and fully completed by two reviewers. This dual-review process played a critical role in reducing subjective bias and improving the reliability of the findings, thereby enhancing the credibility of the review and confidence in its conclusions.

Additionally, the exclusion of studies assessed as having a high risk of bias was a key strength of this review. This decision reflects the review's emphasis on producing robust evidence, as studies with a high risk of bias are more likely to compromise the accurate assessment of intervention effects. While this approach narrowed the pool of included data, it enhanced methodological rigour and strengthened the robustness of the synthesised findings.

3.5 Conclusion

Knowing if there are relationships between neuromuscular impairments and functional abilities in response to exercise-based therapies, currently used in stroke practice, is important (72, 95, 96). This knowledge can inform clinical practice and modify the focus of therapy from primarily functional improvements to achieving these improvements by addressing neuromuscular impairments. Because it is suggested that focusing solely on functional improvements may result in compensatory strategies that could negatively impact stroke survivors' long-term recovery process (72, 86).

This review found that exercise-based therapies improve both neuromuscular impairments and functional abilities post-stroke (**Aim 1a**). While the effect sizes suggest greater benefits for neuromuscular impairments, there is no statistically significant difference between these effects (**Aim 1a**). Importantly, the review showed that there are almost perfect correlations between changes in neuromuscular impairments and functional abilities in response to exercise-based therapies (**Aim 1b**). This indicates that the exercise-based therapies included in this review improve both functional abilities and neuromuscular impairments simultaneously without adversely affecting one or the other. This reinforces the idea that practising functional tasks with a focus on movement quality can enable simultaneous improvements in both neuromuscular impairments and functional abilities, avoiding reliance on compensatory strategies.

Consequently, prioritising neuromuscular impairments through a focus on movement quality, particularly in the early post-stroke period when neuroplasticity is most active, can lead to more effective and sustainable functional recovery in clinical practice. However, the possibility of publication bias and heterogeneity in the included studies raises some concerns about the strength of these findings. Further research is, therefore, needed to minimise bias and heterogeneity. Investigating the effects of exercise-based therapies on more homogeneous study samples, intervention types and outcome measures through subgroup analyses may help reduce this heterogeneity and mitigate the risk of potential bias, thereby providing deeper insights.

Chapter 4. Methods and Instruments Common to Experimental Studies

4.1 Introduction

Many of the methods and instruments employed in the two experimental studies reported in subsequent chapters of this thesis (Chapters 5 and 6) are common to both. To avoid repetition, this chapter outlines these commonalities. The specific methods, procedures, and instruments unique to each study are detailed in their respective chapters.

4.2 Instrumentation

To collect kinematic data, a Vicon three-dimensional (3D) motion capture system (Vicon Motion Systems Ltd, Oxford, UK) with ten cameras operating at a 100 Hz sampling rate was used. During the experimental task, the system tracked participants' movement via passive reflective markers. The system set-up and calibration, real-time visualisation and tracking of motion data, and data processing were performed through the Vicon Nexus software (283).

The system is reported to exhibit a low level of random error, or "noise," in its measurements (284). It can track motion in a large area, minimising the effect of occlusions that occur when one or more markers on an individual are momentarily obscured (285).

To collect muscle activation data, the Delsys surface EMG system (Delsys Trigno Avanti System, Delsys Inc., Boston, MA) with an operating rate of 2000 Hz was utilised. Data was collected using the system's surface EMG electrodes (27mm x 37mm x 13mm) placed on the skin over pre-defined muscles. The research-specific test configuration and EMG sensors' signal quality check were performed using the EMG Work Acquisition software (Delsys Inc., Boston, MA).

The system is reported to be valid in discerning differences in muscle activity under different conditions. (286). The system's wireless technology provides for greater mobility during data collection and reduces the likelihood of cable interference (287). It can identify EMG signals from multiple channels at the same time, allowing data to be collected from a variety of muscles at once (287).

4.2.1 Laboratory Setup

Prior to each data collection session, Vicon system calibration was executed based on the Vicon Nexus Product Guide (283).

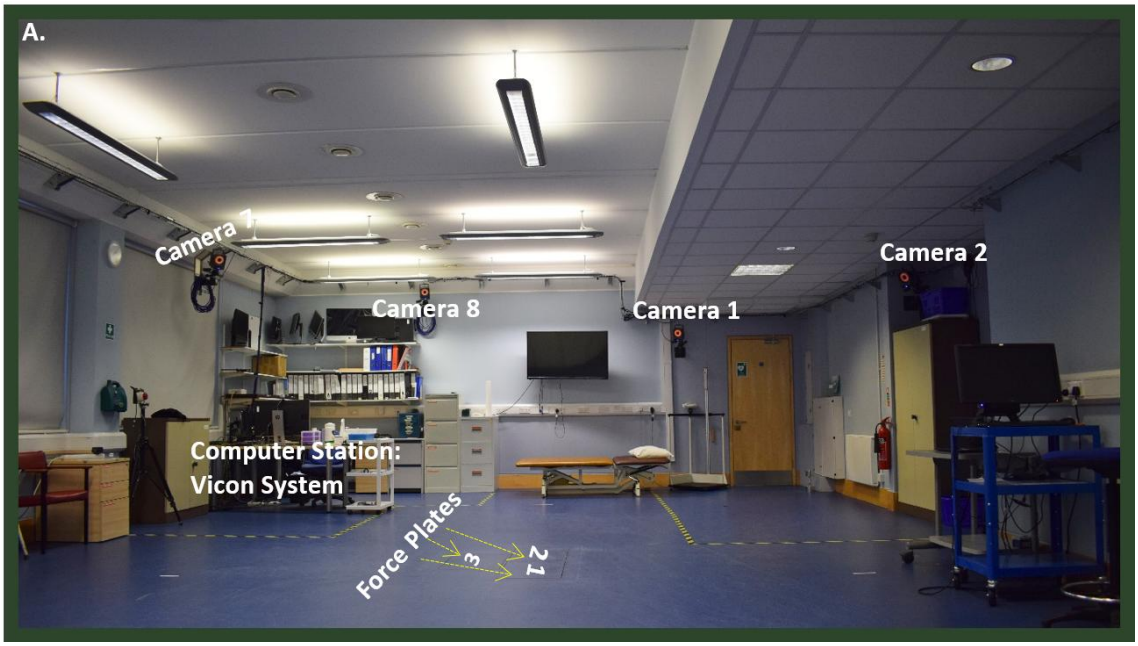
First, camera calibration was completed to determine the position, orientation, and lens properties of each camera (283). This established the capture volume in the system, defining

the spatial area within which accurate 3D data could be produced (283). Then, the volume origin of the system was set to define the centre of the capture volume and its axes (283). This volume's origin and axes are defined as the global coordinate system (283). While the global origin coordinates are set at (0, 0, 0), the global axis coordinates are represented as (x, y, z), where 'x' represents the horizontal axis, 'y' represents the horizontal axis perpendicular to 'x', and 'z' represents the vertical axis (283).

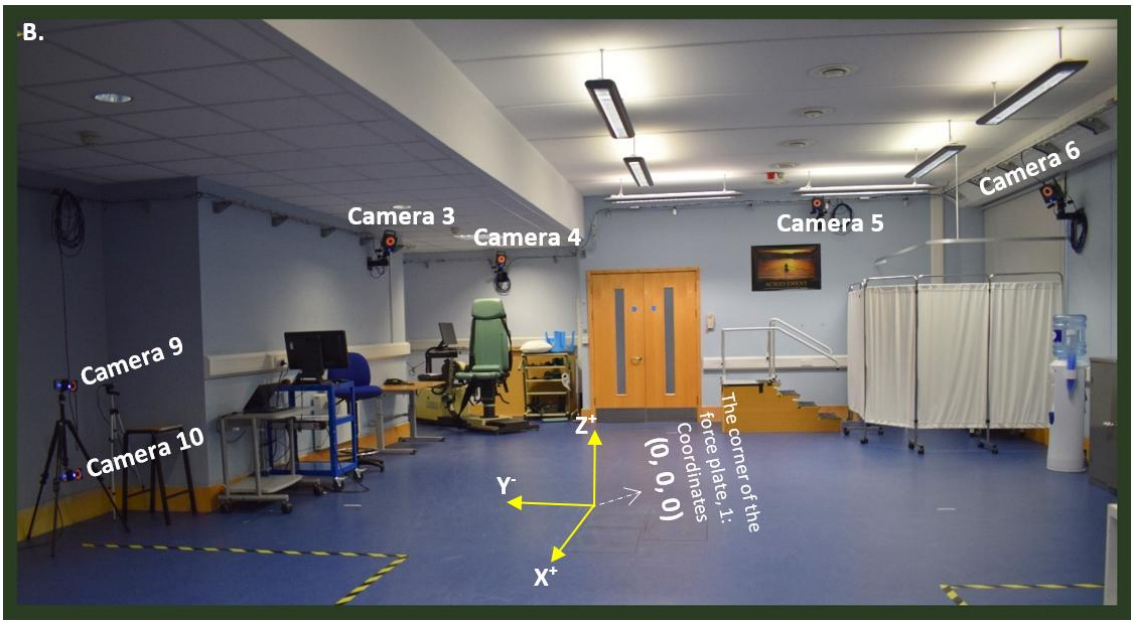
In the laboratory where all data collection sessions were conducted, there are three force plates that are in line with the floor surface. The corner of the first force plate was selected as a reference point for the laboratory's volume origin, and its coordinates were set to (0, 0, 0) as the global origin of the laboratory's coordinate system. All subsequent coordinates within the laboratory were determined relative to this established global origin (Figure 12).

Figure 12. Laboratory Setup (MoveExLab, UEA)

A. First Half of the Laboratory with Cameras, Computer Station, and Force Plates



B. Second Half of the Laboratory with Cameras and the Laboratory's Origin and Coordinates



Note: MoveExLab: Movement and Exercise Laboratory; **UEA:** University of East Anglia

4.2.2 Research-Specific Test Configuration

Before starting data collection for this project, a research-specific test configuration was established in the Delsys surface EMG system. The names of the muscles from which data would be collected were specified and saved on the system, and a unique numbered sensor was assigned to each muscle to ensure consistent data collection across all sessions.

4.2.3 Integration of Vicon and EMG Systems

The EMG system was integrated with the Vicon system to achieve synchronisation with kinematic data and to facilitate data analysis. The EMG system was added to the Vicon Nexus software's device list as a digital device, synchronising the two systems.

4.3 Experimental Procedures

Data collection took place in the MoveExLab at the UEA.

Each participant was asked to visit MoveExLab twice for data collection. All procedures were verbally explained to participants at the first of these two visits. They were given a printed copy of the participant information sheet (PIS), which was reviewed with them, and their project-related questions were addressed. Upon request, participants were reimbursed for their travel expenses up to 50 miles round trip.

During the informed consent process, participants attested to the absence of a latex allergy. Prior to the first data collection session, however, each participant completed the allergy screening questionnaire (Appendix 6) to determine if they had any other allergies that would demand an adaptation to the testing materials and/or environment. Each participant's allergy screening questionnaire was assessed to determine the type of adhesive to be used and whether any aspect of the test should be avoided.

The participants subsequently changed into their sleeveless T-shirts and shorts in a changing area partitioned off from the MoveExLab's main body with a curtain. Participants were given the choice to either bring their own shorts and T-shirt or have them provided for the purpose of data collection.

4.3.1 Specific Procedures to the Vicon Motion Capture System

Measurements: At the beginning of the first data collection session, the required measurements for the Vicon Plug-in Gait full-body model were taken from each participant. These bilateral measurements, performed according to the Vicon Plug-in Gait Reference Guide (288), were

stored in the Vicon Nexus software. Each of these is in Table 11, along with the corresponding measuring procedures.

Table 11. Vicon Plug-in Gait Full Body Model: Measurements and Corresponding Procedures

Measurement	Procedure
Body Mass (kg)	It is measured standing on a scale.
Height (mm)	It is measured standing on the floor.
Inter-ASIS Distance (mm)	The distance between left and right anterior superior iliac spines, measured with a calliper in the supine position.
Leg Length (mm)	The length from the anterior superior iliac spine to the medial malleolus across the knee joint, measured with a tape measure in the supine position.
Knee Width (mm)	The mediolateral width of the knee along the line of the knee flexion axis, measured with a calliper in a seated position with feet resting flat on the floor.
Ankle Width (mm)	The mediolateral distance across the malleoli, measured with a calliper in a seated position with feet resting flat on the floor.
Shoulder Offset (mm)	The vertical distance from the rotation centre of the glenohumeral joint to the base of the shoulder marker on the acromioclavicular joint, measured using a calliper.
Elbow Width (mm)	The width of the elbow along the axis of elbow flexion, measured with a calliper.
Wrist Width (mm)	The anterior-posterior thickness of the wrist at the wrist flexion axis, measured with a calliper.
Hand Thicknesses (mm)	The thickness between the dorsum and palmar surfaces of the hand, measured from the location where the finger marker was affixed with a calliper.

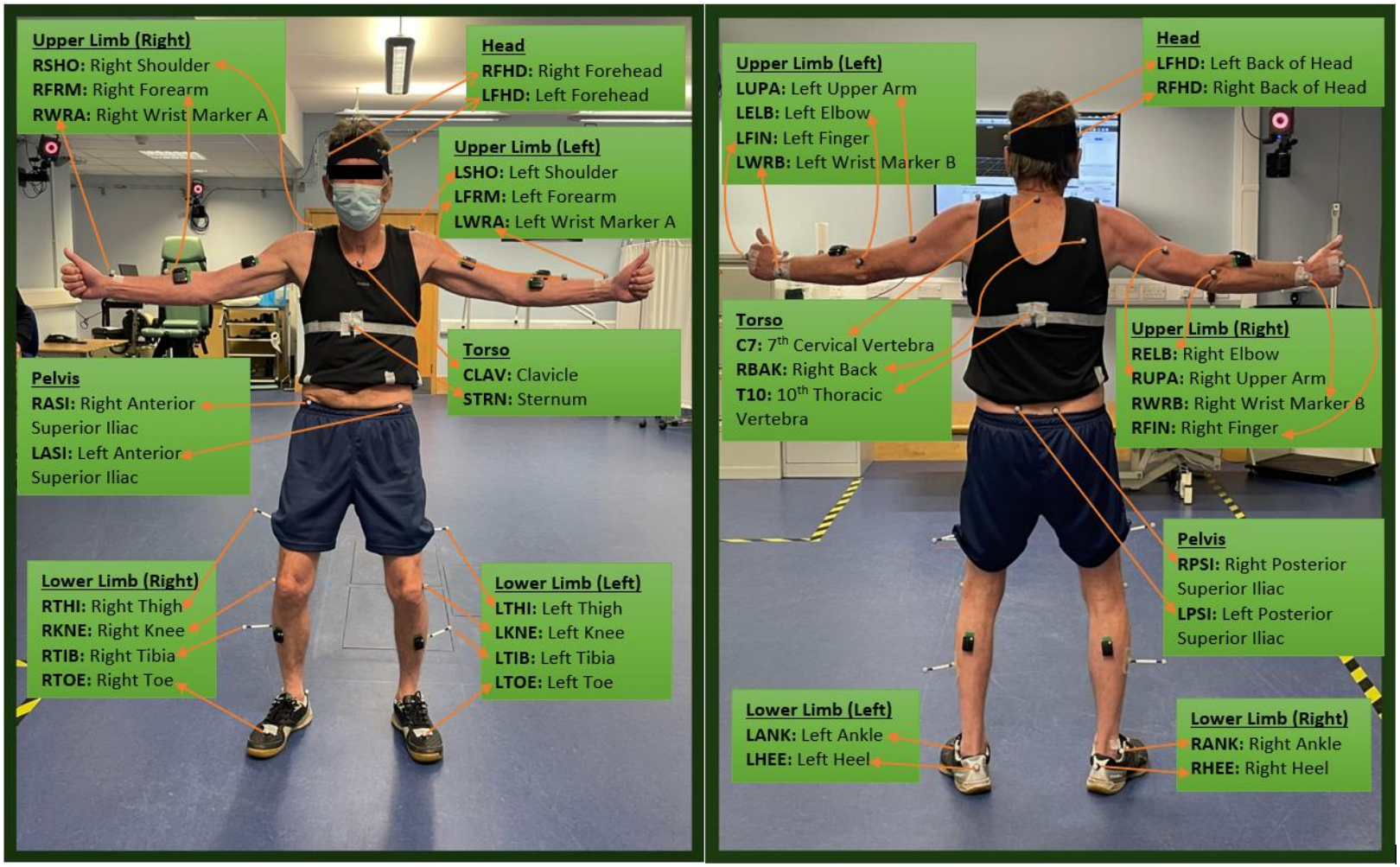
Marker Placement: Prior to each data collection session, thirty-nine passive reflective Vicon markers were placed on each participant's head (n = 4), torso (n = 5), upper limbs (n = 14), pelvis (n = 4) and lower limbs (n = 12) using hypoallergenic tape (Figure 13). These placements were conducted in accordance with the Vicon Plug-in Gait Reference Guide (288).

Capture the Static Trial: Following the marker placement in each session, a static trial was recorded. During this trial, participants were asked to maintain a specific position, referred to as the "Motorbike pose", while the Vicon system recorded the trial (Figure 13). The system then generated a labelling skeleton template to define the marker set and allow the Vicon Nexus software to perform automatic labelling (288).

A comparison between the marker locations that the system automatically generated and those that should be present on the participant's body was done on the labelling skeleton template,

utilising a single frame from the static trial recording in which all markers placed on the subject's body were visible. Any discrepancies were manually corrected to make sure that all markers were placed correctly on the labelling skeleton. Then, a predefined static pipeline was executed. This pipeline included 'Reconstruct', 'Autolabel Static', 'Scale Subject VSK', 'Static Skeleton Calibration - Markers Only', 'Process Static Plug-in Gait model', and 'Save Trial - C3D + VSK' operations and saved the trial at the end to facilitate accurate marker placement in subsequent dynamic trial recordings.

Figure 13. Vicon Plug-In Gait Full-Body Model: Marker Placement and Static Trial Recording Position



Note: The participant photo was taken with consent obtained through the completion of the UEA Model Release Consent Form and then used in this thesis. The form submitted by the individual to the UEA's system is provided in Appendix 7.

4.3.2 Specific Procedures for the Delsy Surface EMG System

In each data collection session, EMG signals were collected from specific muscles of each participant as they performed the experimental task. These muscles were: biceps brachii (BB), flexor carpi radialis (FCR), extensor carpi radialis (ECR), and brachioradialis (BR), chosen for their essential roles in the task's execution. The BB is primarily responsible for elbow flexion, while the FCR is involved in wrist flexion and abduction. The ECR contributes mainly to wrist extension and radial deviation, and BR aids in elbow flexion and forearm pronation/supination. Additionally, all these muscles are superficial, making them practical choices for surface EMG recording.

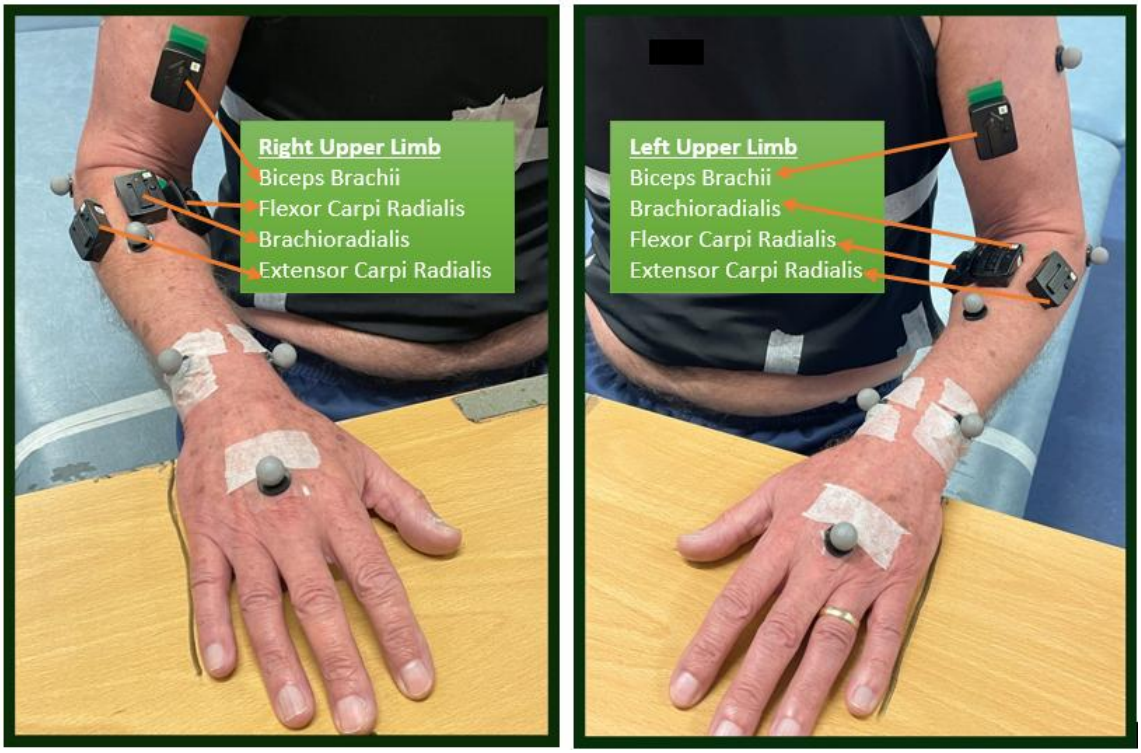
Electrode Placement: Before placing the surface EMG electrodes on these selected muscles, participants' skin was prepared with alcohol-based swabs and skin preparation gel to minimise resistance to signal transmission from muscle to electrode. Eight surface EMG electrodes were adhered to the surface of the ULs using hypoallergenic adhesive tape, with four electrodes on each limb. To minimise any potential movement artefacts, electrodes were carefully secured with additional tape as needed.

Accurate measurement of muscle activity can be achieved by utilising surface EMG, provided that the proper procedure for electrode placement on the skin is followed (289). Electrode placement on the muscles of interest was therefore accomplished by referencing the electrode placement reported in previous studies (290–293). Following the execution of muscle-specific test manoeuvres to palpate the superficial muscle outlines, electrodes were positioned appropriately over the muscle bellies. Table 12 presents the test manoeuvres and electrode placement procedures on muscles, while Figure 14 shows the completed electrode placement.

Table 12. Muscles Assessed, Test Manoeuvres, and Electrode Placement

Muscle	Test Manoeuvre	Electrode Placement Procedure
Right – Left Biceps Brachii (BB)	Flexion of the forearm in supination (291)	Electrodes were placed on the line between the medial acromion and the cubital fossa at one-third of the distance from the cubital fossa (290).
Right – Left Flexor Carpi Radialis (FCR)	Flexion of the wrist (291)	Mid-point between biceps tendon insertion and medial epicondyle was found, and sensors were placed about four finger widths down from this point (290, 291).
Right – Left Extensor Carpi Radialis (ECR)	Dorsiflexion of the wrist (291)	The electrodes were positioned at a distance of two fingers from the lateral epicondyle of the humerus (291, 293).
Right -Left Brachioradialis (BR)	Forearm flexion in a neutral position (291)	Electrodes were placed halfway between the biceps tendon and the lateral epicondyle, just distal to the elbow joint crease, and parallel to the longitudinal axis of the forearm (291, 292).

Figure 14. Electrode Placement



Signal Quality Check: Prior to each data collection session, the quality of EMG signals for each muscle was assessed using EMG Work Acquisition software. This was done while participants performed the relevant test manoeuvre (Table 12). If necessary, the electrode placement was repeated for optimal signal quality.

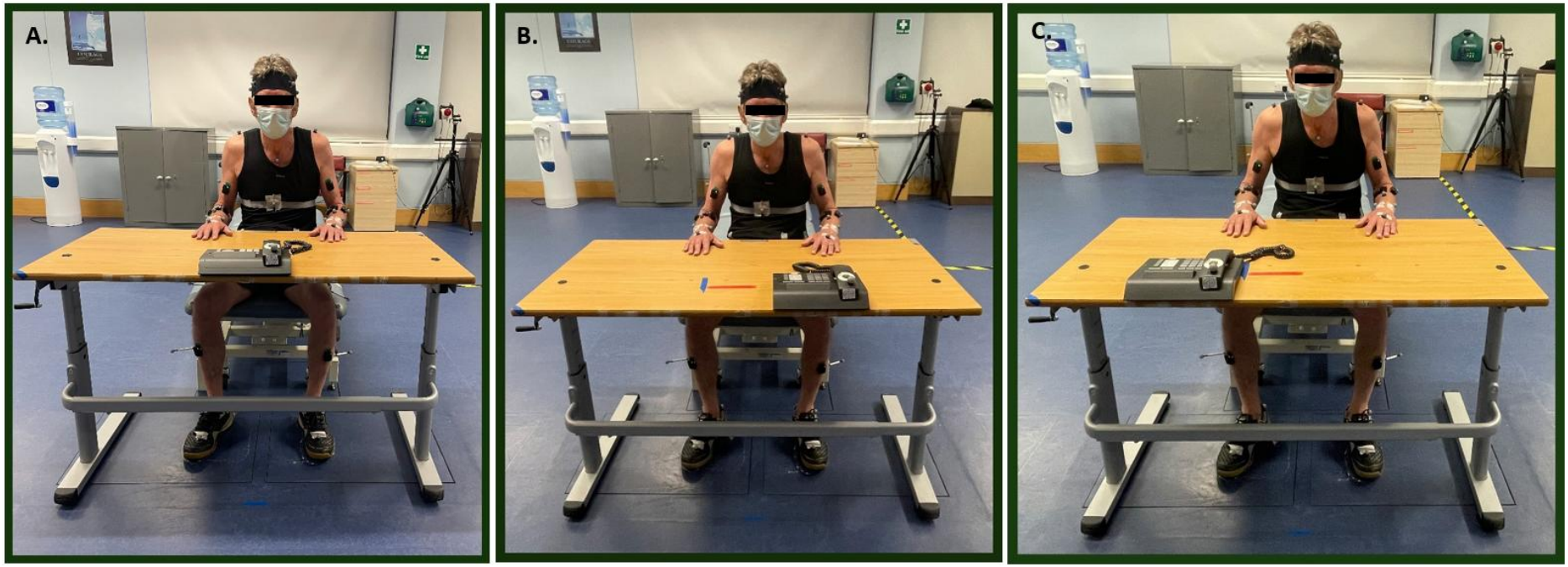
Note: Specifically, the Vicon-system-related measurements, marker placement, and electrode placement, as described above, were completed jointly by the lead researcher (the author of this work) and another researcher, both of whom were well-trained in these procedures and are qualified physiotherapists. This approach was implemented to reduce the preparation time for research participants.

4.3.3 Standardised Upper Limb Task

The telephone answering task, a functional and real-life UL activity, was used in this project (Figure 15). Although the focus was primarily on the 'reaching to grasp' section, participants attempted the entire task. The reasoning is that there may be differences in neuromuscular control strategies used when performing a real-life activity versus simply reaching for a target in a laboratory setting. Therefore, by using such a purposeful, real-life activity, participants are more likely to use 'natural' movement patterns, thus collecting data that is directly applicable to clinical practice.

Additionally, a telephone was chosen as the target because it is safer than other alternatives, such as using a glass or can of liquid, which could cause injury if dropped or spilt across the surface EMG electrodes.

Figure 15. Experimental Setup: **A.** Midline Workspace; **B.** Contralateral Workspace–Right Upper Limb Task; **C.** Contralateral Workspace–Left Upper Limb Task



Note: The figure displays the participant positioning and the telephone positioning for different tasks. Figure A illustrates the midline workspace, where the receiver is aligned with the trunk's midline at the start position. Figure B shows the contralateral workspace for the right upper limb task, aligning the receiver with the midline of the left hand at the start position. Figure C presents the contralateral workspace for the left upper limb task, with the receiver aligned to the midline of the right hand at the start position.

Participant Positioning: In all data collection sessions, participants were seated on an adjustable plinth (Figure 15). The plinth's height and position were carefully tailored and consistently maintained for individuals across all testing occasions. For each participant, the plinth's height was adjusted so that their hips, knees, and ankles formed 90-degree angles while seated. A height-adjustable table was positioned in front of them, set to a height that allowed them to sit upright with relaxed shoulders and elbows flexed at 90 degrees, ensuring that both hands rested comfortably on the table with the wrist creases aligning with the table's edge. The starting position for each hand, directly in front of each shoulder at the table's front edge, was marked to guide participants to return to it during the task. This position was regularly checked to ensure consistency throughout data collection.

Telephone Positioning: Throughout the experimental task, the telephone was placed on the table in three consecutive positions, each at 1.5 times the participants' forearm length from the table's edge nearest to the participant (Figure 15):

1. In the midline workspace, where the task was completed with the right and left hand, respectively, the receiver was aligned with the midline of the participant's trunk (1st position; Figure 15, A).
2. In the contralateral workspace, where the task was completed with the right hand, the receiver was aligned with the midline of the participant's left hand (2nd position; Figure 15, B).
3. In the contralateral workspace, where the task was completed with the left hand, the receiver was aligned with the midline of the participant's right hand (3rd position; Figure 15, C).

Auditory Cuing: The participants were cued to commence the task upon receiving an auditory signal in the form of a buzzer. The buzzer, integrated into the Vicon Nexus software, emitted a signal at a frequency of 2000 Hz and generated a detectable voltage signal, a spike, when pressed. This signal was recorded by the Vicon Nexus software and synchronised with the kinematic and EMG data. This voltage signal precisely indicated the exact moment when participants were prompted to initiate the task.

Instructions for Participants: Prior to beginning data collection, participants were instructed to:

> "Look at the telephone and sit still. When you hear the buzzer, pick up the telephone and answer it with "hello," then replace the receiver, then place your hand back in the start position as marked on the table. I will then check your posture to make sure you are back

in the starting position. You will repeat the task each time you hear the buzzer. In-between repeats of the task you will sit still, with your hand in the start position and look at the telephone. You will repeat the task three times with each hand. Then I will move the telephone to the left-hand side of the table. You will repeat the task three times using your right hand. Then I will move the telephone to the right-hand side of the table. You will repeat the task three times using your left hand. I will be here to prompt you if you need me to and to answer any questions."

All participants were given sufficient time to practice the task to ensure they fully understood the requirements and felt comfortable performing it before data collection began. Once participants indicated they were ready, data collection using the Vicon and Delsys EMG systems commenced.

Note: The ethical approval process established a maximum number of trials for each study: up to 30 trials for participants without mobility-impairing conditions (Chapter 5) and up to 45 trials for stroke survivors (Chapter 6). To balance data quality with practical considerations, such as minimising fatigue and disengagement, each participant was initially asked to complete five trials per hand in each workspace (midline and contralateral), if feasible. This decision was informed by existing research on UL kinematics, which suggests that 3–5 trials are generally sufficient for reliable results (294).

However, after several data collection sessions, observations and participant feedback revealed that completing five trials per condition often caused fatigue and disengagement. To address this, it was decided to immediately assess trial quality after recording using the Vicon Nexus software to ensure that the trial was well reconstructed. The number of trials per reaching condition was amended to three, allowing for up to five trials if the quality of the initial trials was unclear or insufficient, to secure at least three high-quality trials for analysis.

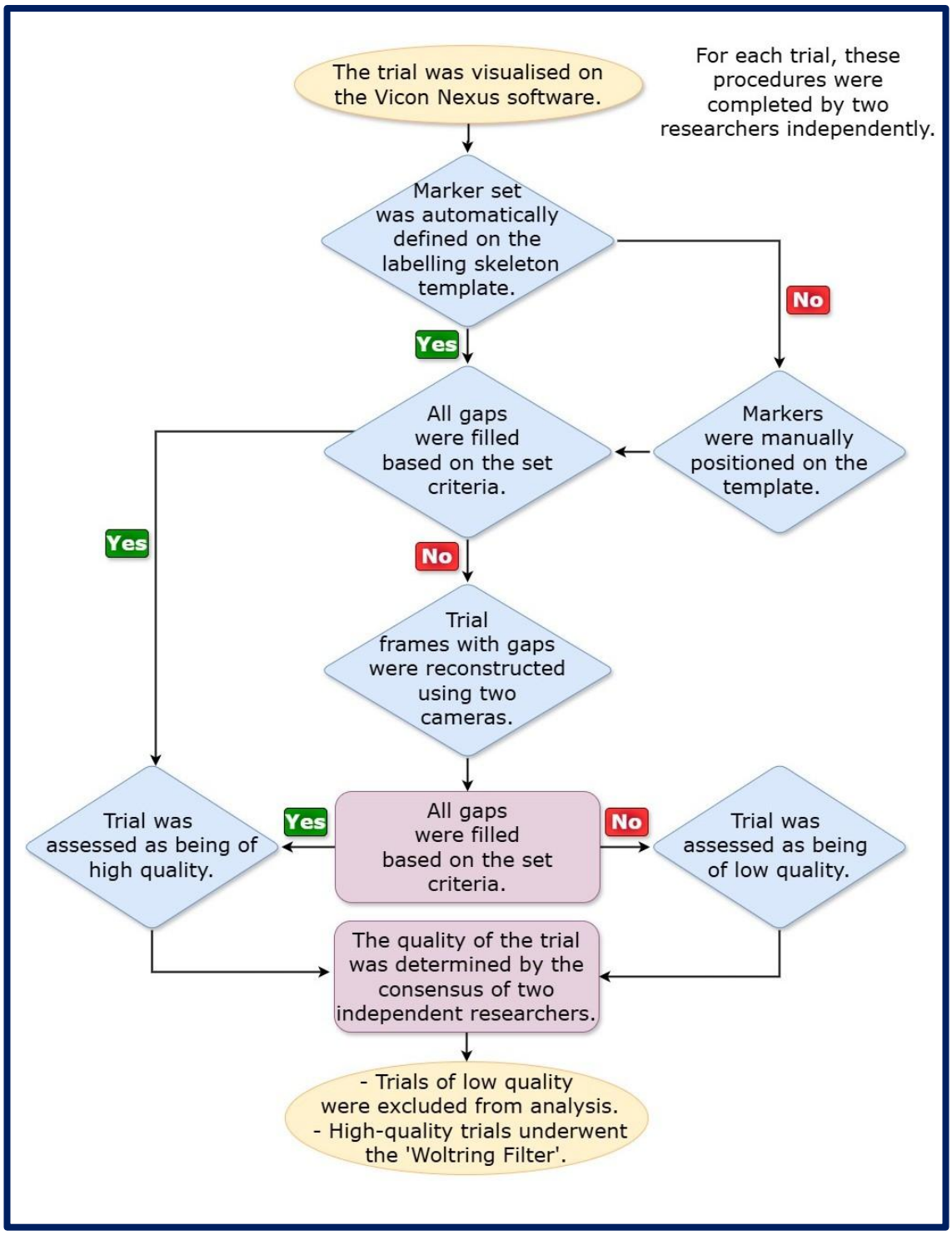
4.4 Data Processing

To obtain accurate and reliable findings from the raw kinematic and EMG data, it is necessary to address any errors or noise that may be present. This involves processing the raw data to cleanse, filter, and transform it into a more understandable and useful form. All the data collected was therefore subjected to meticulous processing prior to analyses.

4.4.1 Processing of the Kinematic Data

The collected kinematic data were processed using the Vicon Nexus software (Figure 16).

Figure 16. Flowchart: Processing of the Raw Kinematic Data



Dynamic trials recorded as participants performed the experimental task were visualised in the Vicon Nexus software. The saved static trials allow automatic marker positioning in dynamic trials. However, marker placement was checked to guarantee their accurate placement. In cases where the marker(s) were identified as misplaced or if the marker set was not automatically placed on the template by the software, manual corrections were made as needed.

Gaps in trials are possible due to issues such as motion blurring, sensor malfunction, signal interference, or markers becoming obstructed during the recording process. These gaps must be filled for the data to be accurate. Therefore, gaps in the trials were filled following preestablished criteria (Table 13). A trial was considered high quality if all gaps could be filled accordingly. For larger gaps, the 'Reconstruct' operation of the Vicon Nexus software was used to reconstruct frames where these gaps occurred using two cameras rather than the standard three. If the marker(s) with gaps became visible, the gaps were filled using the same criteria. Trials with unresolved gaps in essential markers for deriving the project's outcome variables were deemed unusable and excluded from analyses. Noisy data, unusual model outputs, and other anomalies led to the trial being labelled as of dubious quality.

Table 13. Gap-Filling Criteria

Marker	Standard Gap Filling: Type and Maximum Frame Size	Still Participants (Waiting for Buzzer): Type and Maximum Frame Size
Any of the Head Markers	• Rigid body fill, up to 65 frames	• Rigid body fill, up to 100 frames
Either Wrist Marker When the Other is Visible	• Pattern fill, up to 50 frames	• Pattern fill, up to 80 frames
Any Marker on the Torso	• Spline fill, up to 5 frames **OR** • Pattern fill from suitable marker, up to 10 frames	• Rigid body fill, up to 20 frames (Used with caution and only other torso markers are visible.)
Any other Marker	• Spline fill, up to 5 frames **OR** • Pattern fill from suitable marker, up to 10 frames	

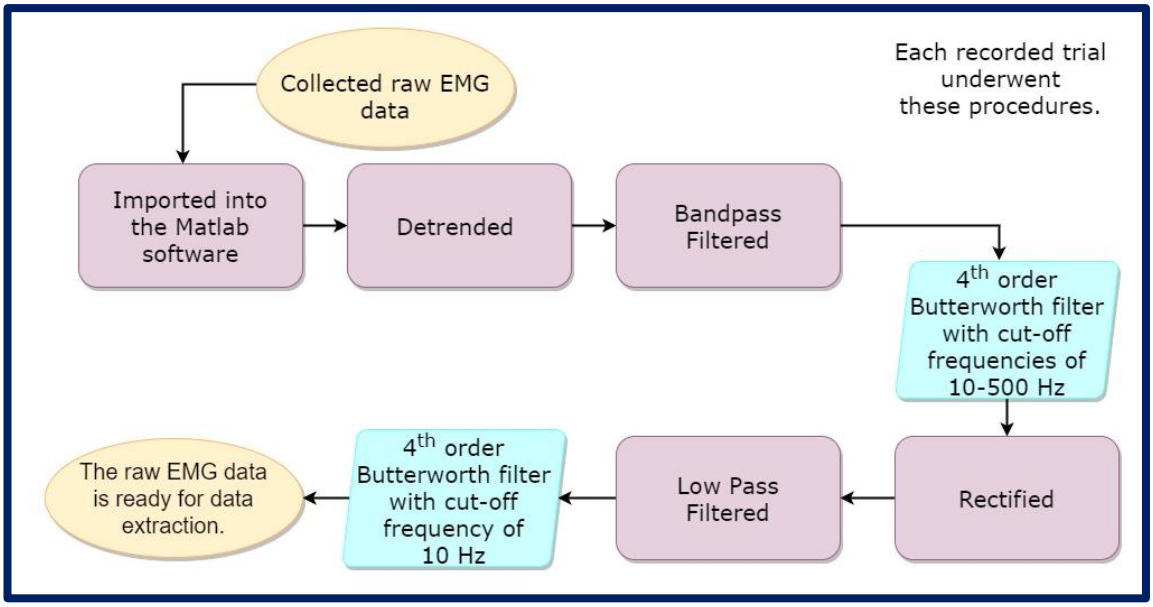
These procedures were completed independently for each recorded trial by the lead researcher and another researcher. Discrepancies in assessing trial quality and trials deemed dubious, were rigorously examined to determine their final quality rating. Trials with unresolved issues that were initially labelled as dubious were classified as low quality.

High-quality trials underwent the 'Woltring Filter' operation in the Vicon Nexus software for trajectory smoothing.

4.4.2 Processing of the EMG Data

Raw EMG data from each recorded trial was processed using MATLAB scripts (Mathworks Inc, Natick, MA, USA). Noise and artefacts were removed from each trial (295, 296). A series of sequential processes was performed on each collected EMG dataset (Figure 17). These processes were determined by visually examining the EMG signals and evaluating various techniques reported in previous research.

Figure 17. Flowchart: Processing of the Raw Surface EMG Data



Sequentially:

Data Importation: The raw EMG data were imported into MATLAB software.

Detrending the Data (Removing Mean): The data underwent pre-processing using MATLAB's *'detrend'* function to remove the best straight-fit line trend (297, 298). This eliminated baseline drifts due to resting muscle activity, and electrode placement fluctuations unrelated to muscle activity being monitored to ensure a more accurate representation of the monitored muscle activity (299).

Bandpass Filtering: The detrended EMG data were filtered using a fourth-order Butterworth bandpass filter with cutoff frequencies of 10-500 Hz to eliminate frequencies outside this range.

After thoroughly evaluating the characteristics of the collected EMG data and the analysis objectives, it was concluded that the chosen filter properties are appropriate for this project. Butterworth filters are known for their advantageous amplitude properties, which enable them to preserve the amplitude of desired signal components while reducing the amplitude of

undesirable interference or noise (300, 301). They also exhibit transient behaviour by not introducing significant distortion or delay to the EMG signal (300, 302). Additionally, the order of a filter has a significant effect on its performance because it affects the steepness (roll-off) of the frequency response (303). Fourth-order filters are frequently used in a variety of settings due to their ability to effectively attenuate high-frequency noise and interference while preserving important lower-frequency components in terms of structure and timing (304). Using the fourth-order Butterworth filter can effectively eradicate unwanted noise and artefacts, which is required for accurate analysis of the muscle activity onset time (MAOT) and electromechanical delay (EMD) (305, 306), two of the outcome variables measured in this project.

Power spectral density analyses (PSD) on arbitrary data samples revealed that the frequency range of interest in the collected data is typically between 10 and 450 Hz. However, cases where the EMG signal increased up to 500 Hz were observed on the PSD graphs; thus, the Butterworth filter with cutoff frequencies of 10-500 Hz was chosen to avoid losing any crucial data.

Rectification: Bandpass-filtered EMG data were full-wave rectified to convert all negative amplitudes to positive (307, 308). EMG data is a "bipolar signal" with both positive and negative values, and rectification ensures that the data is not averaged to zero. (307, 308).

Low Pass Filter: Smoothing the rectified EMG data was accomplished using a fourth-order Butterworth low pass filter with a cutoff frequency of 10 Hz. The fourth-order Butterworth filter was chosen for the same reasons mentioned above in the bandpass filtering stage. The effects of different cutoff frequencies on the linear envelope were visually inspected, and it was determined that a cutoff frequency of 10 Hz provided the best quality linear envelope, which is suitable for accurate MAOT detection. Thus, these filtering properties were decided to be appropriate for obtaining a refined linear envelope and removing any high-frequency fluctuations introduced during the rectification process (309).

4.5 Variables

The current study concentrated on the ‘reaching to grasp’ phase, an essential preliminary stage in the ‘telephone answering’ task. This phase is of utmost importance as it establishes the foundation for the subsequent phases of functional activities involving the UL. Hence, all pertinent computations and analyses were customised exclusively for this preliminary phase.

The kinematics-derived variables in the project were:

- Time to Task Completion (TTC): It quantifies the time required to complete a specific task. It allows for a direct and objective evaluation of performance efficiency. Shorter task completion times usually indicate greater functional ability. This measure can be useful in assessing the practical implications of neuromuscular impairments on everyday functional tasks.
- Movement Smoothness (MS): Improvements in this measure typically signify a transition towards more efficient motor patterns and improved movement control (310).
- Trunk-Hand Displacement Ratio (THDR): It quantifies the extent to which individuals use trunk movement to compensate for reduced neuromuscular control of the UL (311). A higher THDR indicates greater use of compensatory trunk movement, whereas a lower THDR indicates less compensatory trunk movement. This measure can, therefore, serve as an important indicator of neuromuscular impairment and provide useful information for the project.
- Reach Path Ratio (RPR): A lower RPR indicates a more efficient and direct movement, while a higher RPR indicates a more indirect and inefficient movement trajectory (312). Utilising RPR can be effective for assessing the quality of movement and the severity of neuromuscular impairments.

The EMG-derived variables were:

- Muscle Activity Onset Time (MAOT): This variable assesses the timing of muscle activation, which is frequently altered after stroke. Changes or delays in muscle activity onset can indicate underlying neuromuscular disruptions. The assessment of these changes can help in understanding the extent and nature of neuromuscular impairment in stroke survivors.
- Electromechanical delay (EMD): While reported among EMG-derived variables in this text, EMD is actually a combined EMG- and kinematics-derived variable. It reflects disruptions in the integrity of neural pathways that control muscle activation. Post-stroke, these disruptions can lead to prolonged EMD, as the neural system requires more time to generate the necessary muscle activity for initiating movement (17). Implementing this variable into the project can help in understanding the efficiency and health of neural processes involved in motor control.

Among these variables, only TTC is a functional ability variable, while the others are neuromuscular impairment variables.

The selection of the TTC, MS, THDR, RPR, and MAOT as outcome measures is further supported by a recent systematic review. This review analysed 32 studies with 618 stroke survivors and 429 healthy adults. The findings indicated that stroke survivors demonstrated longer time to complete tasks (SMD = 2.04 [1.50, 2.58] s), reduced movement smoothness (SMD = 1.20 [0.89, 1.50]), a more curved reach path ratio (SMD = 0.81 [0.38, 1.24]) and greater trunk displacement (SMD = 1.18 [0.92, 1.44] mm) compared to healthy adults across various workspaces (17). The review's narrative synthesis, which included data from eight studies, indicated that stroke survivors experienced delayed muscle activation compared to healthy adults. These findings, thus, emphasise the critical nature of these measures in representing changes in UL movement abilities following a neurological impairment like a stroke, which may offer valuable insights to the current research.

Following data processing, the values of the aforementioned variables were extracted from the collected data using custom-written MATLAB scripts. Below is a detailed explanation of the variables and the data extraction process.

- **Functional Ability Variable**

Time to Task Completion (TTC): Stroke survivors frequently take longer to complete a given task, indicating the impact of neuromuscular impairments on task performance. TTC, thus, can be an indication of the practical consequences of neuromuscular impairments caused by a stroke. A decrease in functional abilities associated with neurological impairments such as stroke can result in a longer TTC, whereas an increase in functional abilities can result in the opposite (17).

TTC was calculated as the time difference between the onset and the end of the movement in seconds. The onset of movement was the first time point at which the finger marker position deviated from the resting mean by more or less than three standard deviations (3*SD) (313, 314), with this deviation continuing uninterrupted for at least 0.08 seconds. The procedure used to find this point was:

- The resting mean of the finger marker trajectory was calculated using three seconds of data collected while the participants sat still in the starting position immediately before the buzzer cue to begin performing the task.
- The upper and lower thresholds were calculated as the resting mean plus 3*SD and the resting mean minus 3*SD, respectively.
- The first point where the position of the finger marker exceeded the upper threshold and the first point where it fell below the lower threshold were identified, with the

condition that the deviation remained continuous for at least 0.08 seconds (8 consecutive data points) after the buzzer cue.

- Then, the MATLAB min function was used to determine which of these two instances occurred earlier after the buzzer cue; this point was deemed the movement onset.

The movement's end, characterised by the hand grasping the receiver and moving towards the ear, corresponded to the first peak in the finger (FIN) marker's Y-axis position. This peak was detected using MATLAB's *'findpeaks'* function during the telephone answering task. The telephone was positioned on the Y-axis, guiding participants to reach in that direction. The first peak, indicating the hand's contact with the telephone, was marked as the movement's end.

- **Neuromuscular Impairment Variables**

Movement Smoothness (MS): MS encompasses movement fluidity and quality, making it an important determinant of the impact of post-stroke neuromuscular impairments (310, 315). MS can decrease due to stroke-related neuromuscular impairments (17). Smaller MS values signify less smooth movements, whereas greater MS values are indicative of smoother movements.

It is widely used in UL kinematics research, and several smoothness metrics are available (316). A recent systematic review conducted to determine the most valid metrics for assessing the smoothness of UL movements concluded that, of 32 metrics evaluated, only Spectral Arc Length (SPARC) is valid (316). MS was, therefore, decided to be quantified using the SPARC method. The *'SpectralArcLength'* function described by Balasubramanian (317) (SpectralArcLength.m) and computing the spectral arc length of the movement speed profile was imported into Matlab (316, 317). The speed profile for the 'reaching to grasp' phase was calculated. The speed profile was then passed to the *'SpectralArcLength'* function, which calculated the smoothness value using a sampling time of 0.01 seconds.

Trunk-Hand Displacement Ratio (THDR): The trunk plays an important role in UL activities (318). When reaching for an item within arm's length, the trunk stabilises the body's position (318, 319). When reaching beyond the arm's length, the trunk moves in synchronisation with the arm to assist in directing the hand to the target (318, 319). Excessive trunk displacement (TD) during UL movements is a common compensatory strategy for UL neuromuscular impairments following stroke (17, 320). The degree of TD can serve as an indicator of the severity of neuromuscular impairments in individuals with UL impairments after a stroke.

For this project, the decision was made to compute the THDR instead of using the traditional method of TD calculation. This ratio provides an estimate of the TD's contribution to the overall hand displacement (HD). If the THDR is less than 1, it signifies that the hand travelled farther than the trunk during the task, implying that the arm was used more than the trunk. If the THDR is greater than 1, it indicates that the trunk travelled a greater distance than the hand during the task, implying that the trunk was used more than the arm. During the 'reaching to grasp' phase, TD was calculated as the difference between the maximum and minimum values of the T10 marker's position on the Y-axis, which was placed on the 10th thoracic vertebra. MATLAB's '*max*' and *'min'* functions were used to compute these values in millimetres. Similarly, HD was measured in millimetres as the difference between the maximum and minimum values of the FIN marker's position on the Y-axis, which was positioned on the 3rd metacarpophalangeal joint. The THDR was then calculated as the ratio of TD to HD, resulting in a unitless value.

Reach Path Ratio (RPR): The RPR is commonly reported in UL kinematics studies to assess movement linearity (17). An RPR close to 1 indicates a straight path, while an RPR greater than 1 indicates either an abnormally curved path or multiple attempts to reach a target (312). Therefore, RPR can serve as an indicator of the severity of neuromuscular impairments following a stroke.

The RPR is calculated by dividing the actual distance travelled by the straight-line distance between the movement's onset and end (312). The actual path length was determined by the cumulative changes in the X and Y axes of the FIN marker from the movement onset to the end. The total distance travelled accounts for absolute changes in both axes, capturing all directional movements. The straight-line distance was derived using the Euclidean formula, based on differences in the FIN marker's X and Y positions at the movement onset and end, calculated as the square root of the sum of the squares of these horizontal and vertical distances.

Muscle Activity Onset Time (MAOT): MAOT represents the moment when muscle fibres initiate to contract to perform a targeted activity/movement (321) and post-stroke it is often extended (17, 322). Extended MAOT can signify neuromuscular impairments, while decreases in MAOT may indicate neuromuscular restitution.

It was calculated following the steps below, sequentially (323, 324):

- The resting mean of the EMG signal was calculated by averaging the EMG signal over a 3-second period immediately prior to the cue to start (buzzer).
- The SD of the EMG signal during this same 3-second period was calculated.

- Using the resting mean and SD, a threshold was defined as the resting mean plus three times the SD (3*SD) of the EMG signal.
- The first time point at which the EMG signal exceeded this threshold for at least 160 consecutive data points (equivalent to 0.08 seconds) after the cue to start (buzzer) was identified.
- The detected time point was subtracted from the time point of the cue to start (buzzer) to determine the MAOT in milliseconds (ms).

Electromechanical Delay (EMD): The time lag between the onset of muscle electrical activity and the measurable onset of mechanical force production is referred to as EMD, and it reflects the time required for electrochemical processes to activate mechanical contraction (325, 326). Therefore, EMD enables the acquisition of insights into the operation of the neuromuscular system. Prolonged EMD may suggest a potential neuromuscular impairment that hinders the transmission of electrical signals from the nervous system to muscle fibres.

Due to the differing sampling rates of the Vicon and EMG systems, the Vicon data was resampled from its original 100 Hz to match the 2000 Hz sampling rate of the EMG system using MATLAB. The movement onset time, as defined under the 'Time to Task Completion (TTC)' subheading above, was then adjusted to align with the EMG system's 2000 Hz sampling rate. This alignment was crucial for the accurate calculation of EMD. EMD was subsequently calculated by subtracting the MAOT value from the adjusted movement onset time, expressed in milliseconds.

Note: Although the collection of EMG data from the FCR and BR muscles was initially planned, it was later observed that clear readings from these muscles were not obtained during data collection, particularly in the study involving stroke survivors (Chapter 6). Consequently, these muscles were excluded from the analyses.

The primary challenges in obtaining clear signals from the FCR and BR muscles likely stemmed from a combination of factors: their small sizes and deep anatomical locations, which make them inherently difficult to monitor with surface electrodes, as well as post-stroke changes in muscle tone and activation patterns that further complicated signal acquisition. Additionally, while the Delsys surface EMG system is known for its high sensitivity and typically performs well without shaving the electrode placement area, the lack of shaving in cases of excessive hair may have contributed to reduced signal quality in this project (327).

Since the study with individuals without mobility-impairing conditions (Chapter 5) was intended to inform variable selection for assessments in stroke survivors, and the EMG data from the FCR and BR muscles were not viable in the stroke survivors' study (Chapter 6), their exclusion from both studies was considered acceptable within the context of this PhD project. This decision ensured consistency across analyses and maintained their relevance to the study objectives.

Chapter 5. Reference Values, Test-Retest Reliability, and Smallest Detectable Changes for Measures of Functional Ability and Neuromuscular Impairment during a Standardised Upper Limb Task in a Representative Sample of Individuals without Mobility-Impairing Conditions

5.1 Introduction

Rehabilitation outcomes for stroke survivors can be improved by gaining a detailed understanding of the relationships between post-stroke neuromuscular impairments and functional abilities. Such an understanding could potentially facilitate establishing efficient and effective rehabilitation goals.

The systematic review presented in a preceding chapter detected almost perfect correlations between improvements in neuromuscular impairments and functional abilities following exercise-based therapies compared to control interventions. However, these findings largely rely on clinical outcome measures, which have limitations in distinguishing between neuromuscular recovery and compensation and lack the sensitivity to detect subtle changes (71, 106).

In contrast, kinematics- and EMG-derived variables can allow more sensitive and precise assessments of stroke survivors (16, 17, 328). Incorporating these variables into investigating the relationships between neuromuscular impairments and functional abilities post-stoke could yield deeper insights. Despite this potential, the majority of current research on the relationships between neuromuscular impairments and functional abilities post-stroke predominantly relies on clinical outcome measures (29–32). Research employing kinematics- and EMG-derived variables is limited (19–22) and frequently constrained by small sample sizes (19, 22). Additionally, the diversity of available kinematics- and EMG-derived variables poses a challenge in selecting the most appropriate and sensitive ones to investigate these relationships effectively (17, 18, 28, 106, 328), emphasising the need for a standardised core set in clinical trials (106).

Establishing the reference values, test-retest reliability, and SDC of kinematics- and EMG-derived variables in a population without mobility-impairing conditions provides foundational data for understanding the behaviour of these variables, supporting their standardisation and guiding their potential selection for future validation and use in post-stroke assessments (110). Reference values enable the identification of deviations from the norm in stroke survivors, offering insights into neuromuscular impairments and functional limitations (110–112). Test-retest reliability evaluates the inherent variability of these variables, independent of stroke-related factors such as recovery over time or cognitive decline, providing evidence of their consistency under controlled conditions and laying the groundwork for exploring their

applicability in stroke research (110, 113). SDC values, by quantifying the smallest detectable change beyond measurement error, provide a benchmark for reliable measurement and inform their potential relevance in evaluating rehabilitation outcomes (110, 114).

However, high-quality studies on reference values, test-retest reliability, and SDCs for kinematics- and EMG-derived variables in adults without mobility-impairing conditions remain scarce (18, 23–26, 28, 115, 328). Existing research often suffers from small sample sizes (23–26), which limit statistical power, and methodological limitations, including the lack of standardised measurement protocols (18, 28, 115, 328), thereby limiting both the reproducibility and generalisability of findings. Addressing these limitations requires high-quality, large-scale studies that employ rigorously documented protocols to identify reference values, assess reliability, and calculate SDCs for kinematics- and EMG-derived variables in adults without mobility-impairing conditions, providing foundational data for their future validation and potential application in stroke-related research.

To address the thesis's second research question, this experimental study aims to (1) identify the reference values (**Aim 2a**); (2) determine the test-retest reliability (**Aim 2b**); and (3) ascertain the SDC (**Aim 2c**) of neuromuscular impairment and functional ability variables during a standardised UL task using the Vicon motion analysis and Delsys EMG system in a representative adult population without mobility-impairing conditions.

5.2 Methods

5.2.1 Introduction

Chapter 4 describes the common methods and instruments, employed in this study and the study presented in Chapter 6. This section exclusively concentrates on the methods and experimental procedures specific to this study.

5.2.2 Study Design and Participants

This study was designed as a correlational agreement study. The eligibility criteria for participants are set out in Table 14 below.

Table 14. Eligibility Criteria for Recruitment

Inclusion Criteria	Exclusion Criteria
• Aged at least 18 years old • Providing written informed consent	• Have any neurological and/or musculoskeletal pathology, impacting mobility, such as Multiple Sclerosis or osteoporosis • Have a latex allergy

5.2.3 Ethical Approval and Informed Consent

Ethical approval for the study was granted by the UEA's FMH Research Ethics Committee under reference number 2019/20-044 (Appendix 8).

Written informed consent was obtained from each participant prior to being included in the study in adherence with the Declaration of Helsinki (Appendix 9). Each was provided a PIS (Appendix 10) and a Covid-19 PIS (Appendix 11) electronically. Any queries they had were addressed electronically, over the phone, or in person.

5.2.4 Sample Size

A *priori* power analysis indicated that 54 participants were required to estimate the intraclass correlation coefficient (ICC) with a 95% CI width of no more than 0.15, assuming the ICC is 0.85 (329). Considering a 20% participant attrition rate and a 15% poor data quality rate (330, 331), the sample size was set to be 75 participants.

5.2.5 Recruitment

All participants were recruited from the UEA and Norwich and Norfolk local communities.

To reach potential participants, the study advertisement (Appendix 12) was placed around the university, on the RHITE database - https://www.brainmic.nihr.ac.uk/RHITE; the ABIRA website - http://www.abira.ac.uk/; the HSC (School of Health Sciences) Bulletin; the UEA Lasdun (newsletter); and social media. In-person or telephone contact was made with people who approached the research team after hearing about the study.

An ethically approved PIS (Appendix 10) was emailed to all potential participants. They were given as much time and opportunity as needed to thoroughly review the information, ask questions, and consult with others. Those who expressed an interest in participating were asked to fill out a written informed consent form, ideally before their initial scheduled visit to the MoveExLab. Upon their arrival at the MoveExLab for the first data collection session, a hard copy of the PIS was reviewed with them. All relevant procedures were explained, and their questions were answered. Participants were enrolled in the study once they provided written informed consent.

5.2.6 Data Collection

Participants were asked to complete two data collection sessions. The assessments were carried out at intervals ranging from one to four weeks, depending on their preferences. The remaining experimental procedures and detailed information regarding the variables and their extraction processes are outlined in Chapter 4.

5.2.7 Statistical Analyses

Data were categorised by hand dominance and workspace location for the standardised UL task (Section 4.3.3). Analyses were conducted individually and reported for each of the four reaching conditions: midline workspace with dominant hand (MDH); midline workspace with non-dominant hand (MNH); contralateral workspace with dominant hand (CDH); and contralateral workspace with non-dominant hand (CNH). Prior to the analyses, the mean of the variables' values from repeated trials in each session was computed. This approach was adopted because it would give a more accurate depiction of how an individual usually performs.

STATA 17.0 was used for statistical analyses.

Aim 2a: Identification of the Reference Values for the Variables

In the analyses, first-session data was used. Initially, the normality of the data distribution for each variable was visually and statistically assessed using histograms and the Shapiro-Wilk tests. Because of the observed skewness in the data, summary statistics are provided as median

values, as well as the 5th and 95th percentiles (P5 and P95). The median is a dataset's centre value that serves as an estimate of the typical measurement and is less impacted by outliers and skewed data (332). The 5th percentile represents the lowest 5% of the dataset, while the 95th percentile is greater than all but 5% of the values. These percentiles provide insight into the dataset's variability and probable outliers, covering 90% of the data.

Box plots were generated for each variable to graphically display the dataset while also providing information about its central tendency, dispersion, and variability (333).

Aim 2b: Determining the Test-Retest Reliability

Test-retest reliability was determined using ICC point estimates and their accompanying 95% CIs, which indicate the range of plausible values of the ICC, based on data from both sessions. Unlike correlation coefficients, which can only evaluate linear relationships, the ICC provides a more comprehensive measure of reliability, accounting for both agreement and consistency (334). The ICC, supplemented by a 95% CI, ensures precision in the reliability estimate, increasing the generalisability of the findings (334). Individual ICC (2,1) values, which directly represent the consistency of test-retest measurements across two sessions, were employed. The mixed effect model was implemented to account for both fixed and random effects in the analyses. The assumption of normality in the distribution of test-retest differences was adopted.

Conversely to the notion that acceptable levels of reliability should be universally standardised, Butts and Michels (335) propose a context-dependent approach. Therefore, an acceptable reliability cutoff of 0.70 was determined and implemented on the ICC point estimates based on the recommendations for the test-retest reliability in physical activity instruments (336, 337) and previous research on the reliability of kinematics-derived UL neuromuscular impairment variables (338). Additionally, Portney and Watkins' reliability classification guidelines were applied to the 95% CIs to provide a range-based classification of reliability (Table 15) (334, 339).

Table 15. Reliability Coefficient Classification Guidelines

Reliability Coefficient	Interpretation
< 0.50	Poor Reliability
0.5 to 0.75	Moderate Reliability
> 0.75	Good Reliability

The ICC estimates relative reliability, reflecting the measure's consistency and stability across test sessions (340). It does not provide information concerning the consistency of scores for individual participants across repeated testing sessions (341). For a comprehensive evaluation

of reliability, it is essential to include metrics, describing absolute reliability, such as limits of agreement (LOA) and standard error of measurement (SEM) (334). These metrics help in identifying the presence of systematic errors–consistent inaccuracies in a particular direction– or random errors–unpredictable deviations (334). Although a high ICC indicates consistent measurements, it can coexist with these errors (334). Both LOA and SEM were therefore utilised to provide a comprehensive understanding of the reliability of the variables.

The LOA for each variable was determined by calculating the mean of two measurements obtained in two consecutive sessions for each participant. The difference between these two measurements was calculated, and the mean and SD of these differences were derived. The Upper and Lower LOA, representing a 95% confidence range for differences and reported as 95% LOA throughout the text, were calculated as:

- Upper LOA = mean difference + 1.96 × SD of difference
- Lower LOA = mean difference − 1.96 × SD of difference

These calculations were used in generating the LOA plots (Bland-Altman plots) to visualise the individual differences between test sessions, plotted against the mean of the two measurements for each variable (342). In the plots, the mean difference (or bias) and the upper and lower LOAs were represented by horizontal lines, indicating the average discrepancy and the boundaries within which 95% of differences between the two sessions are anticipated to fall, respectively.

The 95% LOA range for each variable was compared to the relevant reference values to evaluate the variable's consistency. A narrow 95% LOA indicates a high level of measurement consistency, while a wide LOA indicates greater variability in relation to the pertinent reference values.

The SEM provides an understanding of the range within which the "true" value of a variable is likely to be located (343). To calculate the SEM for each variable (denoted as '$_x$'), the standard deviation (SD_x) of the variable at the first session was computed. The SEM values were then determined using the following formula: $SEM_x = SD_x \, x \sqrt{1 - R_x}$, where $'R_x'$ represents the ICC value of the associated variable (341, 344). An interval of ± 1 SEM is regarded as having a 68% likelihood of containing the true value of the variable, while intervals of ± 2 SEM and ± 3 SEM are interpreted as having a 95% and 99% probabilities, respectively, of containing the true value of the variable (343). The SEM expressed as a percentage of the mean (SEM%), which becomes particularly relevant when the variability of measurement is influenced by its actual

value (345), was also calculated for each variable using the formula: $SEM\%_x = (\frac{SEM_x}{Mean_x})\ x\ 100$. In this formula, '$Mean_x$' refers to the mean value of the variable in the first session. A smaller SEM and SEM% indicate greater precision in the measurements, while a larger SEM and SEM% suggest greater variability or error (346). An SEM% of 10% or less was deemed an acceptable level of measurement error (347).

Aim 2c. Ascertaining the Smallest Detectable Change of the Variables

The SDC of each variable, representing the minimum score change discernible as a true change with 95% confidence, was calculated using the formula: $SDC_x = SEM_x\ x\ 1.96\ x\ \sqrt{2}$ (348), where SEM was calculated from the first session's data.

In addition to the analyses that included the entire dataset, sensitivity analyses were also conducted by excluding outliers to determine their impact on the findings.

5.3 Results

The study enrolled 75 participants with a mean age of 48 years (SD = 17.3, range 21 to 85 years). Of these participants, 61% (46 out of 75) were females, and 89% (67 out of 75) were right-hand dominant. The characteristics of all participants are provided in Appendix 13.

Three participants out of the initial cohort of 75 did not undertake the second data collection session. One was unreachable, and two were unable to visit within the specified timeframe. Additionally, technological challenges arose with data collection that impeded the derivation of some or all variables for some participants in the first and/or second session/s. Consequently, the number of available datasets varied across variables and analyses per reaching condition. Sample sizes ranged from 72 to 74 for reference values and from 67 to 70 for test-retest reliability and SDC analyses, depending on the variable and reaching condition. Specific sample sizes for each variable and analysis are reported in the respective data presentation tables within the sections for reference values and test-retest reliability below.

During the first data collection session, 1,140 trials were recorded across four reaching conditions: MDH, MNH, CDH, and CNH, with 285 trials per condition (Appendix 14). Of these:

- Seventeen trials had no data extracted due to the absence of the buzzer data.
- Five trials had problematic kinematic models, making it impossible to extract kinematics-derived variables and EMD data from both the ECR and BB muscles.
- Four trials experienced flickering of the T10 marker, preventing the extraction of THDR data.
- Six trials had noisy EMG signals from both the ECR and BB muscles, preventing the extraction of any EMG data.
- One trial had noisy EMG signals from the BB muscle alone, preventing the extraction of EMG data for that muscle.

As a result, 1,107 trials had complete data, while 17 trials had no data extracted, and 16 trials had partial data extraction.

During the second data collection session, 1,096 trials were recorded across four reaching conditions (Appendix 15): MDH, MNH, CDH, and CNH, with 274 trials per reaching condition. Of these:

- Sixteen trials had no data extracted due to the absence of the buzzer data.
- Twenty trials had noisy EMG signals from both the ECR and BB muscles, preventing the extraction of any EMG data.

- One trial had noisy EMG signals from the BB muscle alone, preventing the extraction of EMG data for that muscle.

As a result, 1,059 trials had complete data, while 16 trials had no data extracted, and 21 trials had partial data extraction.

Appendices 14 and 15 provide details on the variables that were not obtained from certain participants, as well as the associated reasons. These appendices also include details on the quality of the dataset.

Aim 2a: Identification of the Reference Values for the Variables

Table 16 provides the identified reference values for each of the variables evaluated. Figure 18 shows the corresponding box plots.

Table 16. Reference Values

Reference Values for the Kinematics-Derived Variables

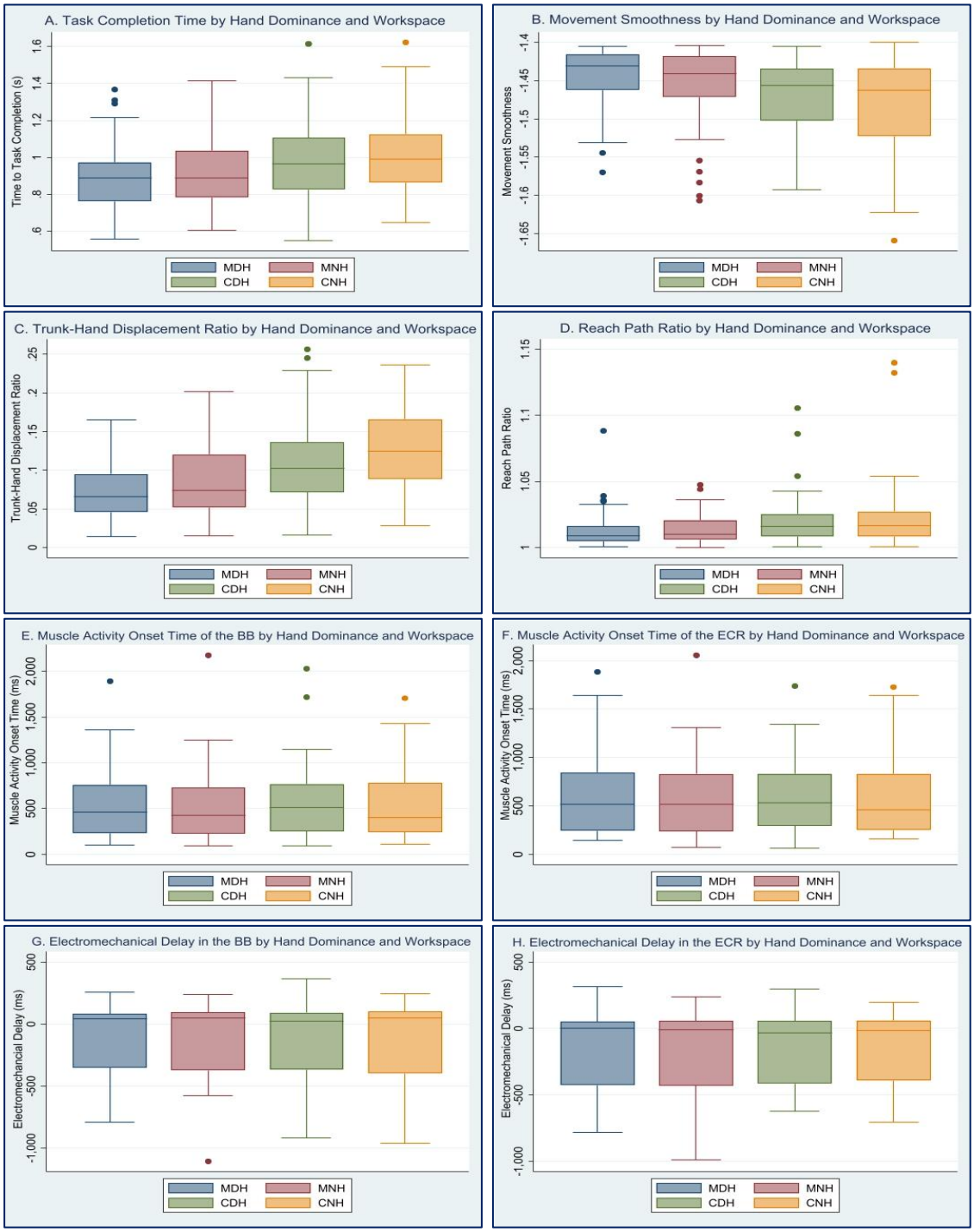
	Functional Ability Variable			Neuromuscular Impairment Variable								
	Time to Task Completion (s)			Movement Smoothness (unitless)			Trunk-Hand Displacement Ratio (unitless)			Reach Path Ratio (unitless)		
Reaching Condition	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**
Midline – Dominant Hand (MDH)	74	0.89	0.63 – 1.22	74	-1.43	-1.53 – -1.41	74	0.07	0.02 – 0.15	74	1.01	1.00 – 1.03
Midline – Nondominant Hand (MNH)	74	0.89	0.66 – 1.27	74	-1.44	-1.57 – -1.41	74	0.07	0.03 – 0.18	74	1.01	1.00 – 1.03
Contralateral – Dominant Hand (CDH)	73	0.96	0.70 – 1.43	73	-1.46	-1.56 – -1.41	72	0.10	0.04 – 0.22	73	1.02	1.00 – 1.04
Contralateral – Nondominant Hand (CNH)	74	0.99	0.74 – 1.35	74	-1.46	-1.59 – -1.41	74	0.12	0.04 – 0.21	74	1.02	1.00 – 1.05

Reference Values for the EMG-Derived Variables

	Neuromuscular Impairment Variable											
	Muscle Activity Onset Time of the Biceps Brachii (ms)			Muscle Activity Onset Time of Extensor Carpi Radialis (ms)			Electromechanical Delay in Biceps Brachii (ms)			Electromechanical Delay in Extensor Carpi Radialis (ms)		
Reaching Condition	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**	**N**	**Median**	**P5 – P95**
Midline – Dominant Hand (MDH)	74	459	170 – 1089	74	518	171 – 1254	74	43	-551 – 128	74	4	-617 – 180
Midline – Nondominant Hand (MNH)	74	426	135 – 1147	74	518	147 – 1238	74	52	-490 – 183	74	-12	-609 – 159
Contralateral – Dominant Hand (CDH)	73	513	148 – 1111	74	536	177 – 1236	72	25	-541 – 199	73	-32	-572 – 173
Contralateral – Nondominant Hand (CNH)	73	397	148 – 1186	73	458	172 – 1293	73	47	-524 – 177	73	-13	-607 – 154

Note: The table provides the median values and interpercentile ranges (P5–P95) for each variable, specific to the following reaching conditions: (1) midline workspace with the dominant hand, (2) midline workspace with the non-dominant hand, (3) contralateral workspace with the dominant hand, and (4) contralateral workspace with the non-dominant hand. 'N' denotes the sample size, 's' represents seconds, and 'ms' denotes milliseconds.

Figure 18. Box Plots of the Variables by Hand Dominance and Workspace



Notes: These boxplots display the data distribution for each variable under four distinct reaching conditions, the numerical details of which are provided in Table 16. The boxes represent the interquartile range, showing the middle 50% of the data, with the median indicated by the internal horizontal line. The boxes' lower and upper edges correspond to the 1st and 3rd quartiles, respectively. The whiskers represent the highest and lowest values unless outliers are present (333). Data points beyond the whiskers, shown as dots, are outliers. Overlapping distributions across conditions indicate similarities in the data. **Conditions:** **MDH** – Midline-Dominant; **MNH** – Midline-Non-Dominant; **CDH** – Contralateral-Dominant; **CNH** – Contralateral-Non-Dominant. **BB** stands for Biceps Brachii and **ECR** for Extensor Carpi Radialis.

Aim 2b and Aim 2c: Determining the Test-Retest Reliability and Ascertaining the Smallest Detectable Change for the Variables

The test-retest reliability for each individual variable is provided in Tables 17 through 24, with corresponding LOA plots in Figures 19 through 26. Appendix 16 contains the adjusted LOA plots produced for the sensitivity analyses.

Functional Ability Variable

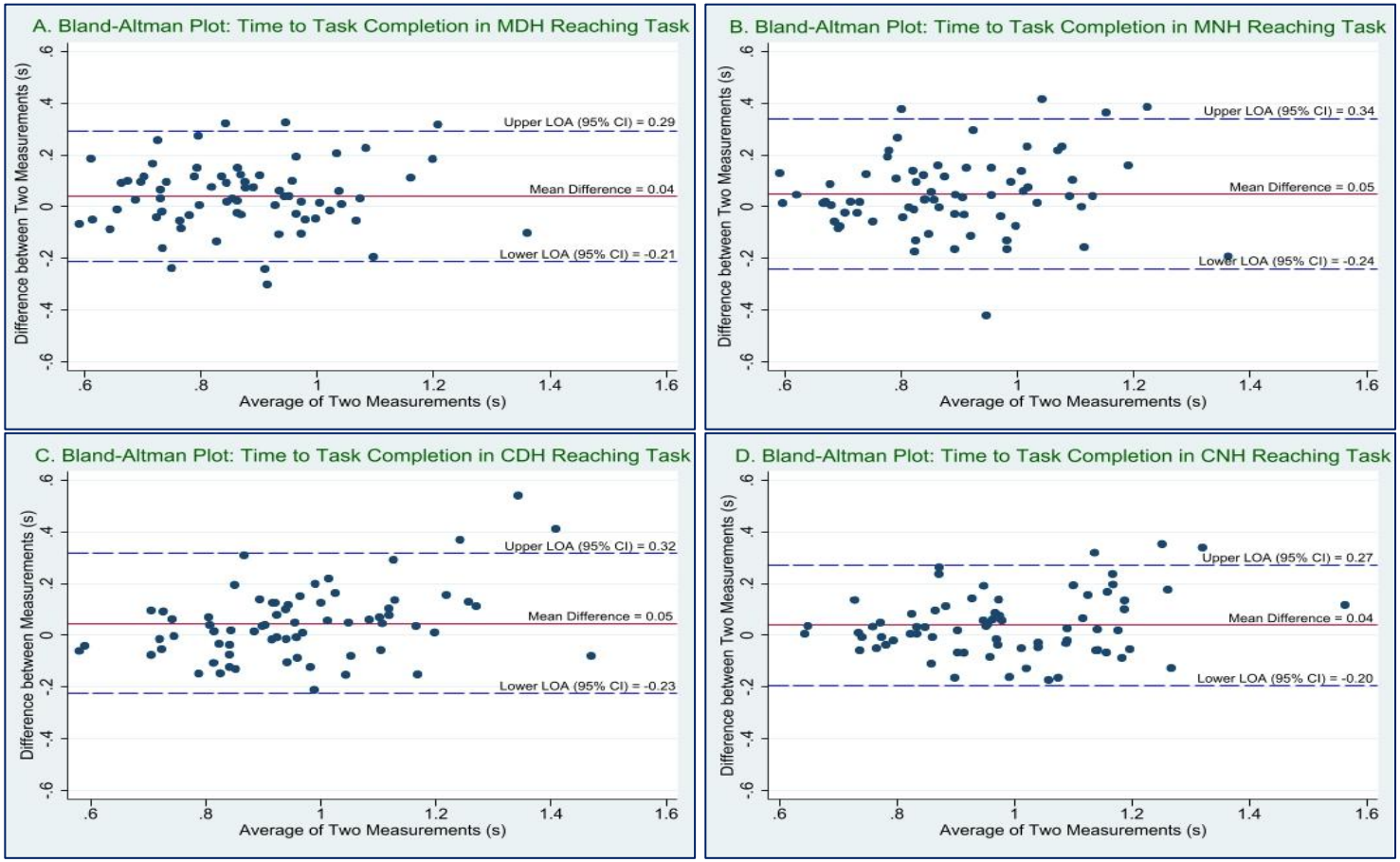
Time to Task Completion (TTC)

Table 17. Test-Retest Reliability and Smallest Detectable Change for the 'Time to Task Completion'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Time to Task Completion**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (s)**	**SEM%**	**95% LOA (s)**	**SDC (s)**
Midline – Dominant Hand (MDH)	70	0.69 (0.53 – 0.80)	Moderate-Good	0.10	10.7	-0.21 to 0.29	0.26
Midline – Nondominant Hand (MNH)	70	0.63 (0.45 – 0.76)	Poor-Good	0.11	12.39	-0.24 to 0.34	0.31
Contralateral – Dominant Hand (CDH)	69	0.73 (0.58 – 0.83)	Moderate-Good	0.11	11.58	-0.23 to 0.32	0.32
Contralateral – Nondominant Hand (CNH)	70	0.79 (0.66 – 0.87)	Moderate-Good	0.09	9.12	-0.20 to 0.27	0.25
B.	**Sensitivity Analyses for Time to Task Completion**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (s)**	**SEM%**	**95% LOA (s)**	**SDC (s)**
Midline – Dominant Hand (MDH)	64	0.79 (0.64 – 0.87)	Moderate-Good	0.07	8.40	-0.16 to 0.24	0.21
Midline – Nondominant Hand (MNH)	65	0.75 (0.61 – 0.84)	Moderate-Good	0.08	9.27	-0.19 to 0.26	0.23
Contralateral – Dominant Hand (CDH)	63	0.75 (0.59 – 0.84)	Moderate-Good	0.11	10.98	-0.19 to 0.24	0.30
Contralateral – Nondominant Hand (CNH)	67	0.83 (0.74 – 0.90)	Moderate-Good	0.07	7.54	-0.18 to 0.23	0.21

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Time to Task Completion (TTC)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 19. Bland-Altman (LOA) Plots of Time to Task Completion (TTC) by Tasks



Notes: These plots show the consistency of the 'Time to Task Completion (TTC)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Higher averages on the x-axis correspond to longer TTCs. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

Neuromuscular Impairment Variables

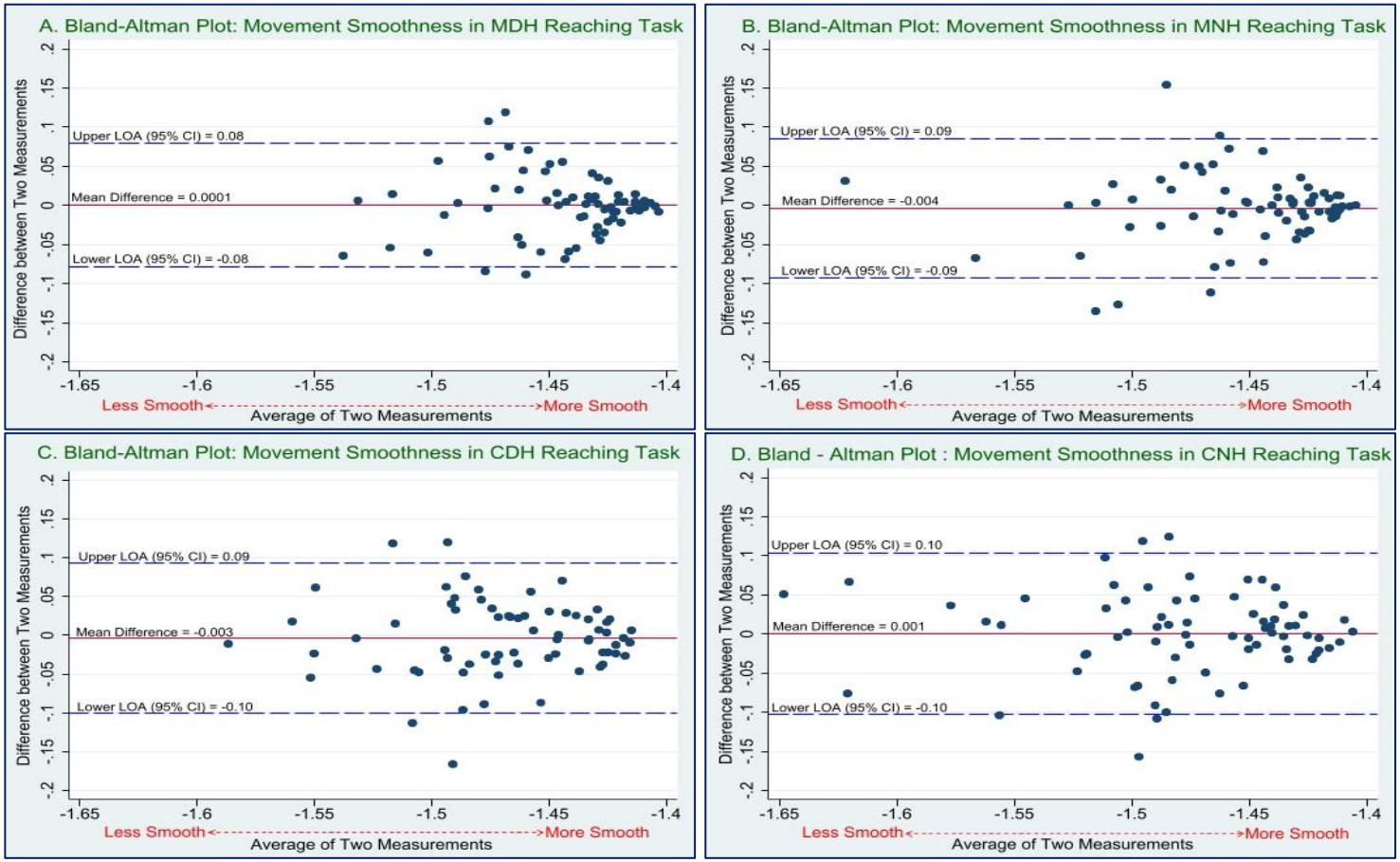
Movement Smoothness (MS) (Unitless Variable)

Table 18. Test-Retest Reliability and Smallest Detectable Change for the 'Movement Smoothness'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Movement Smoothness**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	70	0.43 (0.21 – 0.60)	Poor-Moderate	0.03	1.96	-0.08 to 0.08	0.08
Midline – Nondominant Hand (MNH)	70	0.53 (0.33 – 0.68)	Poor-Moderate	0.03	2.28	-0.09 to 0.09	0.09
Contralateral – Dominant Hand (CDH)	69	0.44 (0.23 – 0.61)	Poor-Moderate	0.03	2.37	-0.10 to 0.09	0.10
Contralateral – Nondominant Hand (CNH)	70	0.58 (0.40 – 0.72)	Poor-Moderate	0.04	2.49	-0.10 to 0.10	0.10
B.	**Sensitivity Analyses for Movement Smoothness**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	66	0.58 (0.39 – 0.72)	Poor-Moderate	0.02	1.63	-0.07 to 0.06	0.07
Midline – Nondominant Hand (MNH)	65	0.74 (0.60 – 0.83)	Moderate-Good	0.02	1.54	-0.06 to 0.06	0.06
Contralateral – Dominant Hand (CDH)	65	0.61 (0.44 – 0.75)	Poor-Moderate	0.03	1.88	-0.08 to 0.07	0.08
Contralateral – Nondominant Hand (CNH)	65	0.71 (0.57 – 0.82)	Moderate-Good	0.03	1.95	-0.08 to 0.09	0.08

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Movement Smoothness (MS)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. For MS values calculated using spectral arc, SEM% is reported in absolute terms due to their inherent negativity. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 20. Bland-Altman (LOA) Plots of Movement Smoothness (MS) by Tasks



Notes: These plots show the consistency of the 'Movement Smoothness (MS)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Lower averages on the x-axis correspond to less smooth movements. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

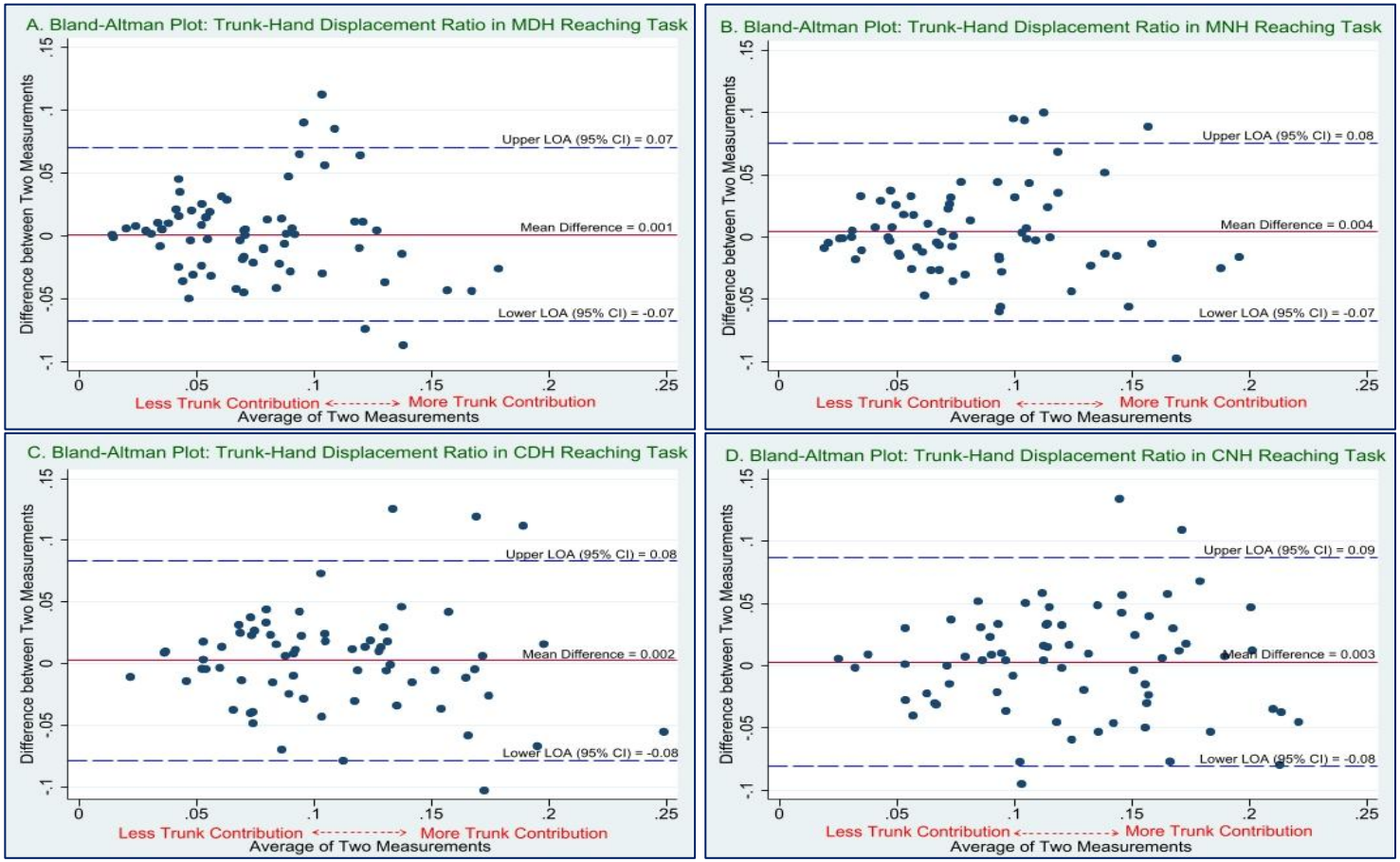
Trunk-Hand Displacement Ratio (THDR) (Unitless Variable)

Table 19. Test-Retest Reliability and Smallest Detectable Change for the 'Trunk-Hand Displacement Ratio'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Trunk-Hand Displacement Ratio**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	70	0.63 (0.47 – 0.75)	Poor-Moderate	0.02	31.37	-0.07 to 0.07	0.07
Midline – Nondominant Hand (MNH)	70	0.67 (0.52 – 0.78)	Moderate-Good	0.03	29.75	-0.08 to 0.07	0.07
Contralateral – Dominant Hand (CDH)	68	0.66 (0.51 – 0.78)	Moderate-Good	0.03	26.24	-0.08 to 0.08	0.08
Contralateral – Nondominant Hand (CNH)	70	0.66 (0.50 – 0.77)	Moderate-Good	0.03	24.43	-0.08 to 0.09	0.08
B.	**Sensitivity Analyses for Trunk-Hand Displacement Ratio**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	65	0.77 (0.65 – 0.85)	Moderate-Good	0.02	24.61	-0.05 to 0.05	0.05
Midline – Nondominant Hand (MNH)	65	0.79 (0.68 – 0.87)	Moderate-Good	0.02	23.03	-0.05 to 0.05	0.05
Contralateral – Dominant Hand (CDH)	63	0.80 (0.69 – 0.88)	Moderate-Good	0.02	18.81	-0.06 to 0.06	0.05
Contralateral – Nondominant Hand (CNH)	67	0.72 (0.58 – 0.82)	Moderate-Good	0.03	21.74	-0.07 to 0.07	0.07

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Trunk-Hand Displacement Ratio (THDR)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 21. Bland-Altman (LOA) Plots of Trunk-Hand Displacement Ratio (THDR) by Tasks



Note: These plots show the consistency of the 'Trunk-Hand Displacement Ratio (THDR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis indicate more trunk movement in relation to the hand. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

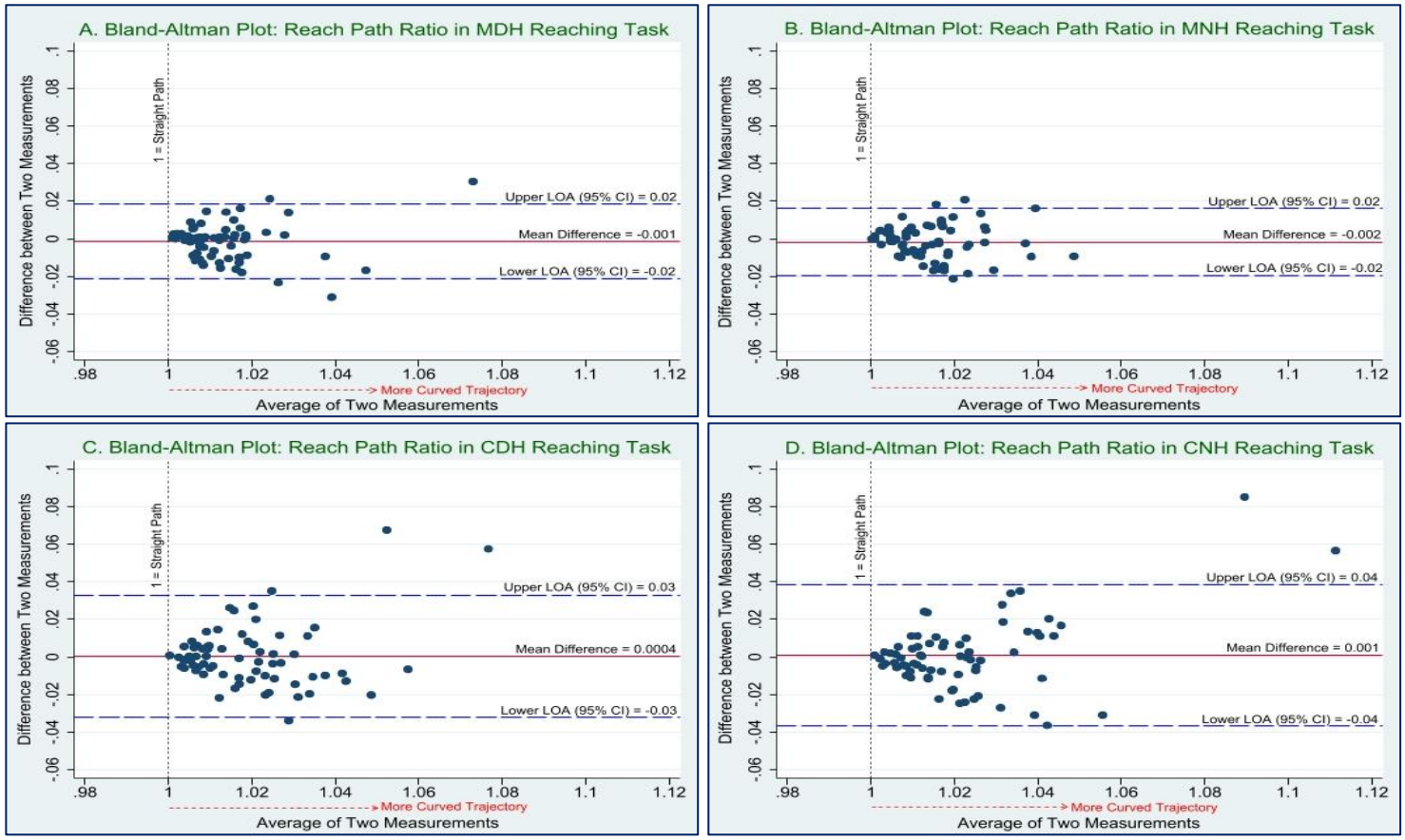
Reach Path Ratio (RPR) (Unitless Variable)

Table 20. Test-Retest Reliability and Smallest Detectable Change for the 'Reach Path Ratio'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Reach Path Ratio**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	70	0.69 (0.54 – 0.79)	Moderate-Good	0.007	0.71	-0.02 to 0.02	0.02
Midline – Nondominant Hand (MNH)	70	0.64 (0.48 – 0.76)	Poor-Good	0.006	0.63	-0.02 to 0.02	0.02
Contralateral – Dominant Hand (CDH)	69	0.51 (0.31 – 0.67)	Poor-Moderate	0.01	1.24	-0.03 to 0.03	0.04
Contralateral – Nondominant Hand (CNH)	70	0.58 (0.40 – 0.72)	Poor-Moderate	0.02	1.55	-0.04 to 0.04	0.04
B.	**Sensitivity Analyses for Reach Path Ratio**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM**	**SEM%**	**95% LOA**	**SDC**
Midline – Dominant Hand (MDH)	66	0.63 (0.47 – 0.76)	Poor-Good	0.005	0.52	-0.02 to 0.01	0.01
Midline – Nondominant Hand (MNH)	66	0.69 (0.53 – 0.80)	Moderate-Good	0.005	0.53	-0.02 to 0.01	0.01
Contralateral – Dominant Hand (CDH)	65	0.64 (0.48 – 0.77)	Poor-Good	0.007	0.72	-0.02 to 0.02	0.02
Contralateral – Nondominant Hand (CNH)	68	0.50 (0.29 – 0.66)	Poor-Moderate	0.01	1.04	-0.03 to 0.03	0.03

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Reach Path Ratio (RPR)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 22. Bland-Altman (LOA) Plots of Reach Path Ratio (RPR) by Tasks



Note: These plots show the consistency of the 'Reach Path Ratio (RPR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. An average of '1' on the x-axis indicates a straight path towards the target. Here, the target is the phone. Greater averages on the x-axis indicate a more curved trajectory. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

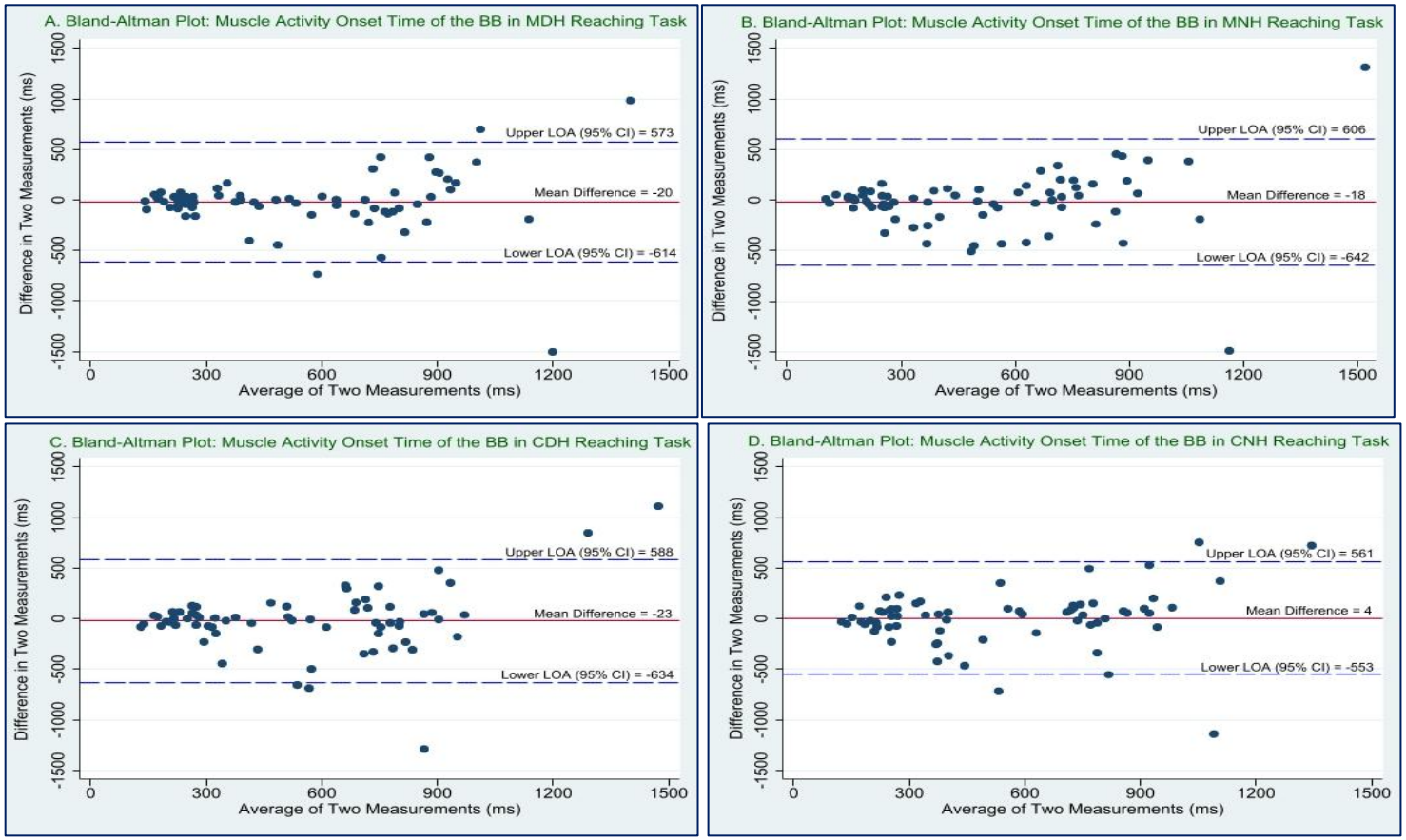
Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB)

Table 21. Test-Retest Reliability and Smallest Detectable Change for the 'Muscle Activity Onset Time of the Biceps Brachii'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Muscle Activity Onset Time of the BB**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	69	0.62 (0.44 – 0.74)	Poor-Moderate	221	41.51	-614 to 573	613
Midline – Nondominant Hand (MNH)	69	0.57 (0.38 – 0.71)	Poor-Moderate	241	47.27	-642 to 606	668
Contralateral – Dominant Hand (CDH)	68	0.57 (0.38 – 0.71)	Poor-Moderate	241	45.31	-634 to 588	668
Contralateral – Nondominant Hand (CNH)	67	0.68 (0.53 – 0.79)	Moderate-Good	202	37.59	-553 to 561	559
B.	**Sensitivity Analyses for Muscle Activity Onset Time of the BB**						
Reaching Task	**N**	**ICC (95% CI)**		**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	65	0.82 (0.72 – 0.89)	Moderate-Good	129	25.54	-359 to 333	207
Midline – Nondominant Hand (MNH)	67	0.73 (0.60 – 0.83)	Moderate-Good	160	32.93	-430 to 399	444
Contralateral – Dominant Hand (CDH)	63	0.79 (0.68 – 0.87)	Moderate-Good	130	25.85	-368 to 340	361
Contralateral – Nondominant Hand (CNH)	62	0.85 (0.76 – 0.91)	Good	123	14.43	-344 to 383	341

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 23. Bland-Altman (LOA) Plots of Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB) by Tasks



Note: These plots show the consistency of the 'Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis correspond to later muscle activity onset. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR)

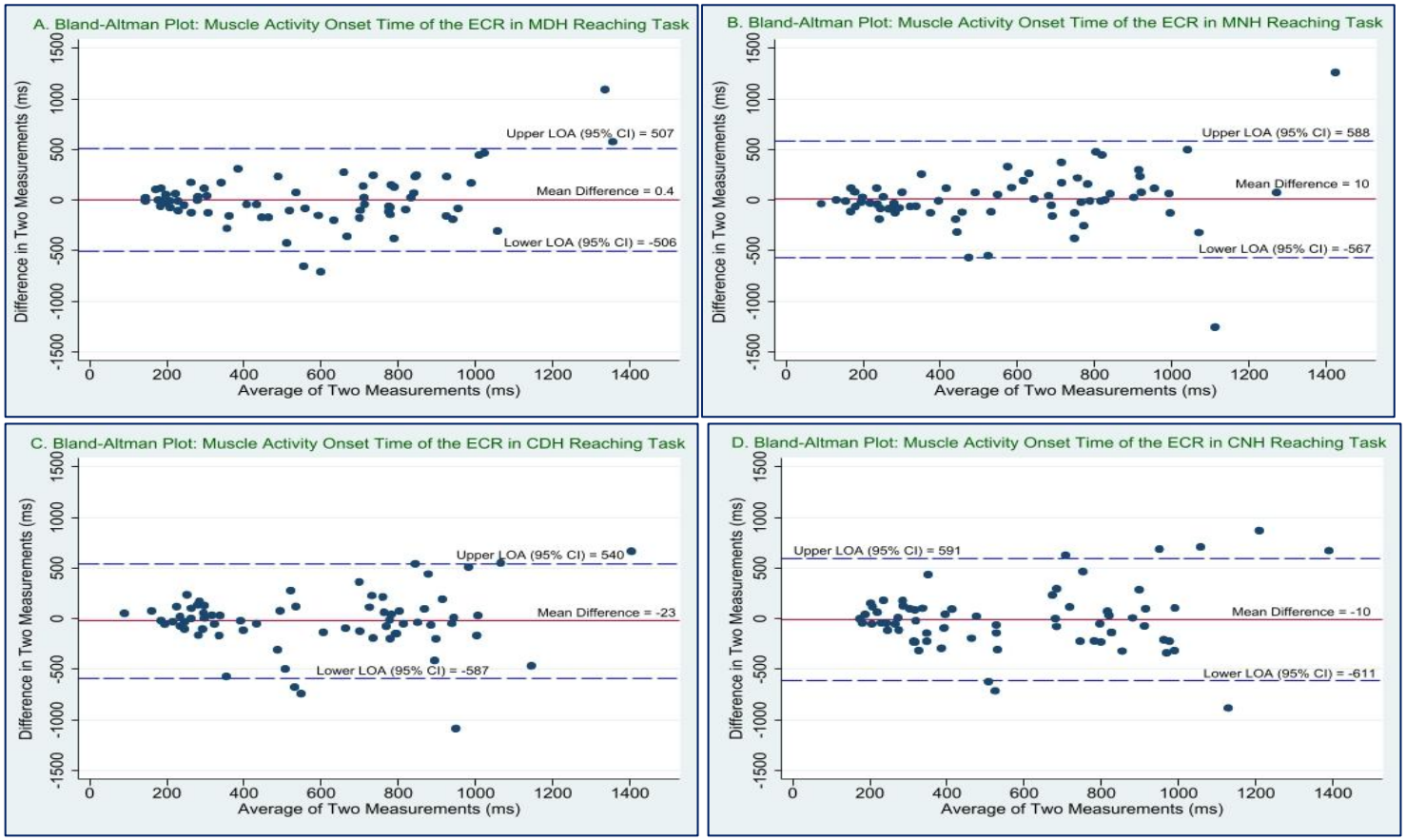
Table 22. Test-Retest Reliability and Smallest Detectable Change for the 'Muscle Activity Onset Time of the Extensor Carpi Radialis'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Muscle Activity Onset Time of the ECR**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	69	0.70 (0.55 – 0.80)	Moderate-Good	200	35.53	-506 to 507	554
Midline – Nondominant Hand (MNH)	69	0.64 (0.47 – 0.76)	Poor-Moderate	224	39.04	-567 to 588	620
Contralateral – Dominant Hand (CDH)	69	0.63 (0.46 – 0.75)	Poor-Moderate	210	36.47	-587 to 540	581
Contralateral – Nondominant Hand (CNH)	68	0.71 (0.56 – 0.81)	Moderate-Good	199	35.07	-611 to 591	550

B.	**Sensitivity Analyses for Muscle Activity Onset Time of the ECR**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	65	0.82 (0.71 – 0.88)	Moderate-Good	130	24.20	-358 to 349	360
Midline – Nondominant Hand (MNH)	67	0.78 (0.67 – 0.86)	Moderate-Good	154	27.81	-388 to 410	426
Contralateral – Dominant Hand (CDH)	63	0.79 (0.67 – 0.86)	Moderate-Good	138	24.98	-401 to 373	382
Contralateral – Nondominant Hand (CNH)	60	0.83 (0.73 – 0.89)	Moderate-Good	115	14.54	-393 to 326	317

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. An SEM% ≤ 10% was deemed acceptable. SEM% represents the SEM as a percentage of the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement.

Figure 24. Bland-Altman (LOA) Plots of Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR) by Tasks



Note: These plots show the consistency of the 'Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis correspond to later muscle activity onset. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

Electromechanical Delay (EMD) in the Biceps Brachii (BB)

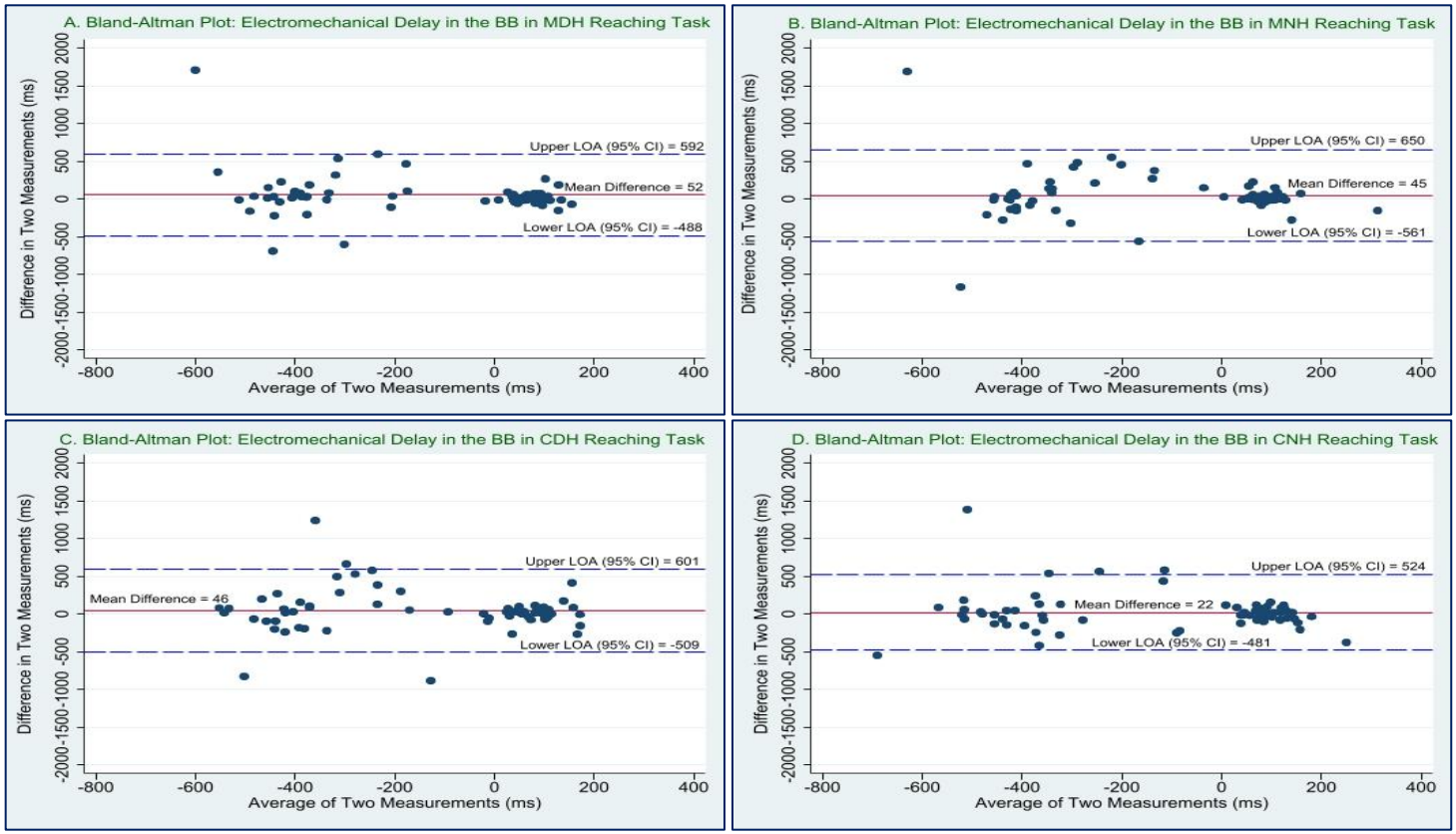
Table 23. Test-Retest Reliability and Smallest Detectable Change for the 'Electromechanical Delay in the Biceps Brachii'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Electromechanical Delay in the BB**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	69	0.50 (0.30 – 0.66)	Poor-Moderate	178	NCC	-488 to 592	494
Midline – Nondominant Hand (MNH)	69	0.41 (0.20 – 0.59)	Poor-Moderate	208	NCC	-561 to 650	576
Contralateral – Dominant Hand (CDH)	68	0.48 (0.28 – 0.64)	Poor-Moderate	194	NCC	-509 to 601	538
Contralateral – Nondominant Hand (CNH)	67	0.60 (0.42 – 0.73)	Poor-Moderate	178	NCC	-481 to 524	493

B.	**Sensitivity Analyses for Electromechanical Delay in the BB**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	65	0.85 (0.75 – 0.90)	Moderate-Good	91	NCC	-219 to 298	252
Midline – Nondominant Hand (MNH)	67	0.71 (0.57 – 0.81)	Moderate-Good	130	NCC	-329 to 405	361
Contralateral – Dominant Hand (CDH)	64	0.75 (0.62 – 0.84)	Moderate-Good	122	NCC	-299 to 391	339
Contralateral – Nondominant Hand (CNH)	62	0.82 (0.72 – 0.89)	Moderate-Good	112	NCC	-289 to 254	309

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Electromechanical Delay (EMD) in the Biceps Brachii (BB)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. SEM% could not be calculated due to the mixed positive and negative values of the variable, which prevent a meaningful indicator of measurement error relative to the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement; **NCC:** Not Calculable.

Figure 25. Bland-Altman (LOA) Plots of the Electromechanical Delay (EMD) in the Biceps Brachii (BB) by Tasks



Note: These plots show the consistency of the 'Electromechanical Delay (EMD) in the Biceps Brachii (BB)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Positive averages suggest muscle activity onset before hand movement, while negative averages indicate the opposite. Smaller positive averages indicate a shorter time interval between muscle activity onset and movement onset. Smaller negative averages suggest a longer delay in muscle activity after the hand movement. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR)

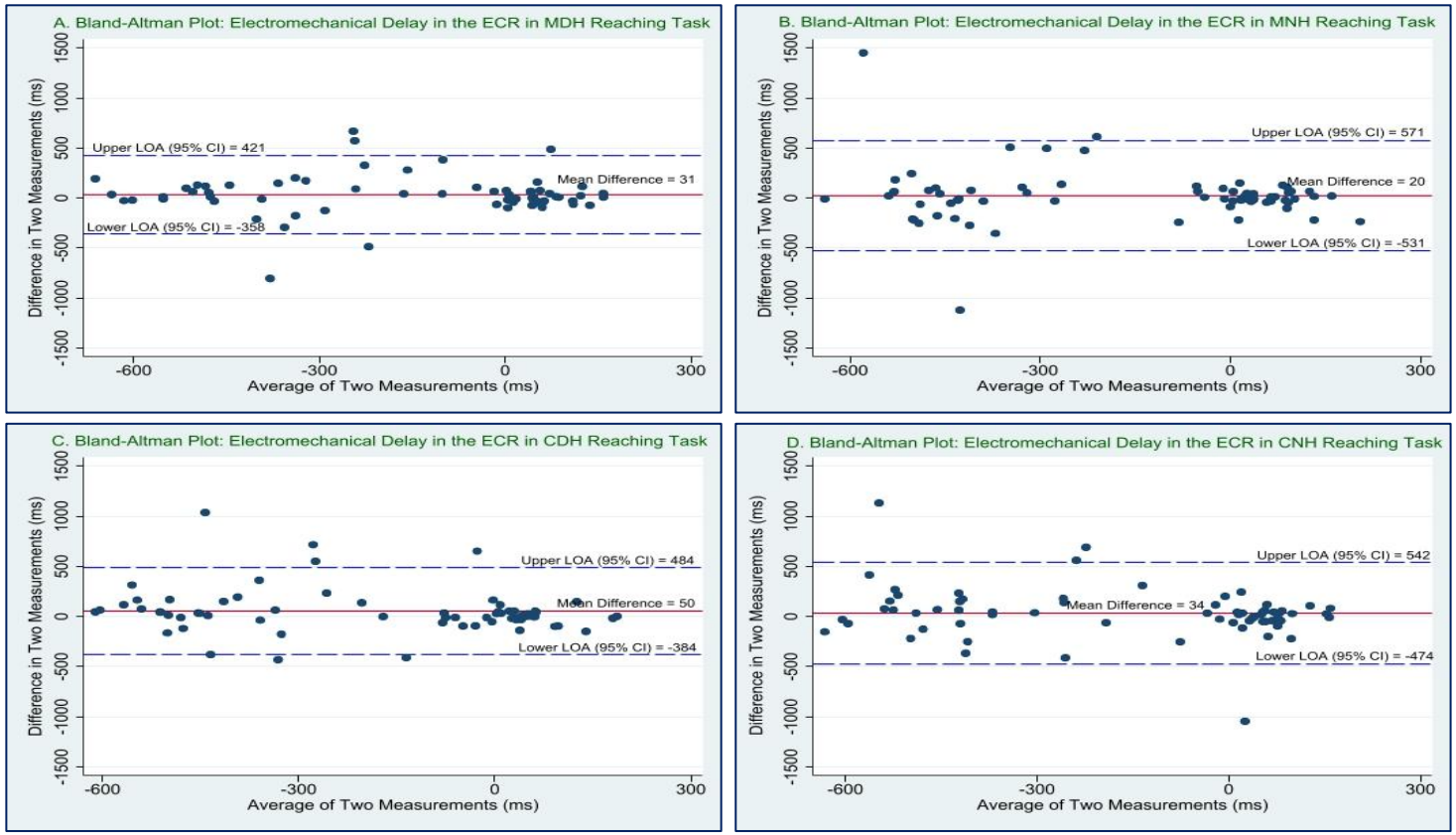
Table 24. Test-Retest Reliability and Smallest Detectable Change for the 'Electromechanical Delay in the Extensor Carpi Radialis'. **A.** Findings from the Entire Dataset; **B.** Findings from Sensitivity Analyses with Outliers Excluded

A.	**Electromechanical Delay in the ECR**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	69	0.72 (0.59 – 0.82)	Moderate-Good	141	NCC	-358 to 421	390
Midline – Nondominant Hand (MNH)	69	0.52 (0.33 – 0.68)	Poor-Moderate	191	NCC	-531 to 571	531
Contralateral – Dominant Hand (CDH)	69	0.65 (0.50 – 0.77)	Moderate-Good	148	NCC	-384 to 484	409
Contralateral – Nondominant Hand (CNH)	68	0.67 (0.51 – 0.78)	Moderate-Good	150	NCC	-474 to 542	416

B.	**Sensitivity Analyses for Electromechanical Delay in the ECR**						
Reaching Task	**N**	**ICC (95% CI)**	**Reliability Classification**	**SEM (ms)**	**SEM%**	**95% LOA (ms)**	**SDC (ms)**
Midline – Dominant Hand (MDH)	64	0.90 (0.84 – 0.94)	Good	79	NCC	-194 to 248	219
Midline – Nondominant Hand (MNH)	66	0.82 (0.72 – 0.88)	Moderate-Good	112	NCC	-306 to 319	309
Contralateral – Dominant Hand (CDH)	63	0.90 (0.84 – 0.94)	Good	78	NCC	-203 to 246	215
Contralateral – Nondominant Hand (CNH)	64	0.84 (0.75 – 0.90)	Moderate-Good	105	NCC	-278 to 308	291

Note: This table presents test-retest reliability and smallest detectable change (SDC) for the 'Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR)' variable across four reaching tasks: MDH, MNH, CDH, and CNH. **Section A** includes findings from the entire dataset. **Section B** details findings from sensitivity analyses excluding outliers. The ICC [2,1] mixed effects model was used. Acceptable reliability was established with an ICC threshold of ≥ 0.70. SEM% could not be calculated due to the mixed positive and negative values of the variable, which prevent a meaningful indicator of measurement error relative to the mean. **N:** Sample Size; **ICC:** Intraclass Correlation Coefficient; **CI:** Confidence Interval; **SEM:** Standard Error of Measurement; **LOA:** Limits of Agreement; **NCC:** Not Calculable.

Figure 26. Bland-Altman (LOA) Plots of the Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR) by Tasks



Note: These plots show the consistency of the 'Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Positive averages suggest muscle activity onset before hand movement, while negative averages indicate the opposite. Smaller positive averages indicate a shorter time interval between muscle activity onset and movement onset. Smaller negative averages suggest a longer delay in muscle activity after the hand movement. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand.

For all variables analysed:

- The 95% CIs were wide, suggesting variability in the measurements.
- LOA plots showed mean differences close to zero, indicating minimal systematic error. The distribution of measurements, both above and below the mean difference, was relatively even and random. This suggests that the observed variability is primarily due to random error, thereby supporting the accuracy of the variables (Figures 19-26).
- The 95% LOA ranges exceeded the SEMs for all variables, suggesting that the variability in test-retest measurements extends beyond the inherent error of the measurements themselves. This indicates the presence of additional sources of variability.
- SDCs continuously remained smaller than the corresponding 95% LOA ranges.
- Sensitivity analyses generally resulted in higher ICC values, narrower 95% CIs, and 95% LOA ranges, and reduced SEM, SEM% and SDC values (Tables 17-24). Consistent outliers were identified across multiple variables (Appendix 16).

Specifically,

For the Functional Ability Variable:

Time to Task Completion (TTC): TTC demonstrated acceptable test-retest reliability for contralateral workspace tasks (ICC = 0.73 for CDH and 0.79 for CNH). However, for midline workspace tasks, the reliability did not meet the acceptable threshold (ICC = 0.69 for MDH and 0.63 for MNH) (Table 17, A). The measurement error remained within acceptable limits for the CNH task (SEM% = 9.12%), but slightly exceeded the 10% threshold for the other tasks (SEM% = 10.7% for MDH, 11.58% for CDH, and 12.39% for MNH). Despite this, the 95% LOA ranges for each reaching condition were narrow, suggesting a generally high level of absolute reliability in TTC measurements (Figure 19). It showed acceptable test-retest reliability for all conditions in the sensitivity analyses (ICCs = 0.75 to 0.83) (Table 17, B; Appendix 16, Figure 1.)

For the Neuromuscular Impairment Variables:

Movement Smoothness (MS): The test-retest reliability of MS did not reach the acceptable threshold (ICCs = 0.43 to 0.58) (Table 18, A). In contrast, the SEM% was consistently ≤ 2.49% across each reaching condition, and the 95% LOA ranges were narrow, indicating high absolute reliability (Figure 20). In the sensitivity analyses, it showed acceptable reliability for non-dominant hand tasks (ICCs = 0.74 for MNH and 0.71 for CNH), but not for dominant hand tasks (ICC = 0.58 for MDH and 0.61 for CDH) (Table 18, B). (LOA plots are in Appendix 16, Figure 2.)

Trunk-Hand Displacement Ratio (THDR): The test-retest reliability of THDR for each reaching condition was below the acceptable level (ICCs = 0.63 to 0.67) (Table 19, A). For all conditions,

the SEM% was 24.43% or higher, and 95% LOA were wide (Figure 21). In the sensitivity analyses, the test-retest reliability of THDR reached an acceptable level for all tasks (ICCs ≥ 0.72) (Table 19, B). Despite a reduction, SEM% values remained above the acceptable cutoff in all conditions (≥ 18.81%). (LOA plots are in Appendix 16, Figure 3.)

Reach Path Ratio (RPR): RPR did not demonstrate acceptable test-retest reliability (ICCs = 0.51 to 0.69). It exhibited SEM% values of 1.55% or less and consistently narrow 95% LOA ranges across all reaching conditions, indicating high absolute reliability (Table 20, A; Figure 22). Sensitivity analyses also did not reveal acceptable test-retest reliability (ICCs = 0.50 to 0.69) (Table 20, B). (LOA plots are in Appendix 16, Figure 4).

Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB): The BB's MAOT did not demonstrate acceptable test-retest reliability (ICCs = 0.57 to 0.68) and had high measurement error (SEM% = 37.59% to 47.27%) across all reaching conditions (Table 21, A). The 95% LOA ranges were consistently wide (Figure 23). Despite acceptable test-retest reliability in the sensitivity analyses (ICCs = 0.73 to 0.85), SEM% remained above 10% across the tasks, and 95% LOA ranges continued to be wide (Table 21, B; Appendix 16, Figure 5).

Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR): The ECR's MAOT demonstrated acceptable reliability in the MDH (ICC = 0.70) and CNH conditions (ICC = 0.71), but not in the MNH (ICC = 0.64) and CDH (ICC = 0.63) conditions (Table 22, A). Across the reaching conditions, its SEM% values always exceeded the acceptable measurement error cutoff (SEM% = 35.07% to 39.04%), and the 95% LOA ranges were consistently wide (Figure 24). Sensitivity analyses showed acceptable reliability in all reaching conditions (ICC = 0.78 to 0.83), but with SEM% values still exceeding the acceptable error threshold (14.54% to 27.81%) and wide 95% LOA ranges (Table 22, B) (LOA plots are in Appendix 16, Figure 6).

Electromechanical Delay (EMD) in the Biceps Brachii (BB): The test-retest reliability of EMD in the BB did not reach an acceptable level in any reaching condition (ICCs = 0.41 to 0.60), with wide 95% LOA ranges observed in each condition (Table 23, A; Figure 25). Sensitivity analyses significantly improved reliability findings (ICCs = 0.71 to 0.85), yet the 95% LOA ranges remained wide (Table 23, B; Appendix 16, Figure 7).

Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR): The test-retest reliability for EMD in the ECR was acceptable only in the MDH condition (ICC = 0.72) but not in the other conditions (ICCs = 0.52 to 0.67) (Table 24, A). Wide 95% LOA ranges were observed in all reaching

conditions (Figure 26). Sensitivity analyses showed acceptable test-retest reliability across all conditions (ICCs = 0.82 to 0.90); however, the 95% LOA ranges remained wide (Table 24, B; Appendix 16, Figure 8).

5.4 Discussion

This study identified reference values (**Aim 2a**) and ascertained the SDCs (**Aim 2c**) for the neuromuscular impairment and functional ability variables (TTC, MS, THDR, RPR, MAOT of the BB and ECR, and EMD in the BB and ECR) during the standardised UL task using the Vicon motion analysis and Delsys EMG systems in a sample of individuals without mobility-impairing conditions. While all variables demonstrated insufficient relative test-retest reliability, the absolute reliability of TTC, MS, and RPR was high (**Aim 2b**).

Despite the paucity of previous studies on reference values, test-retest reliability, and SDCs for variables derived from 3D motion analysis systems in individuals without mobility-impairing conditions (28, 109), the available studies provide a comparative basis for interpreting this study's findings.

The only study identified in the literature on the test-retest reliability of TTC reported ICCs ranging from 0.49 to 0.86 and SEMs between 0.04 and 0.09 for TTC across various UL tasks with nine participants (26). The absence of 95% CIs in this study hinders direct comparison, yet the reported values seem to be consistent with the findings of the current study (Table 17).

The findings of the current study show some similarities in the test-retest reliability of MS with the only existing prior study (Table 18), which similarly utilised the SPARC method (349). This prior study, involving 19 participants, reported ICCs [95% CI] ranging from 0.676 [0.168–0.875] to 0.851 [0.608–0.943] for various UL tasks (349). Despite these findings, which generally exhibit greater test-retest reliability, the overlapping 95% CIs between the two studies indicate some consistency in the findings. Additionally, the SEM values reported in the prior study, which ranged from 0.01 to 0.06, align closely with those in the current study, pointing to comparable measurement precision.

Regarding the test-retest reliability of RPR, the current study's findings (Table 20) show partial alignment with two previous studies, both of which had relatively small sample sizes. The first, involving nine participants, reported ICCs ranging from 0.64 to 0.88 (without 95% CIs) for four different UL tasks (26). The second study, with 19 participants, documented ICCs [95% CI] ranging from 0.667 [0.176–0.869] to 0.893 [0.728–0.958] across various UL tasks (349). While these studies generally suggest greater test-retest reliability for RPR, the overlapping 95% CIs with the current study's findings indicate a level of consistency. The SEM values for RPR in the current study (Table 20) closely align with those reported in the previous research, which ranged from 0 to 0.03 (26) and 0.01 to 0.08 across different tasks (349).

The reference values of TCC in this study (Table 16) share similarities with those of previous research. TTC values reported in previous studies are: median (min., max.) = 1.24 (1.09, 1.41) seconds for a midline reach-to-grasp task (six participants) (16); mean (SD) = 0.66 (0.14) seconds for a contralateral pointing task (six participants) (350); and mean (SD) = ranging from 0.46 (0.06) to 0.75 (0.14) seconds for various midline reach-to-touch and reach-to-grasp tasks (nine participants) (26). The slight differences in the values are most likely due to variations in experimental design, including task-specific instructions such as 'comfortable pace' (16, 26) versus 'as quickly as possible' (26, 350). Additionally, unlike the more generic approaches employed in previous studies (16, 350), this study's methodological approach of customising object placement to each participant's forearm length, may also have influenced the variability in TCC values.

The current study's findings on MS reference values, computed using the SPARC method (Table 16), closely align with those of previous studies that employed the same method. These studies reported the following mean (SD) values: 1.436 (0.038) for a midline reach-to-grasp task performed with the non-dominant hand in 12 participants (112); values ranging from -1.45 (0.03) to -1.43 (0.02) for a forward-reaching task to point at a target and return, performed separately with the dominant and non-dominant hands, in 32 participants (351); and values ranging from -1.60 (0.12) to -1.44 (0.02) for various midline reaching tasks, including reaching for objects on the floor, on a table, and reaching for a door knob, and a glass performed with the right hand in 19 participants (349). Despite task variations, the consistency in MS values across studies points to the SPARC method's potential reliability across diverse experimental setups and populations.

Reference values for THDR have been reported in only one study: a median (min., max.) of 0.38 (0.15, 0.53) in six healthy individuals (16). These findings are in contrast with those of the current study (Table 16). One notable distinction in the studies is the anatomical reference points used. The previous study based its measurements on the cervical 7^{th} vertebra (16), while this study used the thoracal 10^{th} vertebra for its calculations. This variation in reference points is likely to influence THDR measurements, emphasising the significance of standardised measurement protocols for enabling consistent comparisons in research and clinical practice.

The reference values for RPR in this study (Table 16) exhibit similarities with those from one prior study (mean (SD) = 1.03 (0.02) to 1.06 (0.03) in various reaching tasks for nine participants) (26), but are slightly lower than those reported in another study (mean SD = 1.2 (0.1) for 12 individuals) (352), which are the only two studies identified for comparison. The latter study

required participants to reach a point rapidly without making contact with the target, likely necessitating more careful, visually guided movements, which could have led to higher RPR values. This suggests that task-specific demands can significantly impact movement trajectories.

The SDCs for TTC and RPR were reported in only one prior study, with values varying between 0.11 and 0.25 seconds for TTC and between 0 and 0.08 for RPR across various tasks for nine participants (26). These values are closely aligned with the current study's findings (Tables 17 and 20), with only slight differences likely attributable to the experimental variations. Additionally, the observation in the current study that the SDCs for all evaluated variables were smaller than their respective 95% LOA ranges suggests that changes exceeding the SDC yet remaining within the 95% LOA fall within the expected range of variability for repeated measurements. Conversely, changes that surpass the 95% LOA ranges are more likely to signify true changes in the measured variables.

Research on the test-retest reliability and SDCs for THDR is lacking. Likewise, studies on the reference values, test-retest reliability, and SDCs for MAOT in the BB and ECR, as well as EMD in these muscles, are absent, eliminating the opportunity for comparative analysis.

There can be potential reasons for the insufficient test-retest reliability findings of the current study. Firstly, the findings of this study may have been influenced by the unique physiology or behaviour of certain participants. Some participants consistently exhibited outlier values across multiple variables (Appendix 16). Sensitivity analyses, performed after excluding these outliers, indicated acceptable reliability for most variables (Tables 17 through 24). Thus, it is likely that these individual differences significantly impacted the overall reliability of the variables, even considering the study's large sample size. ICCs are sensitive to the normality of data distribution (353). Given the non-normal distribution observed in the data for all variables, this could have influenced the study's findings. However, the exclusion of outliers in the sensitivity analyses, leading to a more normal distribution, may have provided more accurate information about the variables' reliability. To further minimise the impact of outliers on study findings, employing larger sample sizes in future research could be beneficial.

Secondly, low between-subject variability in individuals without mobility-impairing conditions can lead to low ICC values (354). Populations with diverse physiological characteristics, such as stroke survivors, are likely to exhibit greater test-retest reliability for the same variables investigated (26).

Thirdly, the ICC's sensitivity to measurement range may have impacted the findings. When measurement scores are inherently similar and fall within a narrow range across participants, ICC values may be lower (355). In this study, the measurement scores, particularly for the RPR and MS variables, were tightly clustered, which may explain their insufficient test-retest reliability.

Fourthly, crosstalk, where electrodes capture activity from adjacent muscles (356), may have contaminated EMG signals (357) and caused variability between sessions. Especially for the ECR muscle, this can be an important confounding factor in the findings due to its close proximity with other muscles in the forearm and the limited skin surface for electrode placement (357, 358). Crosstalk levels in forearm extensor muscles are reported to potentially reach up to 58% (358). Despite the implementation of standardised electrode placement and post-placement monitoring for crosstalk, this might still have influenced the findings, increasing the within-subject variability between sessions.

Additionally, most participants exhibited negative EMD in both the BB and ECR, suggesting that hand movements began before muscle activation. It is reported that in movements from proximal to distal, individuals often use upper arm joints (shoulder and elbow) to lead movements in distal joints (wrist and fingers) (359). Thus, shoulder, and elbow torques may have initiated hand movements prior to BB and ECR activation. In this study, movement onset, which is crucial for EMD calculations, was detected based on the start of movement in the finger marker (Section 4.5). Using movement in the shoulder or elbow joints to detect movement onset instead of the finger marker might have yielded different results. In addition, the study employed a standardised UL task of reaching for a telephone (Section 4.3.3), which typically does not involve substantial elbow flexion and wrist extension. These factors could be potential explanations for the negative EMD findings. Conversely, a subset of participants displayed positive EMD values. Even for some participants, EMD values switched between positive and negative across sessions, potentially leading to significant within-subject variability. These observed within- and between-subject variabilities in EMD values might have contributed to the observed insufficient test-retest reliability findings for EMD in the BB and ECR.

Strengths of the Study

One significant strength of the study is its large sample size, which was based on a power calculation and effectively achieved. This enhances the statistical power and generalisability of the findings. It also mitigates the impact of random variations, thereby supporting the reliability and accuracy of the findings.

Another strength of the study is the inclusion of sensitivity analyses, which exclude outliers. These analyses enabled the assessment of test-retest reliability through a more typical sample, providing an understanding of the variables' reliability under standard conditions.

Additionally, the placement of Vicon markers and surface EMG electrodes on participants by two researchers across the sessions is a strength of the study. This approach aligns with standard practices in multi-centre clinical research and clinical settings. Thus, the study's findings are directly pertinent to the intended use of the variables assessed.

Limitations

One potential limitation of this study is the sequence of task repetitions conducted by participants. Given that at least 12 repetitions were performed, decreased attentiveness may have affected the performance in subsequent trials.

While the involvement of multiple researchers in placing Vicon markers and surface EMG electrodes is a strength, it also may be a potential limitation. Despite efforts to ensure consistent placement following standardised procedures and the expertise of the involved physiotherapists, variability in marker and electrode placement between sessions might have influenced the findings (360–363).

5.5 Conclusion

This study assessed the test-retest reliability of certain kinematics-derived variables (TTC, MS, RPR, and THDR) and EMG-derived variables (MAOT of the BB and ECR, and EMD in the BB and ECR) in individuals without mobility-impairing conditions (**Aim 2b**). While these variables generally exhibited insufficient test-retest reliability (ICCs < 0.70) (**Aim 2b**), sensitivity analyses accounting for outliers revealed acceptable test-retest reliability (ICCs > 0.70) for most variables (**Aim 2b**). Factors such as outliers, the sensitivity of ICCs to low between-subject variability in a homogeneous sample, and the narrow measurement range of certain variables likely influenced these findings.

Despite insufficient test-retest reliability (relative reliability), TTC, MS, and RPR demonstrated high absolute reliability and accuracy, as evidenced by small SEM% values (< 10%), narrow 95% LOAs, and negligible systematic biases (**Aim 2b**). These findings support their precision in repeated individual measurements and suggest their potential for detecting meaningful changes. The identified reference values for TTC, MS, and RPR provide normative data that can guide the identification of deviations in movement patterns (**Aim 2a**). The identified SDCs for TTC, MS, and RPR were smaller than their corresponding 95% LOA ranges, supporting the use of these LOA ranges as thresholds to detect meaningful changes beyond expected measurement variability (**Aim 2c**). Consequently, these variables may be useful for detecting neuromuscular impairments and functional limitations, particularly for monitoring changes within individuals over time; however, further validation in stroke populations is needed to confirm their clinical utility.

In contrast, THDR and the EMG-derived variables demonstrated insufficient reliability (**Aim 2b**), indicating that their reference values and SDCs (**Aim 2a and 2c**) should be interpreted with caution. However, their low systematic biases and acceptable test-retest reliability values in sensitivity analyses suggest they can still offer valuable insights. While their limitations imply that these variables may require further validation before widespread use, they can contribute to a broader understanding of movement abilities when combined with variables like TTC, MS, and RPR, which exhibit high absolute reliability and accuracy.

In summary, TTC, MS, and RPR emerged as promising variables with high absolute reliability and negligible systematic biases, making them strong candidates for future validation in stroke populations. This study provides foundational reference values and reliability data to support the informed selection of variables and standardisation efforts. These findings underscore the potential utility of these variables for practical applications in clinical and research settings and

suggest their promise when integrated into simplified and accessible assessment methods for broader usability.

Chapter 6. Relationship between Neuromuscular Impairments and Functional Abilities after Stroke: An Observational Repeated Measures Cohort Study

6.1 Introduction

Understanding the relationship between the severity of neuromuscular impairments and functional limitations is critical for making sound clinical decisions and effectively planning stroke survivors' therapy sessions.

Although there are some studies that investigated how neuromuscular impairments correlate with functional abilities post-stroke, these studies employed single-session cross-sectional designs (19–21, 30, 32, 33, 87). Various factors such as compensatory strategies, familiarity with the experimental setting, fatigue, and motivation can impact the observed relationships between neuromuscular impairments and functional abilities, even without true changes in neuromuscular impairments (101–103). Cross-sectional studies can provide information on potential relationships, but only longitudinal studies can truly ascertain whether these relationships are stable or affected by external factors. Understanding which relationships between them are consistent is crucial for developing effective, targeted rehabilitation strategies. However, no longitudinal study has yet investigated the long-term stability of the relationships between them.

Additionally, previous studies exploring these relationships have limited generalisability due to their relatively small sample sizes (19, 22, 33, 87). These studies primarily focused on evaluating the influence of specific neuromuscular impairments on functional abilities, resulting in a limited understanding of the broader relationships (29–32). Incorporating variables derived from kinematics and EMG could enhance this understanding by enabling a more detailed investigation of neuromuscular impairments (16–18). However, the limited application of kinematics- and EMG-derived variables in existing studies continues to constrain a thorough understanding of the relationships between neuromuscular impairments and functional abilities post-stroke (19–22).

To address the thesis's third research question, this experimental study aims to (1) estimate the relationships between measures of neuromuscular impairment and functional ability in people after stroke (**Aim 3a**); and (2) explore whether there are stable relationships between measures of neuromuscular impairment and functional ability collected two to four months apart when improvement is not expected in people after stroke (**Aim 3b**).

6.2 Methods

6.2.1 Introduction

This section only contains study-specific methods and experimental procedures. Chapter 4 provides the common methods and instruments employed in this study and in the study presented in Chapter 5.

6.2.2 Ethical Approval and Informed Consent

Ethical approval for the study was granted by the UEA's FMH Research Ethics Committee under the reference number 2020/21-028 (Appendix 17).

Potential participants were screened against the eligibility criteria (Table 25, below). Those met the criteria received the FMH Ethics Committee-approved PIS (Appendix 18) and written and video-recorded COVID-19 guidelines (Appendix 11) for visiting the MoveExLab, available at http://www.abira.ac.uk/about-abira/research-facilities/. Information was delivered through post or email based on their preferences. They were given sufficient time for questions and consultations with others. Any questions they had were answered online, over the phone, or in person. Per preference, individuals who wished to participate were required to provide informed consent via two options. The first involved returning a completed informed consent form in a stamped addressed envelope provided to them and receiving a hard copy of it on their first MoveExLab visit. The second option allowed electronic consent via email, aligned with the MRHA/HRA joint statement on electronic informed consent (details at https://www.hra.nhs.uk/about-us/news-updates/hra-and-mhra-publish-joint-statement-seeking-and-documenting-consent-using-electronic-methods-econsent/).

Participants were asked to use their personal email accounts to respond to the email containing the informed consent form, which was sent from a UEA email address. They were requested to indicate their consent by initialling each statement and providing their signature, name, and the date on the form. Individuals providing written informed consent were enrolled in the study (Appendix 19).

6.2.3 Study Design and Participants

This study was designed as an observational cohort study with two assessment points, two to four months apart. The study's eligibility criteria for potential participants are in Table 25.

Table 25. Participant Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
• Be at least 18 years old • Have received a clinical diagnosis of stroke at any point in the past • Have been discharged from NHS stroke services • Have provided written informed consent	• Have any other diagnosed neurological and/or musculoskeletal pathology that impacts mobility, such as Multiple Sclerosis or osteoporosis • Having a latex allergy

6.2.4 Sample Size

A *priori* power calculation was performed to determine the required sample size for achieving a power of 0.8 in a one-sample correlation test, assuming a null hypothesis of no population correlation (rho = 0) and an alternative hypothesis of a significant correlation (rho = 0.5), with a significance level of 0.05. The analysis concluded that a sample size of 30 participants with complete data sets would be sufficient. To account for potential challenges such as participant attrition and incomplete data collection, the sample size was set at 45 individuals. This decision was based on the anticipation of approximately a 20% attrition rate and a 15% incidence of data loss due to various factors such as poor data quality or incomplete data collection from some participants (330, 331).

6.2.5 Recruitment

A variety of communication channels were used to reach potential participants. Charities such as 'Headway Norfolk and Waveney,' 'ARNI Stroke Charity,' and local voluntary stroke support groups were contacted about the study, and their help in disseminating the approved study poster (Appendix 20) and PIS was sought. The study's poster was distributed across Norwich Research Park and nearby public buildings (within a 25-mile radius), as well as on the HSC Bulletin, UEA Lasdun (newsletter), HSC Twitter, the RHITE database (https://brainhtc.org/rhite/), the ABIRA website (http://www.abira.ac.uk), and social media. A local radio station broadcasted the study. People who approached the research team after learning about the study or who had previously participated in the studies and granted informed consent to be contacted about future trials were contacted about the study.

6.2.6 Data Collection

Two data collection sessions were undertaken two to four months apart. Even when participants were unable to complete the entire task, measures were collected as planned. This approach was adopted because valuable data can still be obtained from muscles during attempted

movements. Participants were encouraged to perform the task to the best of their ability and to inform the researchers if they experienced fatigue or discomfort. In these instances, breaks or the discontinuation of the experiment were implemented.

Following the completion of the experimental procedures detailed in Chapter 4, participants were assessed using two clinical outcome measures: the FMA – UL Motor Scale and the ARAT. These measures, internationally recommended for stroke recovery trials (106), were only applied to the more affected UL.

- FMA – UL Motor Scale, a widely employed clinical measure in stroke research and practice (364), was utilised to evaluate neuromuscular impairments. It assesses UL movements, coordination, and reflexes, with a maximum score of 66 (365). It has high intra-rater (ICC (95% CI) = 0.95 (0.66 – 1.0)) and inter-rater reliability (ICC (95% CI) = 0.99 (0.97 – 1.0)) among stroke survivors (366). The "FMA-UL Motor Scale" is referred to as "FMA" throughout the text.

- ARAT, another widely used measure in stroke research and clinical practice, was employed to assess functional ability. ARAT evaluates the ability to execute tasks involving object manipulation with a maximum score of 57 (367). It demonstrates excellent test-retest (ICC = 0.965, rho = 0.968) and inter-rater reliability (ICC = 0.998, rho = 0.996) among stroke survivors (182). Its construct validity, in relation to the FMA both pre- and post-treatment, has been established as excellent, with Spearman's rank correlation coefficients of 0.73 (95% CI = 0.58 – 0.83) at pretreatment and 0.74 (95% CI = 0.60 – 0.84) post-treatment ($p < 0.01$) (368).

The remaining experimental procedures and detailed information regarding the variables and their extraction processes are outlined in Chapter 4.

6.2.7 Statistical Analyses

Data were categorised by the more affected UL and workspace for the standardised UL task (Section 4.3.3). Analyses were individually conducted and reported for each of the four reaching conditions: midline workspace with the more affected hand (MMAH); midline workspace with the less affected hand (MLAH); contralateral workspace with the more affected hand (CMAH); and contralateral workspace with the less affected hand (CLAH). Prior to the analyses, the mean of the variables' values from repeated trials in each session was computed. This approach was adopted because it would give a more accurate depiction of how an individual usually performs.

STATA 17.0 was used for the statistical analyses.

Aim 3a: Estimate the relationships between measures of neuromuscular impairment and functional ability

To explore the relationships between neuromuscular impairments and functional abilities, linear regression analyses were conducted using data from both sessions. These analyses involved distinct regression models for each specific pair of functional ability and neuromuscular impairment variables. For each model, functional ability variables (TTC and ARAT) were matched with corresponding impairment variables from the same hand and workspace condition. For instance, TTC data collected from the more affected hand during midline workspace reaching tasks were paired with impairment measures obtained from the more affected hand in the midline workspace condition. For variables like FMA and ARAT, which lack workspace specification, the pairing was conducted with kinematics- and EMG-derived variables from the more affected hand, considering each workspace condition independently.

While correlation statistics are commonly employed to analyse the relative strengths of relationships among two variables, they are not ideal for datasets with repeated measures due to their assumption of observation independence (369). Therefore, for the longitudinal data in this study, a linear regression approach was utilised, executed using the *'reg'* command in STATA. The regression model included the functional ability variable as the dependent variable and the neuromuscular impairment variable as the independent variable. To effectively handle repeated observations per individual and account for inherent similarities in repeated measurements from the same individual, the model adjusted for clustering at the participant level, using the participant identifier (P1_num) in the *'vce(cluster P1_num)'* option (370, 371). This adjustment acknowledges the clustering within the data and enhances the reliability of the findings by addressing potential heteroskedasticity (non-constant variance) in the dataset (370–373), a method often overlooked in correlation analyses (334, 373).

The regression coefficients, coefficient of determination (R^2), 95% CIs, and p-values were provided for each pairwise relationship. The regression coefficient indicates the strength and direction of the linear relationship between the variables (334). It quantifies the expected change in functional ability for each one-unit change in the neuromuscular impairment while controlling for other variables (334). A higher absolute value of the regression coefficient signifies a stronger relationship (334). The R^2 value explains the proportion of variance in the dependent variable (functional ability) that can be explained by the independent variable

(neuromuscular impairment) (374). It contextualises the regression coefficient (Coef.) by indicating the overall strength of the relationship (374). A higher R^2 value suggests that a larger proportion of the variance in functional ability is accounted for by variations in neuromuscular impairment, signifying a stronger relationship (374).

The interpretation of R^2 values is as follows: values below 0.1 indicate very weak strength, 0.1 to 0.3 indicate weak strength, 0.3 to 0.5 indicate moderate strength, 0.5 to 0.7 indicate strong strength and values above 0.7 indicate very strong strength (375). The 95% CIs indicate a range in which the actual values of the estimated regression coefficients are expected to fall with 95% confidence (334). Narrower intervals indicate greater precision and reliability (334). The 95% CI which does not include zero further supports the presence of a statistically significant effect (376). The threshold for statistical significance was established at a p-value of 0.05.

Aim 3b: Explore whether there are stable relationships between measures of neuromuscular impairment and functional ability collected two to four months apart when improvement is not expected

In the analyses, data from both sessions were used, but only for those participants who had data available from both sessions for the pertinent variables in the assessed pairwise relationships.

Each distinct linear regression model for pairwise relationships of neuromuscular impairment and functional ability variables described above was adapted to include the data collection time points (Session 1 or 2) as a categorical variable. An interaction term, combining the session identifier with the independent variable (impairment measure), was incorporated into the model. This modification allowed for the evaluation of whether the effect of the impairment variable on the functional ability variable changes between the sessions. Thus, whether the identified relationships are consistently present over time or are influenced by external factors was assessed.

The p-value of the interaction term, referred to as the stability p-value, was provided for each assessed pairwise relationship. A stability p-value greater than 0.05 indicates that the relationship between impairment and functional ability is stable (377), signifying no significant differences across sessions. In addition, session-specific regression coefficients were provided as supplementary information to provide further insight into the magnitude and potential variations of the relationship between impairment and functional ability at different time points.

In summary, from the combination of statistical analyses, four distinct scenarios emerge regarding the potential relationships between variables:

- Significant and Stable Relationship: A significant, consistent relationship over time (relationship p-value < 0.05, stability p-value > 0.05), suggesting reliable predictability between the variables.
- Significant but Unstable Relationship: This indicates a statistically significant yet fluctuating relationship over time (relationship p-value < 0.05, stability p-value < 0.05), suggesting that while the variables are related, their predictive relationship is inconsistent and possibly influenced by external factors.
- Insignificant and Stable Relationship: This indicates a relationship that consistently lacks statistical significance (relationship p-value > 0.05) across different time points (stability p-value > 0.05). It signifies a persistently weak or non-existent connection between the variables.
- Insignificant and Not Stable Relationship: A statistically insignificant and varying relationship (relationship p-value > 0.05, stability p-value < 0.05), indicating an unreliable and non-predictive relationship.

6.3 Results

The study enrolled 45 individuals who reported a history of stroke. However, one participant (ID: PS034) later disclosed being unaware of their stroke, until this was identified through a 'Magnetic Resonance Imaging' scan. Due to uncertainties about the timing and impact of this undetected stroke, this participant was excluded. Consequently, the total number of stroke survivors who could be included in the data analyses was 44. Table 26 presents the characteristics of these participants, with detailed individual characteristics available in Appendix 21.

Table 26. Participant Characteristics at Recruitment (Sample Size = 44)

Age (Years)	Mean = 62.3, SD = 12.2, Range = 25-85
Biological Sex (Male / Female)	25 / 19
Hand Dominance (Right / Left)	38 / 6
More Affected Hand (Right / Left)	22 / 22
Time Since Stroke Onset (Years)	Mean = 5.7, Range = 0.2-22
Participants with At Least One Prior Stroke (Before the Most Recent)	10
Baseline FMA – UL Motor Scale (0 – 66)	Mean (SD) = 47.59 (24.40) Range = • ≤ 15 = 10 participants • 16-34 = 3 participants • ≥ 35 = 31 participants
Baseline ARAT (0 – 57)	Mean (SD) = 40.27 (23.75) Range = • ≤ 19 = 13 participants • 20-39 = 2 participants • ≥ 40 = 29 participants

Note: FMA – UL: Fugl-Meyer Assessment – Upper Limb Motor Scale, **ARAT:** Action Research Am Test, **SD:** Standard Deviation.

Of the 44 participants, seven did not participate in the second data collection: two were unresponsive to communication efforts, four developed new pathologies affecting movement, and one experienced worsened rheumatoid arthritis symptoms. Due to some participants being unable to fully complete the experimental task and the presence of noisy EMG signals, only partial data extraction was possible. The number of participants included in the analyses therefore varied across variables.

During the first data collection session, 547 trials were recorded across four reaching conditions: MMAH (136 trials), MLAH (135 trials), CMAH (138 trials), and CLAH (135 trials) (Appendix 22). Of these:

- Five trials had no data extracted due to both the inability to complete the task with the more affected hand and the absence of discernible EMG activity from both the BB and ECR muscles.
- Forty-three trials lacked kinematic data due to the inability to complete the task with the more affected hand.
- Twelve trials lacked kinematic data due to the inability to complete the task with the more affected hand, and EMG data from the ECR muscle due to the absence of discernible muscle activity.
- Three trials lacked kinematic data due to the inability to complete the task with the more affected hand, and EMG data from the BB muscle due to the absence of discernible muscle activity.
- One trial lacked EMG data for the BB muscle due to noisy signals.
- One trial lacked kinematic data due to the inability to complete the task with the more affected hand, and EMD data for the ECR muscle because movement onset was undetectable.

As a result, 482 trials had complete data, while five trials had no data extracted, and 60 trials had partial data extraction.

During the second data collection session, 456 trials were recorded across four reaching conditions: MMAH (111 trials), MLAH (117 trials), CMAH (111 trials), and CLAH (117 trials) (Appendix 23). Of these:

- Two trials had no data extracted due to both the inability to complete the task with the more affected hand and the absence of discernible EMG activity from both the BB and ECR muscles.
- Thirty-seven trials lacked kinematic data due to the inability to complete the task with the more affected hand.
- Fourteen trials lacked kinematic data due to the inability to complete the task with the more affected hand, and EMG data from the ECR muscle due to the absence of discernible muscle activity.
- One trial lacked kinematic data due to the inability to complete the task with the more affected hand, and EMG data from the BB muscle due to the absence of discernible muscle activity.

As a result, 402 trials had complete data, while two trials had no data extracted, and 52 trials had partial data extraction.

The variables that were not extracted for certain participants, along with the reasons, are provided in Appendices 22 and 23. These appendices also contain the outcomes of all the recorded trials' quality checks.

Aima 3a and 3b: Estimate the relationships between measures of neuromuscular impairment and functional ability and explore the stability of their relationships

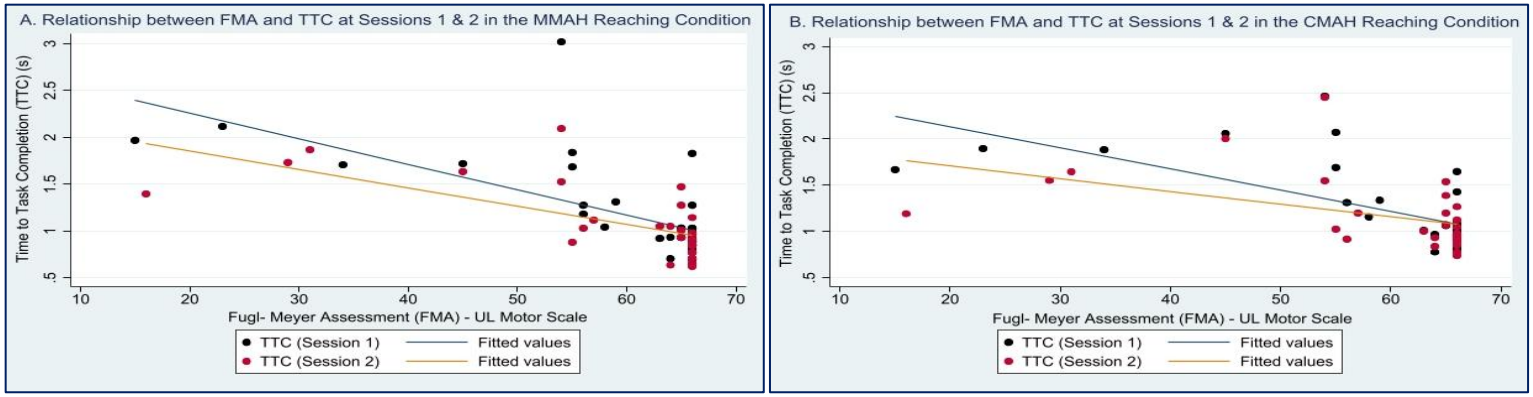
Tables 27 to 34 present the findings for the pairwise relationships between functional ability variables (TTC, ARAT) and neuromuscular impairment variables (MS, THDR, RPR, MAOT of the BB and ECR, and EMD in the BB and ECR) and their stability over time. Corresponding scatterplots are shown in Figures 27 to 34. Explanatory text for the findings is provided following the tables and figures.

The scatterplots illustrate session-specific relationships. The tables present findings from the regression analyses. The reaching conditions stated in the tables and figures relate to the kinematics- or EMG-derived variables collected from both hands in two distinct workspaces (MMAH, MLAH, CMAH, CLAH), while the clinical outcome measures (FMA, ARAT), collected only from the more affected hand, do not include workspace specification.

Relationships between the Fugl-Meyer Assessment (FMA) and Functional Ability Variables

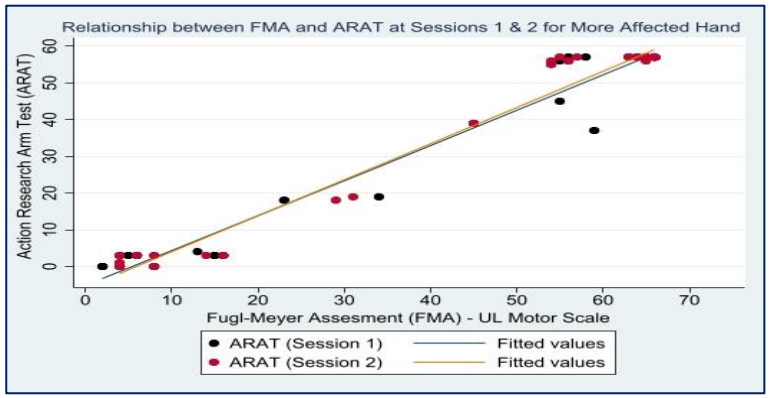
Figure 27. Scatter Plots of Fugl-Meyer Assessment and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between Fugl-Meyer Assessment and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (FMA) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **FMA:** Fugl-Meyer Assessment; **TTC:** Time to Task Completion; **UL:** Upper Limb; **s:** seconds. FMA data were collected only from more affected side. Ceiling effects in the FMA are evident.

B. Relationship between Fugl-Meyer Assessment and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (FMA) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **FMA:** Fugl-Meyer Assessment; **ARAT:** Action Research Arm Test; **UL:** Upper Limb. ARAT and FMA data were collected only from the more affected side. Ceiling effects in the FMA and ARAT are evident.

Table 27. Relationships of the Fugl-Meyer Assessment with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

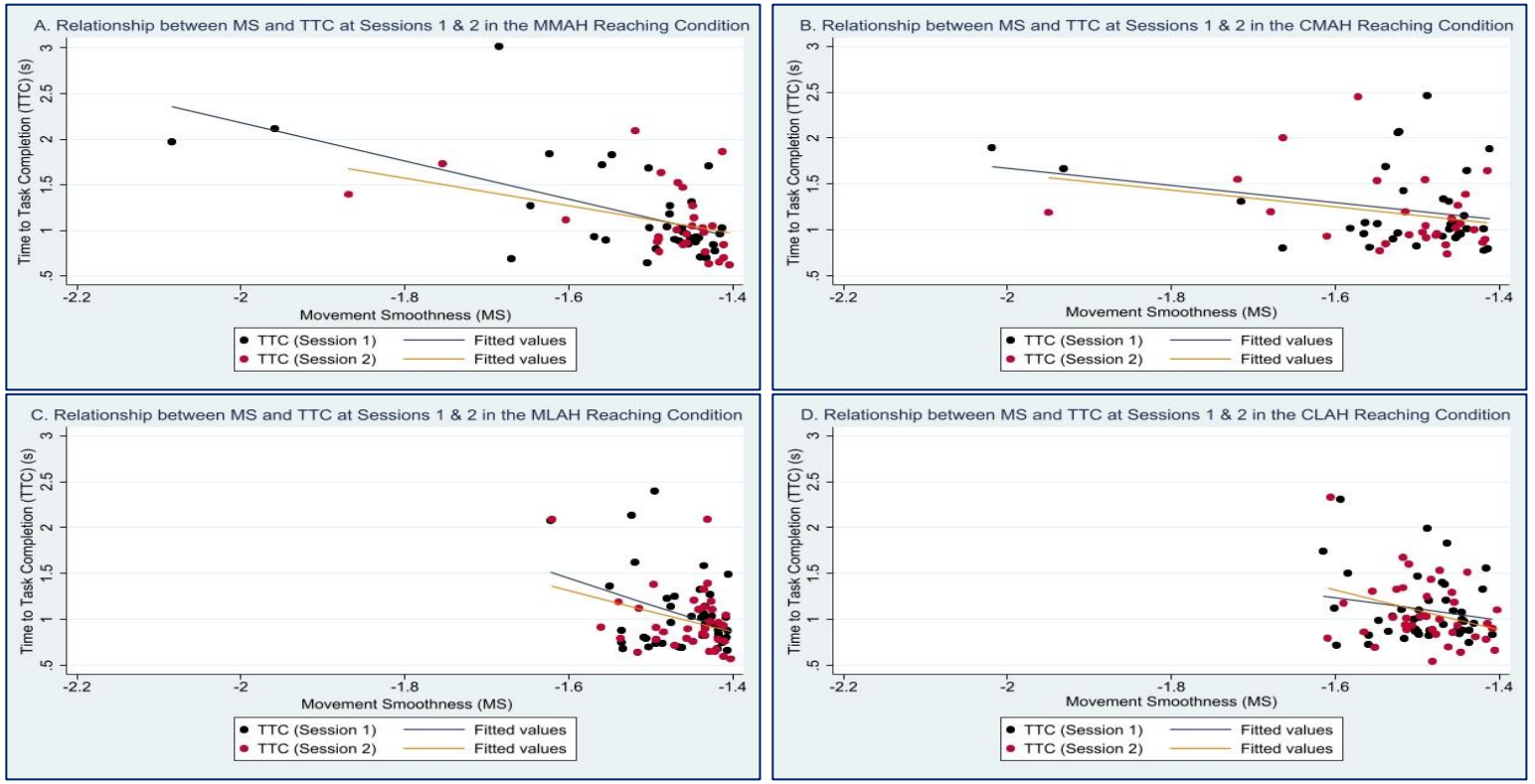
Relationship with Fugl-Meyer Assessment (FMA)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	-0.02	0.41	-0.03; -0.01	< 0.001*	28/28	0.051#	-0.03/-0.02
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	-0.02	0.32	-0.03; -0.01	< 0.003*	28/28	< 0.001	-0.02/-0.01
Action Research Arm Test	More Affected Hand (No Specific Workspace)	44/37	0.97	0.97	0.92; 1.01	< 0.001*	37/37	0.07#	0.96/0.98

Note: This table presents the relationship between the Fugl-Meyer Assessment (FMA) and functional ability variables (Time to Task Completion (TTC) and Action Research Arm Test (ARAT)), categorised by reaching condition. A p-value < 0.05 indicates a statistically significant relationship. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT and FMA data were collected from only the more affected side.

Relationships between the Movement Smoothness (MS) and Functional Ability Variables

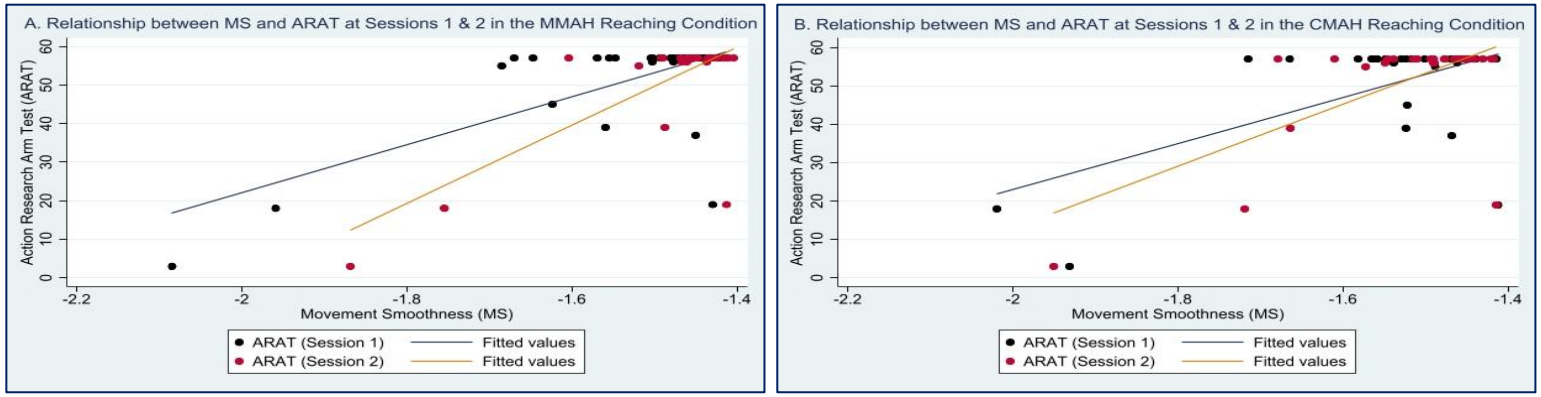
Figure 28. Scatter Plots of Movement Smoothness and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between Movement Smoothness and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MS) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **MS:** Movement Smoothness; **TTC:** Time to Task Completion; **s:** seconds.

B. Relationship between Movement Smoothness and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MS) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MS:** Movement Smoothness; **ARAT:** Action Research Arm Test. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 28. Relationships of the Movement Smoothness with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

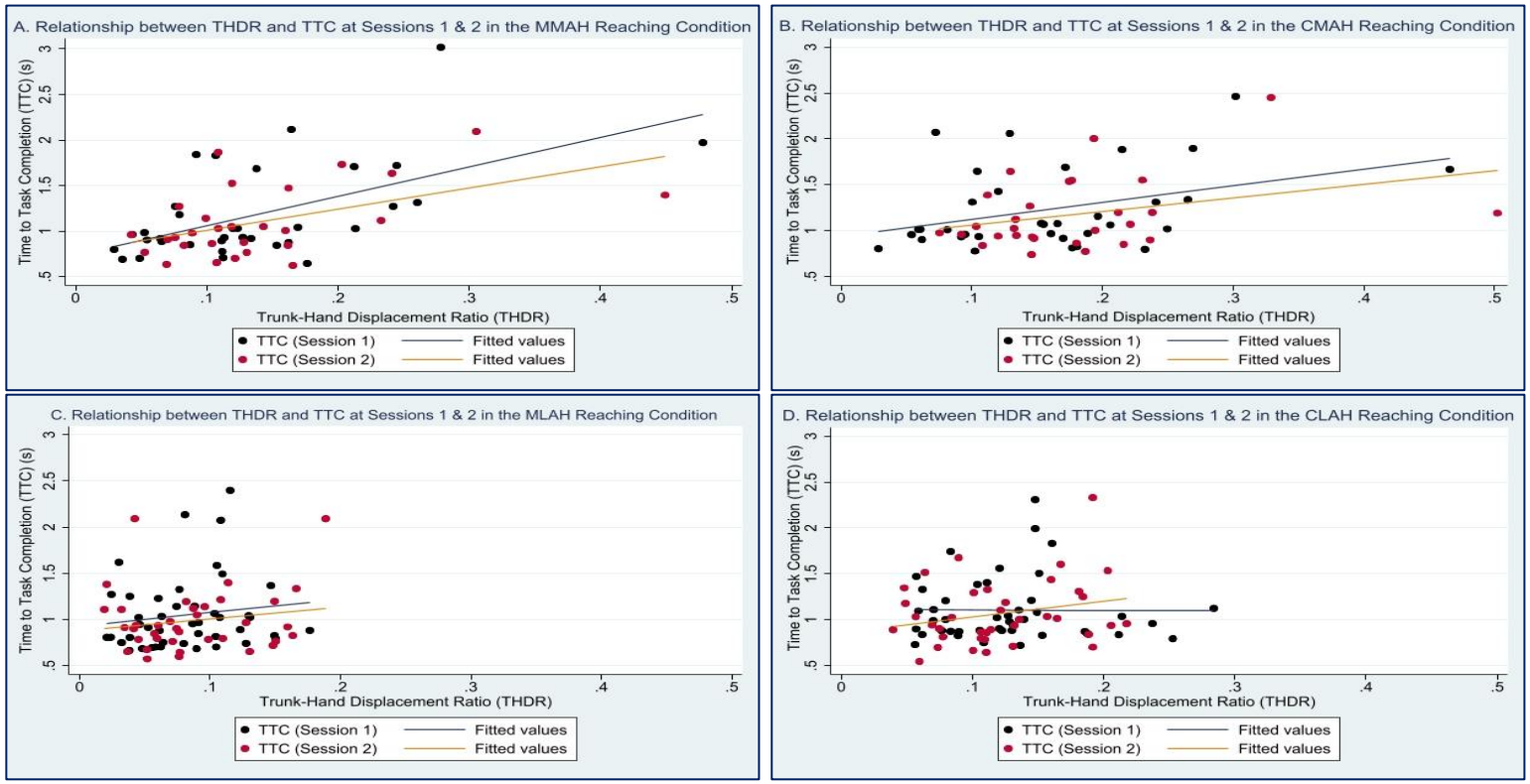
Relationship with Movement Smoothness (MS)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	-1.93	0.29	-2.95; -0.92	< 0.001*	28/28	0.11#	-2.18/-1.51
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	-0.92	0.08	-1.59; -0.26	0.008*	28/28	0.86#	-1.05/-0.93
Time to Task Completion	Midline – Less Affected Hand (MLAH)	44/37	-2.61	0.12	-5.19; -0.03	0.048*	37/37	0.71#	-2.81/-2.25
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	-1.68	0.07	-4.20; 0.83	0.18	37/37	0.48	-1.24/-2.17
Action Research Arm Test	Midline – More Affected Hand (MMAH)	34/28	7.15	0.47	3.93; 10.36	< 0.001*	28/28	0.001	6.74/10.14
Action Research Arm Test	Contralateral – More Affected Hand (CMAH)	34/28	6.82	0.40	2.34; 11.29	0.004*	28/28	0.18#	6.59/8.11

Note: This table presents the relationship between the Movement Smoothness (MS) and functional ability variables (Time to Task Completion (TTC) and Action Research Arm Test (ARAT)), categorised by reaching condition. A p-value < 0.05 indicates a statistically significant relationship. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. For the relationship evaluations between MS and ARAT, MS values are multiplied by 10 to facilitate clearer interpretation. This adjustment does not alter the observed relationships but makes the regression coefficients more comparable and interpretable in the context of the ARAT scores. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT data were collected from only the more affected side.

Relationships between the Trunk-Hand Displacement Ratio (THDR) and Functional Ability Variables

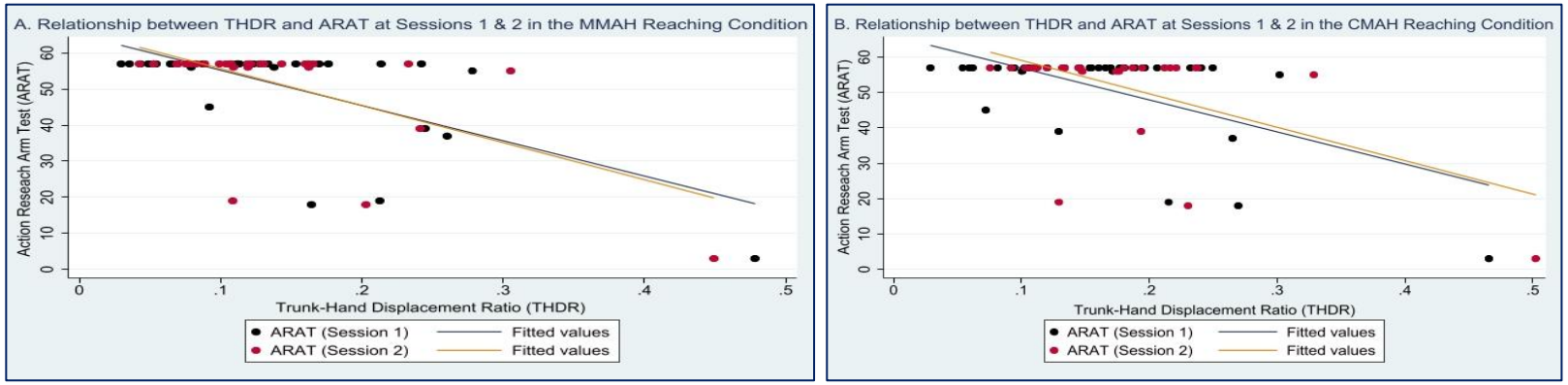
Figure 29. Scatter Plots of Trunk-Hand Displacement Ratio and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between Trunk-Hand Displacement Ratio and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (THDR) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **THDR:** Trunk-Hand Displacement Ratio; **TTC:** Time to Task Completion; **s:** seconds.

B. Relationship between Trunk-Hand Displacement Ratio and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (THDR) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **THDR:** Trunk-Hand Displacement Ratio; **ARAT:** Action Research Arm Test. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 29. Relationships of the Trunk-Hand Displacement Ratio with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

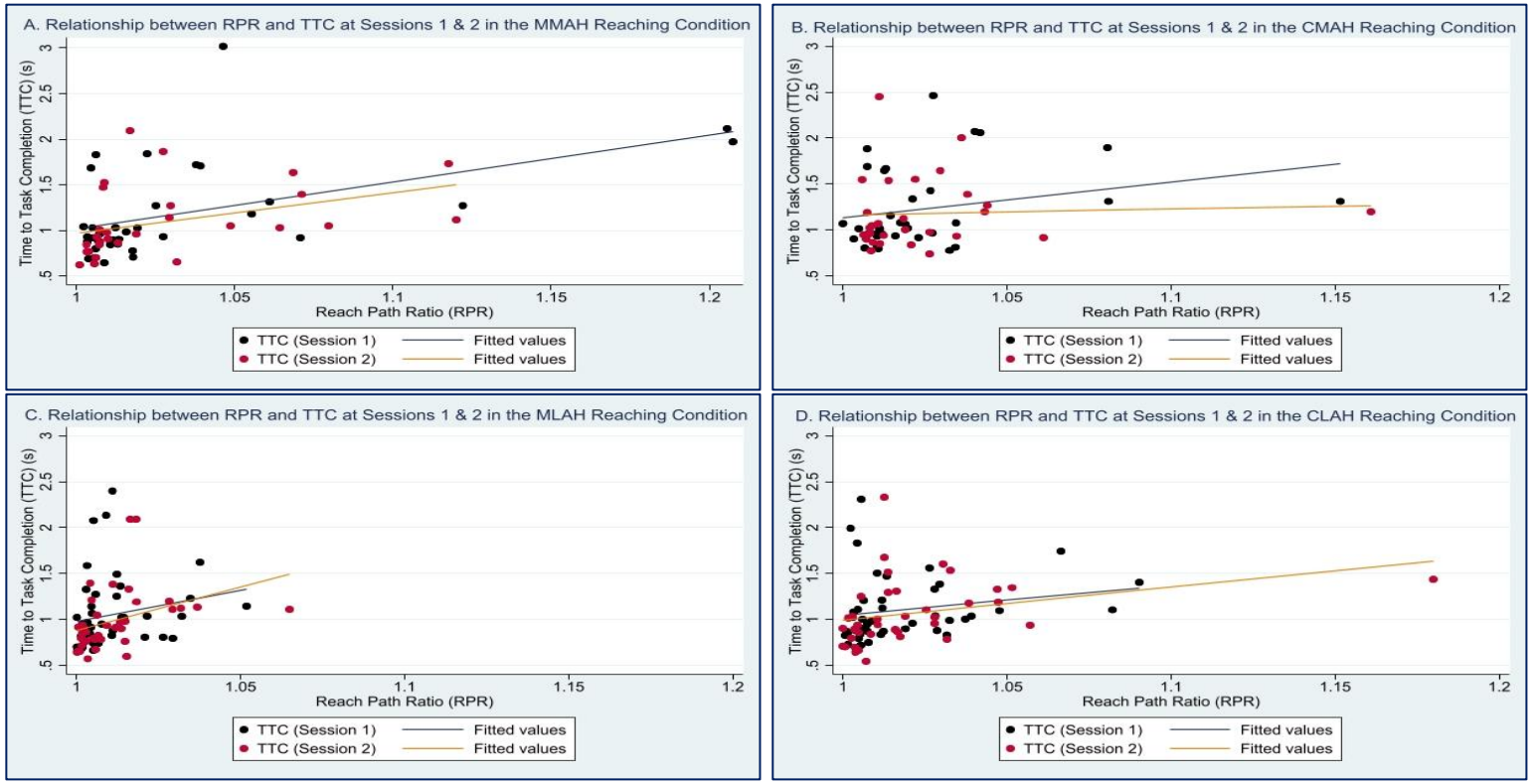
Relationship with Trunk-Hand Displacement Ratio (THDR)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	2.83	0.29	1.06; 4.61	0.003*	28/28	0.02	3.47/2.32
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	1.63	0.12	-0.13; 3.38	0.07	28/28	0.34	2.20/1.49
Time to Task Completion	Midline – Less Affected Hand (MLAH)	44/37	1.30	0.02	-1.20; 3.79	0.30	37/37	0.63	2.21/1.24
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	0.72	0.01	-1.03; 2.47	0.41	37/37	0.15	0.18/1.75
Action Research Arm Test	Midline – More Affected Hand (MMAH)	34/28	-9.98	0.42	-15.69; -4.27	0.001*	28/28	0.98#	-10.27/-10.21
Action Research Arm Test	Contralateral – More Affected Hand (CMAH)	34/28	-9.11	0.34	-15.69; -2.53	0.008*	28/28	0.71#	-10.22/-9.46

Note: This table presents the relationship between the Trunk-Hand Displacement Ratio (THDR) and functional ability variables (Time to Task Completion (TTC) and Action Research Arm Test (ARAT)), categorised by reaching condition. A p-value < 0.05 indicates a statistically significant relationship. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. For the relationship evaluations between THDR and ARAT, THDR values are multiplied by 10 to facilitate clearer interpretation. This adjustment does not alter the observed relationships but makes the regression coefficients more comparable and interpretable in the context of the ARAT scores. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT data were collected from only the more affected side.

Relationships between the Reach Path Ratio (RPR) and Functional Ability Variables

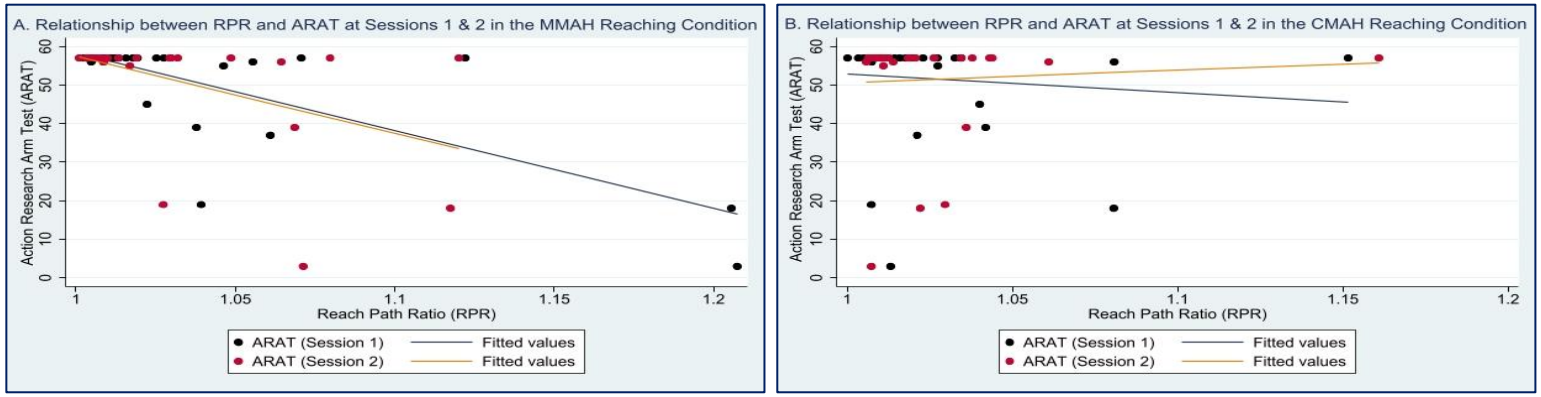
Figure 30. Scatter Plots of Reach Path Ratio and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between Reach Path Ratio and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (RPR) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **RPR:** Reach Path Ratio; **TTC:** Time to Task Completion; **s:** seconds.

B. Relationship between Reach Path Ratio and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (RPR) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **RPR:** Reach Path Ratio; **ARAT:** Action Research Arm Test. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 30. Relationships of the Reach Path Ratio with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

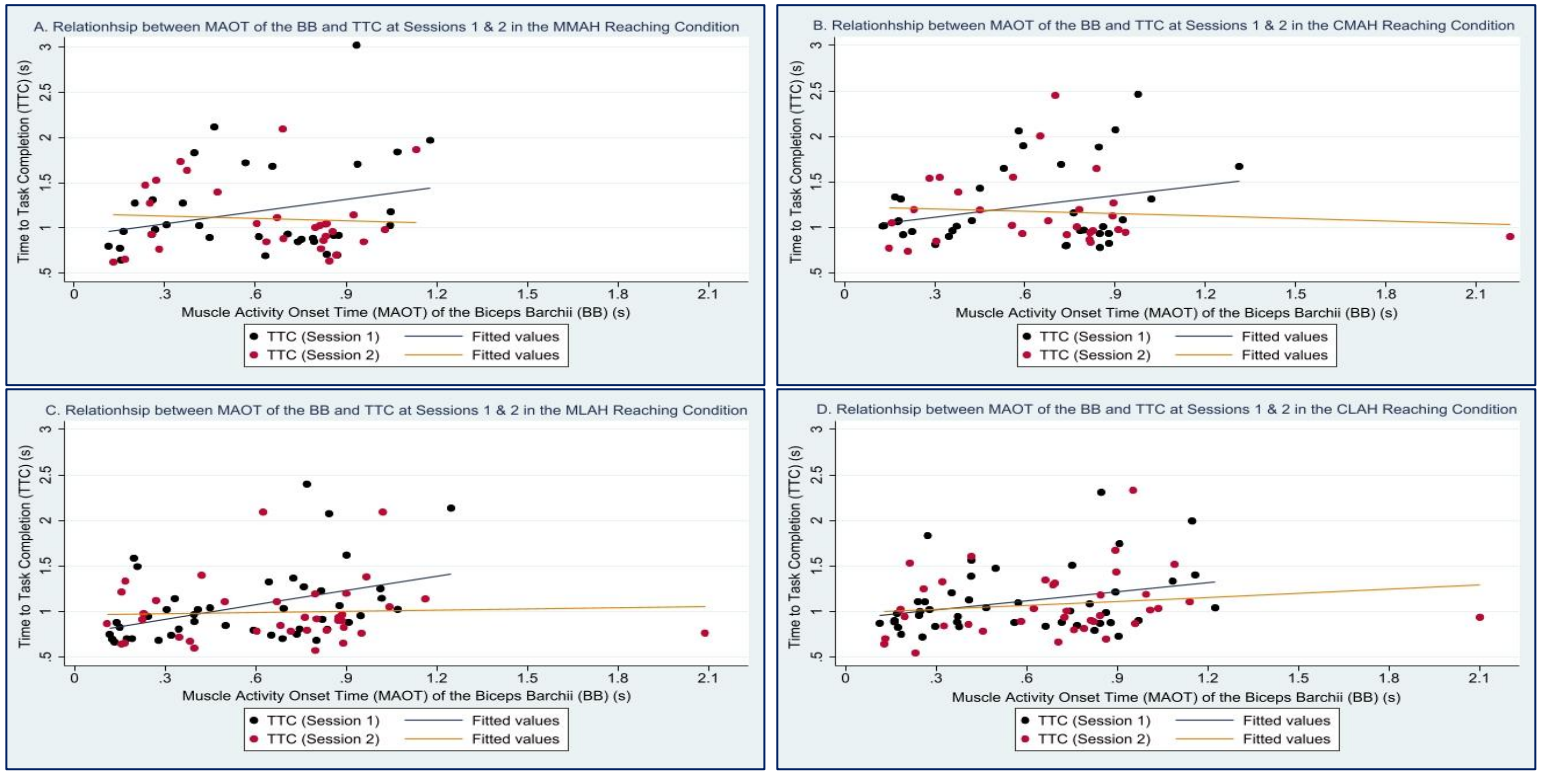
Relationship with Reach Path Ratio (RPR)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	5.00	0.22	3.16; 6.84	< 0.001*	28/28	0.69#	4.99/4.40
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	2.36	0.03	-1.17; 5.90	0.18	28/28	0.24	3.09/0.69
Time to Task Completion	Midline – Less Affected Hand (MLAH)	44/37	7.93	0.07	2.26; 13.60	0.007*	37/37	0.59#	7.07/9.48
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	3.30	0.06	0.95; 5.64	0.007*	37/37	0.80#	2.81/3.41
Action Research Arm Test	Midline – More Affected Hand (MMAH)	34/28	-19.99	0.42	-30.79; -9.19	0.001*	28/28	0.99#	-19.85/-19.94
Action Research Arm Test	Contralateral – More Affected Hand (CMAH)	34/28	-1.06	0.001	-13.18; 11.06	0.86	28/28	0.45	-3.98/3.12

Note: This table presents the relationship between the Reach Path Ratio (RPR) and functional ability variables (Time to Task Completion (TTC) and Action Research Arm Test (ARAT)), categorised by reaching condition. A p-value < 0.05 indicates a statistically significant relationship. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. For the relationship evaluations between RPR and ARAT, RPR values are multiplied by 10 to facilitate clearer interpretation. This adjustment does not alter the observed relationships but makes the regression coefficients more comparable and interpretable in the context of the ARAT scores. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT data were collected from only the more affected side.

Relationships between the Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB) and Functional Ability Variables

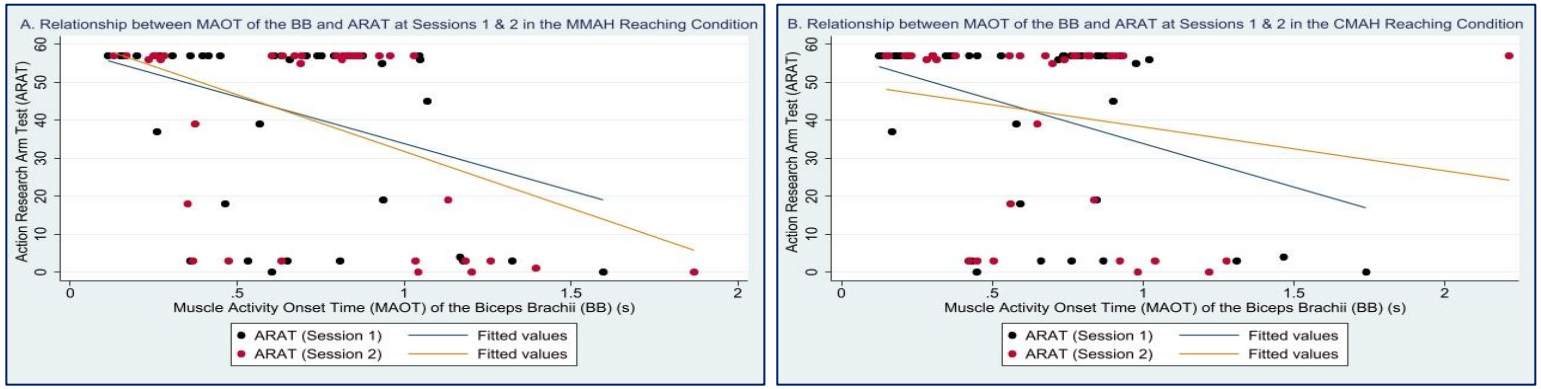
Figure 31. Scatter Plots of the Muscle Activity Onset Time of the Biceps Brachii and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between the Muscle Activity Onset Time of the Biceps Brachii and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MAOT of the BB) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **MAOT:** Muscle Activity Onset Time; **BB:** Biceps Brachii; **TTC:** Time to Task Completion; **s:** seconds. The MAOT values are represented in seconds.

B. Relationship between the Muscle Activity Onset Time of the Biceps Brachii and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MAOT of the BB) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MAOT:** Muscle Activity Onset Time; **BB:** Biceps Brachii; **ARAT:** Action Research Arm Test; **s:** seconds. The MAOT values are represented in seconds. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 31. Relationships of the Muscle Activity Onset Time of the Biceps Brachii with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

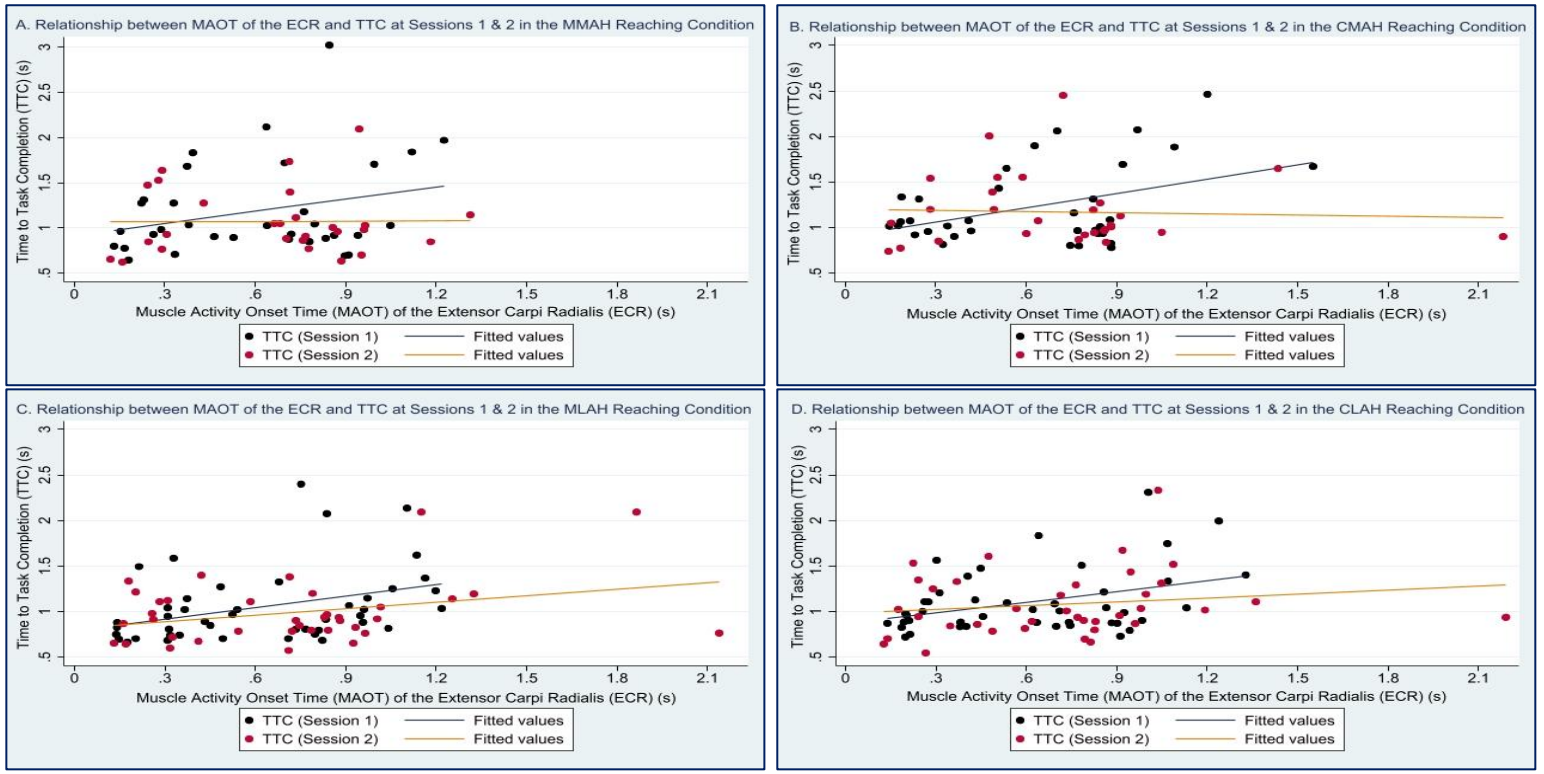
Relationship with Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	0.22	0.02	-0.26; 0.69	0.36	28/28	0.10	0.47/-0.09
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	0.12	0.01	-0.22; 0.45	0.48	28/28	0.03	0.35/-0.09
Time to Task Completion	Midline – Less Affected Hand (MLAH)	43/37	0.23	0.05	-0.08; 0.54	0.14	36/36	0.23	0.39/0.17
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	0.22	0.05	-0.07; 0.50	0.14	37/37	0.30	0.34/0.15
Action Research Arm Test	Midline – More Affected Hand (MMAH)	42/37	-27.44	0.18	-40.61; -14.27	< 0.001*	35/35	0.95#	-24.95/-24.30
Action Research Arm Test	Contralateral – More Affected Hand	42/35	-17.43	0.08	-35.35; 0.49	0.06	35/35	0.45	-21.69/-11.65

Note: This table presents the relationship between the Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB) and functional ability variables (Time to Task Completion (TTC) in seconds and Action Research Arm Test (ARAT), a unitless scale), categorised by reaching condition. The MAOT values are represented in seconds. A p-value < 0.05 indicates statistical significance. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT data were collected from only the more affected side.

Relationships between the Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR) and Functional Ability Variables

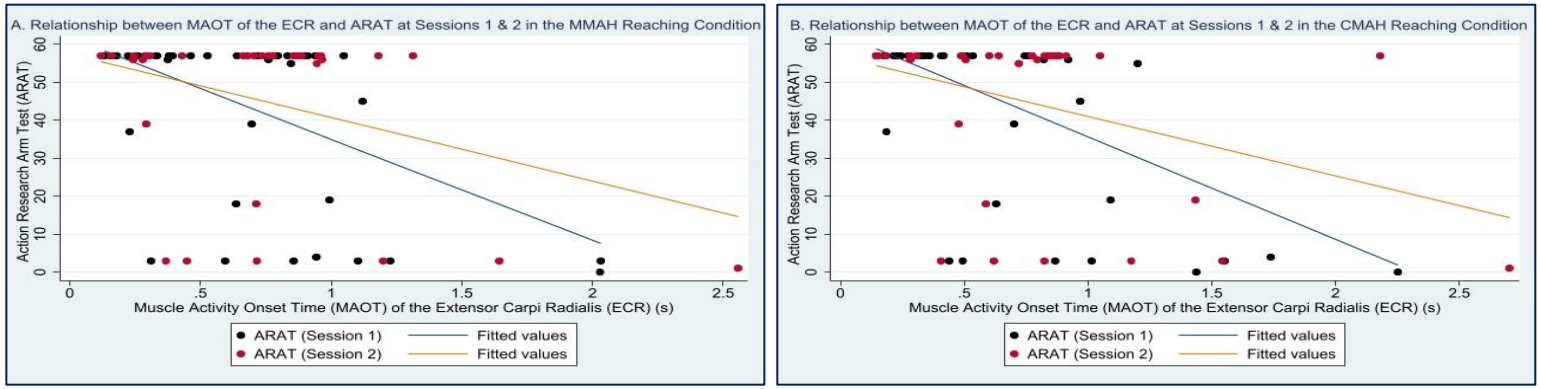
Figure 32. Scatter Plots of the Muscle Activity Onset Time of the Extensor Carpi Radialis and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between the Muscle Activity Onset Time of the Extensor Carpi Radialis and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MAOT of the ECR) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **MAOT:** Muscle Activity Onset Time; **ECR:** Extensor Carpi Radialis; **TTC:** Time to Task Completion; **s:** seconds. The MAOT values are represented in seconds.

B. Relationship between Muscle Activity Onset Time of the Extensor Carpi Radialis and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (MAOT of the ECR) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MAOT:** Muscle Activity Onset Time; **ECR:** Extensor Carpi Radialis; **ARAT:** Action Research Arm Test; **s:** seconds. The MAOT values are represented in seconds. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 32. Relationships of the Muscle Activity Onset Time of the Extensor Carpi Radialis with Functional Ability Variables: Time to Task Completion and Action Research Arm Test

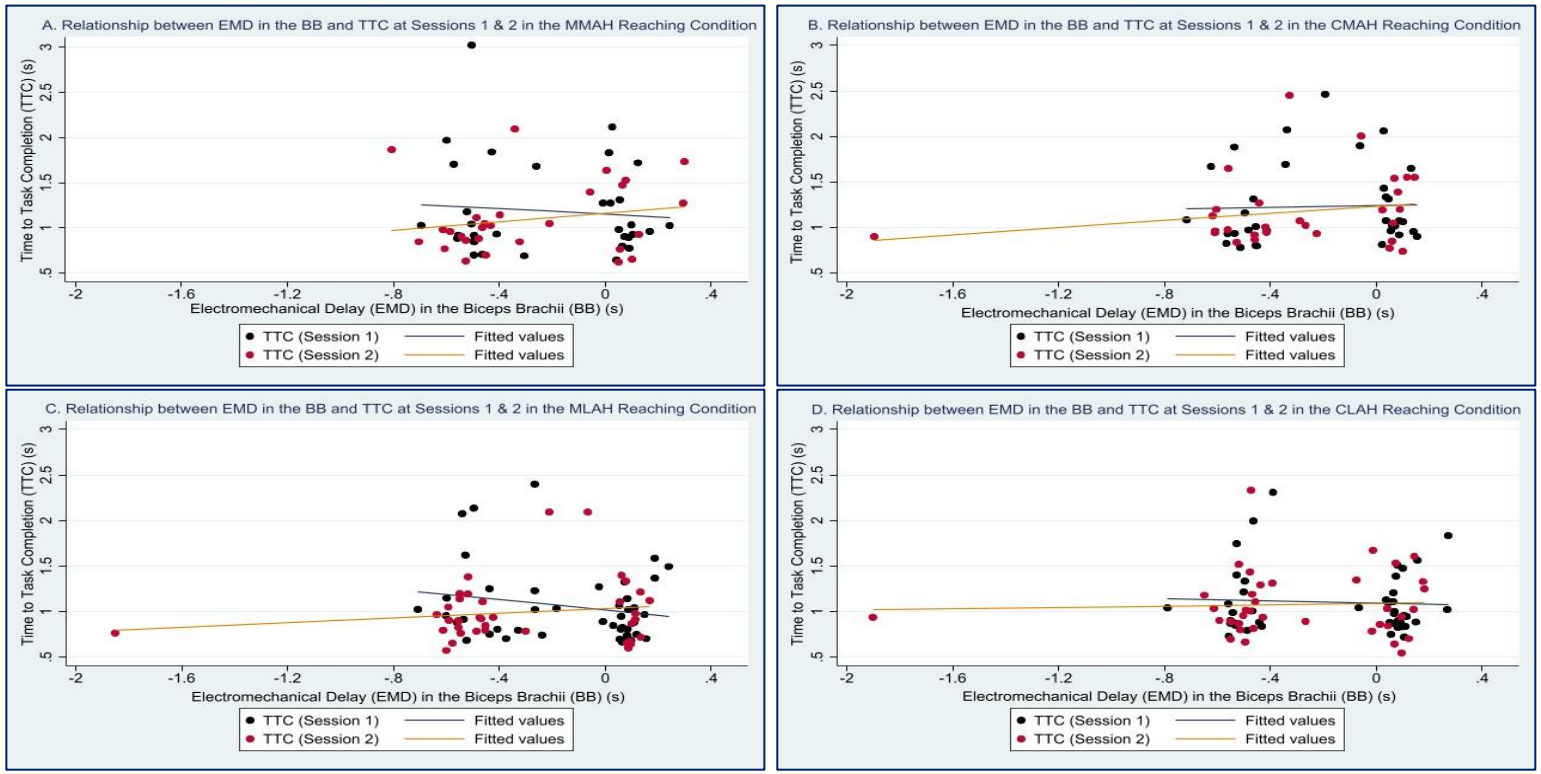
Relationship with Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/27	0.23	0.03	-0.21; 0.67	0.29	27/27	0.13	0.39/0.009
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	0.21	0.04	-0.14; 0.56	0.24	28/28	0.02	0.51/-0.04
Time to Task Completion	Midline – Less Affected Hand (MLAH)	44/37	0.30	0.10	-0.01; 0.60	0.055	37/37	0.57	0.33/0.24
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	0.24	0.07	-0.04; 0.53	0.09	37/37	0.13	0.41/0.14
Action Research Arm Test	Midline – More Affected Hand (MMAH)	41/32	-21.52	0.20	-31.41; -11.63	< 0.001*	32/32	0.13#	-25.72/-16.75
Action Research Arm Test	Contralateral – More Affected Hand	41/33	-20.84	0.22	-31.56; -10.11	< 0.001*	33/33	0.19#	-24.49/-15.67

Note: This table presents the relationship between the Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR) and functional ability variables (Time to Task Completion (TTC) in seconds and Action Research Arm Test (ARAT), a unitless scale), categorised by reaching condition. The MAOT values are represented in seconds. A p-value < 0.05 indicates statistical significance. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. **N:** number of observations; **S1:** Session 1; **S2:** Session 2; **Coef.:** regression coefficient; and **95% CI:** 95% confidence interval. The '*' denotes statistical significance, and '#' indicates significant and stable relationships over time. ARAT data were collected from only the more affected side.

Relationships between the Electromechanical Delay in the Biceps Brachii and Functional Ability Variables

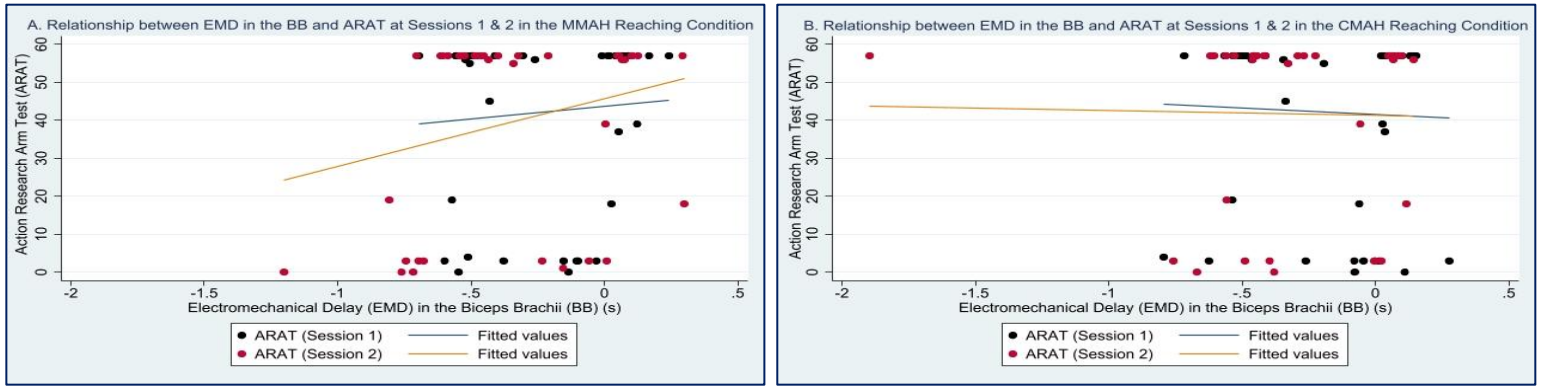
Figure 33. Scatter Plots of the Electromechanical Delay in the Biceps Brachii and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between the Electromechanical Delay in the Biceps Brachii and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (EMD in the BB) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **EMD:** Electromechanical Delay; **BB:** Biceps Brachii; **TTC:** Time to Task Completion; **s:** seconds. The EMD in the BB values are represented in seconds.

B. Relationship between the Electromechanical Delay in the Biceps Brachii and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (EMD in the BB) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **EMD:** Electromechanical Delay; **BB:** Biceps Brachii; **ARAT:** Action Research Arm Test; **s:** seconds. The EMD in the BB values are represented in seconds. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 33. Relationships of the Electromechanical Delay in the Biceps Brachii (BB) with Functional Ability Variables: Time to Task Completion (TTC) and Action Research Arm Test (ARAT)

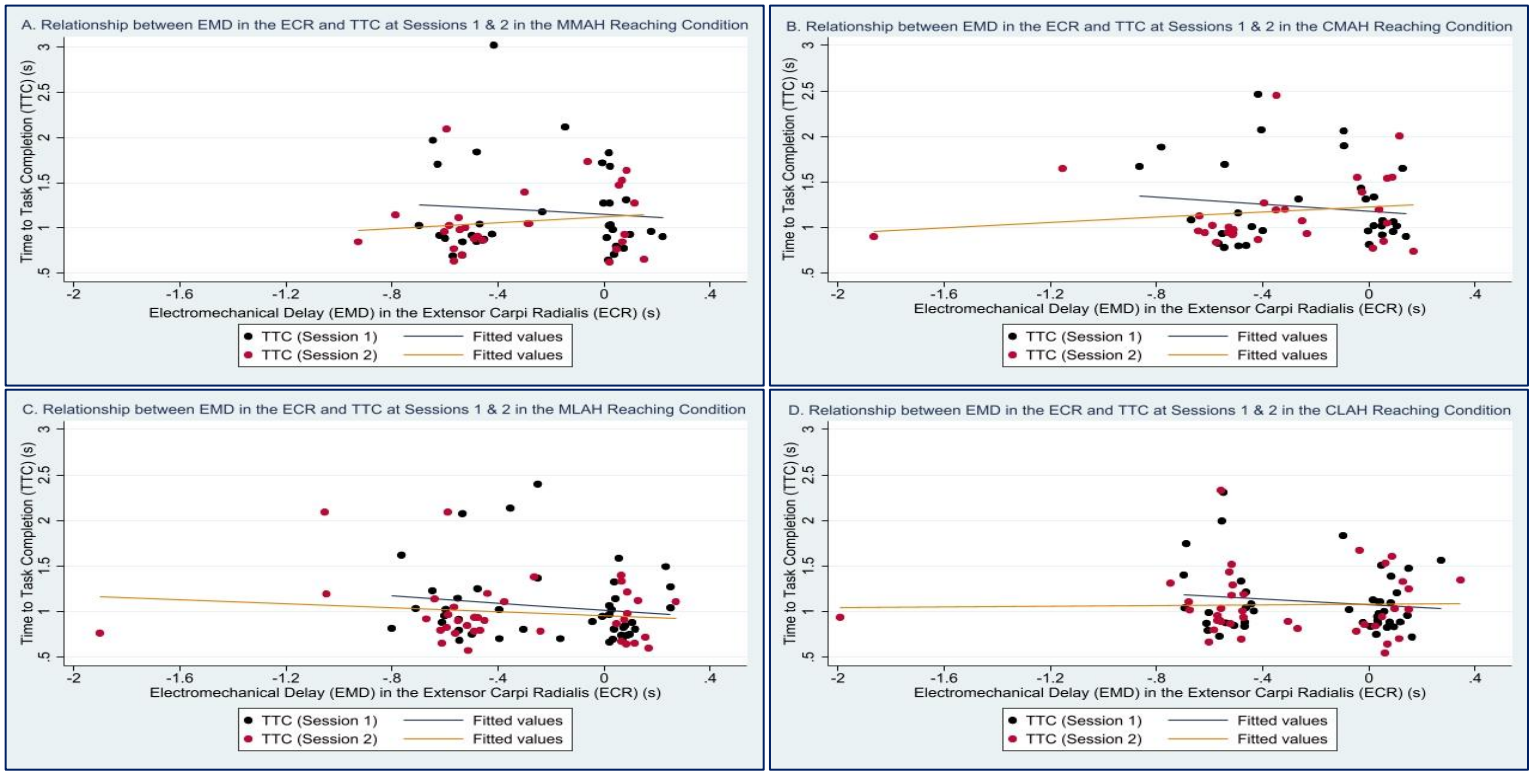
Relationship with Electromechanical Delay (EMD) in the Biceps Brachii (BB)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/28	0.05	0.001	-0.42; 0.53	0.82	28/28	0.15	-0.20/0.24
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	0.15	0.02	-0.10; 0.40	0.22	28/28	0.63	0.10/0.20
Time to Task Completion	Midline – Less Affected Hand (MLAH)	43/37	-0.002	0	-0.21; 0.20	0.98	36/36	0.28	-0.20/0.11
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	0.006	0	-0.22; 0.23	0.96	37/37	0.60	-0.06/0.04
Action Research Arm Test	Midline – More Affected Hand (MMAH)	42/37	13.54	0.03	-4.30; 31.37	0.13	35/35	0.58	6.33/14.29
Action Research Arm Test	Contralateral – More Affected Hand	42/35	-1.83	0.001	-15.51; 11.84	0.79	35/35	0.54	-11.58/-1.29

Note: This table presents the relationship between the Electromechanical Delay (EMD) in the Biceps Brachii (BB) and functional ability variables (Time to Task Completion (TTC) in seconds and Action Research Arm Test (ARAT), a unitless scale), categorised by reaching condition. The EMD values are represented in seconds. A p-value < 0.05 indicates statistical significance. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. **N:** number of observations; **Coef.:** regression coefficient; **95% CI:** 95% confidence interval. ARAT data were collected only from the more affected side.

Relationships between the Electromechanical Delay in the Extensor Carpi Radialis and Functional Ability Variables

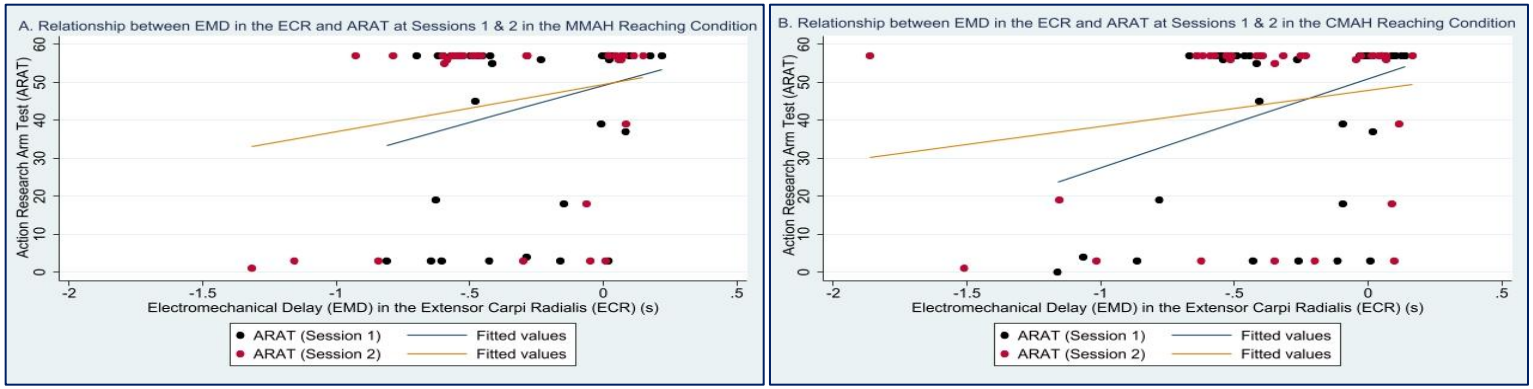
Figure 34. Scatter Plots of the Electromechanical Delay in the Extensor Carpi Radialis and Functional Ability Variables Across Two Sessions (A and B)

A. Relationship between the Electromechanical Delay in the Extensor Carpi Radialis and Time to Task Completion at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (EMD in the ECR) (x-axis) and functional ability (TTC) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Downward slopes signify negative correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **MLAH:** Midline Less Affected Hand; **CLAH:** Contralateral Less Affected Hand; **EMD:** Electromechanical Delay; **ECR:** Extensor Carpi Radialis; **TTC:** Time to Task Completion; **s:** seconds. The EMD in the ECR values are represented in seconds.

B. Relationship between the Electromechanical Delay in the Extensor Carpi Radialis and Action Research Arm Test at Session 1 and Session 2



Note: These plots display the relationships between neuromuscular impairment (EMD in the ECR) (x-axis) and functional ability (ARAT) (y-axis). Black dots represent functional ability values relative to neuromuscular impairment at Session 1, while red dots indicate Session 2. The best-fit lines (blue for Session 1, orange for Session 2) show the data trends. Upward slopes signify positive correlations. **MMAH:** Midline More Affected Hand; **CMAH:** Contralateral More Affected Hand; **EMD:** Electromechanical Delay; **ECR:** Extensor Carpi Radialis; **ARAT:** Action Research Arm Test; **s:** seconds. The EMD in the ECR values are represented in seconds. ARAT data were collected only from the more affected side. Ceiling effects in the ARAT are evident.

Table 34. Relationships of the Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR) with Functional Ability Variables: Time to Task Completion (TTC) and Action Research Arm Test (ARAT)

Relationship with Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR)									
Functional Ability Variable	**Condition**	**N [S1/S2]**	**Coef.**	**R^2**	**95% CI**	**p-value**	**Stability N [S1/S2]**	**Stability p-value**	**Specific Coef. [S1/S2]**
Time to Task Completion	Midline – More Affected Hand (MMAH)	34/27	0.03	0.0003	-0.40; 0.45	0.90	27/27	0.31	-0.08/0.17
Time to Task Completion	Contralateral – More Affected Hand (CMAH)	34/28	0.03	0.001	-0.29; 0.36	0.85	28/28	0.11	-0.17/0.15
Time to Task Completion	Midline – Less Affected Hand (MLAH)	44/37	-0.12	0.02	-0.39; 0.15	0.37	37/37	0.70	-0.17/-0.11
Time to Task Completion	Contralateral – Less Affected Hand (CLAH)	44/37	-0.04	0.002	-0.27; 0.19	0.71	37/37	0.34	-0.18/0.02
Action Research Arm Test	Midline – More Affected Hand (MMAH)	40/32	14.69	0.06	-3.26; 32.63	0.11	31/31	0.44	12.96/4.30
Action Research Arm Test	Contralateral – More Affected Hand	41/33	16.58	0.10	-0.95; 34.12	0.06	33/33	0.18	21.16/9.40

Note: This table presents the relationship between the Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR) and functional ability variables (Time to Task Completion (TTC) in seconds and Action Research Arm Test (ARAT), a unitless scale), categorised by reaching condition. The EMD values are represented in seconds. A p-value < 0.05 indicates statistical significance. The stability p-value assesses whether the observed relationship (or lack thereof) between the variables is consistent over sessions, with a value > 0.05 suggesting stability. **N:** number of observations; **Coef.:** regression coefficient; **95% CI:** 95% confidence interval. ARAT data were collected only from the more affected side.

Relationships between the Fugl-Meyer Assessment (FMA) and Functional Ability Variables: A one-point increase in FMA score was found to lead to a 0.02-second decrease in TTC for the more affected hand, regardless of the workspace (Table 27; Figure 27, A). These relationships were consistently moderate and significant across each reaching condition (R^2 = 0.41 for MMAH and 0.32 for CMAH; $p < 0.005$ for both). The relationship was stable for the MMAH reaching condition between sessions (stability p-value = 0.051), but it was not stable for the CMAH reaching conditions (stability p-value < 0.001).

A one-point increase in the FMA score corresponded to a 0.97-point increase in the ARAT score for the more affected hand (Table 27; Figure 27, B). This relationship was very strong (R^2 = 0.97) and statistically significant ($p < 0.001$), with stability observed over time (stability p-value = 0.07).

Relationships between the Movement Smoothness (MS) and Functional Ability Variables: Each one-point increase in MS corresponded to a decrease in TTC (Table 28; Figure 28, A). The relationship between MS and TTC was weak (R^2 = 0.29 for MMAH; 0.12 for MLAH) but statistically significant ($p < 0.05$) and stable over time (stability p-value > 0.05) in the midline workspace for both hands (Coef.: -1.93 for MMAH; -2.61 for MLAH). In the contralateral workspace, the relationship was very weak for both hands (R^2 = 0.08 for CMAH; 0.07 for CLAH). For the more affected hand (CMAH), the relationship was statistically significant (p = 0.008) and stable between sessions (stability p-value = 0.86). For the less affected hand (CLAH), it was not significant (p = 0.18), and this lack of significance was stable over time (stability p-value = 0.48).

A positive relationship was observed between MS and ARAT, with moderate strength (Table 28; Figure 28, B). Specifically, a 0.1 unit increase in MS corresponded to a 7.15-point increase in ARAT in the MMAH reaching condition (R^2 = 0.47) and a 6.82-point increase in the CMAH condition (R^2 = 0.40) (Table 28). The MS-ARAT relationship was statistically significant for both MMAH and CMAH reaching conditions ($p < 0.005$) while being stable between sessions for the CMAH condition (stability p-value = 0.18) but not for MMAH (stability p-value = 0.001).

Relationships between the Trunk-Hand Displacement Ratio (THDR) and Functional Ability Variables: The analyses revealed a positive, albeit weak, relationship between TTC and THDR for the more affected hand in both workspaces (R^2 = 0.29 for MMAH; 0.12 for CMAH) (Table 29; Figure 29, A). For the less affected hand, the relationship was very weak in both workspaces ($R^2 \leq 0.02$ for MLAH and CLAH) (Table 29). This relationship was statistically significant only in the MMAH reaching condition (p = 0.003) but lacked temporal stability (stability p-value = 0.02).

A moderate, negative relationship was observed between ARAT scores and THDR for the more affected hand in both the midline (R^2 = 0.42) and contralateral (R^2 = 0.34) workspaces (Table 29; Figure 29, B). Specifically, a 0.1 unit increase in THDR was associated with a 9.98-point decrease in ARAT in the MMAH reaching condition and a 9.11-point decrease in ARAT in the CMAH condition. This relationship was statistically significant ($p < 0.005$) and demonstrated stability between sessions (stability p-value > 0.05) in each reaching condition.

Relationships between the Reach Path Ratio (RPR) and Functional Ability Variables: A positive relationship was observed between RPR and TTC across all reaching conditions (Table 30; Figure 30, A). For the more affected hand, in the midline workspace (MMAH), the RPR-TTC relationship was weak (Coef.: 5.00; R^2 = 0.22) but statistically significant ($p < 0.001$) and stable over time (stability p-value = 0.69). However, in the contralateral workspace for the more affected hand (CMAH), this relationship was very weak (Coef.: 2.36; R^2 = 0.03) and not statistically significant ($p = 0.18$). For the less affected hand, the relationship was very weak in both workspaces (Coef.: 7.93, R^2 = 0.07 in MLAH; Coef.: 3.30, R^2 = 0.06 in CLAH), yet statistically significant ($p \leq 0.007$) and stable between sessions (stability p-value > 0.05). The wide 95% CIs, not encompassing zero in the MMAH, MLAH, and CLAH reaching conditions, suggest that the significant yet relatively weak RPR-TTC relationship may be attributed to the considerable data variability.

A negative relationship was observed between ARAT scores and RPR for the more affected hand (Table 30; Figure 30, B). For every 0.1-unit increase in RPR, the ARAT score decreased by 19.99 points in the MMAH condition and by 1.06 points in the CMAH condition. In the midline workspace (MMAH), this relationship was moderate (R^2 = 0.42) and statistically significant ($p < 0.05$), and it remained stable over time (stability p-value > 0.05). In the contralateral workspace (CMAH), the relationship was negligible (R^2 = 0.001) and not statistically significant ($p = 0.86$), with stability over time (stability p-value > 0.05).

Relationships between the Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB) and Functional Ability Variables: Regression analyses indicated positive but very weak relationships between MAOT of the BB and TTC across all reaching conditions (Coef.: 0.12 to 0.23; R^2 = 0.01 to 0.05) (Table 31, Figure 31, A). This relationship did not display statistical significance in any of the reaching conditions ($p > 0.05$).

A negative association was observed between MAOT of the BB and ARAT scores for the more affected hand in both workspaces (Coef.: -27.44 in the MMAH and -17.43 in the CMAH condition) (Table 31, Figure 31, B). While this association was weak (R^2 = 0.18) but statistically significant

($p < 0.001$) and stable over time (stability p-value = 0.95) in the MMAH condition, it was very weak ($R^2 = 0.08$) and not statistically significant ($p = 0.06$) in the CMAH condition.

Relationships between the Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR) and Functional Ability Variables: A very weak to weak positive relationship was observed between the MAOT of the ECR and TTC across the reaching conditions (Coef.: 0.21 to 0.30; R^2 = 0.03 to 0.10) (Table 32; Figure 32, A). This relationship was statistically insignificant ($p > 0.05$) and stable over time (stability p-value > 0.05) in the MMAH, MLAH and CLAH conditions. In the CMAH reaching condition, the relationship was statistically insignificant ($p = 0.24$) and not stable (stability p-value = 0.02). The 95% CIs, consistently encompassing zero, underscore the insignificance of these associations and highlight significant variability in the data.

The relationship between MAOT of the ECR and ARAT scores was negative and weak in both MMAH and CMAH reaching conditions (Coef.: -21.52 in MMAH and -20.84 in CMAH; R^2 = 0.20 and 0.22, respectively) (Table 32; Figure 32, B). This relationship was statistically significant ($p < 0.001$) and demonstrated stability over time (stability p-value > 0.05) in both conditions.

Relationships between the Electromechanical Delay (EMD) in the Biceps Brachii (BB) and Functional Ability Variables: Regression analyses did not reveal any clear trends in the relationships between the EMD in the BB and both TTC and ARAT scores across all reaching conditions (Table 33; Figure 33, A and B). The relationships were either non-existent or very weak, as indicated by zero or near-zero R^2 values. Additionally, the wide 95% CIs highlight substantial variability in the data. All assessed relationships were statistically insignificant ($p > 0.05$) and demonstrated stability over time (stability p-value > 0.05).

Relationships between the Electromechanical Delay (EMD) in the Extensor Carpi Radialis and Functional Ability Variables: The relationship between TTC and EMD in the ECR showed no discernible trend, as evidenced by a mix of positive and negative coefficients, and near-zero R^2 values (Table 34; Figure 34, A). Wide 95% CIs indicated considerable variability in the data. A potential positive trend was observed between ARAT scores and EMD in the ECR (Coef.: 14.69 in the MMAH and 16.58 in the CMAH; R^2 = 0.06 and 0.10, respectively) (Table 34; Figure 34, B). However, all these relationships were statistically insignificant ($p > 0.05$) and demonstrated stability over time (stability p-value > 0.05), indicating a consistent lack of significant association across sessions.

FMA and ARAT consistently exhibited a ceiling effect across analyses.

6.4 Discussion

This study identified several relationships between neuromuscular impairments and functional abilities in stroke survivors post-discharge (**Aim 3a**) (Tables 27-34). Some of these relationships, examined two to four months apart when no improvement was anticipated in stroke survivors, exhibited significance and stability throughout time (**Aim 3b**). The significant and stable relationships identified include:

- FMA-TTC for MMAH: Moderate strength
- FMA-ARAT for the more affected hand: Very strong
- MS-TTC for MMAH, MLAH and CMAH: Either very weak or weak strength
- MS-ARAT for CMAH: Moderate strength
- THDR-ARAT for MMAH, CMAH: Moderate strength
- RPR-TTC for MMAH, MLAH and CLAH: Either very weak or weak strength
- RPR-ARAT for MMAH: Moderate strength
- MAOT of the BB and ARAT for MMAH: Weak strength
- MAOT of the ECR and ARAT for MMAH and CMAH: Weak strength.

Although statistically significant, the relationships between FMA-TTC for CMAH (moderate strength), MS-ARAT for MMAH (moderate strength), and THDR-TTC for MMAH (weak strength) were not consistent over time.

This study's findings of statistically significant negative associations between FMA and TTC (Coef.: -0.02 and $p < 0.05$ for MMAH and CMAH) (Table 27) align with existing research: $r = -0.42$ and $p < 0.05$ in 30 stroke survivors (20), $r = -0.567$ and $p < 0.001$ in 34 stroke survivors (378) and $\beta = -9.39$ and $p < 0.019$ ($R^2 = 0.7164$) in 26 stroke survivors (379). The magnitudes of the associations found in the two of these studies (20, 378) are similar to those in the current study ($R^2 = 0.41$ for MMAH and 0.32 for CMAH), all involving participants with a range of impairments from mild to severe. However, the other available study, predominantly involving participants with mild impairments, suggests a very strong relationship between FMA and TTC (379).

A significant and strong relationship between FMA and ARAT has been consistently reported in the literature, aligning with the findings of the present study ($R^2 = 0.97$, $p < 0.001$) (Table 27). Previous research reports the following relationships: $r = 0.93$ and $p < 0.01$ in a study of 27 stroke survivors with moderate impairment (FMA-UL Mean (SD)) = 29.93 (7.66) (380); $r = 0.70$ and $p < 0.01$ in a study of 30 stroke survivors with mild to moderate impairment (FMA-UL Mean (SD)) = 53.6 (9.1)) (20); and $r = 0.663$ and $p < 0.001$ in a study of 87 predominantly moderately impaired

stroke survivors (FMA-UL (Mean (SD)) = 34.51 (11.69)) (29). These consistent findings across studies involving stroke survivors with varying impairment levels suggest that the relationship between FMA and ARAT remains stable regardless of the impairment level. The current study also found that their relationships were stable over time (stability p-value = 0.07), underscoring the robustness of their relationships and suggesting that they can be predictive markers for each other.

The negative MS-TTC relationship observed in this study (Table 28) is consistent with the only other study in the literature that assessed this relationship in stroke survivors, similarly using the SPARC method to compute MS (381). That study found a moderate, statistically significant correlation between changes in MS and TTC following robotic-assisted therapy in 31 stroke survivors ($r = -0.51$, $p < 0.01$). Additionally, Schiefelbein et al. (100) reported a significant negative correlation of MS, computed using the number of movement units, with the BBT in 34 stroke survivors ($r = -0.56$, $p = 0.025$). All these findings suggest an association between fluid movements and improved functionality.

The absence of research on the relationship between RPR and functional ability post-stroke precludes direct comparisons with the findings of the current study. However, the current study identified positive relationships between RPR and TTC and negative relationships between RPR and ARAT scores across various tasks (Table 30). These findings imply that a lower RPR, indicative of more direct movement trajectories, can be associated with better functioning.

Importantly, this study makes a novel contribution to the literature by revealing predominantly statistically significant and stable relationships between MS and functional ability, as well as between RPR and functional ability, across various reaching conditions post-stroke. Although these relationships were not of strong magnitude, their consistent presence across different tasks and over time suggests a potential, ongoing association between neuromuscular impairments, represented by MS and RPR variables, and functional ability in stroke survivors.

The current study's findings on the positive relationship between THDR and TTC reveal a significant association in the only MMAH reaching condition ($R^2 = 0.29$, $p = 0.003$), yet this relationship was not stable over time (stability p-value = 0.02) (Table 29). These findings partially align with the only available previous study (19), which reported a variable positive relationship between anterior trunk flexion ROM and TTC, significant for cyclic movements ($r = 0.6$, $p < 0.05$) but not for discrete movements ($r = 0.4$, $p > 0.05$) in a cohort of 17 stroke survivors. Thus, while

THDR can be associated with TTC, its reliability as an indicator may vary, especially in consecutive assessments.

Additionally, the current study's findings on the negative, significant, and moderate relationship between THDR and ARAT scores (Coef.: -9.98 for MMAH and -9.11 for CMAH; R^2 = 0.42 and 0.34, respectively; $p < 0.05$ for both) (Table 29) show parallels with prior research on trunk involvement in UL task execution and functional ability as assessed by clinical outcome measures. Prior studies reported a weak, positive correlation between anterior trunk displacement and 'WMFT-Performance Time' scores ($r = 0.37$, $p > 0.05$) in 35 stroke survivors (30), and a moderate, negative correlation between trunk flexion ROM and BBT ($r = -0.4$, $p < 0.05$) in 17 stroke survivors (19). These findings, including those from the current study, indicate that increased trunk involvement in UL tasks may be associated with reduced functional ability, as measured by clinical outcome measures. The stability of the THDR-ARAT relationship across sessions in the current study (stability p-value > 0.05 in both MMAH and CMAH) also indicates there may be a potentially consistent link between trunk involvement and functional ability.

While increased trunk displacement is often expected to aid functional ability (17); the discrepancy in findings between THDR and TTC, and THDR and ARAT, observed in the current study, indicates that THDR may not always be a consistent or reliable indicator of improved task performance in stroke survivors.

The current study suggests a potentially positive relationship between earlier MAOT of both the BB and ECR and functional ability (Tables 31 and 32). These findings are in line with the only available previous research, which reported significant negative correlations between MAOT for ECR and FCR and the 'Arm Motor Ability Test (AMAT)' – functional ability score ($r \approx -0.7$; $p < 0.01$ for both) in 26 chronic stroke survivors (21). This suggests that delayed MAOT may be associated with greater functional limitations. This previous study focused on specific wrist flexion and extension tasks sustained for three to five seconds, requiring focused, rapid, and powerful muscle contractions, which is different from daily, purposeful, functional activities such as the telephone answering task used in the current study. This difference in task demands may account for the lack of significant findings in the MAOT-TTC relationship observed in the current study and may also explain the weak, although mostly significant and stable, relationship between MAOT and ARAT (382).

The absence of prior research on the association between EMD and functional ability precludes a comparison with this study's findings. The substantial variability and the zero or near-zero strength of the relationships observed suggest that EMD in the BB and EMD in the ECR, within the context of the experimental task used in the current study, is unlikely to be reliable predictors of functional ability post-stroke.

In this study, the absence of correlations or the lower magnitude of identified relationships compared to previous research can be attributed to several potential reasons. Firstly, the study's heterogeneous sample, varying in impairment level, stroke severity, time since stroke, age, and gender, may have led to less pronounced relationships by increasing variability in the data (383–386). The wide 95% CIs observed in the analyses, indicative of significant data variability, support this notion.

Secondly, ceiling effects in the clinical outcome measures (FMA and ARAT) likely influenced the findings (Figures 27–34). These effects were particularly pronounced among participants with higher motor abilities, where the FMA and ARAT failed to capture subtle variations in movement performance. By contrast, kinematics- and EMG-derived variables remained sensitive to performance differences. As detailed earlier in the introduction under the subheading 'Impact of COVID-19 Pandemic on Research Progress and Methodology,' the broad inclusion criteria adopted in this study, driven by recruitment challenges during the COVID-19 pandemic, resulted in a sample primarily composed of stroke survivors with mild impairments in their chronic stages. Consequently, 18 out of 44 participants achieved the maximum score of 66 on the FMA-UL Motor Scale, and 25 out of 44 achieved the maximum score of 57 on the ARAT during their first data collection sessions (Appendix 21). The prevalence of these full scores resulted in ceiling effects, as participants who scored at the maximum level left no room for these measures to detect subtle variations in movement performance, particularly among individuals with mild impairments. This limitation likely obscured the strength or presence of relationships assessed using these measures.

The relationships between neuromuscular impairment variables and the ARAT were generally stronger compared to those with TTC, a kinematics-derived functional ability variable, in this study. This difference in the strength of relationships may be attributed to the varying sensitivities of these variables. TTC, as a time-based kinematic variable, is likely more sensitive to subtle motor performance changes, resulting in more variable relationships with impairment measures. In contrast, ARAT, despite potential ceiling effects, appears to maintain a more consistent relationship with neuromuscular impairments, possibly reflecting broader aspects of

UL function that are less sensitive to minute changes. Thus, ARAT may not be as sensitive to changes in neuromuscular impairment variables as time-based variables like TTC.

Strengths of the Study

A key strength of this study is the assessment of participants at two distinct time points, which enabled an investigation into the stability of the relationships between neuromuscular impairments and functional abilities. While statistical significance offers valuable insights, it is also important to consider the stability of these relationships over time to confirm how reliable the established relationships are.

Another strength of this study is its large sample size, contributing to the robustness of the findings. The initial sample size estimation suggested that a cohort of 30 individuals would be sufficient for robust assessments, and this target was met in evaluating the pairwise relationships between impairment and functional ability variables. Despite a slight reduction in participant numbers for the stability analyses, with 27 to 28 participants remaining in some pairwise associations due to dropouts in the second data collection session, the sample size was still considerable, particularly in comparison to prior studies on stroke survivors.

Evaluating how different variables of neuromuscular impairment affect both clinical and kinematics-derived measures of functional ability represents a key strength of this study, enabling a more in-depth and thorough examination of these relationships.

Limitations

A potential limitation of the study is the recruitment of stroke survivors who differed in terms of time since stroke onset, stroke severity, impairment levels, and dominance of the more affected hand. This diversity, although reflective of clinical settings, might have impacted the findings.

Another potential limitation of the study is the order of task repeats performed by participants. Given that at least 12 repetitions were completed, decreasing attentiveness and fatigue may have hampered performance in later trials.

The variability in the placement of Vicon markers and surface EMG electrodes, handled collaboratively by two different researchers across data collection sessions, could be a potential limitation of the study. This approach, while common in multi-centre clinical research and clinical settings, might have introduced minor inconsistencies in placement despite standardised

procedures and the expertise of the physiotherapists involved. Such variations could potentially have influenced the findings regarding the stability of the relationships between variables across sessions (360–363).

Lastly, the inclusion of four participants (PS014, PS015, PS037, and PS038 (Appendix 21)) who were less than six months post-stroke at the time of recruitment may be another potential limitation of this study. One of these participants (PS037) withdrew. However, given that significant recovery after stroke typically occurs within the first three to six months (3, 99), the remaining three participants might have experienced some noticeable improvements between sessions compared to the rest of the research sample. Thus, this situation may have influenced the findings of the stability between neuromuscular impairment and functional ability variables across sessions.

6.5 Conclusion

This study assessed the relationships between neuromuscular impairments and functional abilities in stroke survivors (**Aim 3a**) and evaluated whether these relationships remained stable over a period of two to four months post-discharge when significant improvements are typically not expected (**Aim 3b**). It was found that neuromuscular impairment variables: FMA, MS, and RPR, exhibited significant and stable relationships with functional ability across nearly all reaching conditions. These relationships were consistent regardless of whether functional ability was assessed using the kinematics-derived measure (TTC) or the clinical measure (ARAT). This suggests a reciprocal influence, indicating that targeting these specific neuromuscular impairments–RPR, MS, and those captured by FMA–in therapy could effectively enhance functional ability in stroke survivors.

The study also found that while MOAT and THDR showed some significant and stable relationships with ARAT, they did not exhibit a similar pattern with TTC. Additionally, EMD did not demonstrate a significant association with functional ability. These findings suggest that MOAT, THDR, and EMD may not be reliable predictors of functional ability, and their relationship with functional ability could be influenced by external factors such as fatigue, compensation, and motivation.

The observed relatively weak relationships between neuromuscular impairments and functional abilities in this study may be attributed to the heterogeneous nature of the research sample and the ceiling effects in the clinical outcome measures. Further research with a more homogenous sample could potentially provide deeper insights into these relationships.

Chapter 7. Discussion

7.1 Introduction

The overarching aim of this thesis is to deepen understanding of the relationships between neuromuscular impairments and functional abilities post-stroke. Gaining deeper insights into their interactions could lead to the development of more targeted and adaptive rehabilitation practices, thereby enhancing the effectiveness and efficiency of therapeutic strategies.

7.2 Summary of Key Findings

The first research question was:

"What is the nature of the relationships between UL neuromuscular impairments and functional abilities in response to exercise-based therapies?"

To address this question, meta-analyses and meta-regression analyses were undertaken on 30 eligible studies published from January 1, 2011, to December 16, 2020. The findings revealed that compared to control interventions (no therapy, sham, and conventional therapy):

- Exercise-based therapies significantly improve both neuromuscular impairments and functional abilities (**Aim 1a**).
- Although no statistically significant difference was detected between the effects, exercise-based therapies showed greater improvement in neuromuscular impairments than in functional ability, as indicated by larger effect sizes (**Aim 1a**).
- There is an almost perfect positive and statistically significant correlation between the improvements in neuromuscular impairments and functional abilities in response to exercise-based therapies (**Aim 1b**).

None of the included studies had a high risk of bias. They exhibited substantial heterogeneity. However, due to the wide scope of this review, this observed heterogeneity does not conflict with the aims of the study, as it represents varied conditions encountered in real clinical settings.

The second question was:

"What are the reference values, test-retest reliability, and SDC for UL neuromuscular impairment and functional ability variables, as derived using the Vicon motion analysis and Delsys EMG system, in individuals without mobility-impairing conditions?"

To address this question, a correlational agreement study was performed.

- Reference values for variables of UL neuromuscular impairment and functional ability (TTC, MS, THDR, RPR, MAOT of the BB and ECR, and EMD in the BB and ECR) were calculated (**Aim 2a**).
- Generally, the test-retest reliability of these variables was found to be insufficient (ICC < 0.70). However, the TTC, RPR and MS exhibited high absolute reliability, as demonstrated by small SEM% (< 10%) and narrow 95% LOAs (**Aim 2b**).
- The SDCs of these variables were ascertained and found to be consistently smaller than their corresponding 95% LOA ranges (**Aim 2c**).
- No systematic bias was observed in the measurements of these variables.

Lack of sufficient test-retest reliability does not always render the variables completely unreliable. Outliers, the ICCs' sensitivity to low between-subject variability, and the variables' narrow measurement range may have influenced the findings. TTC, MS, and RPR demonstrated high absolute reliability and accuracy, making them promising variables for detecting neuromuscular impairments and functional limitations. Their reference values and SDCs can guide the identification of deviations in movement patterns and movement assessments. THDR and EMG-derived variables, while exhibiting limitations in reliability, can still offer valuable insights due to their negligible systematic biases and acceptable test-retest reliability in sensitivity analyses, especially when combined with variables that exhibit high absolute reliability. In summary, TTC, MS, and RPR demonstrated potential clinical and research utility and warrant further exploration in stroke populations. These variables may be particularly useful when integrated into simplified and accessible assessment methods for broader usability.

The third question was:

"To what extent do UL neuromuscular impairments in stroke survivors correlate with UL functionality?"

To address this question, a longitudinal observational cohort study was conducted, assessing stroke survivors twice over a period of two to four months. Clinical outcome measures (FMA and ARAT) were used to assess more affected UL. Kinematics- and EMG-derived variables were also used to collect data during a standardised UL task in four conditions: MMAH, MLAH, CMAH, and CLAH. For analyses, each neuromuscular impairment variable (MS, RPR, THDR, MAOT of the BB and ECR, and EMD in the BB and ECR) was paired with each functional ability variable (TTC and ARAT). These pairings were based on data collected under identical conditions. The relationships between these pairs, as well as their stability over time, were evaluated individually.

- Several statistically significant and stable associations were identified. Among these:
  - A notably very strong association was observed between FMA and ARAT.
  - FMA demonstrated a moderate relationship with TTC in the MMAH.
  - Kinematics-derived neuromuscular impairment variables, MS, THDR, and RPR, showed moderate associations with ARAT in specific conditions: MS with ARAT in CMAH; THDR with ARAT in both MMAH and CMAH; and RPR with ARAT in MMAH.
  - MS and RPR were associated with TTC in most conditions despite their weak strength.
- Some statistically significant relationships lacked stability over time. These were the relationships of FMA-TTC in the CMAH, MS-ARAT in the MMAH, and THDR-TTC in the MMAH.
- Although MAOT and THDR exhibited some significant and stable associations with ARAT, they did not display similar patterns with TTC. Additionally, EMD values were not found to have any associations with functional ability.

Consequently, FMA, RPR, and MS can serve as predictive markers of functional ability in post-stroke assessments, while THDR, MAOT and EMD may not. The sample's heterogeneity and ceiling effects in the clinical outcome measures could have led to undetected or weak relationships among some variables.

7.3 All Findings in Relation to the Identified Knowledge Gaps

A significant knowledge gap remains in fully understanding the principles of effective and efficient neurorehabilitation (4, 387). Neuroplasticity is crucial for neuromuscular recovery (388), and physical exercise can enhance it (80–83, 389). Exercise-based therapy, a specialised form of physical exercise, encompasses a wide range of interventions that share the common goal of improving neuromuscular impairments and/or enhancing functional abilities (38). Such therapies, which prioritise neuromuscular recovery, could offer a more efficient path to functional recovery (72, 77, 86). Therefore, discerning whether specific therapies drive functional improvements through neuromuscular recovery is essential to inform clinical practice appropriately (71). In addition, clearly established relationships between neuromuscular impairments and functional abilities can guide clinical decisions and effectively tailor therapy for stroke survivors. Thus, a deeper understanding of the post-stroke relationships between neuromuscular impairments and functional abilities—as well as the impact of exercise-based therapies on these relationships—is critical for the development of effective and efficient rehabilitation strategies. However, accurately identifying these relationships post-stroke

remains a challenge (18, 28, 106). Although kinematics- and EMG-derived variables show promise in enhancing this understanding (16–18), their ability to precisely identify these interactions is still uncertain (18, 28, 115, 328).

In this context, my doctoral research contributes substantially to neurorehabilitation in two critical domains. Firstly, it enhances the understanding of the intricate relationships between neuromuscular impairments and functional abilities. Secondly, it provides foundational insights into the accurate assessment of these impairments and abilities.

This section discusses the findings from my doctoral studies, placing them in the context of the existing literature and the knowledge gaps that the research aimed to address.

Understanding the Relationships between Neuromuscular Impairments and Functional Abilities

Previous reviews often did not report the effects of exercise-based therapies on neuromuscular impairments and functional abilities separately (9–11, 13, 15), or sometimes used distinct sets of studies to assess each aspect (12, 14, 282). This has limited our understanding of how exercise impacts these two aspects individually. Addressing this gap, the systematic review in my research (Chapter 3) used a comparative approach, analysing both neuromuscular impairments and functional abilities individually, based on the same set of studies. This approach enabled a comprehensive understanding of their dual impact.

While this review corroborates earlier findings regarding the positive effects of exercise on impairments and functional abilities (12, 14, 282), it also presents novel evidence showing that exercise-based therapies can similarly improve both neuromuscular impairments and functional abilities. In addition, it establishes a strong correlation between these improvements, offering new insights into their simultaneous impact. These findings are significant as they deepen our understanding of how exercise-based therapies can concurrently improve neuromuscular impairments and functional abilities in stroke survivors.

These findings support the notion that exercise-based therapies can enhance functional abilities by improving neuromuscular impairments (84, 85). Therefore, focusing on neuromuscular impairments early in the post-stroke period can be a more effective approach to harnessing neuroplasticity benefits, challenging the current clinical guidelines that often prioritise functional improvements (92, 93). This perspective is reinforced by Platz and colleagues who recommend concentrating on neuromuscular impairments during the acute and subacute

phases of stroke recovery (76). However, they also suggest that as recovery progresses into the chronic stage, the emphasis can shift towards functional abilities (76).

Although the systematic review in my doctoral studies did not specifically investigate the effects of exercise at different recovery stages, it, encompassing stroke survivors at various recovery stages, consistently demonstrated beneficial effects of exercise-based therapies across most primary studies included (as illustrated in Figures 6, 7 and 8). This observation suggests that exercise-based therapies can improve both neuromuscular impairments and functional abilities at various stages, including during the chronic phase. This finding challenges the traditionally accepted critical recovery window of three to six months post-stroke (3, 99), suggesting a longer potential for recovery. Such an extension aligns with prior research indicating that while improvements in response to exercise are most pronounced in the early months post-stroke, they can continue, albeit at a more modest rate, into the chronic stage (390, 391). The European Stroke Action Plan for 2018-2030 highlights the importance of deepening our understanding of functional recovery mechanisms and potential therapeutic targets in the chronic stage (392). Thus, the suggestion by Platz and colleagues to shift rehabilitation efforts towards functional abilities in the chronic phase of stroke is particularly worth exploring (76). Clarifying the relationships between neuromuscular impairments and functional abilities across all stages of stroke recovery, including the chronic stage, can be beneficial for refining therapeutic strategies across the stroke recovery continuum.

While the review in my research, along with several existing reviews (10, 12, 14, 15, 282), highlights the immediate effects of exercise, understanding the long-term durability of these effects is crucial. This is particularly important for determining whether exercise induces stable changes in neuroplasticity. Given that stroke is a lifelong condition, achieving lasting changes that significantly enhance survivors' daily functional activities is a priority. Therefore, exploring the extent to which these immediate improvements translate into long-term, sustainable improvements is essential for setting effective rehabilitation targets.

Previous reviews have provided insights into the long-term effects of specific therapies. One prior review suggested the potential for long-term maintenance of beneficial effects of mirror therapy on both neuromuscular impairments and functional abilities, based on just two studies (11). Another prior review indicated immediate but not long-term benefits of robotic therapy on neuromuscular impairments, drawing from 17 studies (9). However, these reviews were limited by the small number of studies and lacked a comprehensive assessment of post-stroke improvements in both neuromuscular impairments and functional abilities. This limitation

hinders a full understanding of the long-term benefits of exercise-based therapies, leaving a gap in our knowledge of the long-term progression and stability of how exercise-based interventions influence the relationships between neuromuscular impairments and functional abilities post-stroke.

The observational cohort study in my doctoral research (Chapter 6), which predominantly involved stroke survivors in their chronic stage, with just a few exceptions at the subacute stage at recruitment, and not receiving ongoing therapy from NHS stroke services, provides insights into the potential long-term trajectory of stroke recovery after the cessation of formal rehabilitation. Significant and mostly stable relationships over time between certain neuromuscular impairments and functional abilities found in this study imply that benefits from earlier rehabilitation efforts, potentially including exercise-based therapies, could be enduring. However, due to the lack of specific tracking of therapies received both prior to and after discharge, caution is advised in directly attributing these outcomes to the long-term effects of exercise-based therapies alone, as individual variability in rehabilitation experiences could have significantly influenced these findings. Nonetheless, these results underscore the potential long-term benefits of exercise and highlight the importance of developing effective strategies for exercise-based therapy to maximise benefits for stroke survivors.

In this study, impairment variables that exhibited significant and stable relationships with functional ability, even during recovery stages when substantial improvement is typically not anticipated, were FMA, MS, and RPR. This finding indicates a potential intrinsic link between these impairment variables and functional abilities in stroke survivors. Therapies targeting MS and RPR, along with addressing impairments measured by FMA, may therefore enhance UL function after stroke and lead to lasting functional benefits. Supporting this, Collins and colleagues have identified MS and RPR as significantly altered in stroke survivors compared to healthy individuals (17), highlighting their potential as important focal points for UL rehabilitation in stroke survivors.

This study also revealed that not all relationships between neuromuscular impairments and functional abilities were significant or stable, indicating that improvements in specific impairments may not always lead to enhanced functional abilities. This aligns with findings from previous studies (19, 32, 33, 100). A key contribution of this study is the assessment of the stability of these relationships over time, an aspect not previously explored (19–21, 30, 32, 33, 87). The findings highlight that significant impairment-functional ability relationships may vary over time, even in later recovery stages where substantial improvement is less expected. This

underscores the importance of evaluating the stability of these relationships to truly understand their nature. Identifying which impairment-functional ability relationships are inherently stable can be useful for developing targeted rehabilitation strategies that focus on areas of impairment with a direct and consistent impact on functional abilities, thereby enhancing the functional recovery of stroke survivors.

Challenges in Accurate Assessment of Neuromuscular Impairments and Functional Abilities

The potential limitations of clinical outcome measures in accurately identifying the links between neuromuscular impairments and functional abilities necessitate cautious interpretation, as those measures may not fully capture the subtle changes (16, 17, 71, 106). The systematic review in my doctoral studies (Chapter 3) revealed strong correlations between impairments and functional abilities, predominantly using clinical outcome measures. In contrast, the observational cohort study (Chapter 6) indicated that their relationships were more pronounced when assessed with clinical outcome measures compared to kinematics-derived variables. This suggests that clinical measures may lack sensitivity to subtle changes in impairments and functional abilities, unlike kinematics-derived variables.

Additionally, both studies consistently demonstrated strong correlations between neuromuscular impairments, as measured by the FMA scale, and functional abilities, as assessed by the ARAT. Despite sample heterogeneity, these findings suggest a reliable correspondence between the impairments measured by FMA and the functional ability components assessed by ARAT across diverse stroke survivor populations. However, the cohort study revealed ceiling effects in the FMA and ARAT scores, likely influenced by the broad inclusion criteria adopted to address recruitment challenges during the COVID-19 pandemic. This approach resulted in a sample predominantly composed of individuals with mild impairments and high functional abilities, highlighting the inherent limitations of these measures in detecting subtle differences in motor performance among higher-functioning participants. Thus, these observed ceiling effects underscore the limitations of FMA and ARAT when applied to such populations. There is a clear need to identify more sensitive clinical outcome measures tailored to higher-functioning individuals and to incorporate a broader range of assessment tools, including those utilising kinematics-derived variables, to achieve a more comprehensive understanding of the relationships between neuromuscular impairments and functional abilities in stroke survivors.

In the correlational agreement study (Chapter 5), TTC, MS, and RPR were identified as having high absolute reliability. This distinction is significant, as it highlights the potential of these variables to accurately capture stable relationships between neuromuscular impairments and

functional abilities when such relationships exist. The observational cohort study (Chapter 6) reinforced the importance of these variables, demonstrating that they not only had significant relationships with functional abilities across different reaching conditions but also maintained these relationships over time. This consistency in relationships, likely influenced by their high absolute reliability, suggests that when stable relationships between impairments and functional abilities are present, using variables with high absolute reliability like TTC, MS, and RPR is crucial to accurately detect and assess these relationships. Conversely, variables lacking confirmed reliability did not show such clear, significant, and stable relationships, underscoring the risk of using less reliable variables in clinical assessments. This emphasises the importance of careful selection and validation of assessment tools in clinical practice (104, 105). My research supports the potential selective use of TTC, MS, and RPR in post-stroke assessments, as their high absolute reliability—demonstrated in individuals without mobility-impairing conditions—and their ability to capture stable relationships between neuromuscular impairments and functional abilities, as observed in stroke survivors in the cohort study, suggest that these variables can enhance the precision of evaluations and inform more effective rehabilitation strategies.

7.4 Strengths and Limitations of the Doctoral Research

Strengths

One of the key strengths of my doctoral research is the inclusion of advanced assessment methods, such as kinematics- and EMG-derived variables. Given the potential limitations of clinical outcome measures, their inclusion enabled a nuanced investigation of the interplay between neuromuscular impairments and functional abilities.

Another key strength of the project is the precise categorisation of assessment variables into neuromuscular impairments and functional abilities, a distinction not commonly applied in previous research, often leading to inaccurate reporting (119–125). This clarity, consistently maintained across all three studies, significantly enhances the accuracy and robustness of the findings, contributing to more accurate and reliable reporting in the field.

The methodological rigour of this research is a notable strength, lending significant credibility to its findings through several key measures. In the systematic review, all screening processes and risk of bias assessments were conducted independently by two researchers, reinforcing objectivity and accuracy in study selection. In the correlational agreement and observational cohort studies, Vicon marker and EMG electrode placements were performed by two well-trained researchers following standardised protocols, supporting consistency and precision in

data collection. Also, in both experimental studies, trial quality checks were independently conducted by two researchers, further enhancing reliability.

Additionally, the research benefited from a particularly large sample size across all studies. This substantial sample size enhanced the statistical power and robustness of the findings.

The research's sample encompassed a heterogeneous group of stroke survivors, varying in gender, age, time since stroke onset, and stroke severity. This diversity ensures that the findings are more generalisable and accurately reflective of real-world clinical practice.

Limitations

The research effectively demonstrates the immediate effects of a broad range of exercise-based therapies. However, delving deeper into how specific therapies individually impact neuromuscular impairments and functional abilities could enhance our understanding of their unique effects, paving the way for more personalised rehabilitation approaches.

While the heterogeneous sample of stroke survivors is a strength, the varying influences of age, gender, stroke severity, time since stroke onset, and affected brain hemisphere dominance are reported (383–386, 390, 393–398). Investigating these relationships in more homogeneous samples, particularly focusing on specific types of therapies, could yield a detailed understanding of their interplay. Such insights would be invaluable in developing personalised rehabilitation plans, tailored to the distinct needs and response patterns of each stroke survivor, ultimately leading to more effective treatment outcomes and optimised resource allocation in clinical settings.

Additionally, the scope of this thesis was limited by time constraints, which precluded a long-term assessment of the relationships between neuromuscular impairments and functional abilities. This limitation restricted our ability to track the progression of stroke survivors from the acute phase through to the chronic stages. Conducting such longitudinal studies could provide valuable insights into the evolving nature of these relationships, similarly, offering a deeper understanding that is crucial for developing more effective, individualised therapy strategies tailored to the changing needs of stroke survivors over time.

7.5 Future Directions

This doctoral research emerged from the need to fill knowledge gaps, particularly concerning the relationships between neuromuscular impairments and functional abilities. It has made

significant contributions to the neurorehabilitation literature by providing insight into the effects of exercise-based therapies as well as the intricate interplay between neuromuscular impairments and functional abilities in stroke survivors. Building on the significant contributions of this research, I propose the following future research directions to further elucidate the relationships between neuromuscular impairments and functional abilities among stroke survivors:

1. Differential Effects of Therapies: Investigate how specific exercise-based therapies uniquely influence neuromuscular impairments and functional abilities across diverse stroke survivor groups. This research could provide tailored insights for personalised therapeutic approaches.
2. Longitudinal Studies: Conduct longitudinal assessments of stroke survivors, starting from the acute stage and extending into chronic phases. This approach would offer a dynamic view of the evolving relationships between impairments and functional abilities, contributing to more effective long-term rehabilitation strategies.
3. Homogenous Sub-Groups Analysis: Assess the relationships between neuromuscular impairments and functional abilities in more homogeneous sub-groups of stroke survivors. This could reveal specific conditions under which these relationships vary, aiding in the development of individualised therapy sessions.
4. Sensitive Clinical Assessment Tools and Variables: Identify and validate sensitive post-stroke assessment tools and variables capable of detecting even subtle improvements in stroke survivors. Such tools and variables could significantly enhance the effectiveness of clinical practice.

7.6 Conclusion

My doctoral research has significantly advanced the understanding of interactions between neuromuscular impairments and functional abilities in post-stroke recovery. It demonstrated that exercise-based therapies can effectively improve both domains across various stages of recovery. Additionally, the research identified strong correlations between these improvements, suggesting that there can be a potential bidirectional relationship between them in response to exercise-based therapies where progress in one domain facilitates improvements in the other.

Research on neuroplasticity suggests that prioritising movement quality in rehabilitation can effectively target neuromuscular impairments while reducing reliance on compensatory strategies. Compensatory strategies, though useful for completing tasks in the short term, can hinder long-term recovery by reinforcing maladaptive plasticity and/or learned non-use. Thus, obtaining functional improvements through targeted improvements in neuromuscular impairments may offer a more effective and sustainable approach to post-stroke recovery. The findings of my research, which suggest a reciprocal relationship between neuromuscular impairments and functional abilities in response to exercise-based therapies, further reinforce this perspective. By addressing neuromuscular impairments early in recovery, clinicians can help stroke survivors practice movements that align as closely as possible with typical movement patterns, optimising therapeutic outcomes and promoting sustainable recovery.

Building on these findings and current neuroplasticity research, integrating functional practice into rehabilitation, when paired with a strong emphasis on movement quality rather than mere task completion, can be particularly effective. This integration can facilitate motor skill relearning and enhance the likelihood of sustained functional recovery. Together, these insights provide clinicians with a framework for designing interventions that balance achieving functional goals with addressing underlying neuromuscular impairments, potentially promoting better outcomes for stroke survivors. This approach is particularly important during the initial six months post-stroke—a critical period of heightened neuroplasticity when targeted interventions are most likely to yield meaningful and lasting benefits.

However, these findings are based on the effects of various exercise-based therapies provided to a heterogeneous sample. Investigating the individual effectiveness of specific exercise-based therapies and examining the relationship between neuromuscular impairments and functional abilities in more homogeneous sub-groups of stroke survivors could provide deeper insights.

Such research would further validate these findings for specific groups within the stroke population and support the development of tailored therapeutic approaches.

My research also identified that specific neuromuscular impairments—measured by FMA, MS, and RPR—exhibit significant and stable associations with functional abilities, such as those assessed by ARAT and TTC. These findings reinforce the idea that targeting neuromuscular impairments can be an effective strategy for improving functional recovery in stroke survivors. However, an important and previously unreported observation is that not all significant relationships between neuromuscular impairments and functional abilities remain stable over time. This highlights the complexity of stroke recovery and the need to evaluate whether these relationships are stable over time, reflecting genuine associations, or influenced by external factors. Neuromuscular impairments that demonstrate significant and stable associations with functional abilities can serve as valuable targets for rehabilitation, particularly when prioritising movement quality. By addressing these specific impairments—such as those measured by FMA, MS, and RPR—clinicians can design interventions that promote movement precision and alignment with typical movement patterns, ensuring that improvements in neuromuscular impairments translate into meaningful and sustained functional gains.

However, these findings were based on a heterogeneous sample. Identifying significant and stable relationships within more homogeneous groups could enhance personalised therapy approaches. Additionally, the data were collected at two time points from stroke survivors predominantly in their chronic stages at the time of recruitment. Evaluating stroke survivors over a longer period, from the acute stage to the chronic stage, could provide deeper insights into the evolving relationships between impairments and functional abilities, offering valuable knowledge to refine rehabilitation strategies.

Additionally, my research suggests that traditional clinical outcome measures, such as the FMA and ARAT, have potential limitations in detecting subtle changes in stroke survivors with mild impairments and high functional abilities, as indicated by the ceiling effects observed in the cohort study. To address these limitations, I propose the application and further validation of more sensitive and precise assessment variables, specifically kinematics-derived variables such as MS and RPR (indicators of neuromuscular impairment) and TTC (a functional ability variable). These variables demonstrated high absolute reliability and no systematic biases in individuals without mobility-impairing conditions, suggesting their potential value for tracking recovery and understanding the interplay between neuromuscular impairments and functional abilities in stroke survivors. While the reliability and accuracy of these variables were established in

individuals without mobility-impairing conditions, findings from stroke survivors in my research revealed that MS and RPR consistently demonstrated significant and stable relationships with functional abilities over time. In contrast, variables that lacked sufficient reliability in individuals without mobility-impairing conditions also failed to exhibit consistent associations with functional abilities in the stroke survivor cohort. These findings highlight the potential robustness and precision of kinematics-derived variables such as MS, RPR, and TTC for accurate post-stroke assessment. Furthermore, they underscore the importance of carefully selecting outcome measures in post-stroke assessments to enable accurate evaluations of recovery progress and the effectiveness of therapeutic interventions.

By establishing normative values from individuals without mobility-impairing conditions, as identified in my research, variables with high absolute reliability and accuracy can serve as benchmarks for detecting deviations in movement patterns. These benchmarks enable clinicians to identify differences between typical movement patterns and those observed in stroke survivors. However, while these values offer a valuable reference, their direct application to stroke survivors requires careful consideration of population-specific differences in movement capabilities, an area warranting further exploration. When applied repeatedly over time, these variables may hold promise for tracking improvements in neuromuscular impairments and functional abilities, facilitating dynamic adjustments to rehabilitation strategies. This approach ensures that therapies are both responsive to individual progress and tailored to optimise outcomes. However, the routine application of these variables in clinical settings is limited by the need for advanced equipment and analysis. To address this, future efforts should prioritise the development of simplified, clinically viable tools that retain the critical components of these kinematics-derived variables with high absolute reliability. Such tools could balance sensitivity to change with practicality, allowing clinicians to assess post-stroke recovery in a more accessible and effective manner.

In summary, this research provides a robust foundation for understanding the complex relationships between neuromuscular impairments and functional abilities in stroke recovery. By emphasising the importance of movement quality, sensitive and precise assessment tools, and tailored interventions, it offers actionable insights for optimising rehabilitation outcomes. Future research could build on these findings by investigating the effects of specific therapies, exploring homogeneous sub-groups, and undertaking longitudinal studies. These efforts could refine therapeutic approaches and support the development of more effective and practical strategies for stroke rehabilitation.

Appendices

Appendix 1. Search Strategies Used in Electronic Databases (A, B and C)

A. Search Strategy Used in CENTRAL

1. MeSH descriptor: [Cerebrovascular Disorders] this term only
2. MeSH descriptor: [Basal Ganglia Cerebrovascular Disease] this term only
3. MeSH descriptor: [Brain Ischemia] explode all trees
4. MeSH descriptor: [Carotid Artery Diseases] explode all trees
5. MeSH descriptor: [Intracranial Arterial Diseases] explode all trees
6. MeSH descriptor: [Intracranial Embolism and Thrombosis] explode all trees
7. MeSH descriptor: [Intracranial Hemorrhages] explode all trees
8. MeSH descriptor: [Stroke] explode all trees
9. MeSH descriptor: [Vasospasm, Intracranial] this term only
10. MeSH descriptor: [Vertebral Artery Dissection] this term only
11. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or "cerebral next vasc$" or cva$):ti,ab
12. ((cerebral or brain or subarachnoid) near/5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)):ti,ab
13. ((cerebral or cerebellar or brain$ or vertebrobasilar) near/5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)):ti,ab
14. MeSH descriptor: [Hemiplegia] this term only
15. MeSH descriptor: [Paresis] explode all trees
16. (hemipleg* or hemipar* or paresis or paretic):ti,ab
17. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or 16
18. MeSH descriptor: [Upper Extremity] explode all trees
19. ("upper next limb*" or "upper next extremit*" or arm or shoulder or hand or axilla or elbow* or forearm* or finger* or wrist*):ti,ab
20. #18 or #19
21. #17 and #20
22. MeSH descriptor: [Exercise] this term only
23. (physiotherap$ or physicaltherap$ or exercise$):ti,ab
24. (exercise* near/3 (treat* or program* or train* or therap*)):ti,ab
25. #22 or #23 or #24
26. #21 and #25
27. MeSH descriptor: [Adult] this term only
28. MeSH descriptor: [Adolescent] this term only
29. MeSH descriptor: [Child] this term only
30. MeSH descriptor: [Infant] this term only
31. #28 or #29 or #30
32. #31 not #27
33. #26 not #32 with Publication Year from 2011 to 2020, in Trials

Note: ti = title, ab = abstract

B. Search Strategy Used in EMBASE

1. cerebrovascular disease/ or exp basal ganglion hemorrhage/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp carotid artery disease/ or cerebral artery disease/ or cerebrovascular accident/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$).tw.
3. ((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
4. ((cerebral or brain$ or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg* or hemipar* or paresis or paretic).tw.
7. or/1-6
8. exp upper limb/
9. ("upper limb$" or "upper extremit$" or arm or arms or shoulder or shoulders or hand or hands or elbow$ or forearm$ or finger$ or wrist$).tw
10. 8 or 9
11. Exercise/
12. (physiotherap$ or physicaltherap$ or exercise$).tw.
13. (exercise* adj3 (treat* or program* or train* or therap*)).tw.
14. or/11-13
15. 7 and 10 and 14
16. Randomized controlled trial/
17. randomization/
18. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
19. clinical trial/
20. Double Blind Procedure/
21. Single Blind Procedure/ or triple blind procedure/
22. Crossover Procedure/
23. placebo/
24. (assign$ or allocat$).tw.
25. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
26. (randomi?ed controlled adj1 trial*).tw.
27. (RCT or randomly allocated or allocated randomly or random allocation).tw.
28. (allocated adj2 random).tw.
29. placebo*.tw.
30. or/16-29
31. (((systematic adj review*) or (meta adj analys*)) not (trial or study)).ti,ab.
32. 30 not 31
33. 15 and 32
34. limit 33 to yr="2011 -Current"
35. 34 not ((exp animal/ or animal experiment/ or nonhuman/) not (exp human/ or human experiment/))
36. (Adolescent/ or exp child/ or exp infant/) not exp adult/
37. 35 not 36

Note: ab = abstract, ti = title, tw = text word

C. Search Strategy Used in CINAHL

S1. (MH "Cerebrovascular Disorders")
S2. (MH "Basal Ganglia Cerebrovascular Disease+")
S3. (MH "Carotid Artery Diseases+")
S4. (MH "Cerebral Ischemia+")
S5. (MH "Intracranial Arterial Diseases+")
S6. (MH "Intracranial Embolism and Thrombosis+")
S7. (MH "Intracranial Hemorrhage+")
S8. (MH "Stroke")
S9. (MH "Stroke, Lacunar")
S10. (MH "Cerebral Vasospasm")
S11. (MH "Vertebral Artery Dissections")
S12. TI (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva*) or AB (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva*)
S13. TI ((cerebral or cerebellar or brain* or vertebrobasilar) N5 (infarct* or ischaemi* or thrombo* or emboli* or apoplexy)) or AB ((cerebral or cerebellar or brain* or vertebrobasilar) N5 (infarct* or ischaemi* or thrombo* or emboli* or apoplexy))
S14. TI ((cerebral or brain* or subarachnoid) N5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed*)) or AB ((cerebral or brain* or subarachnoid) N5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed*))
S15. TI (hemipleg* or hemipar* or paresis or paretic) or AB (hemipleg* or hemipar* or paresis or paretic)
S16. (MH "Hemiplegia")
S17. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18. (MH "Upper Extremity+") OR "upper limb"
S19. TI ("upper limb*" or "upper extremit*" or arm or arms or shoulder or shoulders or hand or hands or elbow* or forearm* or finger* or wrist*) or AB ("upper limb*" or "upper extremit*" or arm or arms or shoulder or shoulders or hand or hands or elbow* or forearm* or finger* or wrist*)
S20. S18 OR S19
S21. (MH "Exercise+") OR "exercise"
S22. TI (physiotherap* or physicaltherap* or exercise*) or AB (physiotherap* or physicaltherap* or exercise*)
S23. TI (exercise* N3 (treat* or program* or train* or therap*)) or AB (exercise* N3 (treat* or program* or train* or therap*))
S24. S21 OR S22 OR S23
S25. S17 AND S20 AND S24
S26. (MH "Randomized Controlled Trials+")
S27. (MH "Random Assignment") OR (MH "Random Sample")
S28. TI ("quasi-random*" or "quasi random*" or "pseudo-random*" or "pseudo random*") or AB ("quasi-random*" or "quasi random* or "pseudo-random*" or "pseudo random")
S29. (MH "Clinical Trials")
S30. (MH "Double-Blind Studies")
S31. (MH "Single-Blind Studies")
S32. (MH "Triple-Blind Studies")
S33. (MH "Placebo Effect") OR (MH "Placebos")
S34. TI (assign* or allocat*) or AB (assign* or allocat*)
S35. TI ((singl* or doubl* or tripl* or trebl*) N5 (blind* or mask*)) or AB ((singl* or doubl* or tripl* or trebl*) N5 (blind* or mask*))

S36. TI (controlled N5 (trial* or stud*)) or AB (controlled N5 (trial* or stud*))
S37. TI (RCT or "randomly allocated" or "allocated randomly" or "random allocation") or AB (RCT or "randomly allocated" or "allocated randomly" or "random allocation")
S38. TI (allocated N2 random) or AB (allocated N2 random)
S39. S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38
S40. S25 AND S39
S41. (MH "Child+")
S42. (MH "Adolescence")
S43. (MH "Adult+")
S44. (S41 OR S42) NOT S43
S45. S40 NOT S44
S46. S45 Limiters – Published Date: 20110101-20201231

Note: AB = abstract, MH = subject heading; searches both major and minor headings, TI = title

Appendix 2. Cochrane Risk of Bias Tool for Randomised Trials (ROB 2 Tool)

Risk of bias assessment

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to sign posts to other questions, no formatting is used.

Domain 1: Risk of bias arising from the randomization process

Signalling questions	Comments	Response options
1.1 Was the allocation sequence random?		Y / PY / PN / N / NI
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?		Y / PY / PN / N / NI
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?		Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias arising from the randomization process?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 2: Risk of bias due to deviations from the intended interventions (*effect of assignment to intervention*)

Signalling questions	Comments	Response options
2.1. Were participants aware of their assigned intervention during the trial?		Y / PY / PN / N / NI
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?		Y / PY / PN / N / NI
2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context?		NA / Y / PY / PN / N / NI
2.4 If Y/PY to 2.3: Were these deviations likely to have affected the outcome?		NA / Y / PY / PN / N / NI
2.5. If Y/PY/NI to 2.4: Were these deviations from intended intervention balanced between groups?		NA / Y / PY / PN / N / NI
2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention?		Y / PY / PN / N / NI
2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to deviations from intended interventions?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 3: Missing outcome data

Signalling questions	Comments	Response options
3.1 Were data for this outcome available for all, or nearly all, participants randomized?		Y / PY / PN / N / NI
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?		NA / Y / PY / PN / N
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?		NA / Y / PY / PN / N / NI
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to missing outcome data?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 4: Risk of bias in measurement of the outcome

Signalling questions	Comments	Response options
4.1 Was the method of measuring the outcome inappropriate?		Y / PY / PN / N / NI
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?		Y / PY / PN / N / NI
4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?		NA / Y / PY / PN / N / NI
4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI
4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?		NA / Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias in measurement of the outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Domain 5: Risk of bias in selection of the reported result

Signalling questions	Comments	Response options
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis?		Y / PY / PN / N / NI
Is the numerical result being assessed likely to have been selected, on the basis of the results, from...		
5.2. ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?		Y / PY / PN / N / NI
5.3 ... multiple eligible analyses of the data?		Y / PY / PN / N / NI
Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the predicted direction of bias due to selection of the reported result?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Overall risk of bias

Risk-of-bias judgement		Low / High / Some concerns
Optional: What is the overall predicted direction of bias for this outcome?		NA / Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable

Note: Access to the tool can be obtained via the website hosting the current version of the ROB 2 tool (168). Guidance for using the tool is also available on the website. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License and is shared here in compliance with this licence.

Appendix 3. Neuromuscular Impairment and Functional Ability Measures Used in Eligible Studies Included in Meta-Analyses and Meta-Regressions

Study	Neuromuscular Impairment Measures	Functional Ability Measures

Abdullah et al. (235)	• Chedoke McMaster Stroke Assessment:
	  ○ Impairment Inventory
	  ▪ Arm Subscale
	  ▪ Hand Subscale
		• Chedoke Arm and Hand Activity Inventory - 7

Almhdawi et al. (236)	• Grip Strength
	• Range of Motion[2]:
	  ○ Active Shoulder Flexion
	  ○ Active Shoulder Abduction
	  ○ Active Elbow Extension
	  ○ Active Wrist Extension
	• Muscle strength[3]:
	  ○ Shoulder Flexors
	  ○ Shoulder Abductors
	  ○ Elbow Extensors
	  ○ Wrist Extensors
		• Wolf Motor Function Test:
		  ○ Performance Time

Amasyali and Yaliman (237)	• Fugl-Meyer Assessment * • Grip Strength[4] • Range of Motion: ○ Active Wrist Extension[5]	• Box and Block Test
Antoniotti et al. (238)	• Fugl – Meyer Assessment* *	• Action Research Arm Test[+]

Askin et al. (239)	• Fugl – Meyer Assessment**
	• Brunnstrom Recovery Stages
	  ○ Upper Extremity
	  ○ Hand
	• Modified Ashworth Scale
	• Motricity Index
	• Range of Motion[2]:
	  ○ Active shoulder flexion
	  ○ Active shoulder abduction
	  ○ Active shoulder internal rotation
	  ○ Active elbow flexion
	  ○ Active wrist flexion
	  ○ Active shoulder extension
	  ○ Active shoulder adduction
	  ○ Active shoulder external rotation
	  ○ Active elbow extension
	  ○ Active wrist extension
		• Box and Block Test

Carmeli et al. (240)	• Fugl-Meyer Assessment**
	• Performance Accuracy on[6]:
	  ○ X Axis (Track Speed)
	  ○ Y Axis (Track Width)
		• Box and Block Test

[2] Measured with a goniometer
[3] Measured with a dynamometer
[4] Measured with a Jamar dynamometer
[5] Measured with a 6''Jamar Goniometer
[6] These variables were derived from the HandTutor™ software

Study	Neuromuscular Impairment Measures	Functional Ability Measures

Ehrensberger et al. (241)	• Muscle strength[7]:
	  ○ Elbow extensors:
	  ▪ Highest Peak Torque
	  ▪ Highest Rate of Torque Development
	  ▪ Highest Average Torque
	• Modified Ashworth Scale[8]:
	  ○ Shoulder muscles
	  ○ Elbow muscles
	  ○ Wrist muscles
		• Chedoke Arm and Hand Activity Inventory - 8

Graef et al. (242)	• Fugl-Meyer Assessment Scale**
	• Range of Motion[2]:
	  ○ Active Shoulder Flexion
	• Modified Ashworth Scale
	• Grip strength[3]
	• Muscle strength[9]:
	  ○ Shoulder Flexors (kg)
	• The Upper-Extremity Performance Test:
	  ○ Task Analysis:
	  ▪ Unilateral Tasks
	  ▪ Bilateral Tasks
	  ▪ Unilateral Total
	  ▪ Bilateral Total
	  ▪ Unilateral and Bilateral Combined
		• The Upper-Extremity Performance Test:
		  ○ Functional Rating :
		  ▪ Unilateral Tasks
		  ▪ Bilateral Tasks

Hsieh et al. (243)	• Fugl-Meyer Assessment Scale** • Grip strength	• Box and Block Test
Hunter et al. (244)	• Grip Strength [10] • Pinch Strength[10]	• Action Research Arm test+ • Wolf Motor Function Test: ○ Performance Time

Huseyinsinoglu, Ozdincler and Krespi (245)	• Motor Evaluation Scale for Arm in Stroke Patients	• Wolf Motor Function Test:
		  ○ Performance Time
		  ○ Functional Ability Scale

Johnson et al. (246)	• Fugl-Meyer Assessment Scale**
	• Modified Ashworth Scale[11]:
	  ○ Shoulder
	  ○ Elbow
	  ○ Wrist
	  ○ Fingers
		• Action Research Arm Test+
		• Box and Block Test

Lee et al. (247)	• Fugl-Meyer Assessment Scale**	• Box and Block Test
Meng et al. (248)	• Fugl-Meyer Assessment Scale**	• Action Research Arm Test+

[7] Maximal voluntary isometric elbow extension strength, assessed using the Biodex System
[8] The muscles from which the spasticity was measured were not reported individually.
[9] Muscle Strength was measured using a load cell.
[10] Measured using a myometer
[11] The study report makes no reference to which muscles were explicitly evaluated.

Study	Neuromuscular Impairment Measures	Functional Ability Measures

Michielsen et al. (249)	• Fugl-Meyer Assessment Scale**
	• Grip Strength[3]
	• Tardieu Scale:
	  ○ Elbow Muscles
	  ○ Wrist Muscles
		• Action Research Arm Test+

Milot et al. (250)	• Fugl-Meyer Assessment Scale**
	• Grip Strength
	• Wolf Motor Function Test:
	  ○ Arm Strength (lb.)
	• Modified Ashworth Scale
	  ○ Elbow Flexors
	  ○ Wrist Flexors
	  ○ Finger Flexors
	  ○ Thumb Flexors
		• Wolf Motor Function Test:
		  ○ Performance Time
		  ○ Functional Ability Scale

Park et al. (251)	• Grip Strength[4]	• Box and Blocks Test

Park et al. (252)	• Fugl-Meyer Assessment Scale***
	• Active Range of Motion:
	  ○ Shoulder Flexion
	  ○ Shoulder Abduction
	  ○ Shoulder Internal Rotation
	  ○ Shoulder Adduction
	  ○ Shoulder External Rotation
		• Wolf Motor Function Test:
		  ○ Performance Time
		  ○ Functional Ability Scale

Prange et al. (253)	• Fugl-Meyer Assessment** • Maximal reach distance measured with the Arm Support device[12]	• Stroke Upper Limb Capacity Scale

Rodrigues et al. (254)	• Fugl-Meyer Assessment Scale**
	• The Upper Extremity Performance Test – Task Analysis[13]:
	  ○ Unilateral Tasks
	  ○ Bilateral Tasks
	  ○ Total
		• The Upper Extremity Performance Test – Function Rating[13]:
		  ○ Unilateral Tasks
		  ○ Bilateral tasks
		  ○ Total

Shimodozono et al. (255)	• Fugl-Meyer Assessment Scale**	• Action Research Arm Test++

Thrane et al. (256)	• Fugl-Meyer Assessment Scale**
	• Wolf Motor Function Test
	  ○ Grip Strength (kg)
	  ○ Arm Strength (kg)
		• Wolf Motor Function Test:
		  ○ Performance Time[14]
		  ○ Functional Ability Scale
		• Nine-Hole Peg Test

Timmermans et al. (257)	• Fugl-Meyer Assessment Scale Scale**
	• Wolf Motor Function Test
	  ○ Grip Strength (kg)
	  ○ Arm Strength (kg)
		• Wolf Motor Function Test:
		  ○ Performance Time
		  ○ Functional Ability Scale
		• Frenchy Arm Test

[12] Measured using the Arm Support device, which tracks the hand's location in the horizontal plane via a reflective marker.

[13] Measured with the Brazilian version of the test.

[14] The Wolf Motor Function Test (WMFT) - Performance Time was reported as WMFT time (s) and logWMFT time, with the latter calculated using a base-10 logarithmic transformation (log10). As the SD values of changes were not provided, the reported p-values for logWMFT time values were used to estimate the SD of changes from baseline. For analyses, logWMFT time variables were used to represent the WMFT - Performance Time scores.

Study	Neuromuscular Impairment Measures	Functional Ability Measures
Timmermans et al. (258)	• Fugl-Meyer Assessment Scale Scale**	• Action Research Arm Test+

Turkbey, Kutlay and Gok (259)	• Brunnstrom Motor Recovery Stage - UL	• Box and Block Test
		• Wolf Motor Function Test:
		  ○ Performance Time
		  ○ Functional Ability Scale

Tyson et al. (260)	• Grip strength • Motricity Index • Modified Ashworth Scale: ○ Elbow Flexors	• Action Research Arm Test+ • Box and Block Test

Wolf et al. (261)	• Fugl-Meyer Assessment Scale****	• Action Research Arm Test+++
		• Wolf Motor Function Test – Performance Time
		  ○ Total
		  ○ Gross
		  ○ Fine

Wu et al. (262)	• Kinematics-derived motor impairment measure/s[15]:
	  ○ Shoulder Flexion Range of Motion
	  ○ Elbow Flexion Range of Motion
		• Action Research Arm Test++

Wu et al. (263)	• Fugl-Meyer Assessment Scale****
	• Kinematics-derived motor impairment measure/s[16]:
	  ○ Normalised Shoulder Flexion Range of Motion
	  ○ Normalised Elbow Extension Range of Motion
	  ○ Normalised Shoulder Abduction Range of Motion
	  ○ Reaction Time
	  ○ Maximum Shoulder-elbow Cross-Correlation
	  ○ Normalised Total Displacement[17]
		• Kinematics-derived functional ability measure/s:
		  ○ Normalised Movement Time[18]

[15] Normalised to correct for variations in task distance.

[16] Participants pressed a desk bell at 90% of arm length. If the maximum reach was less than the functional arm length, it was adjusted to the maximum reachable distance, and values were normalised by dividing by the reachable distance.

[17] It refers to the path of the index finger in a three-dimensional space.

[18] It refers to the time interval between the movement's start and end.

Study	Neuromuscular Impairment Measures	Functional Ability Measures

Zondervan et al. (264)	• Fugl-Meyer Assessment****
	• Range of Motion[19]:
	  ○ Active Shoulder
	  ○ Active Elbow
	• Modified Ashworth Scale[7]
		• Box and Block Test

[19] The study did not specify the movement directions for those values.

* The total score and sub-scores for shoulder-elbow-forearm, wrist, hand, and coordination were reported.

** Only the total score of the scale was reported.

*** The total score and the proximal, distal, and coordination sub-scores of the scale were reported.

**** The total score and the proximal and distal sub-scores of the scale were reported.

+ Only the total score of the test was reported.

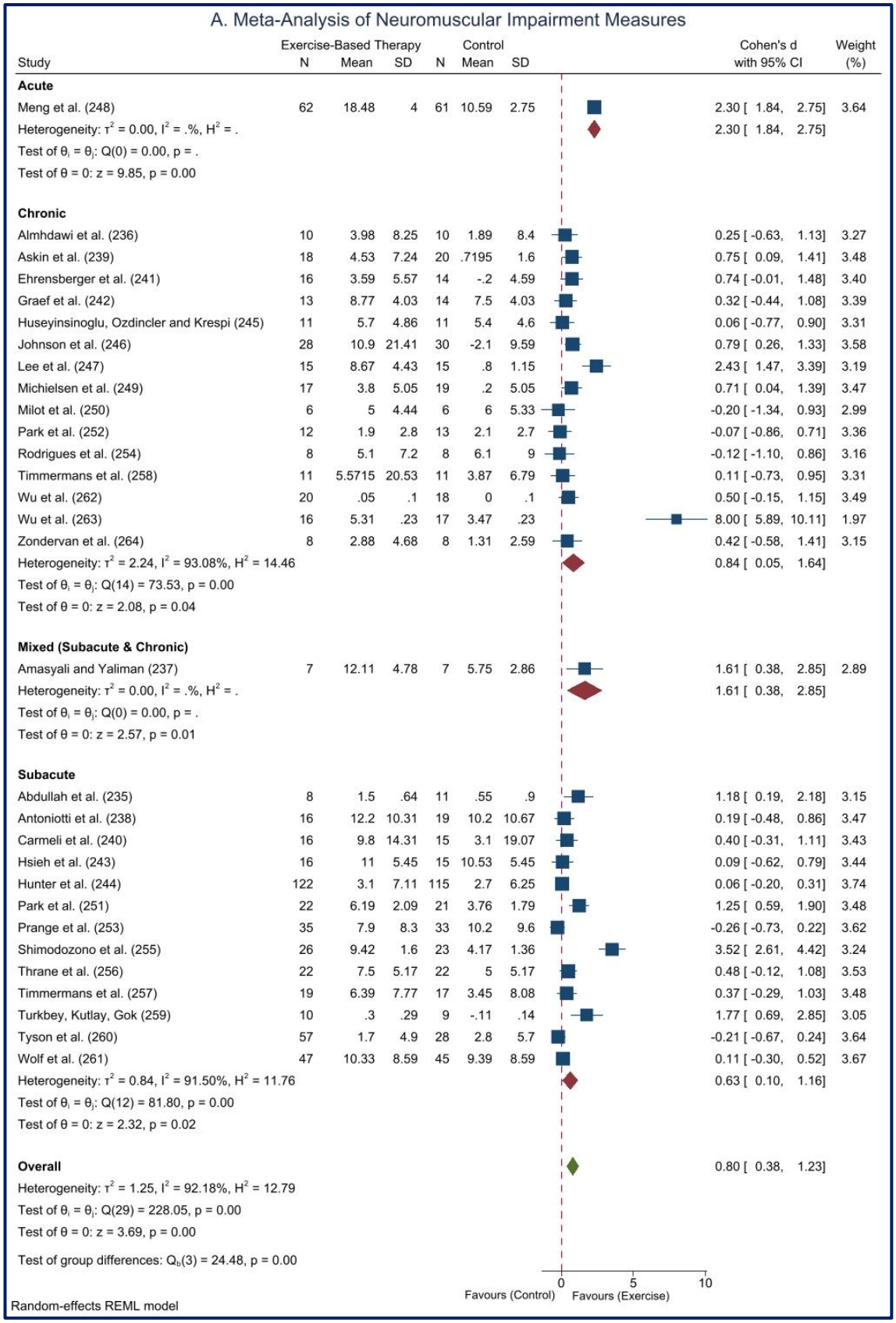
++ The total score and grasp, grip, pinch and gross movement sub-scores of the test were reported.

+++ The total score and grasp, grip and pinch sub-scores of the test were reported.

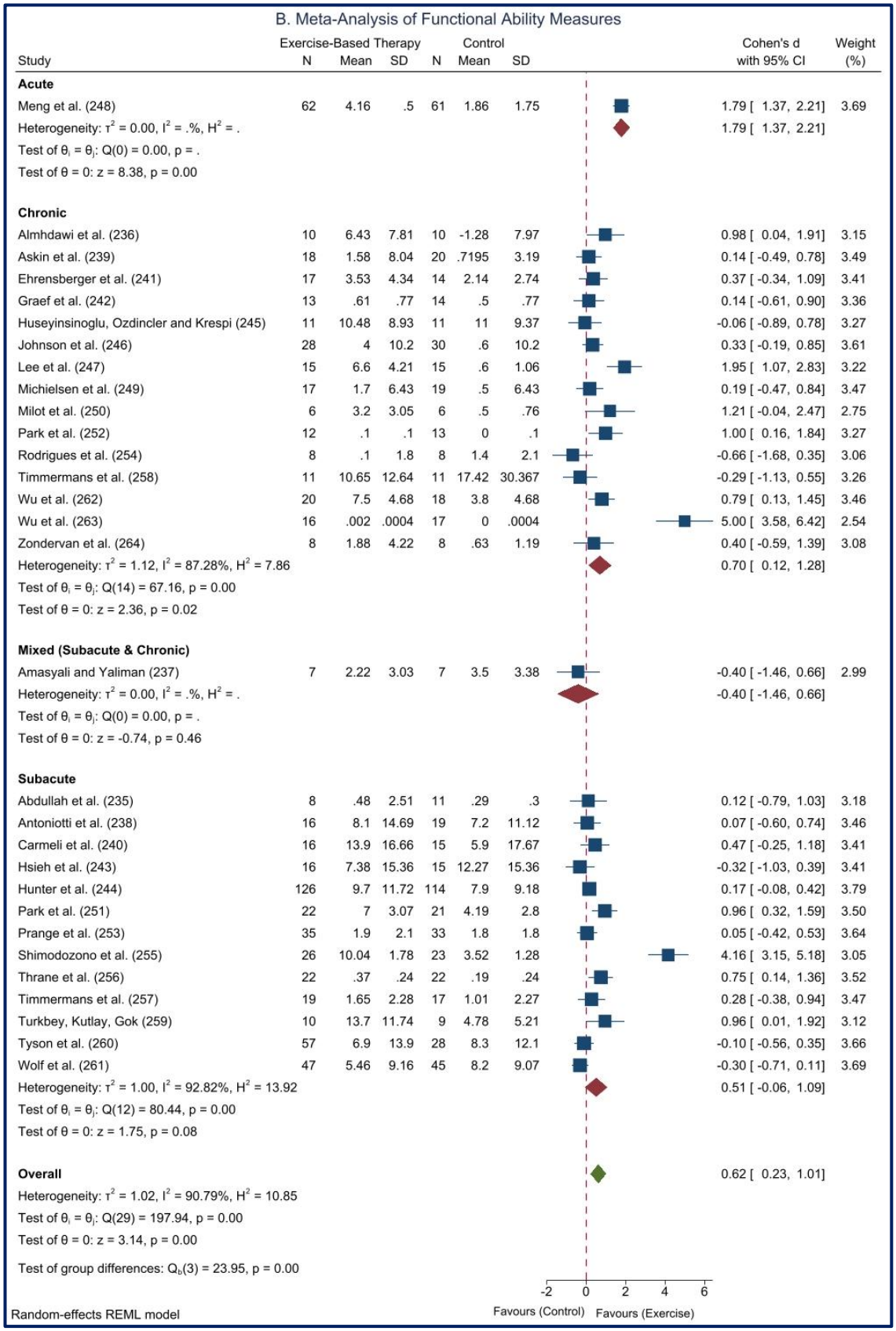
Appendix 4. Additional Analyses

Figure 1. Forest Plots: Meta-Analyses of Comparative Effects of Exercise-Based Therapy by Post-Stroke Stages (A and B)

A. Neuromuscular Impairment



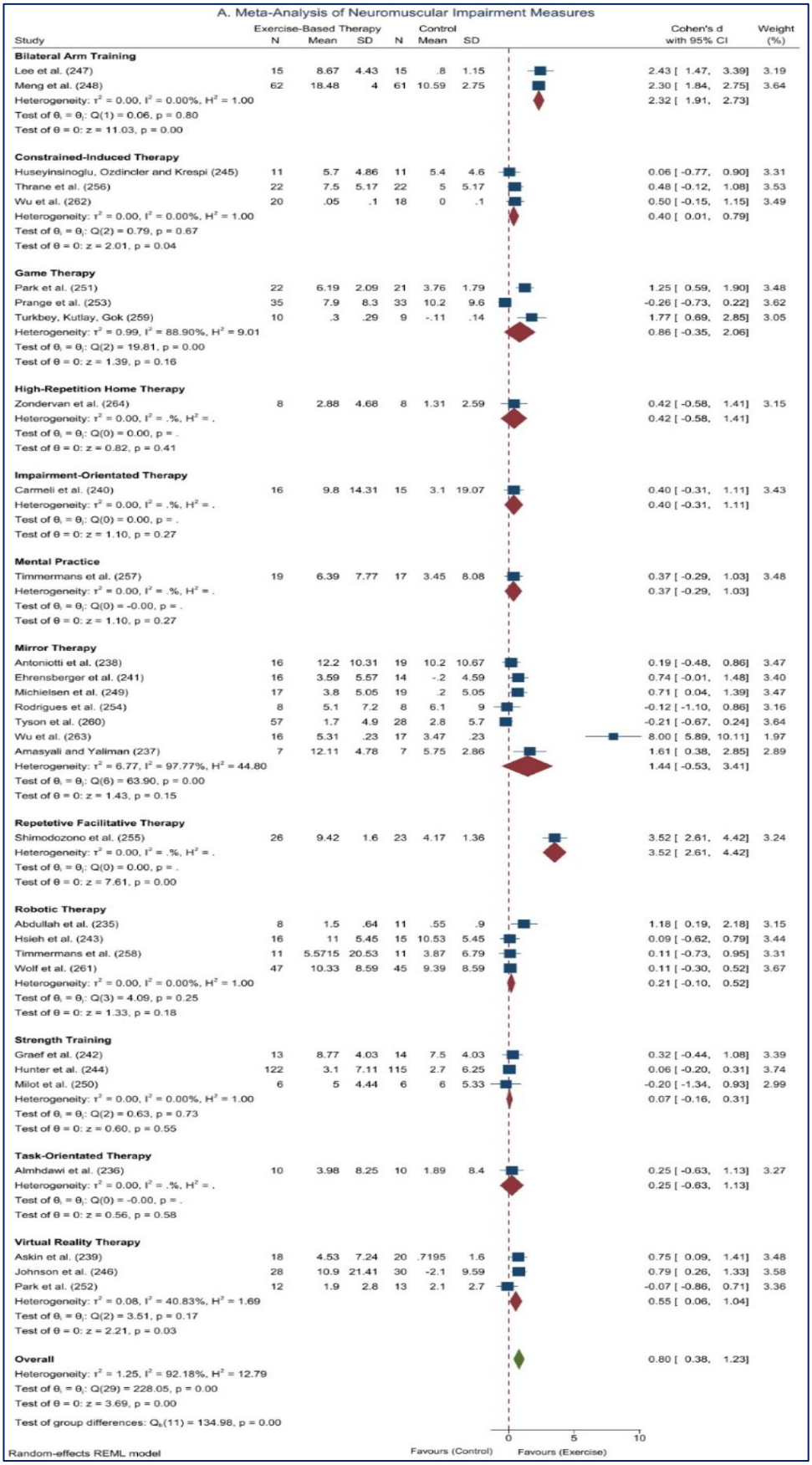
B. Functional Ability



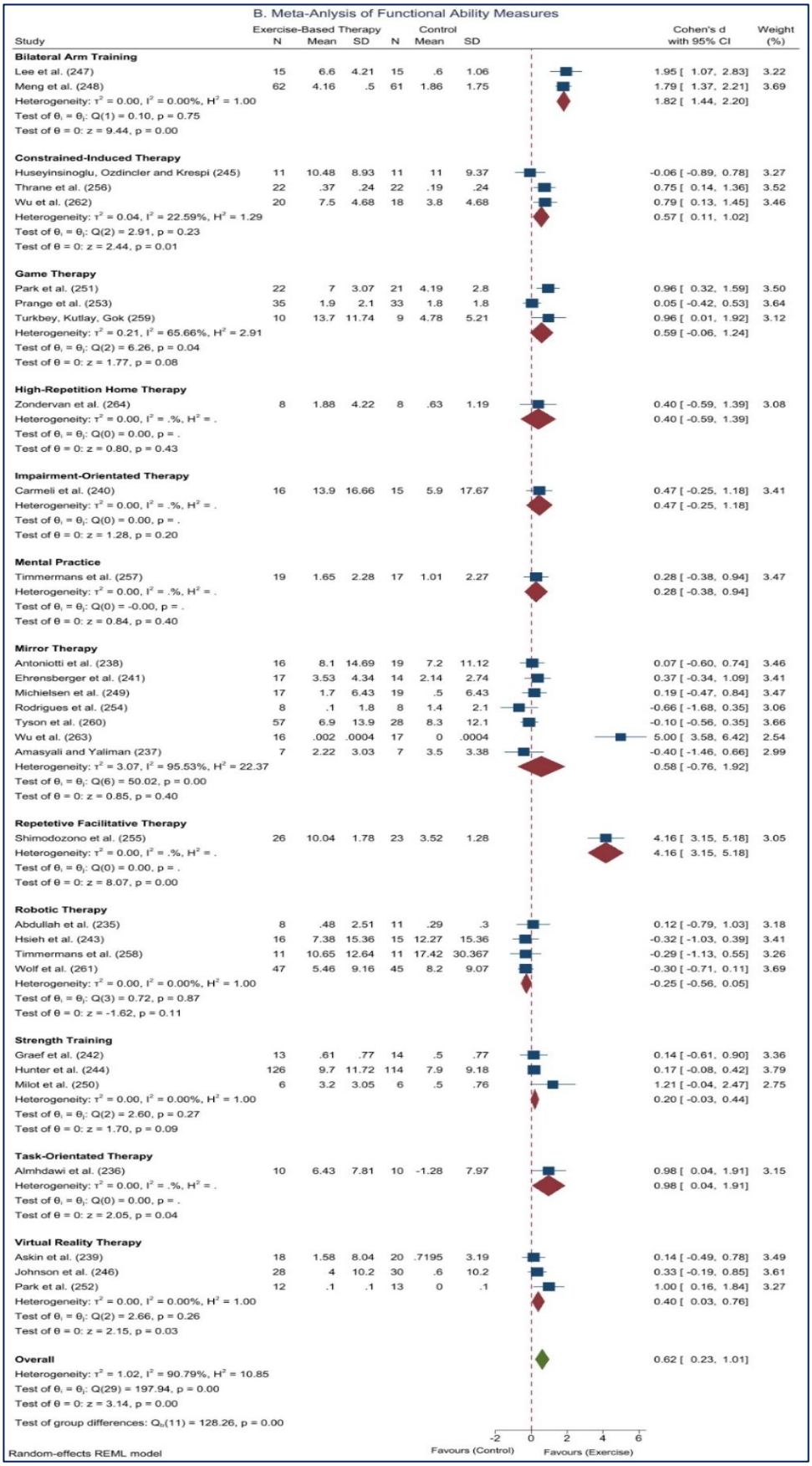
Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Figure 2. Forest Plots: Meta-Analyses of Comparative Effects of Exercise-Based Therapy by Exercise Type (A and B)

A. Neuromuscular Impairment



B. Functional Ability

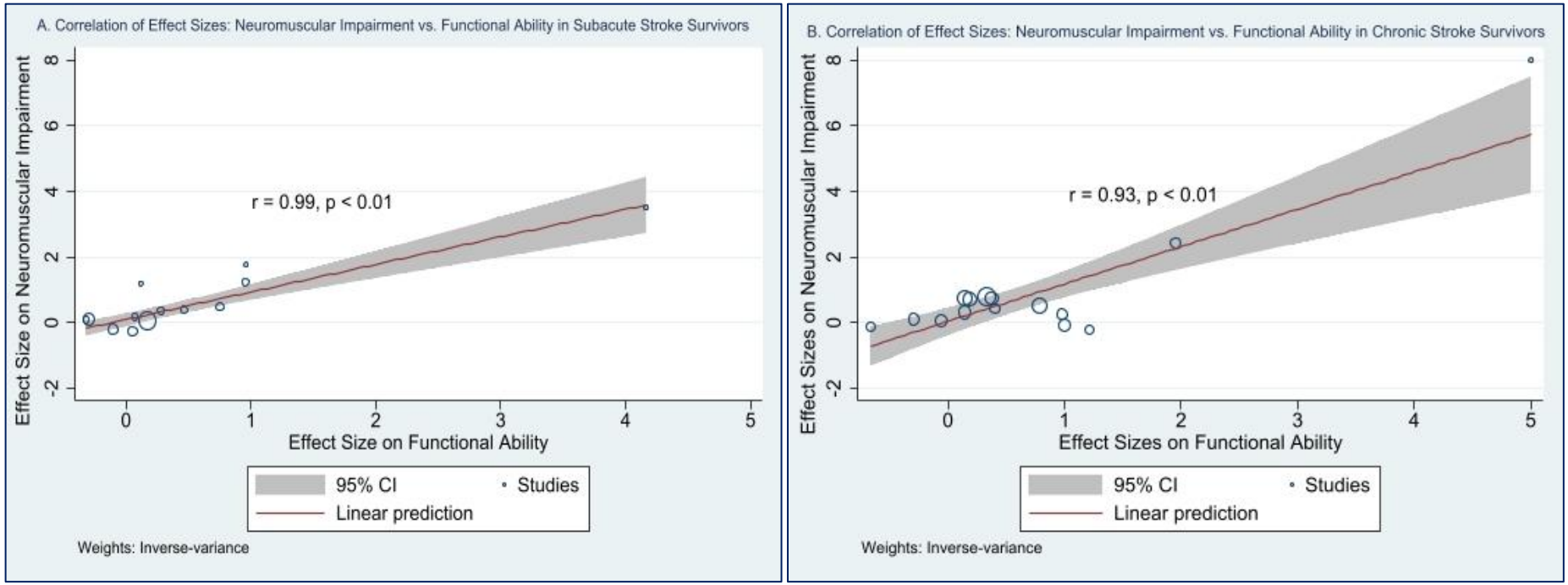


Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Figure 3. Meta-Regression Bubble Plots Illustrating the Correlations between Changes in Neuromuscular Impairments versus Changes in Functional Abilities in Response to Exercise-Based Therapies Compared to Control Interventions, by Post-Stroke Stages (A and B)

A. Subacute Stage

B. Chronic Stage

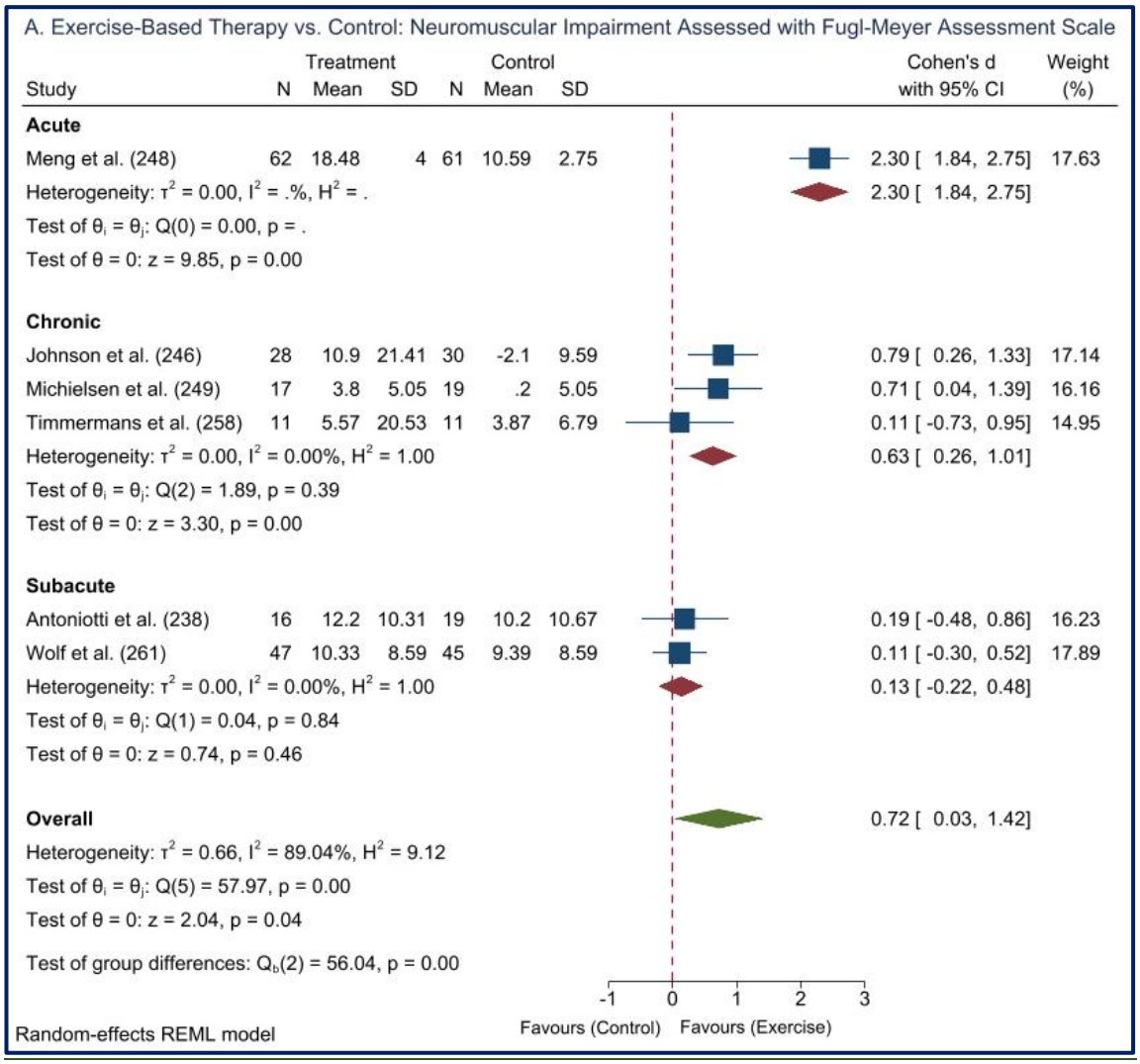


Note: Blue circles reflect the studies' effect sizes. Larger circles correspond to larger effects. The red line represents the regression line of best fit. The grey-shaded area represents the 95% confidence interval for the predicted values of the regression line.

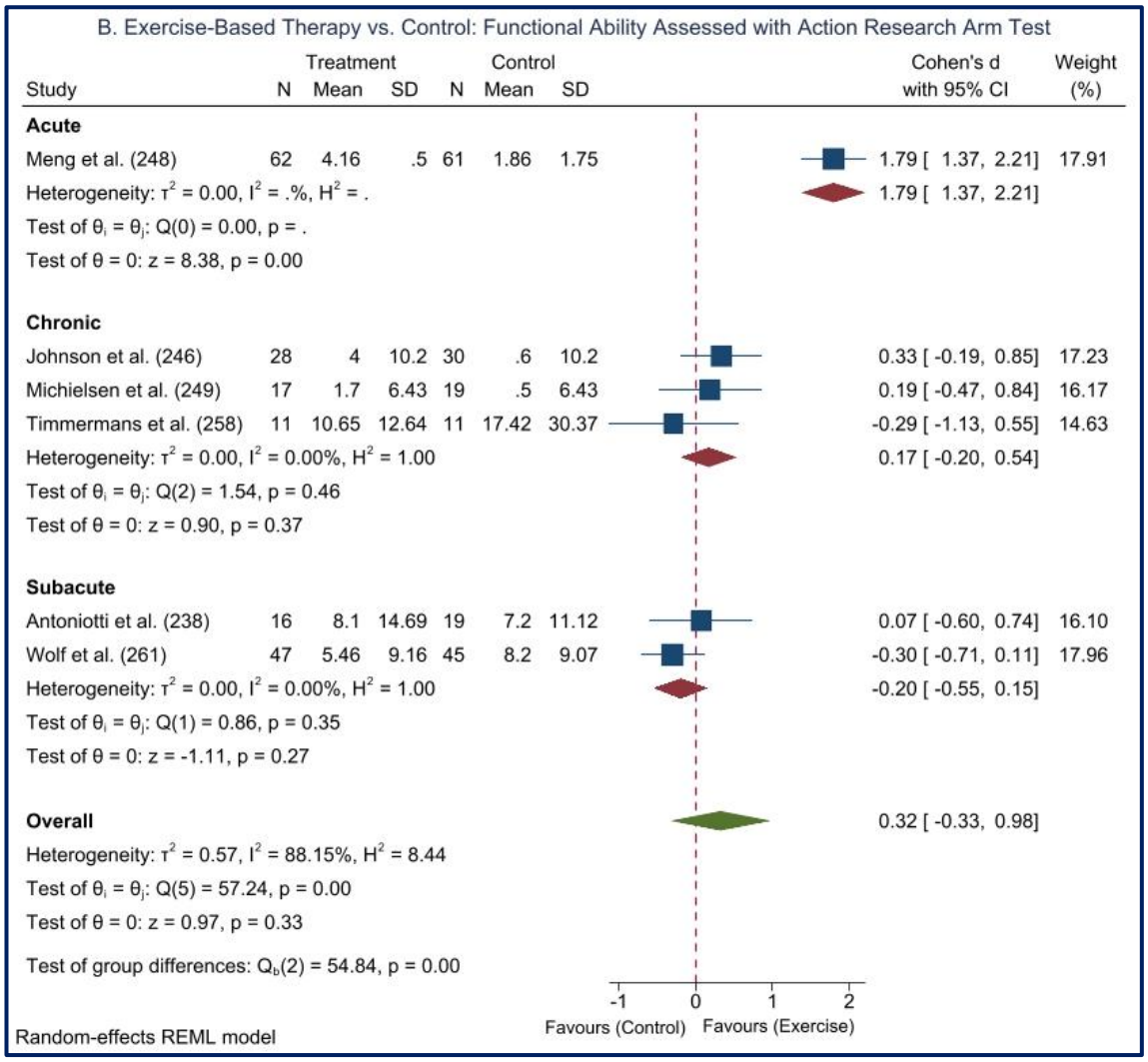
Appendix 5. Sensitivity Analyses

Figure 1. Forest Plots: Sensitivity Meta-Analyses of Comparative Effects of Exercise-Based Therapy (A and B)

A. Neuromuscular Impairment Assessed with Fugl-Meyer Assessment Scale



B. Functional Ability Assessed with Action Research Arm Test



Note: In the plot, the right side indicates a greater effect favouring exercise-based therapy, and the left side favours control intervention. I^2 indicates heterogeneity. 'Weight' shows each study's influence on the overall result. The p-value < 0.05 for the 'Test of θ' indicates the statistically significant effect. **N:** Sample Size; **SD:** Standard Deviation; **Cohen's d:** Effect Size; **CI:** Confidence Interval.

Appendix 6. Allergy Screening Questionnaire

University of East Anglia

MoveExLab H&S Doc No: 005

abira linking research & practice

MoveExLab Allergy Screening Questionnaire (Research)

Section: 1 General Information

Trial Name:

_____

Participant Number:

_____

Section 2: Screening Questions

Please tick a Yes or No box to answer the questions below.

1. Are you aware that you have an allergy of any type? Yes ☐ No ☐

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

2. Do you have any known food allergies? Yes ☐ No ☐

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

3. Do sufferer from any skin complains? **Yes** ☐ **No** ☐

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

4. Have you ever had an allergic reaction to latex products? **Yes** ☐ **No** ☐

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

5. Have you ever had an allergic reaction to any type of metal when placed on your skin?

Yes ☐ **No** ☐

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

6. Have you ever had an allergic reaction to cosmetic products such as creams and gels?

Yes ____ No ____

(If yes please provide further details)

_____

_____

_____

_____

_____

_____

7. Have you ever had an allergic reaction to adhesive products such as tapes and pads when placed on your skin?

Yes ____ No ____

_____

_____

_____

_____

_____

_____

Section 3: Additional Information Requested (Principle Tester Only)

Further information requested: Yes ☐ No ☐

GP letter requested: Yes ☐ No ☐

Other medical documentation requested: Yes ☐ No ☐

Details:

_____

_____

_____

_____

_____

_____

Please copy and attach the requested information to this form when received from the participant.

Participant can proceed with the participation of an exercise test or exercise training program. Yes ☐ **No** ☐

Principle Tester Signature:

_____

Print Name: _____

Date: _____

Section 4: DECLARATION AND AUTHORISATION

I confirm that the information given is a true and accurate statement at today's date. I understand that if I have declared any of the conditions listed, further information may be requested.
I am aware that it is my responsibility to inform the UEA MovExLab if there is a change to any the answers I have already provided in this document.

Participant Signature: **Date:**

The information that you have provided constitutes personal data and as such will be processed in accordance with the Data Protection Act 2018 by the University of East Anglia, being a public authority, as a data controller defined in the act. Further details regarding the processing of your data may be found in the University's data protection policy available on the UEA'S portal internet page.

Appendix 7. University of East Anglia (UEA) Model Release Consent Form

Subject: Thank you for submitting your UEA Model Release Consent Form
To: [redacted]

UEA Model Release Consent Form

I hereby consent to the use of personal case study information, testimonials (comments), videos, audio recordings and photographs of myself taken by members of the University of East Anglia (UEA) or by agents authorised on behalf of UEA for promotional purposes. Please see our privacy notice(s) for further information https://portal.uea.ac.uk/information-services/strategy-planning-and-compliance/regulations-and-policies/information-regulations-and-policies/data-protection/privacy-notices

The personal data that we hold will be used for the purposes stated above and will be processed in accordance with relevant UK Data Protection laws.

Full name of model

[redacted]

Parent/Carer consent required

Name of Parent/Carer

Contact email

[redacted]

Please upload a head-and-shoulders digital photograph to verify your identity:

img_1782.jpg

Project name:

Neuromechanical Correlates of Movement Recovery After Stroke

Project manager email:

v.pomeroy@uea.ac.uk

I give my consent to my data being used as described and understand that I have the right to withdraw my consent at any time:

I consent

Policy statement:

It is UEA's policy, that where we are planning to use personal case study information, testimonials, videos, audio recordings and photographs for promotional purposes in the public domain, consent must be obtained by the appropriate person as set out in the Model Release Consent Form.

The purpose of the consent form is:

- to provide information for the person giving consent so they can make an informed decision.
- to be clear about which areas of work the consent applies to.

The consent form should be completed before the capturing of materials for promotional purposes takes place.

Who should read this guide for models?

Those asked to give consent, including children and young people, parents, legal guardians, models, UEA's staff and students.

How are the images used?

We use images in a range of materials to promote UEA as a whole and also to illustrate particular areas of our work. This includes advertisements and other publicity materials such as leaflets, prospectuses, brochures and posters, direct mail, books, social media channels, newspapers, magazine articles, television programmes and publications for the Internet. For more information on how we use your personal data please visit our website or email enquiries@uea.ac.uk:

https://portal.uea.ac.uk/information-services/strategy-planning-and-compliance/regulations-and-policies/information-regulations-and-policies/data-protection/further-information

How long does consent last?

Consent continues with no time limit, as the purposes for which we use your information will remain as described in this form. However, you have the right to withdraw your consent to any future use of materials containing your personal data at any time by emailing enquiries@uea.ac.uk

Who can give consent?

It is good practice to involve children and young people in the consent process.

- Models who are 16 years old and older, who understand the consent process, can sign for themselves.
- Models under 16 years old – A signature of the parent/legal guardian should be obtained.
- Models who are 13 years old or under – Inform them how their images, comments etc. may be used.
- Be responsive to the child's feelings and respect their wishes.
- Models who are 13-16 and who have a sufficient understanding of the consent process and its implications may sign the consent form in addition to the parent/legal guardian.
- Models who are 16 years old and older and have insufficient understanding of the consent process – The consent form needs to be signed by a parent/legal guardian. Try to engage the model in the process, be responsive to their feelings and respect their wishes.

The personal data that we hold will be used for the purposes stated above and will be processed in accordance with relevant UK Data Protection laws.

Appendix 8. Ethical Approval with the reference number: 2019/20-044

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Valerie Pomeroy
Queen's Building
University of East Anglia
Norwich Research Park
NR4 7TJ

NORWICH MEDICAL SCHOOL
Bob Champion Research & Educational Building
James Watson Road
University of East Anglia
Norwich Research Park
Norwich NR4 7UQ

Email: fmh.ethics@uea.ac.uk
www.med.uea.ac.uk

16th January 2020

Dear Valerie

Title: Developing measurement of movement performance using the "gold-standard" Vicon and novel Biokido motion analysis systems: normal values, test-retest reliability, criterion validity and smallest detectable difference

Reference: 2019/20-044

Thank you for your email of 6th January 2020 notifying us of the amendments you would like to make to your above proposal. These have been considered and I can confirm that your amendments have been approved.

Please can you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance, and that any adverse events which occur during your project are reported to the Committee.

Approval by the FMH Research Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Please can you arrange to send us a report once your project is completed.

Yours sincerely

Prof Alastair Forbes
Chair
FMH Research Ethics Committee

University of East Anglia

NORWICH MEDICAL SCHOOL
Bob Champion Research & Educational Building
Rosalind Franklin Road
University of East Anglia
Norwich Research Park
Norwich NR4 7UQ

Email: fmh.ethics@uea.ac.uk
www.med.uea.ac.uk

Prof Valerie Pomeroy
School of Health Sciences
University of East Anglia
Norwich Research Park
Norwich
NR4 7TJ

17th February 2021

Dear Val

Project title: Developing measurement of movement performance using the "gold-standard" Vicon and novel Biokido motion analysis systems: normal values, test-retest reliability, criterion validity and smallest detectable difference

Reference: 2019/20-044

Thank you for your email 5th February 2021 notifying us of the amendments you would like to make to your above proposal. These have been considered and I can confirm that your amendments have been approved.

Please can you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance, and that any adverse events which occur during your project are reported to the Committee.

Approval by the FMH Research Ethics Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Please can you arrange to send us a report once your project is completed.

Yours sincerely

Dr Jackie Buck
Chair
FMH Research Ethics Committee

COVID-19: The FMH Research Ethics Committee procedures remain as normal. Please note that our decisions as to the ethics of your application take no account of changes in Government measures and UEA guidelines relating to the coronavirus pandemic and all approvals granted are, of course, subject to these.

Appendix 9. Informed Consent Form for Correlational Agreement Study (Chapter 5)

Date of visit |__|__|-|__|__|-|__|__|__|__| (DD-MM-YYYY)

Participant Identification Number: |_____|

University of East Anglia

Developing measurement of movement performance for use in rehabilitation: normal values, reliability, validity and smallest detectable difference

Consent Form for volunteers

Name of Researcher: _____

Name of Participant: _____

Participant Identification Number: |_____|

	Please initial the box
I have read and understood the participant information sheet (PIS Version 3, 6 January 2020)	
I understand that I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	
I understand that my participation is voluntary and that I am free to withdraw at any time until the point that my data are anonymised without giving any reason.	
I agree to complete a form to provide asking for: my demographic information (e.g., age, sex) and information about any allergies of relevance to this project.	
I understand that I will attend the MoveExLab at the University of East Anglia on two separate occasions and that any necessary travel expenses will be reimbursed.	
I understand that I will undertake assessments for measurement of my muscle activity and my movement at the MoveExLab at the University of East Anglia.	
I understand that while information gained during the study may be published, I will not be identified and all information (demographic, muscle activity and movement) will be anonymised.	
I agree to take part in the study.	

	Please initial the appropriate box	
	YES	NO
I agree to my name and contact details being held on a secure database at the University of East Anglia so that I can be contacted regarding follow-up to this study and opportunities for future research that has been ethically approved.		
I agree for my anonymised data captured with the Biokido system to be sent to the manufacturer in Turkey so that it can be analysed. I understand that my anonymised data will be in blurred pictorial format as in the illustration of the Biokido system in the information sheet. My data transferred to Turkey for analysis will only be identifiable by the anonymised study number.		

Name of participant	
Signature	
Date	

Name of person taking consent	
Signature	
Date	

One original copy of this form should be completed. The original should be stored in the investigator site file. Photocopies should be made of the original and given to the participant

Appendix 10. Participant Information Sheet for Correlational Agreement Study (Chapter 5)

University of East Anglia

abira
linking research & practice

Developing measurement of movement performance for use in rehabilitation: normal values, reliability, validity and smallest detectable difference

Information Sheet for potential volunteers

Researchers from the University of East Anglia (UEA) extend an invitation for you to take part in a research project.

We are developing measures of the movement needed for the everyday activity of answering the telephone. Our purpose is to provide new measures that can be used to find out how the brain recovers after stroke and how brain recovery can be improved by physiotherapy. This project will increase knowledge about the movement characteristics of people who have not suffered a stroke. Therefore, this study will provide the reference values needed to improve clinical care of individual stroke survivors.

You do not have to take part if you do not want to.

Talk about the project with others if you would like to.

If you need more information, please ask the researcher, Valerie Pomeroy at UEA. Or get in touch with her personal assistant: Pel Fordham. Both of them will be happy to answer your questions. Their contact information is at the bottom of this page.

Thank you for reading this information sheet and for considering taking part in this project.

Contact Details

Researcher's name: Professor Valerie Pomeroy
Email: v.pomeroy@uea.ac.uk
Phone: 01603 59 1923

Researcher's personal assistant: Pel Fordham
Email: p.fordham@uea.ac.uk
Phone: 01603 59 **1923**

What is the purpose of this project?

There is strong evidence that physiotherapy improves the ability of people to move and be independent after suffering a stroke. But at six months after stroke many people remain unable to produce the movement needed for every-day activity such as picking up a telephone. This situation could be improved by using physiotherapy interventions to aid the recovery of movement after stroke. It is therefore important to be able to recognise if a physiotherapy intervention is aiding movement recovery for stroke survivors to enable them to undertake every-day activity. This requires knowledge of the movement characteristics of people who have not suffered a stroke. This project will provide the required knowledge by using the specialised equipment in the Movement and Exercise Laboratory at the University of East Anglia (MoveExLab).

However, if movement measures are to be used routinely in clinical practice then relying on specialist facilities such as the MoveExLab will not be practical. This equipment is also expensive. So, this project will find out if new equipment, that costs less and is designed for use in small spaces, also provides movement measures that are sensitive to change.

This project will provide the reference values for measures needed in clinical practice to improve movement recovery for stroke survivors. This project will also find out if the movement measures can be made equally as well with new equipment, called Biokido, that is more suitable for use clinically.

Am I eligible to take part in this project?

You are potentially eligible to participate if:

- You are aged 18 or above and
- You do not have or have had an illness that has affected your ability to move e.g.:a painful knee, osteoporosis, multiple sclerosis
- You do not have an allergy to latex

If you are interested, then I (Valerie Pomeroy) would like to talk to you about if you can be involved in this project. My contact details and those of my personal assistant are provided on page 1 of this leaflet.

Do I have to take part?

No, you do not have to take part.

It is entirely up to you to decide. If you would prefer not to take part, that is OK. If you do take part, **you may withdraw at any time without giving a reason.**

If you do withdraw, we can only destroy your data up to the point they are anonymised. After that point, it will not be possible to separate your data.

What will I have to do if I am interested?

If you are able to take part in the project, then we will invite you to attend the Movement and Exercise Laboratory at the University of East Anglia (MoveExLab) for some assessments at a time of your convenience. All necessary travel will be reimbursed, and pre-paid taxis can be arranged if you wish us to do so.

What will I have to do if I take part?

You will be invited to undertake two assessments at the MoveExLab. These assessments will be between 1 and 4 weeks apart depending on your preference. The assessments will take **around 1 hour** to complete at **the MoveExLab** (picture on right of this paragraph). Y**ou may stop at any time**.

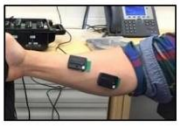
First: We will ask you to **fill in a form** to gather demographic data. We will also ask questions about any allergies you have to ensure that you are unlikely to have any reactions from sticky tape and other materials in the MoveExLab. If you do have allergies, e.g. to sticky tape, then we can adjust the materials we use for testing or aspects of the MoveExLab environment. However, if you have an allergy to latex then we are unable to make adjustments and you will be unable to take part.

Second: We will ask you to change into shorts and a sleeveless T-shirt in a curtained-off private changing area. You can bring your own clothing, or you can use the MoveExLab clothing which is

freshly laundered for each participant. You can decide. We will also ask you to take off your shoes and socks.

We will then measure your height and weight. Then we will measure your body size e.g. the width of your hands and length of your legs. These measurements are needed by the motion analysis software to produce the movement measures.

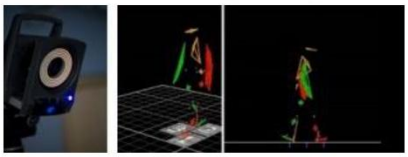
Third: We will place electromyography (EMG) electrodes on your skin using hypoallergenic sticky tape. These EMG electrodes will measure your muscle activity as you move. The picture on the right shows the EMG electrodes in place. These EMG electrodes do not hurt. They just record your natural muscle activity during movement.



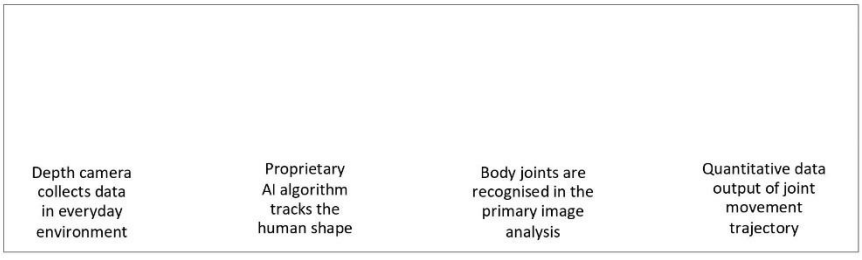
We will also place reflective markers on your skin using hypoallergenic sticky tape. These reflective markers are tracked by infra-red cameras placed at the top of the walls of the MoveExLab. On the right of this text is a picture to illustrate these reflective markers in place. These markers do not hurt. They just record movement of your body.

Fourth: As part of this study we will use electroencephalography (EEG). EEG measures the electrical activity of the brain using electrodes (small metal discs or sensors) which are mounted on a cap and placed on the head with gel. The EEG cap does not hurt, and the entire procedure usually takes about 15 minutes. The gel used to put the sensors on the head can sometimes be slightly sticky and the EEG cap in rare instances may cause slight discomfort.

Fifth: You will be asked to stand still in the middle of the MoveExLab. The eight infra-red cameras placed around the top of the walls will record the light signals from the reflective markers on your body. The motion analysis software will then use the collected information to calibrate your body in the space in which you are going to move. Placed at the right of this paragraph is a photograph of one infra-red camera and examples of the 'pictures' of movement captured.



Your movement will also be 'captured' by a new motion analysis system called the Biokido Motion Analysis system. The Biokido motion analysis system is illustrated in the pictures placed at the bottom of this



paragraph. The system consists of a depth camera and a portable computer with specialist software. The system is fully portable and can be used in small spaces. Therefore, if the measures made with the Biokido system agree with those made by the MoveExLab system then it may be placed in clinical settings for routine measures that are unable to be made now.

Sixth: You will be seated with a telephone placed on a table 3 metres in front of you. Your task will be to go and answer the telephone when you hear a buzzer. You will be instructed in exactly what to do and given time to practice. When you are confident in doing this task, we will record your movement and muscle activity whilst you do it. You will repeat this task until the technician tells you that there are 5 trials which have reconstructed well on the computer. Please note that most trials reconstruct well so it is unlikely that you will have to do this task more than 5 times. The maximum number of times we will ask you to complete this task will be ten if there are problems with computer reconstruction.

Seventh: You will stay seated and we will bring the table in front of you so that you can rest your forearm on it. Your task will be to answer the telephone placed directly in front of you, with your dominant hand, when you hear the buzzer. You will be instructed in exactly what to do and given time to practice. When you are confident in doing this task, we will record your movement and muscle activity whilst you do it. You will repeat this task until the technician tells you that there are 5 trials which have reconstructed well on the computer. Then you will do another 5 trials with the telephone on the left of the table. Followed by 5 trials with the telephone on the right of the table. Please note that most trials reconstruct well so it is unlikely that you will do more than 15 trials of this task. The maximum number of times we will ask you to complete this task will be 30 if there are problems with computer reconstruction.

Eighth: We will remove the EEG cap, EMG electrodes and reflective markers that were placed on your skin. The sticky tape is similar to a sticking plaster. Most people do not experience any discomfort. You will then change back into your normal clothes in the curtained-off private changing area.

The assessment is then completed.

What will happen to my information?

Information will include your **age, gender and ethnicity.**

We will also store personal information such as your **telephone number** and/or **email address** so that we may **arrange your appointment** with us.

Your contact details will be **stored safely.**

Personal information will not be associated with the results in any way.

You will be given a project number for the purpose of collecting and analysing data. This means you **will remain anonymous.**

The data will be **accessible only by authorised people** within the research team. Who must **follow strict ethical protocols** in the **handling and storage** of all project **data** and observe the **General Data Protection Regulation** (2018).

What if I want to take part in future research?

The consent form also has an option to take part in **further research**. **You do not have to tick this.**

If you want to be involved with future stroke rehabilitation research, your name and contact details will be available on a **secure database accessible only by members of the Acquired Brain Injury Rehabilitation Alliance** (ABIRA) here at UEA. **You can withdraw from this database at any point**.

Will my taking part in this project be kept confidential?

All data will be **anonymised so that your name will not be used in any records** made in connection with the project.

The only time that **we would pass on identifiable information** would be if **you disclosed information of a serious incident** or information that made us think that **you or someone else, was at risk of serious harm**.

If during analysis of your movement data, we identify a movement difficulty then the research team will advise you to visit your GP for medical advice.

How will my information be stored?

Fully anonymised **data** will be **stored** securely in the **research office and on password-protected computers** during the project.

Long-term data is then stored in a secure room on a password protected computer at **UEA** for **10 years after the end of the project**. After the 10 years the anonymised database will be retained on the servers of UEA for any required analysis.

All procedures for the handling, processing, storage and destruction of data are **compliant with the General Data Protection Regulation** (2018)

What will happen to the results of the research project?

The results of the project will be used to inform a subsequent investigation of the usefulness of movement measures for stroke survivors.

The anonymised results will be presented at scientific conferences, professional meetings and t scientific seminars. Anonymised results will also be published in scientific journals.

The anonymised results will also be available to participants who took part in the project and the general public by placement of the ABIRA website, the UEA website and on social media. Again, no participants will be identifiable.

The anonymised results will also form part of the PhD theses of two research students who are involved in this project.

Are there any possible risks with this project?

There are no know risks associated with taking part in this project.

What are the possible benefits of taking part?

The data we obtain from your participation will provide new knowledge about how to make measures of movement needed for every-day tasks. We do not anticipate any direct benefits for participants in this project.

We greatly appreciate the contribution of participants to this research and to future potential research which, we hope, will benefit stroke survivors

What if there is a problem?

If you have **any complaints** about the way you have been dealt with or any harm is caused during the project **this will be addressed**.

You can **contact the researchers** at any point (whose information is at the beginning of this sheet).

What if I no longer wish to continue with the project?

You may withdraw from the project **at any time** without giving a reason.

Who has reviewed this project?

This project has been reviewed extensively by experts in the research team and has been granted ethical approval by the Ethical Committee of the UEA Faculty of Medicine and Health who protect the dignity, rights, safety and well-being of participants and researchers.

Who is organising this project?

This project is organised by UEA and the Acquired Brain Injury Research Alliance (ABIRA) and is in collaboration with the creators of the Biokido motion analysis system

Thank you for taking the time to read this leaflet.

If you choose to participate, you will keep a copy of this participant information sheet and the signed informed consent form

MoveExLab COVID-19 Participant Information Sheet

Introduction

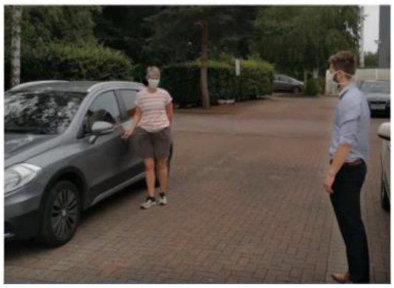
Following the COVID-19 pandemic, the way in which you participate in a research projects has changed. This document will inform you of the processes we have put in place to minimise the risk for you and ourselves. Please take your time to read this document carefully to ensure you fully understand its contents. Contact details are at the bottom of this document.

Section 1: Prior to your visit to the MoveExLab

Before visiting the MoveExLab, you will be contacted by the lead researcher of the project to assess the likelihood that you have COVID-19 or have been possibly exposed to it. In the event that there is a high possibility of you having COVID-19 your visit to the MoveExLab may be postponed. You will also be asked to bring a face covering with you so that it can be worn upon your arrival.

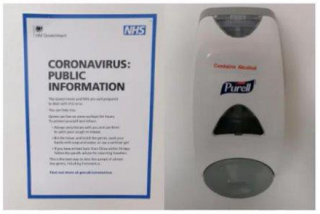
Section 2: On the day of your visit and arriving at the MoveExLab

On the day of your MoveExLab visit, you will need to follow the directions provided to you and make your way to the back of the Norwich Medical School carpark. When you have arrived, you must contact the researcher by mobile telephone to notify them of your arrival. Please wait in your car until the lead researcher has come to meet you.



Section 3: Entering the Norwich Medical School Building and MoveExLab

Once greeted by the lead researcher you will be escorted into the Norwich Medical School and the MoveExLab. Social distancing of two metres will be maintained throughout this route. As you walk through a specially designed one-way route to the MoveExLab, you will be asked to sanitise your hands using one of the many dispensers that are positioned throughout the route.



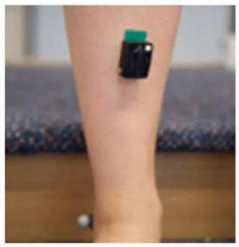
Once you have entered the MoveExLab you will be offered a range of additional Personal Protective Equipment (PPE) to wear if you want to. Hand washing practices will be implemented where necessary.

Section 4: Data Collection Process

You will be asked to change in your MoveExLab testing attire in a designated area. The testing attire will consist of either shorts or t-shirt depending on the research activities. The testing attire provided to you will have been washed in line with Government guidelines.

To reduce the number of people you have to come into contact with there will normally only be yourself and two other researchers in the MoveExLab at any one time. However, on occasions, there could be up to four researchers in the MoveExLab during your visit. The lead researcher will be in close proximity to you throughout most of the data collection process, but the other researchers will be in designated marked out (2m) areas where they will work away from you.

Where possible social distancing guidelines will be followed. For some parts of the data collection process the lead researcher will need to place markers and sensors on your skin meaning that the two metres social distancing rule cannot be maintained. The lead researcher will spend the minimal amount of time as possible doing this. To minimise the risk of infection both the lead researcher and you will be wearing PPE and hand washing practices will be implemented when skin-to-skin contact is made.



Section 6: Completion of data collection and leaving the MoveExLab

Once all the testing procedures are completed, you will change back into attire you arrived in. You will place the testing attire you have worn into the bag provided. You must continue to wear the PPE you have been provided with until you have left the MoveExLab and the Norwich Medical School Building. The lead researcher will take you back to your car using the one-way system that is in place.

Section 7: Post visit follow up.

Forty-eight hours after your visit to the MoveExLab, you will receive a phone call from the lead researcher to see if you have developed any COVID-19 symptoms.

Section 8: Contact Information

Please contact Jacob Wells on 01603 593092 or email Jacob.wells@uea.ac.uk

Appendix 12. Study Advertisement for Correlational Agreement Study (Chapter 5)

Faculty of Medicine and Health
University of East Anglia

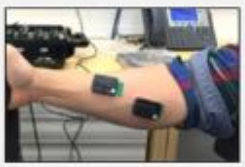
Brain recovery after stroke is a puzzle
Would you like to be part of the solution?

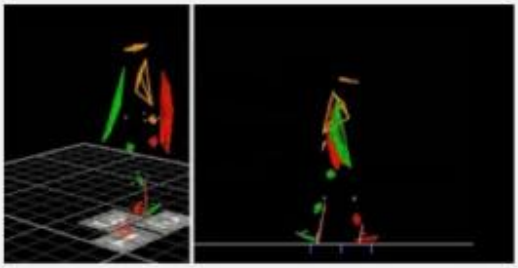
We are developing new measures of movement to find out how the brain recovers after stroke

We need healthy people to compare the measures

The measures involve answering a telephone placed on a table. First, moving from a chair to reach the table. Second, seated next to the table. We will record your movement during these tasks.

In detail we are recruiting adults who do not have any neurological or musculoskeletal condition impacting on their ability to move or have a latex allergy. This project will involve measuring your movement whilst you undertake the every-day task of picking up a telephone several times. To measure your movement, we will stick small reflective markers and sensors on your skin. No painful or intrusive methods are used. You will need to attend two 60-minute sessions in the Movement and Exercise Laboratory at the University of East Anglia.





For more information please contact:
v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk

For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
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For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk
For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk

Appendix 13. Individual Participant Characteristics in Correlation Agreement Study (Chapter 5)

Participant ID	Age at the First Session	Gender	Hand dominanance	Participant ID	Age at the First Session	Gender	Hand dominanance
PH001	57.4	Female	Left	PH039	57.2	Female	Right
PH002	50.9	Female	Right	PH040	42.8	Female	Right
PH003	42.7	Female	Right	PH041	49.8	Female	Right
PH004	21.6	Female	Right	PH042	70.8	Male	Right
PH005	47.8	Male	Right	PH043	76.4	Male	Right
PH006	20.5	Female	Right	PH044	41.2	Male	Right
PH007	40.5	Male	Right	PH045	37.0	Female	Right
PH008	33.3	Female	Right	PH046	32.3	Female	Left
PH009	23.2	Female	Right	PH047	54.9	Female	Right
PH010	52.0	Female	Left	PH048	58.3	Female	Right
PH011	25.2	Male	Right	PH049	69.7	Male	Right
PH012	46	Male	Right	PH050	35.8	Female	Right
PH013	44.8	Female	Right	PH051	53.4	Female	Right
PH014	23.9	Male	Right	PH052	73.3	Female	Right
PH015	26.3	Female	Right	PH053	68.2	Male	Right
PH016	22.3	Male	Right	PH054	46.2	Female	Right
PH017	24.3	Female	Right	PH055	28.6	Female	Right
PH018	21.8	Female	Right	PH056	26.5	Female	Right
PH019	24.8	Female	Right	PH057	50.7	Female	Right
PH020	55.6	Male	Right	PH058	80.6	Female	Right
PH021	57.5	Female	Right	PH059	65.8	Female	Left
PH022	46.9	Female	Right	PH060	55.6	Male	Right
PH023	50.0	Female	Right	PH061	60.9	Male	Right
PH024	30.3	Male	Right	PH062	49.0	Female	Right
PH025	21.8	Male	Right	PH063	41.4	Male	Right
PH026	27.0	Male	Right	PH064	62.4	Female	Left
PH027	22.8	Female	Right	PH065	63.5	Female	Right
PH028	52.4	Female	Right	PH066	41.3	Male	Right
PH029	32.6	Male	Right	PH067	71.9	Female	Right
PH030	63.3	Female	Right	PH068	67.5	Male	Right
PH031	69.3	Female	Right	PH069	56.9	Male	Right
PH032	66.4	Female	Right	PH070	85.4	Male	Right
PH033	38.3	Male	Left	PH071	27.8	Female	Right
PH034	70.1	Female	Right	PH072	60.7	Male	Right
PH035	65.8	Male	Left	PH073	36.2	Male	Right
PH036	63.3	Female	Right	PH074	36.7	Female	Right
PH037	62.4	Male	Right	PH075	29.4	Male	Left
PH038	75.0	Female	Right				

Appendix 14. Quality Check Results of the Collected Data at the First Data Collection Sessions in Correlational Agreement Study (Chapter 5)

A. All Reaching Conditions for Participants PH001-PH030

	Trial ID																		
P. ID	MDH-1	MDH-2	MDH-3	MDH-4	MDH-5	MNH-1	MNH-2	MNH-3	MNH-4	MNH-5	CDH-1	CDH-2	CDH-3	CDH-4	CDH-5	CNH-1	CNH-2	CNH-3	CNH-4	CNH-5
PH001																				
PH002																				
PH003																				
PH004																				
PH005																				
PH006																				
PH007																				
PH008																				
PH009																				
PH010																				
PH011																				
PH012																				
PH013																				
PH014											No Extracted THDR Data (Flickering T10 Marker)	No Extracted THDR Data (Flickering T10 Marker)	No Extracted THDR Data (Flickering T10 Marker)		No Extracted THDR Data (Flickering T10 Marker)			No Extracted Variables (No Buzzer		
PH015																				
PH016	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No EMG Data (Noisy Signals)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No EMG Data (Noisy Signals)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No EMG Data (Noisy Signals)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No EMG Data (Noisy Signals)
PH017																				
PH018				No Kinematic Data (Problematic Kinematic Model); Only MAOT Data Available							No Kinematic Data (Problematic Kinematic Model); Only MAOT Data Available	No Kinematic Data (Problematic Kinematic Model); Only MAOT Data Available		No Kinematic Data (Problematic Kinematic Model); Only MAOT Data Available	No Kinematic Data (Problematic Kinematic Model); Only MAOT Data Available					
PH019		No EMG Data (Noisy Signals)																		
PH020																				
PH021																				
PH022																				
PH023																				
PH024																				
PH025																				
PH026																				
PH027																				
PH028																				
PH029																				
PH030																				

Note: P. ID: Participant Identification Number; **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand; **EMG:** Electromyography; **MAOT:** Muscle Activity Onset Time; **THDR:** Trunk-Hand Displacement Ratio.

High-Quality Data: Trial with all variables extracted

Unusable: No variable could be extracted

Partial Data: Trials with some variables missing

No Recorded Trial

B. All Reaching Conditions for Participants PH031 -PH075

P. ID	Trial ID																		
	MDH-1	MDH-2	MDH-3	MDH-4	MDH-5	MNH-1	MNH-2	MNH-3	MNH-4	MNH-5	CDH-1	CDH-2	CDH-3	CDH-4	CDH-5	CNH-1	CNH-2	CNH-3	CNH-4	CNH-5
PH031																				
PH032																				
PH033																				
PH034																				
PH035																				
PH036																				
PH037																				
PH038																				
PH039																				
PH040																				
PH041																				
PH042																				
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PH050																				
PH051																				
PH052																				
PH053																				
PH054																				
PH055																				
PH056																				
PH057																				
PH058													No EMG Data from the BB Muscle (Noisy Signals)			No EMG Data (Noisy Signals)				
PH059																				
PH060																				
PH061																				
PH062																				
PH063																				
PH064																				
PH065																				
PH066																				
PH067																				
PH068																				
PH069																				
PH070																				
PH071																				
PH072																				
PH073																				
PH074																				
PH075																				

Note: P. ID: Participant Identification Number; **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand; **EMG:** Electromyography; **BB:** Biceps Brachii; **ECR:** Extensor Carpi Radialis.

High-Quality Data: Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

Appendix 15. Quality Check Results of the Collected Data at the Second Data Collection Sessions in Correlational Agreement Study (Chapter 5)

A. All Reaching Conditions for Participants PH001-PH030

P. ID	Trial ID																			
	MDH-1	MDH-2	MDH-3	MDH-4	MDH-5	MNH-1	MNH-2	MNH-3	MNH-4	MNH-5	CDH-1	CDH-2	CDH-3	CDH-4	CDH-5	CNH-1	CNH-2	CNH-3	CNH-4	CNH-5
PH001																				
PH002																				
PH003																				
PH004																				
PH005																				
PH006																				
PH007																				
PH008																				
PH009																				
PH010																				
PH011																				
PH012																				
PH013		No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)		No Extracted Variables (No Buzzer Data)		No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)		No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)	No Extracted Variables (No Buzzer Data)
PH014																				
PH015																				
PH016																				
PH017																				
PH018	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)	No EMG Data (Noisy Signals)
PH019	WITHDREW																			
PH020																				
PH021																				
PH022																				
PH023																				
PH024																				
PH025																				
PH026																				
PH027																				
PH028																				
PH029																				
PH030																				

Note: P. ID: Participant Identification Number; **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand; **EMG:** Electromyography.

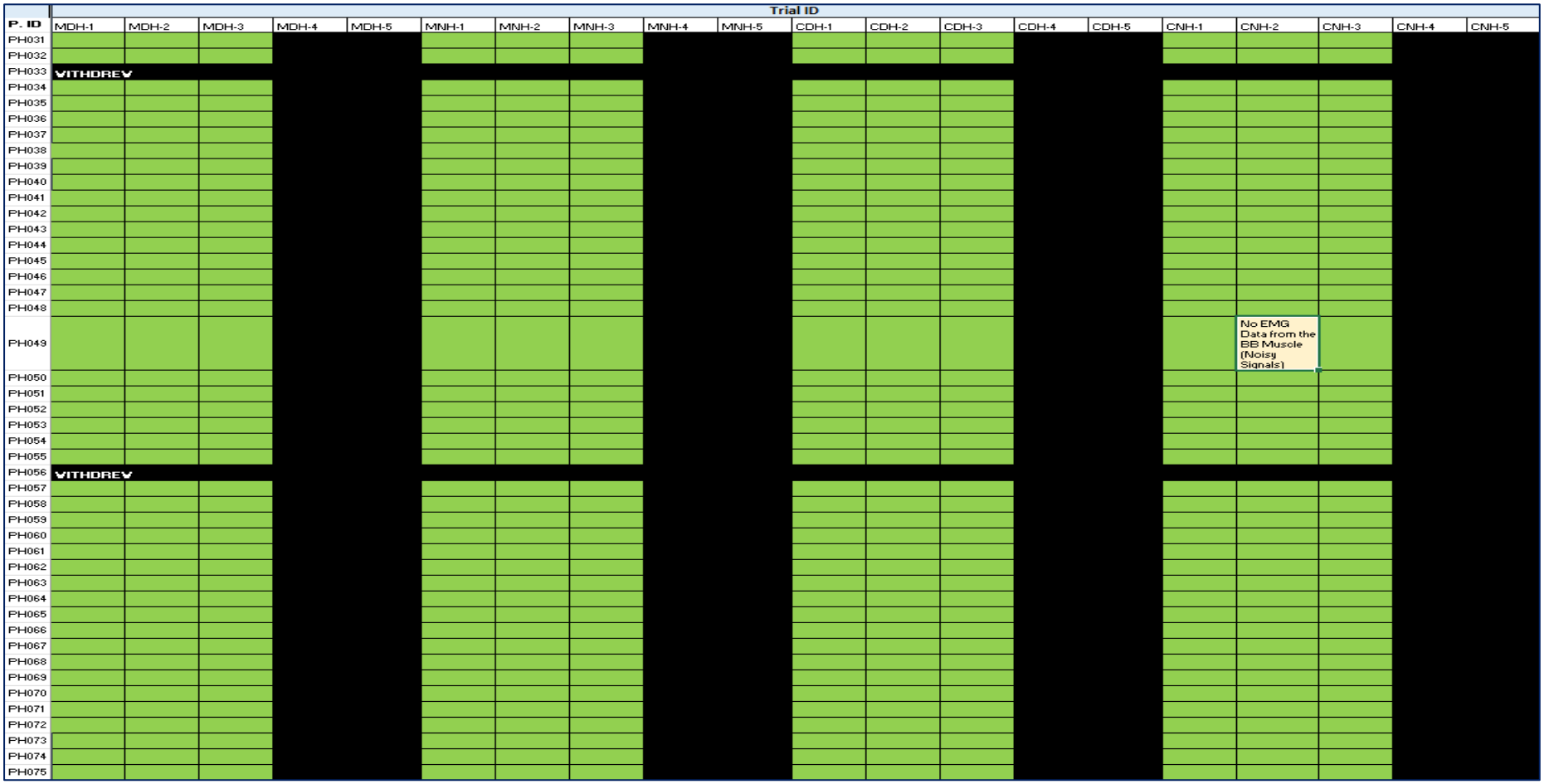
High-Quality Data: Trial with all variables extracted

Unusable: No variable could be extracted

Partial Data: Trials with some variables missing

No Recorded Trial

B. All Reaching Conditions for Participants PH031-PH075

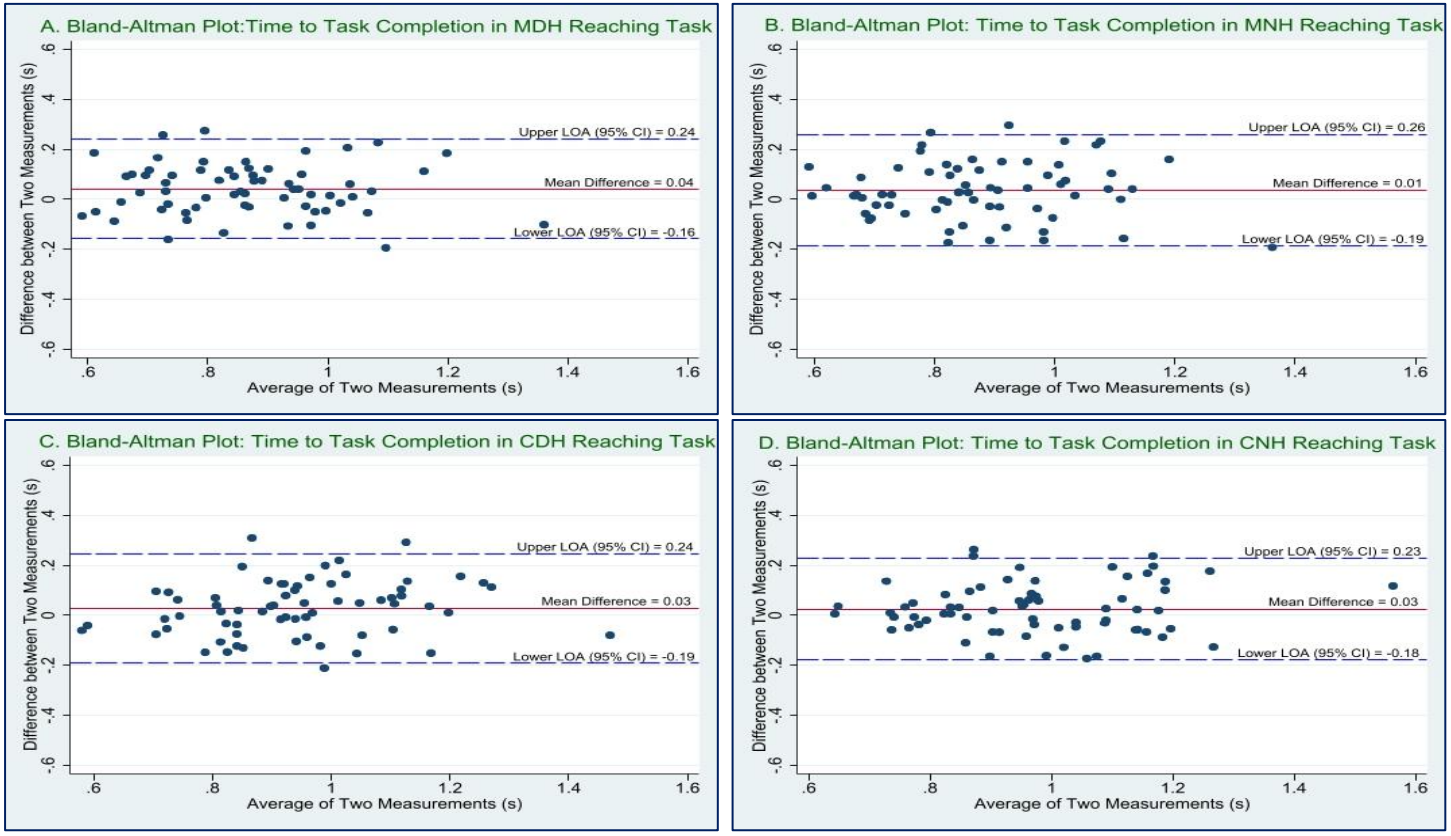


Note: P. ID: Participant Identification Number; **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand; **EMG:** Electromyography; **BB:** Biceps Brachii.

High-Quality Data: Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

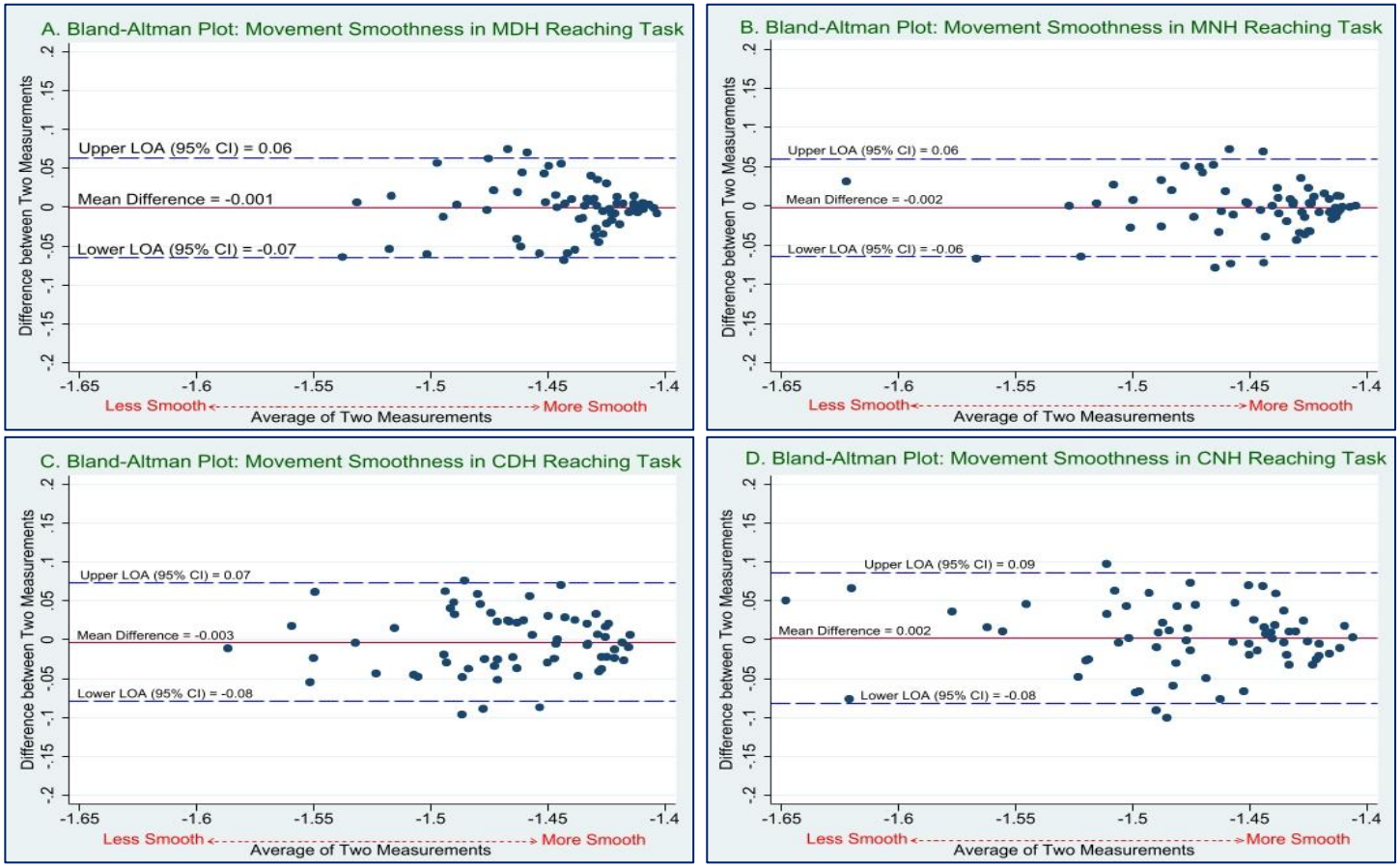
Appendix 16. Sensitivity Analyses in the Bland-Altman Plots

Figure 1. Sensitivity Analyses: Bland-Altman Plots of Time to Task Completion (TTC) Variable Excluding Outliers for Each Individual Reaching Task



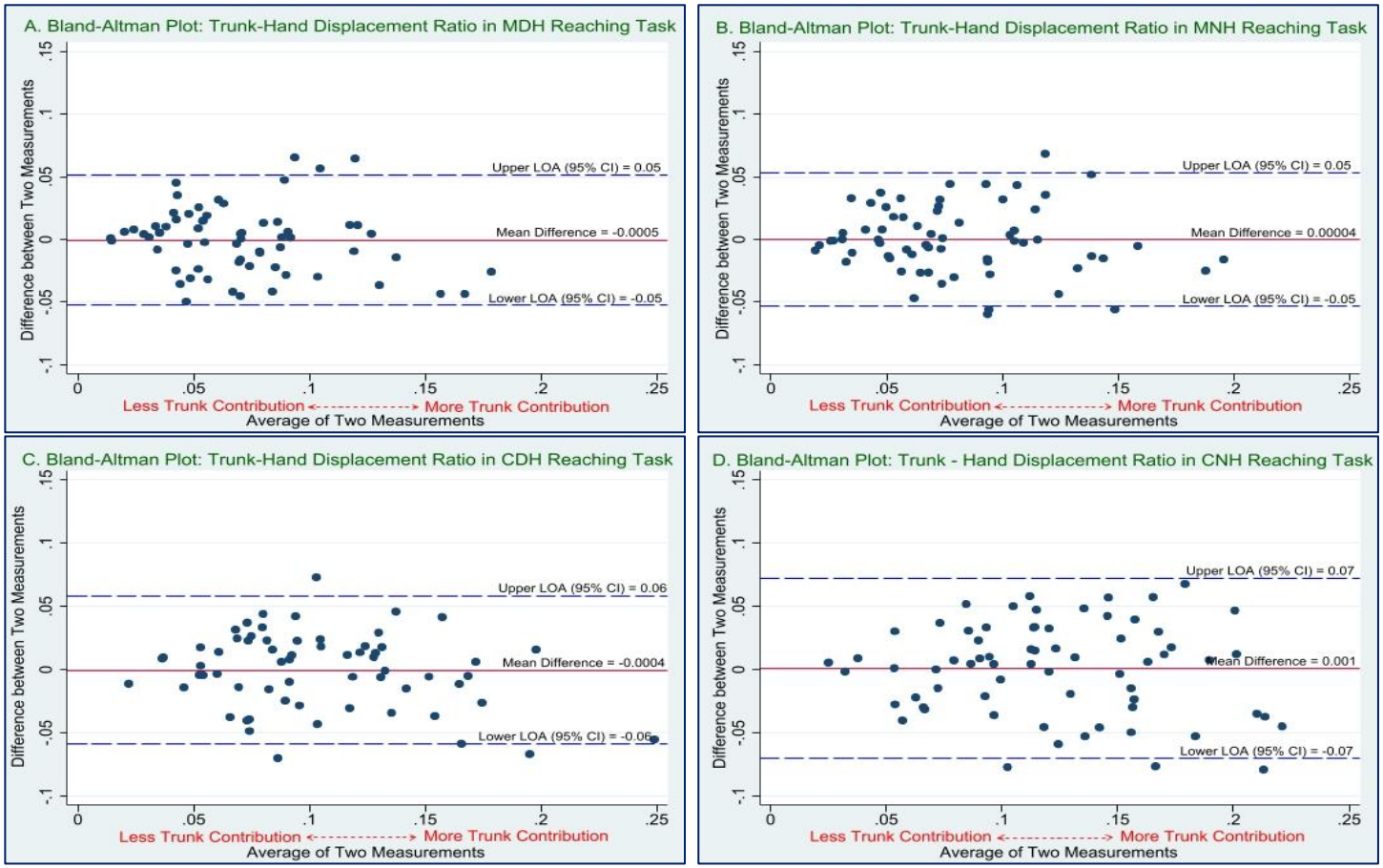
Notes: These plots show the consistency of the 'Time to Task Completion (TTC)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Higher averages on the x-axis correspond to longer TTCs. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH022, PH026, PH028, PH035, PH039, PH068; (B) MNH: PH012, PH017, PH022, PH068, PH074; (C) CDH: PH022, PH026, PH028, PH035, PH039, PH068; (D) CNH: PH012, PH022, PH067.

Figure 2. Sensitivity Analyses: Bland-Altman Plots of Movement Smoothness (MS) Variable Excluding Outliers for Each Individual Reaching Task



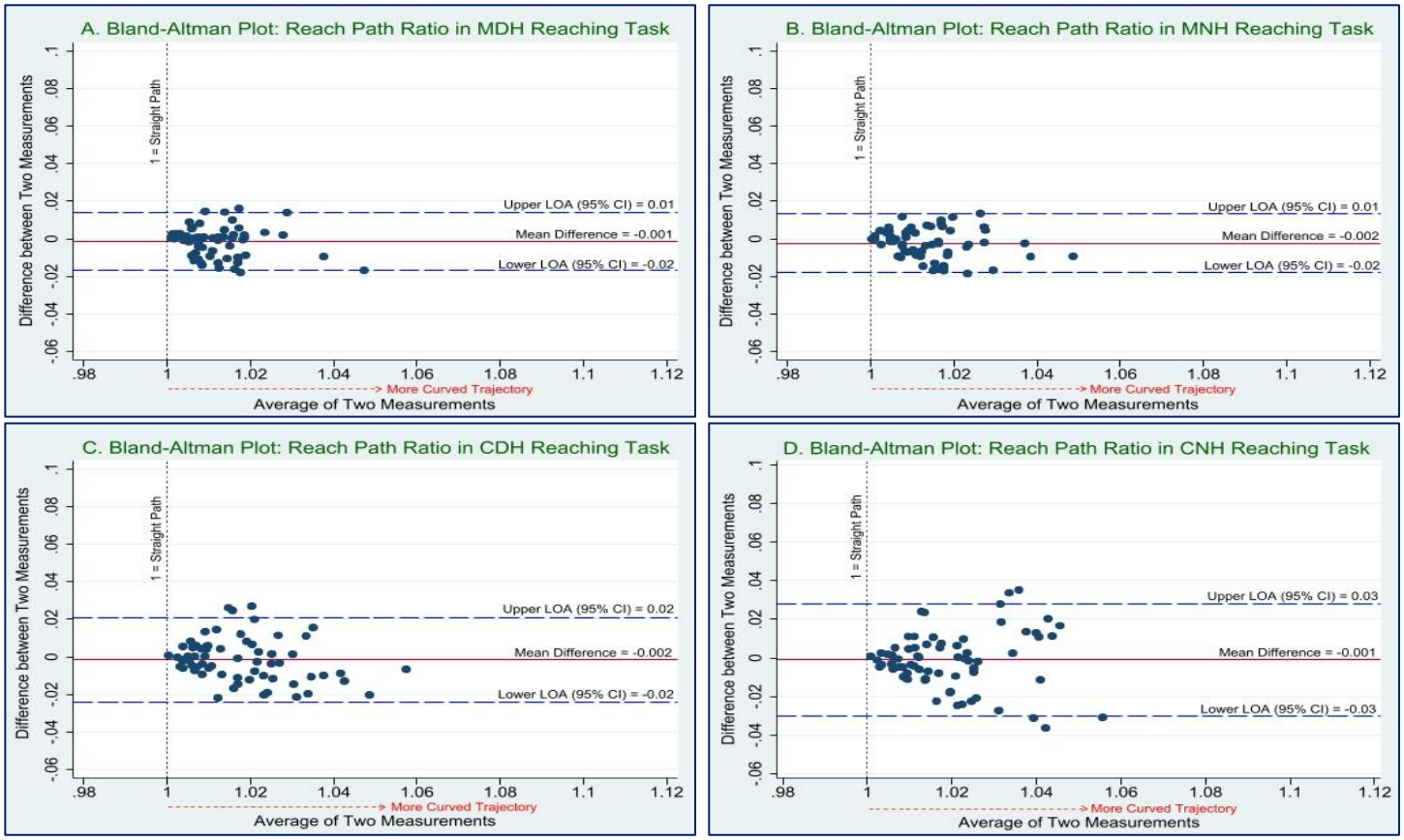
Notes: These plots show the consistency of the 'Movement Smoothness (MS)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Lower averages on the x-axis correspond to less smooth movements. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH020, PH046, PH049, PH061; (B) MNH: PH001, PH011, PH037, PH042, PH066; (C) CDH: PH003, PH049, PH070, PH074; (D) CNH: PH012, PH028, PH036, PH038, PH054.

Figure 3. Sensitivity Analyses: Bland-Altman Plots of Trunk-Hand Displacement Ratio (THDR) Variable Excluding Outliers for Each Individual Reaching Task



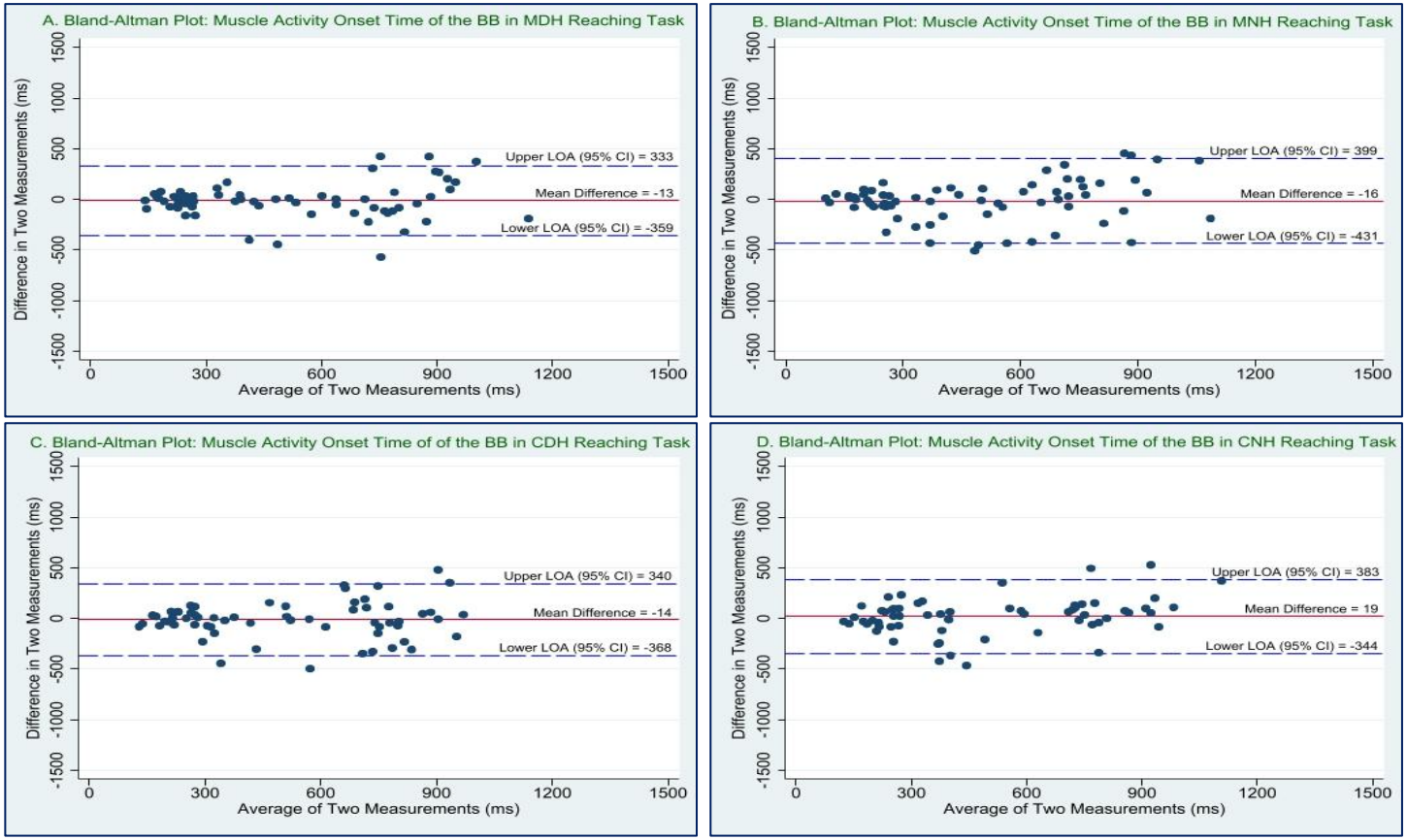
Note: These plots show the consistency of the 'Trunk-Hand Displacement Ratio (THDR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis indicate more trunk movement in relation to the hand. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH001, PH005, PH043, PH049, PH075; (B) MNH: PH001, PH005, PH010, PH012, PH049; (C) CDH: PH001, PH005, PH049, PH062, PH065; (D) CNH: PH001, PH005, PH062.

Figure 4. Sensitivity Analyses: Bland-Altman Plots of Reach Path Ratio (RPR) Variable Excluding Outliers for Each Individual Reaching Task



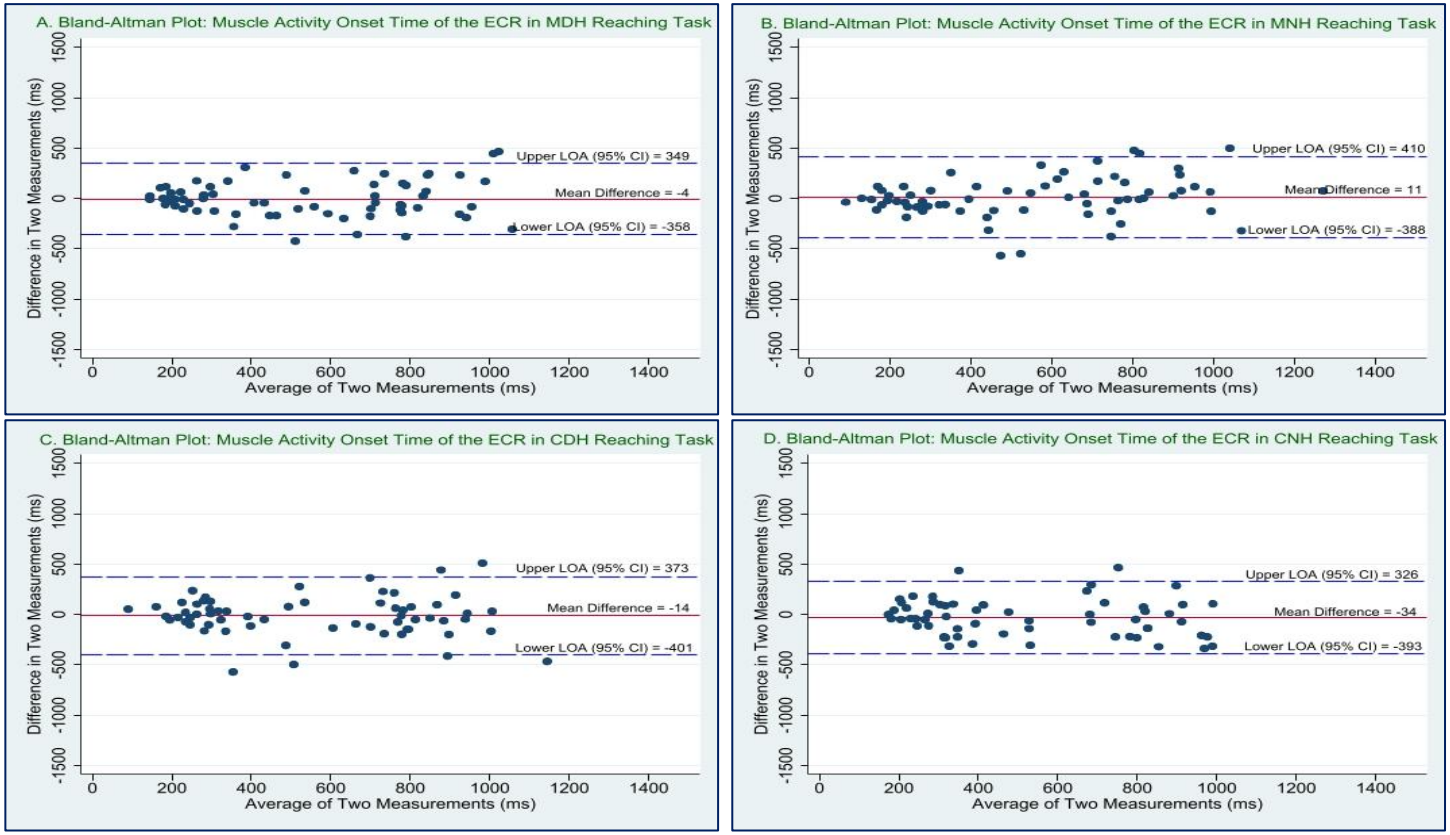
Note: These plots show the consistency of the 'Reach Path Ratio (RPR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. An average of '1' on the x-axis indicates a straight path towards the target. Here, the target is the phone. Greater averages on the x-axis indicate a more curved trajectory. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH017, PH042, PH059, PH075; (B) MNH: PH012, PH017, PH058, PH059; (C) CDH: PH002, PH015, PH059, PH062; (D) CNH: PH062, PH070.

Figure 5. Sensitivity Analyses: Bland-Altman Plots of Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB) Variable Excluding Outliers for Each Individual Reaching Task



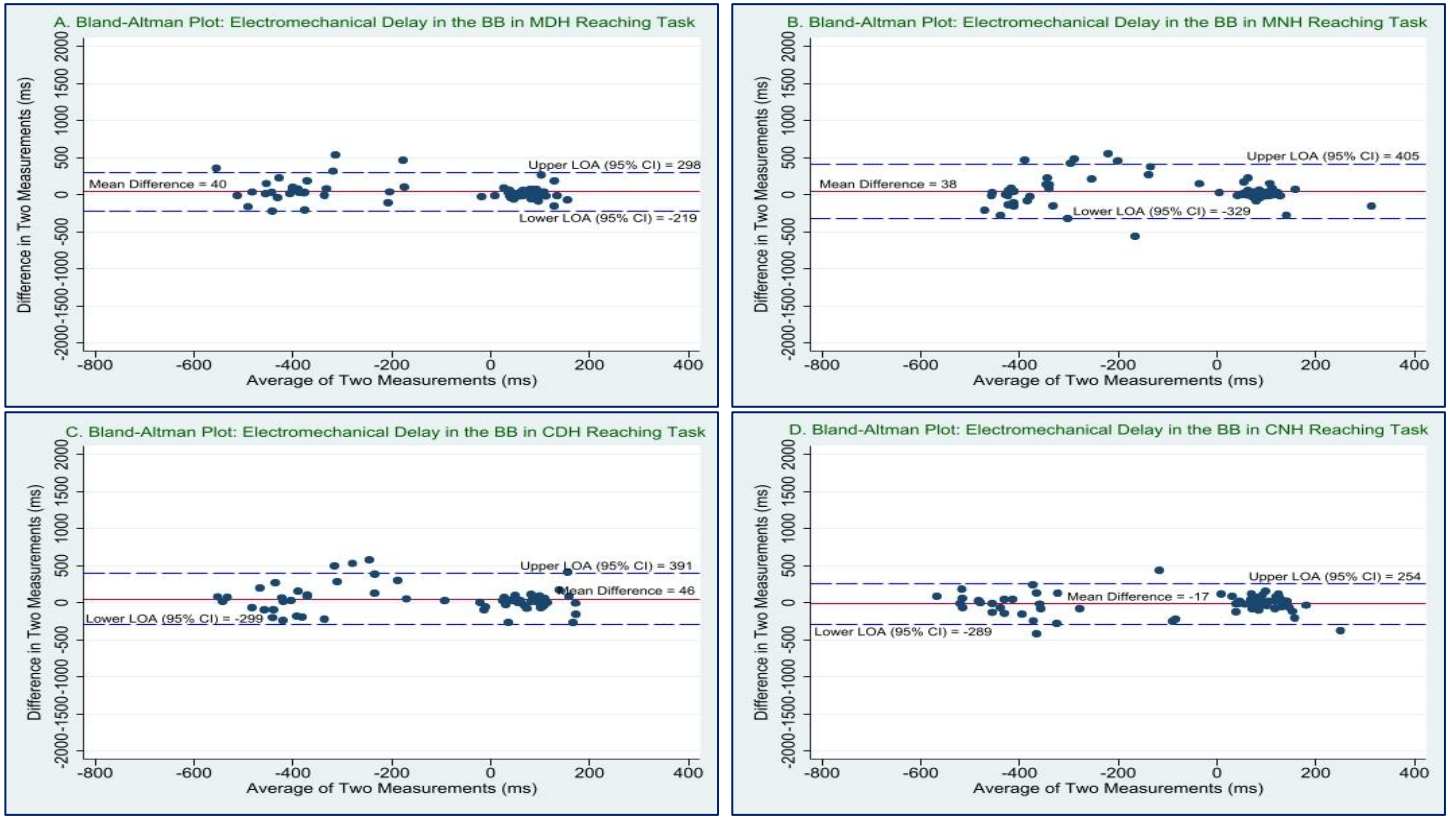
Note: These plots show the consistency of the 'Muscle Activity Onset Time (MAOT) of the Biceps Brachii (BB)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis correspond to later muscle activity onset. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH011, PH022, PH065, PH066; (B) MNH: PH011, PH066; (C) CDH: PH011, PH022, PH064, PH065, PH066; (D) CNH: PH011, PH022, PH023, PH065, PH066.

Figure 6. Sensitivity Analyses: Bland-Altman Plots of Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR) Variable Excluding Outliers for Each Individual Reaching Task



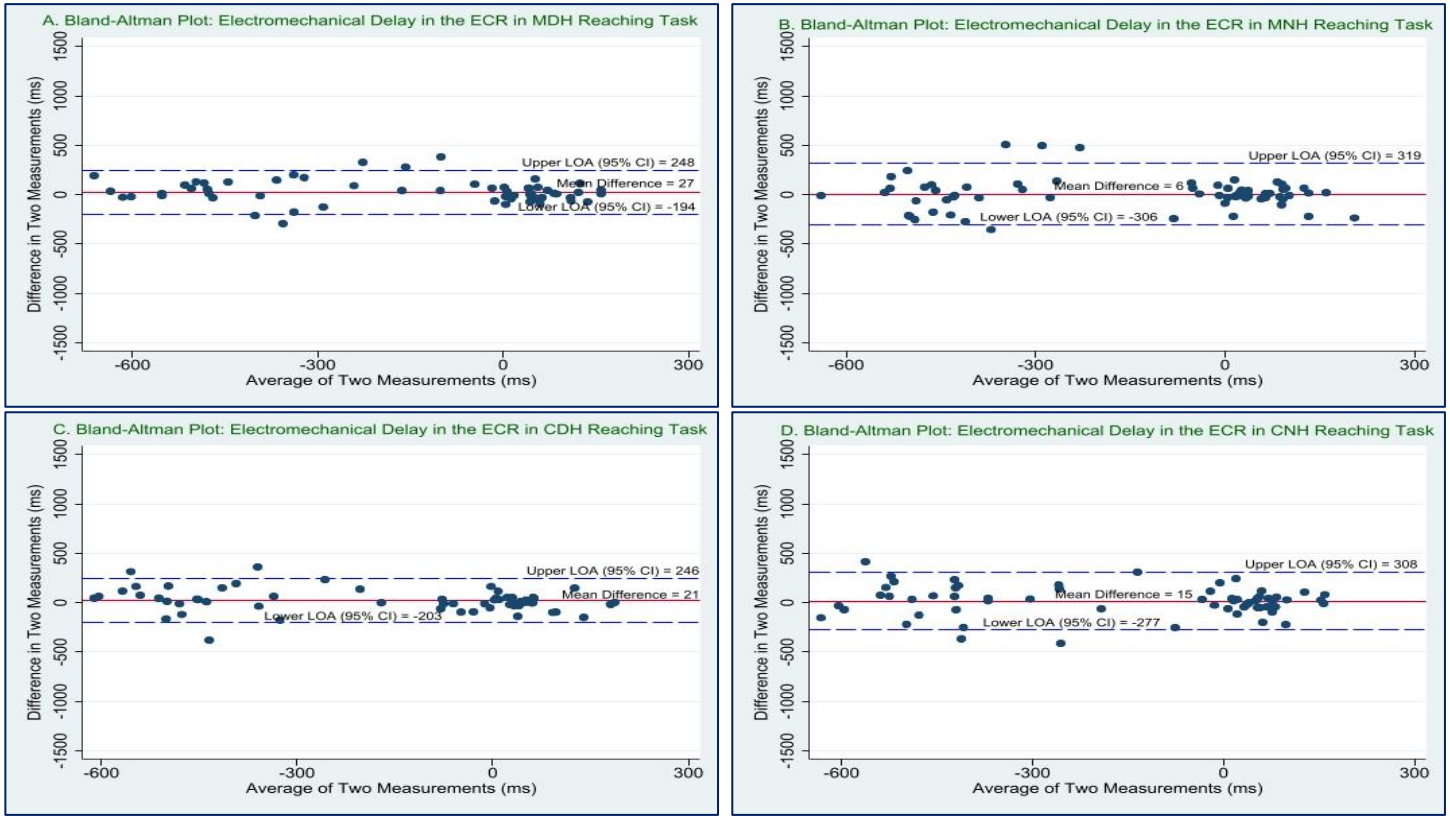
Note: These plots show the consistency of the 'Muscle Activity Onset Time (MAOT) of the Extensor Carpi Radialis (ECR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Greater averages on the x-axis correspond to later muscle activity onset. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH011, PH022, PH064, PH065; (B) MNH: PH011, PH066; (C) CDH: PH008, PH011, PH022, PH064, PH065, PH066; (D) CNH: PH003, PH011, PH017, PH022, PH030, PH064, PH065, PH066.

Figure 7. Sensitivity Analyses: Bland-Altman Plots of Electromechanical Delay (EMD) in the Biceps Brachii (BB) Variable Excluding Outliers for Each Individual Reaching Task



Note: These plots show the consistency of the 'Electromechanical Delay (EMD) in the Biceps Brachii (BB)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Positive averages suggest muscle activity onset before hand movement, while negative averages indicate the opposite. Smaller positive averages indicate a shorter time interval between muscle activity onset and movement onset. Smaller negative averages suggest a longer delay in muscle activity after the hand movement. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH011, PH014, PH065, PH066; (B) MNH: PH011, PH066; (C) CDH: PH011, PH014, PH064, PH066; (D) CNH: PH023, PH065, PH066, PH067, PH068.

Figure 8. Sensitivity Analyses: Bland-Altman Plots of Electromechanical Delay in the Extensor Carpi Radialis Variable Excluding Outliers for Each Individual Reaching Task



Note: These plots show the consistency of the 'Electromechanical Delay (EMD) in the Extensor Carpi Radialis (ECR)' measurements across two sessions. Differences between the two measurements (y-axis) were plotted against their averages (x-axis). The red line indicates the mean difference (bias). The dashed lines denote the 95% Limits of Agreement. Positive averages suggest muscle activity onset before hand movement, while negative averages indicate the opposite. Smaller positive averages indicate a shorter time interval between muscle activity onset and movement onset. Smaller negative averages suggest a longer delay in muscle activity after the hand movement. The plots suggest that the variability in measurements is due to random error. **MDH:** Midline Dominant Hand; **MNH:** Midline Non-Dominant Hand; **CDH:** Contralateral Dominant Hand; **CNH:** Contralateral Non-Dominant Hand. **Outliers Excluded from Plots:** (A) MDH: PH003, PH011, PH014, PH064, PH065; (B) MNH: PH011, PH064, PH066; (C) CDH: PH008, PH014, PH064, PH065, PH066, PH067; (D) CNH: PH017, PH064, PH065, PH066.

Appendix 17. Ethical Approval with the Reference Number: 2020/21-028

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Prof Valerie Pomeroy
School of Health Sciences
University of East Anglia
Norwich Research Park
Norwich
NR4 7TJ

NORWICH MEDICAL SCHOOL
Bob Champion Research & Educational Building
Rosalind Franklin Road
University of East Anglia
Norwich Research Park
Norwich NR4 7UQ

Email: fmh.ethics@uea.ac.uk
www.med.uea.ac.uk

26th November 2020

Dear Val

Project Title: Relationship between neuromuscular recovery, functional ability and sleep after stroke, and, criterion validity of measures made by the Vicon and Biokido motion analysis systems

Reference: 2020/21-028

Your resubmission was considered by the Faculty Research Ethics Committee at their meeting on 26th November 2020 and I can confirm that your proposal has been approved.

Please can you ensure that any amendments to either the protocol or documents submitted are notified to us in advance, and that any adverse events which occur during your project are reported to the Committee.

Approval by the FMH Research Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Please could you also arrange to send us a report once your project is completed.

Yours sincerely

Dr Jackie Buck
Chair
FMH Research Ethics Committee

COVID-19: The FMH Research Ethics Committee procedures remain as normal. Please note that our decisions as to the ethics of your application take no account of changes in Government measures and UEA guidelines relating to the coronavirus pandemic and all approvals granted are, of course, subject to these.

University of East Anglia

Prof Valerie Pomeroy
School of Health Sciences
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Email: fmh.ethics@uea.ac.uk
www.med.uea.ac.uk

17th February 2021

Dear Val

Project Title: Relationship between neuromuscular recovery, functional ability and sleep after stroke, and, criterion validity of measures made by the Vicon and Biokido motion analysis systems

Reference: 2020/21-028

Thank you for your email of 5th February 2021 notifying us of the amendments you would like to make to your above proposal. These have been considered and I can confirm that your amendments have been approved.

Please can you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance, and that any adverse events which occur during your project are reported to the Committee.

Approval by the FMH Research Ethics Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Please can you arrange to send us a report once your project is completed.

Yours sincerely

Dr Jackie Buck
Chair
FMH Research Ethics Committee

COVID-19: The FMH Research Ethics Committee procedures remain as normal. Please note that our decisions as to the ethics of your application take no account of changes in Government measures and UEA guidelines relating to the coronavirus pandemic and all approvals granted are, of course, subject to these.

Appendix 18. Participant Information Sheet for Observational Cohort Study (Chapter 6)

University of East Anglia

University of East Anglia

abira linking research & practice

Relationship between neuromuscular recovery, functional ability and sleep after stroke, and, criterion validity of measures made by the Vicon and Biokido motion analysis systems

Information Sheet for potential volunteers

Researchers from the University of East Anglia (UEA) extend an invitation for you to take part in a research project.

We are investigating how physiotherapy can be directed at the biological underpinnings of movement to improve recovery after stroke. These biological underpinnings are called neuromuscular function. Neuromuscular function includes: the ability to use weak muscles in the right order and at the right time during movement and performing everyday tasks such as answering the telephone in the same way as you did before the stroke. Also being investigated is whether sleep patterns may influence recovery of neuromuscular function

We are also developing measures of the movement needed for the everyday activity of answering the telephone. Our purpose is to provide new measures for finding out how the brain recovers after stroke and how physiotherapy may be focused at the biological underpinnings of movement recovery after stroke.

You do not have to take part if you do not want to.

Talk about the project with others if you would like to.

If you need more information, please ask the researcher, Valerie Pomeroy at UEA. Or get in touch with her personal assistant: Pel Fordham. Both of them will be happy to answer your questions. Their contact information is at the bottom of this page.

Thank you for reading this information and for considering taking part in this project.

Contact Details

Researcher's name: Professor Valerie Pomeroy
Email: v.pomeroy@uea.ac.uk **Phone:** 01603 59 1923

Researcher's personal assistant: Pel Fordham
Email: p.fordham@uea.ac.uk **Phone:** 01603 59 **1923**

What is the purpose of this project?

There is strong evidence that physiotherapy improves the ability of people to move and be independent after suffering a stroke. But at six months after stroke many people remain unable to produce the movement needed for every-day activity such as answering a telephone. This situation could be improved by using physiotherapy interventions to aid the recovery of movement after stroke and changing an individual's sleep pattern. It is therefore important to be able to recognise if a physiotherapy intervention is aiding movement recovery for stroke survivors to enable them to undertake every-day activity. This requires a deeper knowledge of the biological underpinnings of movement called neuromuscular function. This project will provide the required knowledge by using the specialised equipment in the Movement and Exercise Laboratory at the University of East Anglia.

However, if movement measures are to be used routinely in clinical practice then relying on specialist facilities such as the Movement and Exercise Laboratory (MoveExLab) will not be practical. This equipment is expensive and can only be used in large specialised laboratories So, this project will find out if new equipment, that costs less and is designed for use in small spaces, also provides movement measures that are sensitive to change. This is important as most stroke rehabilitation takes place in people's own homes.

This project will identify the aspects of neuromuscular function that may be targeted by physiotherapy treatment to improve movement recovery. It will also inform knowledge of the sleep patterns that are beneficial for movement recovery after stroke. This project will also find out if the

movement measures can be made equally as well with new equipment, called Biokido, that is more suitable for use in everyday routine rehabilitation.

Am I eligible to take part in this project?

You are potentially eligible to participate if:

- You are aged 18 or above and
- You have had a stroke at any point in the past
- You are discharged from NHS stroke services
- You do not have an allergy to latex

If you are interested, then I (Valerie Pomeroy) would like to talk to you about if you can be involved in this project. My contact details and those of my personal assistant are provided on page 1 of this leaflet.

Do I have to take part?

No, you do not have to take part.

It is entirely up to you to decide. If you would prefer not to take part, that is OK. If you do take part, **you may withdraw at any time without giving a reason.**

If you do withdraw, we can only destroy your data up to the point they are anonymised. After that point, it will not be possible to separate your data.

What will I have to do if I am interested?

If you are able to take part in the project, then we will invite you to attend the Movement and Exercise Laboratory at the University of East Anglia (MoveExLab) for some assessments at a time of your convenience. All necessary travel will be reimbursed up to a maximum of a 50-mile return

journey. We can arrange a pre-paid taxi return journey if you wish us to do so. Other than reimbursement of travel expenses there is no payment for taking part in this project.

What will I have to do if I take part?

You will be invited to undertake two assessments at the MoveExLab. These assessments will be between 2 and 4 months apart depending on your preference. The assessments will take **around 90 minutes** to complete at **the MoveExLab** (picture on right of this paragraph). Y**ou may stop at any time**. **Some of the measures are undertaken by you in your own home.**

We have put in place additional procedures to **keep you and us as safe as possible during the COVID-19 pandemic**. Before you arrive at the MoveExLab we will send you an additional information sheet and the URL to a video explaining the additional procedure that meets the requirements of our UEA-approved risk assessment. The **additional information is provided for you as an appendix at the end of this project information sheet**. **The video can be viewed using this link:** http://www.abira.ac.uk/about-abira/research-facilities/. Both the COVID-19 information sheet and video have received ethical approval by the UEA Faculty of Medicine and Health Sciences Ethical Committee.

When you arrive at the MoveExLab to undertake the assessment session you will undertake activities in the following order. You will have **rest periods as and when you need them**.

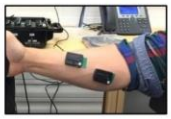
First: We will ask you to **fill in a form** to gather demographic data. We will also ask questions about any allergies you have to ensure that you are unlikely to have any reactions from sticky tape and other materials in the MoveExLab. If you do have allergies, e.g. to sticky tape, then we can adjust the materials we use for testing or aspects of the MoveExLab environment. However, if you have an allergy to latex then we are unable to make adjustments and you will be unable to take part.

Second: We will ask you to change into shorts and a sleeveless T-shirt in a curtained-off private changing area. This clothing is freshly laundered at 60°C for each participant. We will also ask you to take off your socks. You keep your shoes on. The shoes you need to wear are a walking shoe

(not hiking boot) or a trainer without reflective strips. You will need to wear the same shoes for both of your visits to the MoveExLab.

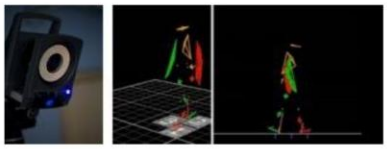
We will then measure your height and weight. Then we will measure your body size e.g. the width of your hands and length of your legs. These measurements are needed by the motion analysis software to produce the movement measures.

Third: We will place electromyography (EMG) electrodes on your skin using hypoallergenic sticky tape. These EMG electrodes will measure your muscle activity as you move. The picture on the right shows the EMG electrodes in place. These EMG electrodes do not hurt. They just record your natural muscle activity during movement.

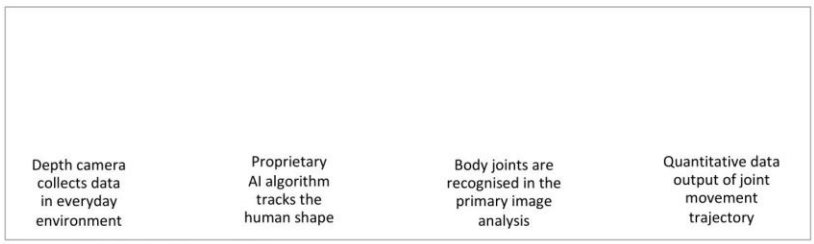


We will also place reflective markers on your skin using hypoallergenic sticky tape. These markers are tracked by infra-red cameras placed at the top of the walls of the MoveExLab. On the right of this text is a picture to illustrate these reflective markers in place. These markers do not hurt. They just record movement of your body.

Fourth: You will be asked to stand still in the middle of the MoveExLab. You will have support if you need it. The eight infra-red cameras placed around the top of the walls will record the light signals from the reflective markers on your body. The motion analysis software will then use the collected information to calibrate your body in the space in which you are going to move. Placed at the right of this paragraph is a photograph of one infra-red camera and examples of the 'pictures' of movement captured.



Your movement will also be 'captured' by a new motion analysis system called the Biokido Motion Analysis system. The Biokido motion analysis system is illustrated in the pictures placed at the bottom of this page. The system



consists of a depth camera and a portable computer with specialist software. The system is fully portable and can be used in small spaces. Therefore, if the measures made with the Biokido system agree with those made by the MoveExLab system then it may be placed in clinical settings for routine measures that are unable to be made now.

Fifth: **You will be seated with a telephone placed on a table 3-metres in front of you. Your task will be to go and answer the telephone when you hear a buzzer.** You will be instructed in exactly what to do and given time to practice. When you are confident in doing this task, we will record your movement and muscle activity whilst you do it. You will repeat this task until the technician tells you that there are 10 trials which have reconstructed well on the computer. Please note that most trials reconstruct well so it is unlikely that you will have to do this task more than 10 times. The maximum number of times we will ask you to complete this task will be 15 if there are problems with computer reconstruction. And please be assured that if you become tired that you will be provided with sufficient rest time between trials or we will reduce the number of trials for you.

Sixth: **You will stay seated and we will bring the table in front of you so that you can rest your forearm on it. Your task will be to answer the telephone placed directly in front of you, with your weaker hand, when you hear the buzzer**. You will be instructed in exactly what to do and given time to practice. When you are confident in doing this task, we will record your movement and muscle activity whilst you do it. You will repeat this task until the technician tells you that there are 10 trials which have reconstructed well on the computer. Then you will do another 10 trials with the telephone on the left of the table. Followed by 10 trials with the telephone on the right of the table. Please note that most trials reconstruct well so it is unlikely that you will do more than 10 trials of each part of this task. The maximum number of times we will ask you to complete this task will be 45 if there are problems with computer reconstruction. And please be assured that if you become tired that you will be provided with sufficient rest time between trials or we will reduce the number of trials for you.

Seventh: You will then be seated in a chair at one end of the MoveExLab whilst the researchers move the plinth from the middle of the space. **You will stand up from the chair, get your balance and then be asked to walk forwards** to the other end of the MoveExLab**. You will only walk as far as you can safely without any support** from a walking aid or another person**. If you cannot walk without support, you will not do this assessment.** You will do 10 walks if you can.

Eighth: We will **remove EMG electrodes and reflective markers** that were placed on your skin. The sticky tape is similar to a sticking plaster. Most people do not experience any discomfort. Then you will undertake some **clinical measures** called the Fugl-Meyer Assessment and the Action Research Arm Test. These involve **assessment of your: reflexes, joint mobility and ability to pick up small objects with your weaker hand.**

Ninth: You will then **change back into your normal clothes** in the curtained-off private changing area.

Tenth: Once you have changed back into your normal clothes you will complete some **short questionnaires** to assess: your **mood, how well you sleep, and how active you are each day**. Please note that **if you are tired** then it is possible for you to **complete many of these questionnaires at home**.

Eleventh: The Researcher will then provide you with a **sleep diary to record how well you sleep each day**. You will **take this home with you**. The Researcher will also **give you two motion watches, one for each wrist**. You will be given an **instruction leaflet** for using the motion watches for a 7-day period. This instruction leaflet is provided as an appendix at the end of this information sheet. You will be provided with a stamped addressed padded envelope to post us the motion watches after the 7-day period.

The assessment is then completed.

The **Researcher will keep in touch with you** by telephone and email **in the time in-between your first and second visits**. **You will also be able to contact the Researcher**. The Researcher will be able to **help you if you have any challenges in using the sleep diary or motion watches**. Also, the Researcher will liaise with you to fix a suitable time for you to attend he MoveExLab for your second visit.

What will happen to my information?

Information will include your **age, gender and ethnicity**.

We will also store personal information such as your **telephone number** and/or **email address** so that we may **arrange your appointments** with us and **keep in contact with you during your period of taking part in this study**.

Your contact details will be **stored safely.**

Personal information will not be associated with the results in any way.

You will be given a project number for the purpose of collecting and analysing data. This means you **will remain anonymous.**

The data will be **accessible only by authorised people** within the research team. Who must **follow strict ethical protocols** in the **handling and storage** of all project **data** and observe the **General Data Protection Regulation** (2018).

What if I want to take part in future research?

The consent form also has an option to take part in **further research**. **You do not have to tick this.**

If you want to be involved with future stroke rehabilitation research, your name and contact details will be available on a **secure database accessible only by members of the Acquired Brain Injury Rehabilitation Alliance** (ABIRA) here at UEA. **You can withdraw from this database at any point**.

Will my taking part in this project be kept confidential?

All data will be **anonymised so that your name will not be used in any records** made in connection with the project.

The only time that **we would pass on identifiable information** would be if **you disclosed information of a serious incident** or information that made us think that **you or someone else, was at risk of serious harm**.

If during the study, we identify a potential health problem then the research team will advise you to visit your GP for medical advice.

How will my information be stored?

Fully anonymised **data** will be **stored** securely in the **research office** (paper versions of forms) **and on password-protected computers** (digital versions of forms) during the project. This includes all forms completed during data collection. These data will only be accessible to the UEA members of the research team (see last page of this leaflet).

Until the end of the project we will store your contact details separately to the fully anonymised data. Your contact details data will be stored **securely on a password-protected secure section of the UEA server**. Contact details data will only be accessible to Professor Pomeroy (Chief Investigator), Canan Yuksel (PhD student) and Merve Kizilay (PhD student). **Your contact details for this project will be kept for one year after completion of the data collection and then destroyed.**

Long-term data will be stored in a secure room on a password protected computer at **UEA** for **10 years after the end of the project**. After the 10 years, only the anonymised database will be retained on the secure servers of UEA for any required analysis.

All procedures for the handling, processing, storage and destruction of data are **compliant with the General Data Protection Regulation** (2018)

What will happen to the results of the research project?

The results of the project will be used to inform subsequent investigations of how to improve the effects of physiotherapy treatment and understand more about how neuromuscular recovery happens after stroke.

The anonymised results will be presented at scientific conferences, professional meetings and scientific seminars. Anonymised results will also be published in scientific journals.

The anonymised results will also be available to participants who took part in the project and the general public by placement of the ABIRA website, the UEA website and on social media. Again, no participants will be identifiable.

The anonymised results will also form part of the PhD theses of two research students who are involved in this project.

Are there any possible risks with this project?

There are no know risks associated with taking part in this project.

What are the possible benefits of taking part?

The data we obtain from your participation will provide new knowledge about how to improve stroke rehabilitation. We do not anticipate any direct benefits for participants in this project.

We greatly appreciate the contribution of participants in this research and to future potential research which, we hope, will benefit stroke survivors in the future.

What if there is a problem?

If you have **any complaints** about the way you have been dealt with or any harm is caused during the project **this will be addressed**.

You can **contact the researchers** at any point (whose information is at the beginning of this sheet).

If you have a complaint about this project please contact: Professor Sally Hardy, Dean of Health Sciences, Queen's Building, University of East Anglia, Norwich Research Park, Norfolk, NR4 7TJ. Tel: 01603 593940. E-mail: S.Hardy@uea.ac.uk

What if I no longer wish to continue with the project?

You may withdraw from the project **at any time** without giving a reason.

Who has reviewed this project?

This project has been reviewed extensively by experts in the research team whose details are provided in the last section of this information sheet. Specifically, the project has been reviewed for clinical relevance, scientific accuracy, medical statistics and practicality. The project has been granted ethical approval by the Ethical Committee of the UEA Faculty of Medicine and Health who protect the dignity, rights, safety and well-being of participants and researchers.

Who is organising this project?

This project is organised by UEA and the Acquired Brain Injury Research Alliance (ABIRA) and is in collaboration with the creators of the Biokido motion analysis system

Who are the team members of this project?

Chief Investigator:

- Professor Valerie Pomeroy, Professor of Neurorehabilitation, School of Health Sciences, University of East Anglia

Investigators:

- Ms Canan Yuksel, PhD student, School of Health Sciences, University of East Anglia
- Ms Merve Kizilay, PhD student, School of Health Sciences, University of East Anglia
- Dr Alpar Lazar, Associate Professor in Dementia and Complexity in Later Life, School of Health Sciences, University of East Anglia
- Dr Nicola Hancock, Lecturer in Physiotherapy, School of Health Sciences, University of East Anglia
- Dr Allan Clark, Senior Lecturer in Medical Statistics, Norwich Medical School, University of East Anglia
- Ms Elizabeth Chandler, Clinical Movement Analyst, School of Health Sciences, University of East Anglia
- Mr Jacob Wells, Research Associate, School of Health Sciences, University of East Anglia
- Mr David Payne, Movement Analysis Research Technician, School of Health Sciences, University of East Anglia
- Ms Louise Gilbert, Specialist Physiotherapist, Early Supported Discharge service (stroke), Norfolk Community Health and Care NHS Trust

Thank you for taking the time to read this leaflet.

If you choose to participate, you will keep a copy of this participant information sheet and the signed informed consent form

Appendix 19. Informed Consent Form for Observational Cohort Study (Chapter 6)

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Date of first visit |__|__|-|__|__|-|__|__|__|__| (DD-MM-YYYY)

Participant Identification Number: |_____|

University of East Anglia

Relationship between neuromuscular recovery, functional ability and sleep after stroke, and, criterion validity of measures made by the Vicon and Biokido motion analysis systems

Consent Form for volunteers

Name of Researcher: _____

Name of Participant: _____

Participant Identification Number: |_____| (Researcher use only)

	Please initial the box
1. I have read and understood the participant information sheet (PIS Version 3, February 2021)	
2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily	
3. I understand that my participation is voluntary and that I am free to withdraw at any time until the point that my data are anonymised without giving any reason.	
4. I agree to complete a form to provide asking for: my demographic information (e.g., age, sex) and information about any allergies of relevance to this project.	
5. I understand that I will attend the MoveExLab at the University of East Anglia on two separate occasions and that any necessary travel expenses will be reimbursed. Up to a maximum of a 50-mile return journey.	
6. I understand that I will undertake assessments for measurement of my muscle activity and my movement at the MoveExLab at the University of East Anglia.	
7. I understand that I will undertake questionnaires of my mood and cognition (e.g. memory). These will be undertaken at the MoveExLab at the University of East Anglia or I will self-complete them at home.	
8. I understand that I will undertake questionnaires about my sleeping pattern. These will be undertaken at the MoveExLab at the University of East Anglia or I will self-complete them at home.	
9. I understand that I will keep a sleep diary to record my sleep pattern during the time in-between my two visits to the MoveExLab at the University of East Anglia.	

10. I understand that I will wear a motion watch on each of my wrists for 7 days following each visit to the MoveExLab at the University of East Anglia and that I will then post these in the stamped addressed padded envelope given to me by the Researcher.	
11. I understand that while information gained during the study may be published, I will not be identified and all information (demographic and measures) will be anonymised.	
I agree to take part in the study. I understand that the study will involve me undertaking the activities outlined in boxes 4-10 above	

	Please initial the appropriate box	
	YES	NO
I agree to my name and contact details being held on a secure database at the University of East Anglia so that I can be contacted regarding follow-up to this study and opportunities for future research that has been ethically approved.		
I agree for my anonymised data captured with the Biokido system to be sent to the manufacturer in Turkey so that if can be analysed. I understand that my anonymised data will be in blurred pictorial format as in the illustration of the Biokido system in the information sheet. My data transferred to Turkey for analysis will only be identifiable by the anonymised study number.		

Name of participant	
Signature	
Date	

Name of person receiving consent	
Signature	
Date	

One original copy of this form should be completed. The original, paper or electronic, should be stored in the relevant section of the investigator site file. Photocopy of a paper form should be made of the original and given to the participant

Appendix 20. Study Advertisement for Observational Cohort Study (Chapter 6)

Faculty of Medicine and Health
University of East Anglia

Brain recovery after stroke is a puzzle
Would you like to be part of the solution?

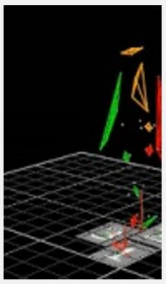
We are investigating how movement recovers after stroke and whether this is influenced by sleep.

We need people who have had a stroke to undertake measures of movement, sleep and daily activity, twice.

Measures involve answering a telephone placed on a table. First, moving from a chair to the table. Second, seated next to the table. Sleep questionnaires will also be completed. Everyday activity will be recorded by motion watches

In detail we are recruiting adults who have had a stroke and do not have a latex allergy. This project will involve measuring your movement whilst you pick up a telephone several times. To measure your movement, we will stick small reflective markers and sensors on your skin. You will complete some questionnaires about how you sleep. No painful or intrusive methods are used. You will need to attend two 90-minute sessions in the Movement and Exercise Laboratory at the University of East Anglia. And you will wear a motion watch on each wrist for 7 days to measure your everyday activity at home.






For more information please contact:
v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk

For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk	For more information: v.pomeroy@uea.ac.uk or p.fordham@uea.ac.uk

Appendix 21. Individual Participant Characteristics in Observational Cohort Study (Chapter 6)

Participant ID	Notes on Reasons for No Session 2 Data	Age at Visit 1 (Years)	Time after Stroke (Years)	Gender	More Affected Side	Hand Dominance	Number of Previous Strokes Reported	FMA-UL Motor Scale Score (Total 66) Session 1	ARAT Score (Total 57) Session 1	FMA-UL Motor Scale Score (Total 66) Session 2	ARAT Score (Total 57) Session 2
PS001		69.0	1.3	Female	Right	Right	0	2	0	4	0
PS002		67.0	15.0	Male	Right	Right	0	4	0	4	1
PS003		53.0	6.3	Female	Left	Right	0	15	3	16	3
PS004		59.0	7.6	Male	Left	Left	1	5	3	8	3
PS005		61.0	6.8	Male	Left	Right	0	15	3	16	3
PS006		46.0	1.4	Male	Right	Left	0	66	57	66	57
PS007		57.0	13.4	Male	Left	Right	1	45	39	45	39
PS008	Another stroke between visits	59.0	8.0	Male	Right	Right	0	59	37	Withdrawn	Withdrawn
PS009		72.0	3.5	Male	Left	Right	0	66	57	65	57
PS010		72.0	10.8	Male	Right	Right	0	55	56	54	56
PS011		48.0	3.7	Male	Left	Right	0	23	18	29	18
PS012	Another health problem	76.0	4.3	Male	Right	Right	0	66	57	Withdrew	Withdrew
PS013		85.0	6.0	Female	Right	Right	0	66	57	65	56
PS014		67.0	0.2	Male	Left	Right	0	66	57	66	57
PS015		64.0	0.4	Female	Left	Left	0	66	57	66	57
PS016		61.0	10.0	Male	Left	Right	0	65	57	65	57
PS017		53.0	12.1	Female	Left	Right	0	16	3	14	3
PS018		71.0	2.0	Female	Right	Right	0	66	57	66	57
PS019	Rheumatoid arthritis flare occured between visits.	54.0	7.3	Female	Right	Right	0	66	57	Withdrawn	Withdrawn
PS020		53.0	3.6	Male	Left	Right	1	8	0	8	0
PS021		53.0	1.8	Female	Right	Left	0	56	57	57	57
PS022		61.0	5.0	Female	Left	Right	0	4	3	4	3
PS023		51.0	2.3	Female	Right	Right	0	6	3	6	3
PS024		68.0	4.9	Female	Left	Right	0	2	0	4	0
PS025		44.0	1.1	Male	Right	Right	0	66	57	66	57
PS026		44.0	1.7	Male	Left	Right	0	66	57	66	57
PS027		47.0	17.2	Female	Left	Right	0	65	57	65	57
PS028		63.0	14	Female	Right	Right	1	66	57	66	57
PS029		35.0	11.1	Female	Left	Right	0	64	57	64	57
PS030		65.0	5.3	Female	Left	Right	0	66	57	66	57
PS031		83.0	3.7	Male	Right	Right	0	66	57	66	57
PS032	Did not respond to communications	73.0	12.5	Male	Right	Right	1	13	4	Withdrew	Withdrew
PS033		42.0	0.6	Male	Right	Right	1	64	57	64	57
PS034	Withdrawn										
PS035		75.0	7.4	Male	Right	Right	0	66	57	66	57
PS036		52.0	7.3	Male	Left	Right	0	34	19	31	19
PS037	Another health problem	49.0	0.3	Female	Left	Right	0	66	57	Withdrew	Withdrew
PS038		73.0	0.4	Female	Left	Right	0	66	57	66	57
PS039		79.0	0.6	Female	Right	Right	0	66	57	66	57
PS040		65.0	3.1	Male	Right	Right	1	56	56	56	56
PS041		68.0	1.4	Male	Left	Left	1	58	57	55	57
PS042	Did not respond to communications	78.0	22	Male	Right	Right	0	55	45	Withdrew	Withdrew
PS043		70.0	2	Female	Left	Right	0	54	55	54	55
PS044		85.0	0.7	Male	Right	Left	1	63	57	63	57
PS045	Onset of another pathology	73.0	0.8	Male	Right	Right	1	66	57	Withdrawn	Withdrawn

Appendix 22. Quality Check Results of the Collected Data at the First Data Collection Sessions in Observational Cohort Study (Chapter 6)

A. Midline Reaching Tasks for Participants PS001-PS024

	Trial ID									
P. ID	MMAH-1	MMAH-2	MMAH-3	MMAH-4	MMAH-5	MLAH-1	MLAH-2	MLAH-3	MLAH-4	MLAH-5
PS001	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)					
PS002	No Kinematic Data (Task Incompletion) / No EMG Data from BB Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from BB Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMD Data from ECR Muscle (Movement Onset Undetectable)							
PS003	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS004	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS005										
PS006										
PS007										
PS008										
PS009										
PS010										
PS011										
PS012										
PS013										
PS014										
PS015										
PS016										
PS017	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS018										
PS019										
PS020	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)							
PS021										
PS022	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS023	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS024	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							

Note: P. ID: Participant Identification Number; **MMAH:** Midline More Affected Hand; **MLAH:** Midline Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted; **Unusable:** No variable could be extracted; **Partial Data:** Trials with some variables missing; **No Recorded Trial**

B. Midline Reaching Tasks for Participants PS025-PS045

	Trial ID									
P. ID	MMAH-1	MMAH-2	MMAH-3	MMAH-4	MMAH-5	MLAH-1	MLAH-2	MLAH-3	MLAH-4	MLAH-5
PS025										
PS026										
PS027										
PS028										
PS029										
PS030										
PS031										
PS032	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS033										
PS034	**WITHDRAWN**									
PS035										
PS036										
PS037										
PS038						No EMG Data from BB Muscle (Noisy Signals)				
PS039										
PS040										
PS041										
PS042										
PS043										
PS044										
PS045										

Note: P. ID: Participant Identification Number; **MMAH:** Midline More Affected Hand; **MLAH:** Midline Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

C. Contralateral Reaching Tasks for Participants PS001-PS024

	Trial ID									
P. ID	CMAH-1	CMAH-2	CMAH-3	CMAH-4	CMAH-5	CLAH-1	CLAH-2	CLAH-3	CLAH-4	CLAH-5
PS001	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data (Noisy Signals)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)					
PS002	No Kinematic Data (Task Incompletion) / No EMG Data from BB Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS003	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS004	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS005										
PS006										
PS007										
PS008										
PS009										
PS010										
PS011										
PS012										
PS013										
PS014										
PS015										
PS016										
PS017	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS018										
PS019										
PS020	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS021										
PS022	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS023	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No ECR Muscle EMG Data (No Detectable Signal)							
PS024	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)							

Note: P. ID: Participant Identification Number; **CMAH:** Contralateral More Affected Hand; **CLAH:** Contralateral Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted; **Unusable:** No variable could be extracted; **Partial Data:** Trials with some variables missing; **No Recorded Trial**

D. Contralateral Reaching Tasks for Participants PS025-PS045

	Trial ID									
P. ID	CMAH-1	CMAH-2	CMAH-3	CMAH-4	CMAH-5	CLAH-1	CLAH-2	CLAH-3	CLAH-4	CLAH-5
PS025										
PS026										
PS027										
PS028										
PS029										
PS030										
PS031										
PS032	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS033										
PS034	**WITHDRAWN**									
PS035										
PS036										
PS037										
PS038										
PS039										
PS040										
PS041										
PS042										
PS043										
PS044										
PS045										

Note: P. ID: Participant Identification Number; **CMAH:** Contralateral More Affected Hand; **CLAH:** Contralateral Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

Appendix 23. Quality Check Results of the Collected Data at the Second Data Collection Sessions in Observational Cohort Study (Chapter 6)

A. Midline Workspace Reaching Tasks for Participants PS001-PS024

	Trial ID									
P. ID	MMAH-1	MMAH-2	MMAH-3	MMAH-4	MMAH-5	MLAH-1	MLAH-2	MLAH-3	MLAH-4	MLAH-5
PS001	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)							
PS002	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS003	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS004	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS005										
PS006										
PS007										
PS008	**WITHDRAWN**									
PS009										
PS010										
PS011										
PS012	**WITHDREW**									
PS013										
PS014										
PS015										
PS016										
PS017	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS018										
PS019	**WITHDRAWN**									
PS020	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)							
PS021										
PS022	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS023	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)							
PS024	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)							

Note: P. ID: Participant Identification Number; **MMAH:** Midline More Affected Hand; **MLAH:** Midline Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted; **Unusable:** No variable could be extracted; **Partial Data:** Trials with some variables missing; **No Recorded Trial**

B. Midline Workspace Reaching Tasks for Participants PS025-PS045

	Trial ID									
P. ID	MMAH-1	MMAH-2	MMAH-3	MMAH-4	MMAH-5	MLAH-1	MLAH-2	MLAH-3	MLAH-4	MLAH-5
PS025										
PS026										
PS027										
PS028										
PS029										
PS030										
PS031										
PS032	**WITHDREW**									
PS033										
PS034	**WITHDRAWN**									
PS035										
PS036										
PS037	**WITHDREW**									
PS038										
PS039										
PS040										
PS041										
PS042	**WITHDREW**									
PS043										
PS044										
PS045	**WITHDRAWN**									

Note: P. ID: Participant Identification Number; **MMAH:** Midline More Affected Hand; **MLAH:** Midline Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

C. Contralateral Workspace Reaching Tasks for Participants PS001-PS024

	Trial ID									
P. ID	CMAH-1	CMAH-2	CMAH-3	CMAH-4	CMAH-5	CLAH-1	CLAH-2	CLAH-3	CLAH-4	CLAH-5
PS001	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)							
PS002	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No EMG Data from BB Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)							
PS003	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS004	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS005										
PS006										
PS007										
PS008	**WITHDRAWN**									
PS009										
PS010										
PS011										
PS012	**WITHDREW**									
PS013										
PS014										
PS015										
PS016										
PS017	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS018										
PS019	**WITHDRAWN**									
PS020	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)							
PS021										
PS022	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion)							
PS023	No Kinematic Data (Task Incompletion)	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion)							
PS024	No Kinematic Data (Task Incompletion) / No EMG Data from ECR Muscle (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)	No Kinematic Data (Task Incompletion) / No EMG Data (No Discernible Muscle Activity)							

Note: P. ID: Participant Identification Number; **CMAH:** Contralateral More Affected Hand; **CLAH:** Contralateral Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted; **Unusable:** No variable could be extracted; **Partial Data:** Trials with some variables missing; **No Recorded Trial**

D. Contralateral Workspace Reaching Tasks for Participants PS025-PS045

	Trial ID									
P. ID	CMAH-1	CMAH-2	CMAH-3	CMAH-4	CMAH-5	CLAH-1	CLAH-2	CLAH-3	CLAH-4	CLAH-5
PS025										
PS026										
PS027										
PS028										
PS029										
PS030										
PS031										
PS032	**WITHDREW**									
PS033										
PS034	**WITHDRAWN**									
PS035										
PS036										
PS037	**WITHDREW**									
PS038										
PS039										
PS040										
PS041										
PS042	**WITHDREW**									
PS043										
PS044										
PS045	**WITHDRAWN**									

Note: P. ID: Participant Identification Number; **CMAH:** Contralateral More Affected Hand; **CLAH:** Contralateral Less Affected Hand; **BB:** Biceps Brachii, ECR: Extensor Carpi Radialis, **EMD:** Electromechanical Delay.

Key: **High-Quality Data:** Trial with all variables extracted
Unusable: No variable could be extracted
Partial Data: Trials with some variables missing
No Recorded Trial

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