

Vibrotactile Stimuli For Functional Rehabilitation In Neurological Individuals.

by

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requirements of the degree of PhD*

***“Dedicated to my dear friend, Uzair Ulhaq,
who lured me into this abyss.”***

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Statement of Originality

I declare that the work in this dissertation was carried out under the requirements of the University's Regulations and Code of Practice for Research Degree Programmes and has not been submitted for any other academic award. Except where indicated by the specific reference in the text, the work is the candidate's work. Any views expressed in the dissertation are those of the author.

This thesis investigates the engineering, scientific and clinical evidence for use of focal muscle vibration (FMV) in neurorehabilitation, with these different elements of the research inspected in different experiments/ chapters, leading to various peer-reviewed publications.

The following research output fully/directly contributed and was used in this PhD thesis:

1. Contents of Chapter 2 is partially based on following peer-reviewed systematic literature review publication:

Ashfaq M, Pujari AN, Niazi IK, et al. "Effectiveness of focal muscle vibrations in improving sensorimotor performance, mobility and strength in spinal cord injury population: a systematic review." *BMJ Open* 2025;15:e110054. doi:10.1136/bmjopen-2025-110054

2. Contents of Chapter 4 are based on following peer-reviewed book chapter:

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4. Contents of Chapter 4 are based on two manuscripts submitted for peer-review:

Ashfaque M, Khushnood K, Ghani U, Naizi I, Amjad I, Mehmood Q, Pujari A, “8 Weeks of Focal Muscle Vibration Alters Functional Connectivity and Cortical Potentials in Children with Cerebral Palsy”, under review in IEEE Transactions in Neural Systems and Rehabilitation Engineering

Preprint- <https://www.techrxiv.org/doi/full/10.36227/techrxiv.176238211.17782193>

Ashfaque M, Khushnood K, Ghani U, Naizi I, Amjad I, Mehmood Q, Pujari A, “8 Weeks of Focal Muscle Vibration Shows Improvements in Muscle Co-ordination and Co-contraction in Cerebral Palsy Children”, under review in IEEE Journal Journal of Translational Engineering in Health and Medicine

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These published/ under publication research presented above address specific disease related investigations and findings with rigorous testing in cerebral palsy (CP), spinal cord injury (SCI) and stroke conditions, looking at evidence individually. The thesis extends this, combining the evidences to present a cohesive picture and overall landscape of neurorehabilitation via FMV, addressing the commonalities in rehabilitation needs and the effectiveness of FMV in each of them.

Signed: Moeez Ashfaque

Dated: 02-04-2026

Abbreviations

ADL	activities of daily living
ANOVA	analysis of variance
CAD	computer-aided design
CCI	co-contraction index
CP	cerebral palsy
DF	dorsiflexion
EEG	electroencephalography
EMG	electromyography
ERM	eccentric rotating mass
FAC	functional ambulation category
FC	functional connectivity
FCR	flexor carpi radialis
FDI	first dorsal interosseous
fMRI	functional magnetic resonance imaging
FMUE	Fugl Meyer Upper Extremity
FMV	Focal muscle vibration
GM	gastrocnemius medialis
GMFM	Gross Motor Function Measure
GRT	grip-and-release test
ICA	Independent component analysis
LL	lower limb
LMM	linear mixed-effects model
LTD	long-term depression
LTP	long-term potentiation

MAS	modified Ashworth scale
MDF	median frequencies
MRCPs	movement-related cortical potentials
NRS	numerical rating scale
PENN	Penn Spasm Frequency Scale
PICO	population-intervention-comparison-outcomes
PICs	Persistent inward currents
PLV	phase locking value
PNF	proprioceptive neuromuscular facilitation
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRPS	Pittsburgh Rehabilitation Participation Scale
REML	restricted maximum likelihood
RF	rectus femoris
RMS	root mean square
ROBINS-I	Risk Of Bias In Non-randomised Studies – of Interventions
ROM	range of motion
SCI	spinal cord injury
Sol	Soleus
TA	tibialis anterior
TFL	tensor fasciae latae
TMS	transcranial magnetic stimulation
TRC	timed up-and-go
TRT	trunk control test
TVR	tonic vibration reflex
UL	upper limb
WBV	whole-body vibration

Abstract

Background:

Neurological disorders such as Spinal Cord Injury (SCI), Cerebral Palsy (CP), and stroke pose significant challenges to sensorimotor function in affected individuals, with traditional therapies often yielding incomplete recovery. This thesis investigates Focal Muscle Vibration (FMV) as a non-invasive intervention to enhance motor and sensory rehabilitation in neurological diseases, addressing gaps in mechanistic understanding, functional performance and clinical efficacy.

Objective:

The overarching aim of this thesis is to investigate FMV's role in sensorimotor rehabilitation by understanding its neurophysiological impacts following its use as an exercise intervention in people suffering from neurological diseases. Three specific research objectives were pursued:

Objective 1 (OB1) — Device Engineering: To engineer a wearable FMV device capable of delivering precise and reproducible vibrations suitable for neuromuscular and sensory rehabilitation.

Objective 2 (OB2) — Neurophysiological Effects: To investigate the specific effects of prolonged FMV exposure on motor function, spasticity, and brain activity in individuals with SCI and CP, and how these effects vary with different vibration frequencies.

Objective 3 (OB3) — Device Feasibility: To evaluate the feasibility, usability, and short-term clinical effects of a co-designed wearable FMV device on spasticity and upper limb function in stroke survivors.

Methods:

An FMV device was developed using ERM vibration motor and characterized for frequency output using accelerometers. An electronic circuitry using was designed to operate the device at the desired frequencies (60-120 Hz) after the frequency characterization. This device was then used for the experimental studies.

Experimental evaluations included three cohort studies investigating the neurophysiological impacts and usability of the FMV device in CP, SCI and stroke cohorts as detailed below:

CP: Effects of 8 weeks of FMV applied to quadriceps at 80 Hz and 100 Hz was assessed via EEG and EMG in a cohort of 65 CP children. Resting-state functional connectivity (FC) and movement related cortical potentials (MRCs) were used to see the cortical impacts of FMV through the EEG assessments. Muscle activations, fatigue and co-contraction metrics were assessed through EMG assessments.

SCI: Three weeks of FMV to the Achilles tendon was delivered to 10 SCI patients, and their EEG FC was investigated.

Stroke: An FMV device usability study in stroke (n= 12) was also conducted using a specifically modified commercial FMV device, with a view to establish for its potential for translation from laboratory to home-based use. Patient feedback was collected to update the original device design. After the updated device design, a single 30-minute dose of FMV was delivered to the arms, and clinical assessments of Fugl-Meyer Upper Extremity (FMUE) and modified Ashworth scores (MAS) were conducted.

Results:

OB1 — Fully Met: A wearable FMV device was designed and developed, delivering vibration frequencies at four levels (60, 80, 100 and 120 Hz) with a mean accuracy of 96.83%. The device was wearable, lightweight (65 g), and low-cost (under £100), meeting all pre-specified engineering requirements.

OB2 — Fully Met (CP); Partially Met (SCI): In CP, FMV demonstrated frequency-dependent enhancements in beta-band functional connectivity, reduced movement-related cortical potentials, improved muscle activation, and delayed fatigue, with 100 Hz yielding superior motor outcomes. In SCI, significant alpha- and beta-band EEG connectivity changes in central-parietal regions were observed, suggesting neuroplasticity; however, clinical spasticity reductions were modest and the sample size (n = 10) precluded definitive conclusions, making this objective partially met for the SCI cohort.

OB3 — Partially Met: The co-designed device was found to be comfortable and easy to use by stroke patients and clinicians. A single session of FMV produced improvements in FMUE scores but no significant changes in spasticity (MAS). Given the feasibility-study design with a small cohort (n = 12) and a single-session protocol, the clinical effectiveness component of OB3 is considered partially met, warranting further investigation in powered randomised trials.

Conclusion:

Findings support FMV's role in modulating cortical and neuromuscular pathways, with implications for personalised, accessible rehabilitation. OB1 was fully met through the development of a characterised, wearable, low-cost FMV device. OB2 was fully met for the CP cohort, demonstrating cortical and neuromuscular benefits, while SCI findings remain promising but preliminary, partially meeting OB2 for that population. OB3 was partially met, confirming device usability and short-term upper limb gains in stroke, with further powered trials needed to confirm clinical efficacy. Limitations include small samples and short follow-up periods, warranting larger trials. This work advances wearable FMV therapy toward evidence-based practice, bridging engineering innovation and clinical application for improved neurological outcomes.

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Chapter 1: Introduction

1.1 Background and Context

Neurological disorders such as spinal cord injury (SCI), cerebral palsy (CP), and stroke disrupt the sensorimotor networks critical for movement, sensation, and functional independence (Sadeghi et al., 2014; Viganò et al. 2023; Celletti et al., 2011). These conditions, affecting millions globally, present persistent challenges to rehabilitation of affected individuals due to their complex interplay of motor deficits, sensory impairments, and limited neuroregenerative capacity (Li et al., 2019; Kuriakose & Xiao, 2020). Traditional interventions—physiotherapy, pharmacotherapy, and surgical approaches—often yield incomplete recovery (Kriger et al., 2006; Christine et al., 2010), particularly in chronic or severe cases, as they predominantly target motor function while under-addressing sensory feedback (Fattorini et al., 2023), a key determinant of rehabilitation success. This therapeutic gap has spurred interest in non-invasive neuromodulation techniques capable of holistically engaging both motor and sensory pathways.

Spinal cord injury: Globally, SCI affects over 750,000 individuals annually (>1200 of which are in the UK), predominantly young adults, incurring lifetime costs exceeding millions in high-income settings due to medical care and lost productivity (McDaid et al., 2019) (Li et al., 2019). Treatment landscape comprises a range of modalities, including surgical interventions, pharmacological therapies, and rehabilitative approaches (Lanig et al. 2018), (Gohritz & Friden, 2018), (Russo et al., 2020). Surgical procedures carry operative risks. Pharmacological treatments manage pain/spasticity non-selectively, with habituation risk. Limited intrinsic repair in the spinal cord yields only modest chronic physiotherapy gains (Kirshblum et al., 2011; Toscano et al., 2019).

Cerebral palsy: CP affects 2–3 per 1,000 live births worldwide (Patel et al., 2020). CP's clinical expression evolves with growth, as skeletal deformities and contractures emerge from muscle imbalances (Patel et al., 2020). The economic and societal toll of CP is substantial, with lifetime costs often exceeding millions in high-income settings due to medical, therapeutic, and assistive needs (Pulgar et al., 2019) (Utsana et al., 2018). In resource-limited contexts, these burdens intensify due to restricted access to specialized care, amplifying disparities in outcomes (Jahan

et al., 2021). Rehabilitation faces a heterogeneous landscape: spasticity limits range of motion, weakness hampers strength, and sensory impairments compromise balance (Patel et al., 2020) (Beckung & Hagberg, 2002). Population-based studies reveal persistent functional limitations, with majority of CP individuals experiencing associated conditions like epilepsy (35%) or intellectual disability (40%), further complicating care (Beckung & Hagberg, 2002).

CP rehabilitation aims to mitigate symptoms and enhance motor function. Physical therapy strengthens muscles, coordination and mobility (Anttila et al., 2008; Das et al., 2019), but is labour-intensive with frequent efficacy plateaus. Occupational therapy improves daily living through fine motor development and adaptations (Steultjens et al., 2004) but does not target core neurological deficits. Pharmacological options (muscle relaxants, botulinum toxin) reduce spasticity (Kriger et al., 2006), though limited by sedation, fatigue and cognitive side effects (Rinaldis et al., 2010; Kolaski et al., 2010; Paoloni et al., 2013). Surgical procedures (orthopaedic surgery, selective dorsal rhizotomy) provide lasting spasticity relief (Wilson et al., 2014; Steinbok et al., 2007) at the expense of significant risks and prolonged recovery.

Stroke: Stroke, a leading cause of disability and second leading of death, arises from interrupted cerebral blood flow. Annually, 13.7 million new cases emerge and 5.5 million die, predominantly older adults, though rising incidence in younger populations (from 12.9% to 18.6%, age 20-54) reflects lifestyle risk factors (e.g., hypertension, obesity) (Kuriakose & Xiao, 2020). Rehabilitation landscape offers a similar picture, with physiotherapy, pharmacological and surgical options used, carrying similar risks of stagnation, habituation and surgery risks respectively. Due to its high occurrence, a number of non-invasive rehabilitation modes have also received attention, including electrical stimulations and focal muscle vibration (FMV).

These established modalities for rehabilitation of SCI, CP and stroke, while critical, reveal inherent constraints that emphasize the demand for innovative and supplementary therapeutic options to tackle the multifaceted motor challenges of these neurological conditions. Traditional approaches, though beneficial, often come with challenges such as invasiveness, side effects, or limited efficacy. There is an increasing need for non-invasive strategies that emphasize sensory rehabilitation, transcending the confines of conventional motor-focused approaches. This unmet need underscores the promise of focal muscle vibration (FMV) therapy as a means to improve sensory-motor integration. Among these, vibration therapy has emerged as a promising intervention due to its ability to stimulate both peripheral and central nervous systems without requiring surgical procedures or systemic drugs.

1.2 Focal muscle Vibration

Vibration therapy, which delivers mechanical oscillations to stimulate neuromuscular and sensory systems (Guang et al. 2018), has emerged as a promising modality in this rehabilitation context. It is widely regarded because of its non-invasive nature, ease of use and cost-effectiveness.

FMV is a targeted form of vibration therapy where vibrations at specific frequencies (50-120 Hz) are applied directly to specific muscle bellies or tendons. This approach has shown promise in both healthy individuals and patients with neuromuscular disorders. The vibrations stimulate muscle spindles, leading to enhanced motor unit recruitment (Fattorini et al., 2023) and improved muscle function, reduced spasticity (Paoloni et al., 2013), and amplifying proprioceptive feedback (Camerota et al., 2016). FMV also influences central nervous system pathways by modulating cortical excitability, which is critical for motor learning and recovery. Its non-invasive nature, ease of use, and low risk of side effects make it an attractive option for clinical and home-based rehabilitation settings. Given the described challenges in traditional rehabilitation methods for these neurological disorders, this thesis aims to check the effectiveness of FMV as a neurological rehabilitation tool, and its application in laboratory and clinical contexts.

The mechanisms underlying vibration therapy make it uniquely suited to address the challenges of neuromuscular rehabilitation. Unlike traditional methods that primarily target motor recovery, vibration therapy simultaneously engages sensory pathways, enabling a more holistic approach to rehabilitation. By directly stimulating muscle spindles and cutaneous mechanoreceptors, vibration therapy can potentially restore lost sensory feedback, which is often a limiting factor in functional recovery.

Despite its promise, the application of vibration therapy in clinical settings remains underexplored, particularly in terms of understanding how these techniques impact neurophysiological processes, such as cortical activation patterns and motor unit recruitment, which is essential for designing effective interventions.

This thesis aims to address this gaps by focusing on application of FMV devices in populations with SCI, CP, and stroke in order to elucidate the neurophysiological mechanisms driving the observed functional improvements. The ultimate goal is to provide evidence-based recommendations for integrating these techniques into clinical practice, improving outcomes for individuals with neuromuscular disorders.

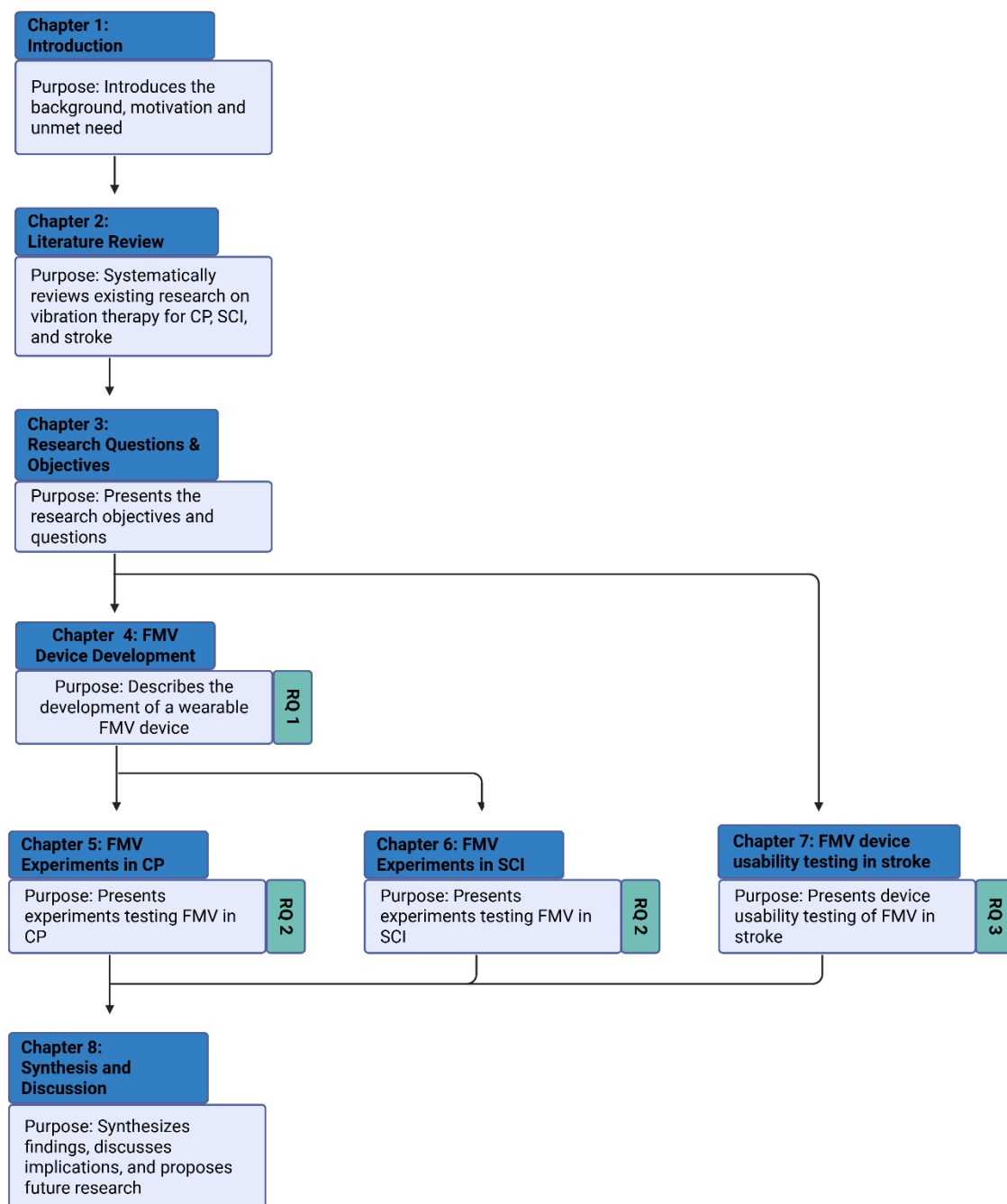


FIGURE 1.1 Flow chart of the thesis structure, illustrating the main purpose of each chapter in exploring FMV therapy's effect on rehabilitation in neurological diseases.

1.3 Thesis Structure

This thesis is structured across eight chapters to systematically address the research problem and objectives. Chapter 1 establishes the context and lays down the unmet need and the problem. Chapter 2 synthesizes the literature on SCI, CP, stroke, and FMV therapy, incorporating

a systematic review of FMV in SCI to critically evaluate the evidence base informing this thesis' studies, and leading to the identification of research gaps. Chapter 3 then delineates the research gaps, establishing the research questions and hypotheses, providing a roadmap for the experimental work. Chapter 4 details the design, construction, and characterization of the FMV device, establishing its technical foundation. Chapter 5 presents the design, findings, and analysis of the experimental investigations of the FMV studies, for CP populations, whereas Chapter 5 presents the FMV investigations on SCI population. Chapter 6 presents the experimental investigations of the FMV usability and feasibility in stroke. Chapter 7 synthesizes the results, discusses their implications for theory and practice, and addresses limitations and future directions. Chapter 7 also concludes with a summary of contributions and their broader impact on neurological rehabilitation. This structure ensures a cohesive progression from problem identification to solution validation, aligning with the interdisciplinary scope of my research. The detailed flow and structure of this thesis are presented in Figure 1.1

Chapter 2: Literature Review

Part of this chapter (Section 2.3) is published as a systematic literature review in BMJ (British Medical Journal) Open

Ashfaque M, Pujari AN, Niazi IK, et al. "Effectiveness of focal muscle vibrations in improving sensorimotor performance, mobility and strength in spinal cord injury population: a systematic review." BMJ Open 2025;15:e110054. doi:10.1136/bmjopen-2025-110054

2.1 Brief Overview of Neurological Disorders

Neurological disorders disrupt the intricate sensorimotor networks of the human body that govern movement, sensation, and coordination, posing substantial challenges to rehabilitation of affected individuals. Conditions such as spinal cord injury (SCI), cerebral palsy (CP), and stroke exemplify this complexity, each characterized by distinct aetiologies yet unified by shared impairments—motor deficits, sensory loss, and limited neural repair capacity. These disorders collectively affect millions globally, exerting profound clinical and socioeconomic burdens (Kuriakose & Xiao, 2020; Li et al., 2019). Representing acquired (stroke), developmental (CP) and traumatic (SCI) occurrences these three disorders offer a diverse representation of neurological disorders. While their pathophysiology varies, the resultant dysfunctions in motor control and sensory feedback underscore a critical need for interventions that address both domains (sensory and motor) concurrently, a need inadequately met by conventional therapies like physiotherapy and pharmacotherapy (Anttila et al., 2008; Christine et al., 2010). This section synthesizes the essential features of SCI, CP, and stroke, focusing on their sensorimotor sequelae and rehabilitation challenges to contextualize the application of vibration therapy explored in subsequent sections.

The literature reveals a consistent limitation across these conditions: incomplete recovery due to the central nervous system's constrained regenerative potential (Nas et al., 2015). Traditional approaches, though foundational, often prioritize motor rehabilitation, neglecting sensory restoration critical for functional outcomes (Fattorini et al., 2023). Moreover, secondary complications—spasticity, muscle atrophy, and chronic pain—exacerbate these

impairments, further complicating recovery (Boulay et al., 2025). FMV therapy, by stimulating neuromuscular and sensory pathways, offers a promising avenue to address these dual deficits, yet its efficacy hinges on understanding the specific challenges posed by each disorder. The following subsections outline these challenges, drawing on foundational studies to frame the therapeutic gaps this thesis targets.

2.1.1 Spinal Cord Injury (SCI)

SCI results from traumatic or non-traumatic damage to the spinal cord, severing neural communication between the brain and periphery, with outcomes ranging from paraplegia (affecting lower limb only) to tetraplegia (affecting all four limbs) depending on lesion level and severity (Nas et al., 2015). Depending on injury location on spine it classifies as cervical (usually tetraplegia), lumbar, thoracic, or sacral (remaining usually paraplegia). The severity of the disease can be complete – stopping neural flow completely, or incomplete – sparing some neural communication (Nas et al., 2015; Kirshblum et al., 2011). Clinicians also use the American Spinal Injury Association Impairment Scale (AIS) categorizing the injury into five grades A, B, C, D or E based on the level of residue activity helping in accessing the motor and sensory functions (Kirshblum et al., 2011). The pathophysiology unfolds in two phases: an irreversible primary injury from mechanical trauma followed by a secondary cascade— inflammation, oxidative stress, and excitotoxicity—that amplifies neural loss (Russo et al., 2020; Hachem et al. 2017). This dual mechanism yields a hostile microenvironment, with glial scarring and limited axonal regeneration impeding recovery (Hachem et al. 2017). Initial weeks after injury lead to an acute phase where secondary changes are still taking place, six months later a chronic stage is reached where damage has become permanent.

Treatment landscape comprises a range of modalities, including surgical interventions, pharmacological therapies, and rehabilitative approaches (Lanig et al. 2018), (Gohritz & Friden, 2018), (Russo et al., 2020). Surgical procedures aim to stabilise and repair the spinal cord related damage yet come along with surgery-associated risks; pharmacological treatments focus on managing symptoms like pain and spasticity but usually have non-selective actions and can lead to habituation. Rehabilitation plays a pivotal role in optimising function and quality of life for individuals with SCIs, encompassing physical therapy, occupational therapy, and assistive devices (Nas et al., 2015), (Lanig et al. 2018), (Gohritz & Friden, 2018), (Elbasiouny et al. 2010). Rehabilitation confronts formidable obstacles: paralysis restricts mobility, spasticity induces involuntary contractions, and sensory deficits impair

proprioception, increasing fall risk (Elbasiouny et al., 2010) (Russo et al., 2020). Studies highlight the spinal cord's minimal self-repair capacity as a primary barrier (Kirshblum et al., 2011), with even intensive physiotherapy yielding modest gains in chronic cases (Toscano et al., 2019). Sensory recovery, crucial for motor coordination, remains particularly elusive, as evidenced by persistent proprioceptive deficits in incomplete SCI cohorts (Moreno-López et al., 2021) (Russo et al., 2020). These challenges, compounded by secondary complications like pressure ulcers, underscore the inadequacy of motor-centric approaches and the potential of FMV therapy to modulate reflex pathways and enhance sensory feedback, as explored in Section 2.2.

2.1.2 Cerebral Palsy (CP)

CP encompasses a group of non-progressive disorders arising from early brain injury, affecting 2–3 per 1,000 live births worldwide (Patel et al., 2020). Damage to the motor cortex, basal ganglia, or cerebellum—often linked to prematurity or hypoxia—disrupts movement and posture, manifesting as spastic, dyskinetic, or ataxic subtypes (Paul et al., 1997). Spastic CP, the most prevalent, features hypertonia and stiffness, impairing voluntary control, while dyskinetic and ataxic forms present involuntary movements and coordination deficits, respectively (Christine et al., 2007) (Patel et al., 2020). Though static neurologically, CP's clinical expression evolves with growth, as skeletal deformities and contractures emerge from muscle imbalances (Patel et al., 2020).

Rehabilitation strategies aim on mitigating symptoms and enhancing motor function. Physical therapy, cornerstone of CP rehabilitation, focuses on strengthening muscles, improving coordination, and enhancing mobility through targeted exercises (Anttila et al., 2008), (Das et al., 2019). While effective in promoting motor skills and preventing secondary complications, it can be labour-intensive, requiring sustained effort over long periods, and efficacy may plateau in some patients. Occupational therapy, designed to enhance daily living skills via fine motor development and adaptive environmental modifications (Steultjens et al., 2004), addresses practical functionality but typically does not directly ameliorate the core neurological deficits. Pharmacological treatments, including muscle relaxants and botulinum toxin injections, are utilized to alleviate spasticity (Kriger et al., 2006); however, their transient effects are frequently offset by adverse reactions such as sedation, fatigue, and cognitive compromise (Rinaldis et al., 2010; Kolaski et al., 2010; Paoloni et al., 2013). Surgical interventions, such as orthopaedic procedures and selective dorsal rhizotomy, provide

enduring relief for severe spasticity (Wilson et al., 2014; Steinbok et al., 2007), yet they entail considerable risks and protracted recovery phases.

These established modalities, while critical, reveal inherent constraints that emphasize the demand for innovative and supplementary therapeutic options to tackle the multifaceted motor challenges of CP. There is an increasing need for non-invasive strategies that emphasize sensory rehabilitation, transcending the confines of conventional motor-focused approaches. This unmet need, combined with the variable presentation of CP, underscores the promise of FMV therapy as a means to improve sensory-motor integration—an avenue that will be elaborated upon in Section 2.2 of this thesis.

2.1.3 Stroke

Stroke, a leading cause of disability and second leading of death, arises from interrupted cerebral blood flow, classified as ischemic (85% of cases, due to arterial occlusion) or haemorrhagic (15%, from vessel rupture) (Kuriakose & Xiao, 2020; Stephen et al., 2020). Ischemic stroke, often precipitated by thrombosis or embolism, induces focal deficits like hemiparesis, while haemorrhagic variants, linked to hypertension or aneurysms, elevate mortality through intracranial pressure (Kuriakose & Xiao, 2020). Annually, 13.7 million new cases emerge and 5.5 million die, predominantly older adults, though rising incidence in younger populations (from 12.9% to 18.6%, age 20-54) reflects lifestyle risk factors (e.g., hypertension, obesity) (Kuriakose & Xiao, 2020). Brain damage disrupts motor cortices, sensory pathways, and cognitive networks, with lesion location dictating deficits—e.g., motor cortex injury yields weakness and impaired motor control, while thalamic damage impairs sensation.

2.1.4 Shared Challenges in Neurological Rehabilitation

Spinal cord injury (SCI), cerebral palsy (CP), and stroke, though distinct in aetiology and clinical presentation, converge on a set of shared rehabilitation challenges that underscore the limitations of current therapeutic paradigms and highlight the potential of FMV therapy. The literature identifies four primary obstacles that impede comprehensive recovery across these conditions, providing a critical framework for this thesis's investigation.

First, incomplete recovery persists due to the nervous system's constrained regenerative capacity. Axonal regeneration and synaptic plasticity, fundamental to functional restoration, are curtailed by inhibitory microenvironments—glial scarring in SCI, cortical damage in CP, and

ischemic necrosis in stroke—resulting in permanent deficits despite intensive intervention (Paul et al., 1997; Hachem et al. 2017; Kuriakose & Xiao, 2020). Second, sensory rehabilitation remains suboptimal, as traditional approaches like physiotherapy and constraint-induced movement therapy prioritize motor outcomes over proprioceptive or tactile recovery exercises (Anttila et al., 2008; Hachem et al. 2017). Recent reviews confirm that sensory deficits—e.g., spatial awareness, object perception, and tactile feedback—are persistent and ill-attended across these disorders, highlighting importance of integrated sensorimotor rehabilitation approaches (Moreno-López et al., 2021; Hoh et al., 2025). Third, secondary complications amplify disability. Spasticity, prevalent in all three conditions, restricts mobility and induces pain, while muscle atrophy and chronic neuropathic pain further erode quality of life (Elbasiouny et al. 2010; Krigger et al., 2006). Pharmacological management, such as baclofen or gabapentin, offers partial relief but introduces side effects like fainting, somnolence and ataxia that compromise long-term efficacy (Krigger et al., 2006; Christine et al., 2010; Lee et al. 2014).

Fourth, psychosocial burdens—depression, anxiety, and social isolation—emerge from prolonged functional dependence and reduced autonomy, diminishing adherence to rehabilitation protocols (Post et al., 2012; Horsman et al. 2010). These challenges reveal a critical gap: conventional therapies, while foundational, fail to integrate motor and sensory restoration holistically, a limitation compounded by their variable success in mitigating secondary sequelae. FMV therapy, by stimulating neuromuscular pathways and enhancing sensory feedback through mechanisms like reflex modulation and cortical activation, presents a mechanistically promising alternative (Jevtic et al., 2016; DeForest et al., 2020). This thesis leverages these shared deficits to evaluate FMV therapy's efficacy, critically assessing its capacity to address the sensorimotor and functional impairments that define SCI, CP, and stroke, as elaborated in Section 2.2.

2.2 Vibration Therapy in Neurological Rehabilitation

2.2.1 Principles and Evolution of Vibration Therapy

Vibration therapy constitutes the application of mechanical oscillations to stimulate neuromuscular and sensory systems, offering a non-invasive neuromodulation strategy distinct from conventional rehabilitation methods like physiotherapy or pharmacotherapy. The literature positions it as a versatile intervention, capable of engaging muscle spindles, reflex

pathways, and cortical networks to address motor and sensory deficits in neurological disorders (Marotta et al., 2025). Unlike invasive techniques (e.g., deep brain stimulation), vibration therapy requires minimal infrastructure and does not need specialized trainings, enhancing its accessibility across clinical and community settings—a feature critical to its relevance in resource-diverse contexts (Guang et al. 2018). This thesis leverages these attributes to explore its potential in SCI, CP, and stroke, conditions marked by sensorimotor impairments inadequately addressed by traditional approaches.

The evolution of vibration therapy traces back to mid-20th-century observations of the tonic vibration reflex (TVR), where sustained muscle contractions were elicited by tendon vibrations (Hagbarth & Eklund, 1966). Initial applications in physiotherapy and sports science focused on generalized whole-body vibration (WBV) to enhance muscle performance (Pujari et al., 2019). However, the advent of portable/ wearable devices in the late 20th century shifted emphasis toward targeted modalities— FMV and stochastic vibration—tailored for neurological rehabilitation. FMV delivers frequency specific (50–120 Hz), localized oscillations to specific muscles or tendons, aiming to modulate motor function and proprioception (Marotta et al., 2025). Stochastic vibration, employing randomized, low-amplitude oscillations, exploits stochastic resonance to amplify sensory thresholds (Richardson et al., 1998). The literature critiques WBV’s lack of specificity for neurological applications (Moggio et al., 2021; Lee et al., 2014), underscoring FMV as mechanistically precise alternatives central to this thesis’s investigative scope, as elaborated in Sections 2.2.2 and 2.2.3.

2.2.2 Focal Muscle Vibration (FMV)

FMV represents a targeted neuromodulation technique that applies specific frequency band mechanical oscillations, typically within the 50–120 Hz range, to specific muscles or tendons (Guang et al. 2018). The literature positions FMV as a non-invasive intervention designed to enhance motor function, reduce spasticity, and amplify sensory feedback in neurological disorders such as SCI, CP, and stroke (Sadeghi et al., 2014; Viganò et al. 2023; Celletti et al., 2011). Unlike WBV, which delivers generalized oscillations, FMV’s precision enables localized stimulation, making it a mechanistically distinct modality suited to addressing the sensorimotor deficits central to this thesis. This section delineates FMV’s definition, theoretical underpinnings, and physiological mechanisms, establishing the foundation for its experimental evaluation in subsequent chapters.

FMV can be defined as the controlled delivery of mechanical vibrations to discrete musculoskeletal targets—muscles or tendons—using portable or wearable devices that generate oscillations at frequencies optimized for neuromuscular and sensory activation (Guang et al. 2018). The literature highlights its therapeutic intent: to stimulate muscle spindles and reflex pathways, thereby modulating motor output and proprioceptive input (Marotta et al., 2025). Typically administered via handheld or strap-on vibrators, FMV operates at amplitudes generally ranging from 0.2 to 4 mm, with durations typically varying from seconds to minutes depending on clinical goals (Guang et al. 2018). This modality's adaptability distinguishes it from pharmacological or surgical interventions, offering a cost-effective, accessible approach that aligns with this thesis's aim to develop practical non-invasive rehabilitation tools.

The theoretical foundation of FMV rests on its capacity to exploit the neurophysiology of muscle spindles—sensory receptors sensitive to length and tension changes within skeletal muscle. Muscle spindle primary endings (or commonly known as Ia afferents) are responsible for detecting stretch-induced changes in muscles. Vibratory stimuli mimics stretch-induced spindle activation by continually activating Ia afferents. Consequently, inducing persistent after-effects in proprioceptive circuits, increasing the sensitivity and discrimination of the sensory system (Fattorini et al., 2023). The prolonged spindle activation results in a sustained depression of Hoffman-reflex (HR) activity—a neural measure of spinal excitability—a phenomenon termed as post vibration depression (PVD). It is attributed to a long-term depotentiation of the underlying sensorimotor pathways post vibration. Particularly, a long-term depression (LTD) like plasticity at the synapse between the Ia afferent and motoneuron (Rochi et al., 2018). The literature extends this concept to neurological rehabilitation, positing that FMV can counteract paresis (Viganò et al., 2023), mitigate hypertonia (Paoloni et al., 2013), and promote cortical reorganization (Jevtic et al., 2016) — mechanisms critical for conditions with disrupted sensorimotor pathways. This thesis builds on this framework, hypothesizing that optimized FMV parameters can amplify these effects across neurological populations (SCI, CP).

FMV's physiological effects span neuromuscular, sensory, and neuroplastic domains, each underpinned by distinct neural processes. From neuromuscular standpoint, FMV activates muscle spindles via Ia afferent fibres, triggering a monosynaptic reflex that increases motor unit recruitment and sustains muscle contraction (Fattorini et al., 2023). This mechanism

enhances voluntary control in paretic (i.e. affected by disorder) muscles, as evidenced by increased EMG activity in SCI cohorts (Ribot-Ciscar et al., 2003). Concurrently, FMV modulates reflex arcs to reduce spasticity, inhibiting hyperactive alpha motor neurons through pre/postsynaptic mechanisms (Murilo et al., 2010). Studies report decreased H-reflex amplitudes following FMV, suggesting a stabilizing effect on the motor neuron activity (Murilo et al., 2010).

Sensory effects centre on proprioceptive enhancement, as FMV amplifies input from muscle spindles, improving positional awareness and coordination (Camerota et al., 2016). From neuroplasticity standpoint, FMV drives cortical activation, with EEG studies detecting changes in oscillatory activity in the primary motor (M1) and somatosensory (S1) cortices during application (Kolbasi et al., 2022). Repeated stimulation induces long-term potentiation (LTP), strengthening synaptic connections within sensorimotor networks and encouraging motor learning—a process linked to sustained functional gains in chronic rehabilitation (Filippi et al. 2023). These mechanisms collectively position FMV as a multifaceted intervention, though their interdependence and optimal triggers require further elucidation.

Establishing the current landscape of FMV application in addressing neurological diseases (CP and SCI) is an essential element for designing suitable stimulation devices and designing effective experimentation protocols. The following sections systematically review the literature for vibration parameters, experimental protocols, outcomes and underlying neurophysiological changes, with an aim to a) adopt best practices in FMV delivery, including device aspects, b) identify gaps in understanding its neurophysiological impact, and c) setting up empirically backed protocols for experimental designs.

2.2.3 Use of FMV in cerebral palsy (CP)

In the context of CP, FMV has emerged as a promising modality to address motor impairments and associated symptoms. This section reviews the evidence supporting FMV's efficacy in CP populations, drawing on systematic reviews, longitudinal studies, and case reports, while identifying gaps in the understanding of its neurophysiological mechanisms.

2.2.3.1 Methodology

The following reports the methodology of the pre-existing systematic review by Ritzmann et al. (2019) on which this section is based. Due to pre-existing systematic literature review

(Ritzmann et al., 2018) on the application of FMV on CP a de-novo systematic literature review was not conducted for the thesis, instead results from the preexisting systematic literature review on the topic are presented here. The following details the methodology of the PRISMA-guided literature review.

A note to mention here that the bespoke literature review studies CP population for any type of vibration intervention (such as WBV, FMV etc.). Therefore, to fit the scope of this thesis I extracted out the studies that use FMV in their application from the total studies present in the review.

2.2.3.1.1 Eligibility criteria

The review was designed according to the population–intervention–comparison–outcomes (PICO) format as follows:

- **Participants:** Studies were included if they involved human participants diagnosed with CP, belonging to any age, or type (spastic, dyskinetic, ataxic, or mixed), reflecting the condition’s clinical diversity
- **Intervention:** The intervention required vibration application, irrespective of frequency (e.g., 50–120 Hz), amplitude, duration, or session number, to capture the full spectrum of protocols. Comparisons included CP individuals exposed to FMV versus those unexposed (e.g., controls or pre-intervention baselines).
- **Comparison:** Comparisons included CP individuals exposed to vibration versus those unexposed (e.g., controls or pre-intervention baselines).
- **Outcome:** Following outcomes were considered:
 - 1) Studies that assessed the sensory and motor function
 - 2) Studies that assessed mobility and strength.

2.2.3.1.2 Information sources

The literature search spanned three databases: PubMed, Google Scholar, and Web of Knowledge. These sources were selected for their common use in rehabilitation and neuroscience research. The keywords “cerebral palsy” AND “vibration” were included in the final Boolean search strategy. Results were limited to articles in English and German languages and studies published in the period from January 1900 to December 2017.

2.2.3.1.3 Inclusion criteria

To be included in the review, an article had to meet the following criteria:

- 1) Studies that assessed the application of vibration on CP patients and followed the listed PICO design listed above
- 2) Involved human participants with a diagnosis of CP
- 3) Delivered intervention of vibration treatment
- 4) Were full-text original articles
- 5) studies with an experimental design: randomized controlled trials, controlled trials, cohort studies, case-control studies, pre-post studies, or case reports
- 6) no inconsistencies in “Methods” and “Results” sections
- 7) complete data.

Further to this, only those studies from the CP review are included in this thesis for synthesis which addressed FMV, and other vibration interventions (such as WBV) are not considered due to falling out of the scope of this thesis.

2.2.3.1.4 Screening and data extraction

Available data identified by the electronic search were extracted independently by two researchers (Ritzmann et al., 2018) to determine whether the article met the inclusion criteria. In cases of disagreement, a third author was consulted. If the title or abstract did not provide sufficient information to determine eligibility, the article was obtained to determine whether it met the criteria. The number of articles that were included or excluded and the reasons for exclusion are detailed in the PRISMA diagram presented in Figure 2.1A.

Three reviewers from (Ritzmann et al, 2018) extracted the data from each of the studies independently and cross-checked the results to eliminate any errors. Key demographic characteristics of the participants, vibration-intervention protocols, and outcomes of each study were systematically collected. Articles were divided into categories based on the type of study design and vibration intervention the participants received, in order to compare effectiveness of vibration in patients with CP. The categories longitudinal and cross-section study designs and focal and WBV (whole body vibration) with side-alternating, vertical vibration or “other” were used.

2.3.1.5 Methodological Quality Assessment

The PEDro scale was used to estimate the quality of evidence. This scale assesses the methodological quality of a study based on such criteria as concealed allocation, intention-to-treat analysis, and adequacy of follow-up. These characteristics make the PEDro scale a useful tool for assessing the quality of therapy and rehabilitation trials (Higgins et al, 2006).

Methodological quality was independently assessed by two researchers. Studies were scored on the PEDro scale based on a Delphi list (Olivo et al., 2008) that consisted of eleven items. One item on the PEDro scale (eligibility criteria) is related to external validity and is generally not used to calculate the method score, leaving a score range of 0–10.

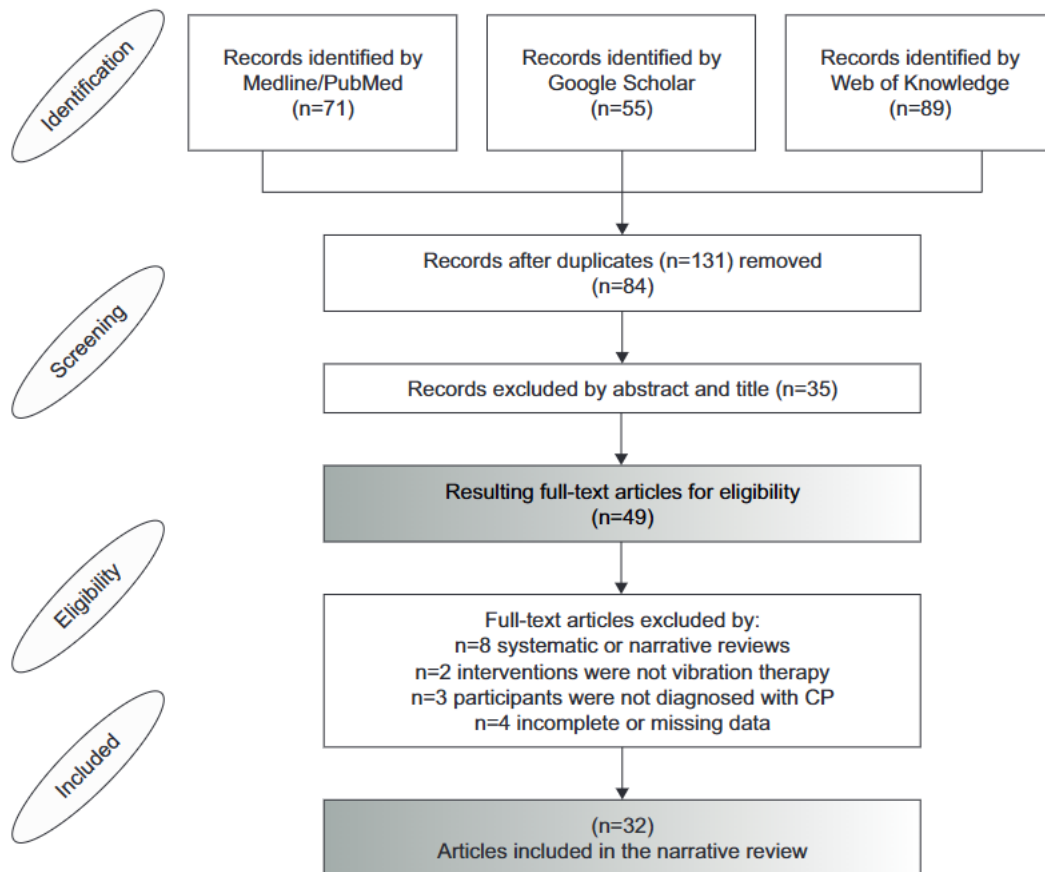


FIGURE 2.1A PRISMA flow diagram for papers identification and screening of the systematic review on CP. Taken from (Ritzmann et al., 2019)

2.2.3.2 Results of the CP Review

The systematic literature review by (Ritzmann et al., 2018) examined the application of FMV in individuals with CP. The search identified a total of 32 studies that addressed the use of vibration therapy in CP population, of these 6 studies were identified to be using FMV for CP population. These six studies targeted various motor and functional deficits associated with the neurological condition. The review reported that FMV interventions, applied at frequencies ranging from 30–37 Hz to 100–200 Hz, yielded improvements in several domains. These included enhanced motor function, increased movement speed, and improved muscle awareness, motor memory, and kinesthesia. FMV was also found to reduce coordination deficits.

and positively influence scores on the Gross Motor Function Measure (GMFM). Notably, the review suggested that FMV may induce supraspinal changes, potentially affecting brain structure, which warrants further investigation. Additionally, FMV was associated with increased muscle strength and reduced hypertonicity, with the latter effect being particularly pronounced in individuals with spasticity-related hypertonicity. Quality of life improvements were also reported, with enhanced well-being measures attributed to FMV interventions.

TABLE 2.1A: Risk of Bias Assessment of Selected Studies for CP review using PEDro. (Ritzmann et al., 2018). CR case report.

Study	1	2	3	4	5	6	7	8	9	10	11	Sum
Cannon et al, 1987	x			x	x			x	x		x	5
Eklund et al, 1969				x	x				x			3
Leonard et al, 1990	x			x				x	x	x	x	5
Tardieu et al, 1984	x			x	x				x	x	x	5
Reyes et al, 2011	x	x		x	x		x	x	x	x	x	8
Camerota et al, 2011											x	CR

2.2.3.2.1 Quality of the included studies

The PEDro quality assessment revealed the following findings: One study (Eklund et al., 1969) had a sum score of 3, three studies (Cannon et al, 1987; Leonard et al, 1990; Tardieu et al, 1984) had a score of 5, one study (Camerota et al., 2011) was a case report, and one study (Reyes et al., 2011) had a sum score of 8. Showcasing that most of the studies were in medium confidence (medium risk) range, apart from one in the high confidence (low risk) zone. These are presented in Table 2.1A.

2.2.3.3 Discussion of the CP Review

This section focuses primarily on synthesising review-level findings and identifying remaining gaps. The following are the key findings.

While four of the studies in (Ritzmann et al., 2018) were cross-sectional (n = 1, 6, 22, 200) and focused on short-term outcomes, two longitudinal studies (duration: 3 days, 6 months; n = 1, 61) explored the sustained effects of FMV, specifically on bone properties and gait parameters.

These studies demonstrated improvements in both areas, suggesting FMV's potential for long-term functional benefits. Beyond the systematic review, additional studies have reported further benefits of FMV in CP populations. For instance, (Russo et al., 2019) found that FMV reduced drooling, a common issue in CP that impacts quality of life. Case reports by (Rutović et al., 2019) and (Boulay et al., 2025) highlighted FMV's role in reducing wheelchair dependency, alleviating ankle dorsiflexor paresis, mitigating plantar flexor overactivity, improving passive extensibility, and decreasing spastic co-contraction.

Despite the promising findings, the literature reveals significant gaps in understanding the neurophysiological mechanisms underlying FMV's effects in CP. Tools such as EEG and EMG could provide insights into the supraspinal and neuromuscular changes induced by FMV, yet these have been underutilized in existing studies. The variability in vibration frequencies (e.g., 30–37, 60, 70, 90, 119, and 100–200 Hz) across studies also complicates comparisons and the establishment of optimal protocols. Furthermore, the predominance of cross-sectional designs limits insights into the long-term efficacy and sustainability of FMV interventions. Future research should prioritize longitudinal studies and employ advanced neurophysiological tools to elucidate the mechanisms driving FMV's therapeutic effects, thereby informing standardized clinical applications.

Due to the extensive systematic literature reviews available on this topic, this thesis focused on finding the gaps in the literature (of FMV's use in CP), which are described above. These gaps directly informed the experimental design of Chapter 5.

2.2.4 Use of FMV in stroke

Focal muscle vibration (FMV) has emerged as a promising non-invasive modality for the rehabilitation of neurological sequelae following stroke, particularly targeting motor deficits and spasticity (Viganò et al., 2023; Fattorini et al., 2025). This section reviews the evidence supporting FMV's role in post-stroke rehabilitation, drawing on multiple systematic reviews and meta-analyses, while identifying the specific gaps that motivated the experimental work in Chapter 7.

2.2.4.1 Methodology

Unlike the CP literature (Section 2.2.3), where a single pre-existing systematic review (Ritzmann et al., 2019) comprehensively covers the field and was adopted as the primary

source, the stroke FMV literature is served by multiple independent systematic reviews and meta-analyses. At the time of writing, more than seven such reviews have been published, including: Moggio et al. (2021), Avvantaggiato et al. (2021), Wang et al. (2020), Giorgi et al. (2024), Sambe et al. (2022), Viganò et al. (2023), and Fattorini et al. (2025). Conducting a de novo systematic review of primary studies would therefore be redundant. Instead, this section adopts a narrative synthesis approach, synthesising findings across the available systematic reviews to identify the state of evidence and locate the specific gap that the experimental work in Chapter 7 addresses. Where reviews report conflicting findings, the position of the more recent or higher-powered review is reported, and the conflict is noted.

The following documents the search strategy and parameters used to identify the systematic reviews synthesised in this section.

2.2.4.1.1 Eligibility Criteria

The review was designed according to the population–intervention–comparison–outcomes (PICO) format as follows:

- **Participants:** Studies were included if they involved adult human participants with a confirmed diagnosis of stroke (ischaemic or haemorrhagic), of any severity, chronicity, or affected limb.
- **Intervention:** The intervention required focal muscle vibration (FMV) application, irrespective of frequency (e.g., 60–120 Hz), amplitude, duration, site of application, or number of sessions, to capture the full spectrum of therapeutic protocols used in the stroke literature.
- **Comparison:** Comparisons included stroke survivors exposed to FMV versus those receiving no intervention, sham vibration, or conventional physiotherapy alone.
- **Outcomes:** The following outcomes were considered: (1) spasticity and muscle tone (e.g., Modified Ashworth Scale); (2) motor function and upper limb kinematics (e.g., Fugl-Meyer Assessment); (3) functional independence and activities of daily living; and (4) balance and mobility.

Only systematic reviews and meta-analyses were included as primary synthesis sources, given their higher level of evidence and the existence of sufficient reviews to support synthesis.

Primary studies were included only where they addressed aspects not covered by available reviews, or where their findings were specifically cited in support of mechanistic explanation.

2.2.4.1.2 Information Sources

Database: Google Scholar.

Keywords: "focal muscle vibration" OR "local muscle vibration" OR "proprioceptive stimulation" OR "localized vibration" AND "stroke".

Date of search: November 2025.

2.2.4.1.3 Inclusion Criteria

To be included in the synthesis, an article had to meet the following criteria:

- 1) Involved adult human participants with a confirmed diagnosis of stroke.
- 2) Delivered intervention of focal muscle vibration (FMV) — whole-body vibration (WBV) studies were excluded as falling outside the scope of this thesis.
- 3) For systematic reviews: used a documented search strategy across at least two databases, with pre-specified eligibility criteria.
- 4) Were full-text articles published in a peer-reviewed journal in English.
- 5) For primary studies included to support mechanistic discussion: used an experimental design (RCT, controlled trial, cohort study, pre-post study, or case series).

2.2.4.1.4 Exclusion Criteria

- 1) Studies investigating whole-body vibration (WBV) only, with no FMV arm.
- 2) Conference abstracts and proceedings without accompanying full-text publication.
- 3) Animal studies.
- 4) Narrative reviews without documented search methodology, as these could not be assessed for coverage or bias.

2.2.4.1.5 Screening and Data Extraction

Titles were screened first against the PICO criteria, followed by abstracts, and then full texts for potentially eligible articles. Systematic reviews and meta-analyses were prioritised as the primary synthesis sources. Where multiple reviews covered the same topic, their conclusions were compared; where discrepancies existed between reviews, the finding of the more recent review with the larger included sample was reported, and the discrepancy noted in the text. Screening was conducted by the primary author.

2.2.4.1.6 Quality of Evidence

As this section synthesises across systematic reviews rather than primary studies, formal risk-of-bias assessment of individual primary studies (e.g., using PEDro, as applied in Section 2.2.3) was not conducted here. The quality of the evidence base is instead characterised at the review level. The seven or more systematic reviews synthesised here collectively cover a large primary study base and consistently employ standardised outcome measures (MAS, Fugl-Meyer). Where individual reviews report quality assessments of their included studies (e.g., PEDro, GRADE, ROBINS-I), their conclusions are noted in the discussion below. The overall evidence quality for FMV in stroke is considered moderate, with most reviews noting heterogeneity of protocols and a need for larger RCTs as the primary limitation (Wang et al., 2020; Moggio et al., 2021; Giorgi et al., 2024).

2.2.4.2 Results

The evidence suggests that FMV plays a valuable role primarily in spasticity reduction and motor function improvement after stroke. Multiple systematic reviews and meta-analyses (Moggio et al., 2021; Avvantaggiato et al., 2021; Fattorini et al., 2025) demonstrate that, when applied to the appropriate muscles, often the antagonist of the spastic muscle, FMV can reduce muscle tone as measured by the Modified Ashworth Scale (MAS) and facilitate voluntary movement. Improvements have been seen not only in muscle tone, but also in upper limb kinematics, balance, mobility, and activities of daily living when integrated into rehabilitation programmes (Giorgi et al., 2024; Wang et al., 2020; Sambe et al., 2022).

Mechanistically, the action of FMV is thought to involve intense and repeated activation of muscle spindles, leading to central modulation of sensorimotor circuits through increased afferent Ia fibre input. This input can reshape the excitatory/inhibitory balance in the primary motor cortex (Marconi et al., 2011; Celletti et al., 2019; Viganò et al., 2023), enhance intracortical inhibition, and decrease hyperexcitable proprioceptive reflex activity seen in post-

stroke spasticity. Repetitive protocols at optimal parameters (typically 75–120 Hz frequency, 0.2–0.5 mm amplitude) can induce lasting neuroplastic effects, resulting in enduring improvements in both spasticity and complex motor behaviours (Fattorini et al., 2025; Wang et al., 2020).

State-of-the-art FMV protocols in stroke typically use high-frequency (75–120 Hz), low-amplitude (0.2–0.5 mm, occasionally up to 2 mm) sinusoidal vibrations applied to the muscle or tendon, most often during a mild isometric contraction (Celletti et al., 2019; Fattorini et al., 2025; Wang et al., 2020). Treatment is usually implemented across several sessions over consecutive days or weeks, with evidence supporting both acute and long-term benefits depending on protocol intensity and duration (Giorgi et al., 2024; Viganò et al., 2023).

FMV can be delivered as a standalone intervention, but many studies indicate that combining FMV with conventional rehabilitation techniques (physiotherapy, robotics, and modular rebalancing) yields superior and longer-lasting outcomes (Giorgi et al., 2024; Calabrò et al., 2017). In addition to spasticity reduction, FMV has been associated with improved grip strength, motor coordination, functional independence, and, to a lesser extent, pain modulation (Giorgi et al., 2024).

2.2.4.3 Discussion

Despite the promising findings across multiple systematic reviews, the clinical application of FMV in stroke is hampered by the heterogeneity of protocols (frequency, amplitude, session number), variability in target muscle selection, and short follow-up periods, which limit consensus on optimal dosing and long-term efficacy (Wang et al., 2020; Moggio et al., 2021; Giorgi et al., 2024). Most reviews call for further high-quality, large-sample RCTs to clarify ideal parameter sets, therapeutic windows (acute versus chronic stroke), and combinations with other therapies (Sambe et al., 2022; Viganò et al., 2023). The risk of adverse effects is consistently reported as low, and FMV is regarded as a safe and accessible adjunct to comprehensive neurorehabilitation protocols.

A specific and consistent gap across all seven reviews is the near-total absence of research into the design and usability of the FMV delivery device itself. No review identified a study that co-designed an FMV device with stroke survivors and clinicians, or evaluated device usability as a primary outcome alongside clinical efficacy. This matters because stroke survivors frequently have upper limb impairment that limits their ability to self-apply handheld vibration devices,

and the absence of wearable, user-centred devices represent a barrier to both clinical adoption and home-based use. This gap directly motivated the experimental work in Chapter 7, which describes the co-design, usability evaluation, and preliminary clinical assessment of a wearable FMV device in a stroke cohort.

In summary, focal muscle vibration stands as a well-evidenced adjunctive therapy for post-stroke rehabilitation, with moderate-quality evidence from multiple systematic reviews supporting its role in spasticity reduction and upper limb motor recovery. The principal remaining gap: the lack of co-designed, wearable delivery systems evaluated for usability in this population, is directly addressed in Chapter 7 of this thesis.

2.3 Systematic review of FMV and spinal cord injury (SCI)

This thesis section evaluates the therapeutic potential of focal muscle vibration (FMV) in individuals with SCI through a systematic literature review. A prior review by (Sadegi et al., 2014) explored FMV's role in reducing spasticity in SCI populations; however, its narrow focus and publication over a decade ago render it insufficient for capturing the broader applications of FMV in contemporary research. To address this gap, the present review systematically examines the efficacy of FMV in enhancing mobility and muscle strength, as well as its impact on sensorimotor function and underlying neurophysiological mechanisms in SCI. This updated synthesis aims to provide a comprehensive foundation for advancing clinical applications of FMV in SCI rehabilitation.

This systematic review synthesizes empirical studies on FMV in SCI up to February 2025, aiming to evaluate its efficacy and elucidate its mechanistic underpinnings across motor and sensory outcomes. The literature reveals a dual focus: understanding FMV's neurophysiological effects (e.g., H-reflex modulation) and assessing its clinical impact on mobility and strength. Yet, methodological variability—e.g., diverse vibration frequencies (60–120 Hz), inconsistent control groups—limits comparative analysis and mechanistic clarity (Gomez-Sariano et al., 2018). Adopting the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework, this review addresses the question: How does FMV application in SCI populations influence sensorimotor function, mobility, and strength, and what insights does it provide into underlying mechanisms? By critically appraising the evidence, this section informs this thesis's experimental design, highlighting the need for robust, longitudinal assessments to advance FMV's role in SCI rehabilitation.

2.3.1 Methods

This systematic review was conducted to assess the efficacy and mechanistic insights of focal muscle vibration (FMV) in individuals with spinal cord injury (SCI), adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The review addressed the question: How does FMV application in SCI populations influence sensorimotor function, mobility, and strength, and what does it reveal about underlying neurophysiological mechanisms? The methodology followed the population-intervention-comparison-outcomes (PICO) framework to structure eligibility criteria and ensure comprehensive evidence synthesis.

2.3.1.1 Eligibility criteria

The effectiveness review was designed according to the population–intervention–comparison–outcomes (PICO) format as follows:

- **Participants:** Studies were included if they involved SCI participants of any age, injury severity (complete or incomplete), or chronicity (acute or chronic), reflecting the condition's clinical diversity
- **Intervention:** The intervention required FMV application, irrespective of frequency (e.g., 50–120 Hz), amplitude, duration, or session number, to capture the full spectrum of protocols. Comparisons included SCI individuals exposed to FMV versus those unexposed (e.g., controls or pre-intervention baselines).
- **Comparison:** Comparisons included SCI individuals exposed to FMV versus those unexposed (e.g., controls or pre-intervention baselines).
- **Outcome:** Following outcomes were considered:
 - 1) Studies that assessed the sensory and motor function
 - 2) Studies that assessed mobility and strength.

2.3.2 Inclusion criteria

To be included in the review, an article had to meet the following criteria:

- 1) Studies that assessed the application of FMVs on SCI patients and followed the listed PICO design listed above
- 2) Measured one or more of the outcomes criteria listed above
- 3) Should be conducted on humans and not in animals
- 4) Must be published in the English language.

- 5) Should not be a thesis
- 6) Should not be investigating penile vibration, or sexual or related functions

2.3.3 Information sources

The literature search spanned six databases—ScienceDirect, PubMed, Cochrane Library, PEDro, Google Scholar, and Springer—covering publications up to February 2025. These sources were selected for their breadth in rehabilitation and neuroscience research, ensuring comprehensive retrieval of relevant studies.

TABLE 2.1B- Keywords Used for the Systematic Review Search Strategy

Keywords search
Springer, Science Direct, PEDro and Cochrane library
"Spinal cord injury", muscle vibration
Google Scholar
"focal muscle vibration" OR "local muscle vibration" OR "segmental muscle vibration" OR "localized mechanical vibration" OR "focal tendon vibration" OR "muscle vibration" OR "Focal Vibro-Tactile Stimulation" OR "hand-arm vibration" OR "focal vibration" OR "proprioceptive stimulation" OR "repetitive sensory input" OR "vibration" OR "vibration stimulation" OR "local vibration" OR "localized vibration" AND "spinal cord injury" OR "Tetraplegia" OR "quadriplegia" OR "paraplegia" OR "spasticity" OR "spasm" OR "spastic paraplegia" OR "spastic paresis" OR "spinal cord lesion" OR "traumatic spinal lesion" OR "hypertonia"
PubMed
"Spinal Cord Injuries"[Mesh] OR "Quadriplegia"[Mesh] OR "Paraplegia"[Mesh] OR "spinal cord lesion"[tw] OR "traumatic spinal cord lesion" OR "Spasm"[Mesh] OR "spastic*"[tw] OR "hyperton*"[tw] OR "spastic paresis"[tw] AND "focal muscle vibration"[tw] OR "local muscle vibration"[tw] OR "segmental muscle vibration"[tw] OR "mechanical vibration"[tw] OR "tendon vibration"[tw] OR "muscle vibration"[tw] OR "focal vibration"[tw] OR "vibration"[tw] OR "vibration stimulation"[tw] OR "local vibration"[tw] OR "localized vibration"[tw] OR "Vibrotactile Stimulation"[tw] OR "hand-arm vibration"[tw] OR "proprioceptive stimulation"[tw] OR "repetitive sensory input"[tw].

2.3.4 Search strategy

Keywords used for the search are provided in Table 2.1B for each of the database. Titles were screened initially, followed by abstracts and then full texts. Any theses/doctoral dissertations were not considered as it was not clear if they were peer reviewed. One review article (Sadegi et al., 2014) was also removed for not being an original research article. Furthermore, if articles were investigating penile vibration, or sexual or related functions, they were also screened out. A PRISMA flow diagram (Figure 2.1A) outlines the screening process.

2.3.1.5 Screening and data extraction

One reviewer (Moezz Ashfaque (MA)) performed the article search identifying the potential studies for the review. Two reviewers (MA and Amit Narahar Pujari (ANP)) independently assessed these identified articles for the screening criteria and any conflicts were mutually resolved. Data extraction was performed by the first reviewer (MA) which was then reassessed by the second reviewer (ANP), any outstanding conflicts were consensually resolved.

Following information was extracted from each of the included study:

- 1) Meta data: Author, year and country of the study. And the experimental design of the study (Case-series design, randomised control trial (RCT), cohort designs or case-reports)
- 2) Outcomes: The outcome measures used,
- 3) Participant demographics: mean age and gender,
- 4) SCI characteristics: Characteristic of the disease: chronic/ acute, complete/incomplete, medications being used, sample size of the cohort
- 5) Intervention elements: Details of the device, frequency and amplitude of vibration, duration and number of sessions, muscle location and target (antagonist/agonist), limb of therapy

Data extraction was divided into intervention for the upper limb (UL) and lower limb (LL). This is due to the disease characteristics of SCI, which can either effect the lower limb only (paraplegia) or all four limbs (tetraplegia). Hence mechanism of FMV action can be different and a separate presentation provides an individual picture for these two cases. The meta data and medication are presented collectively.

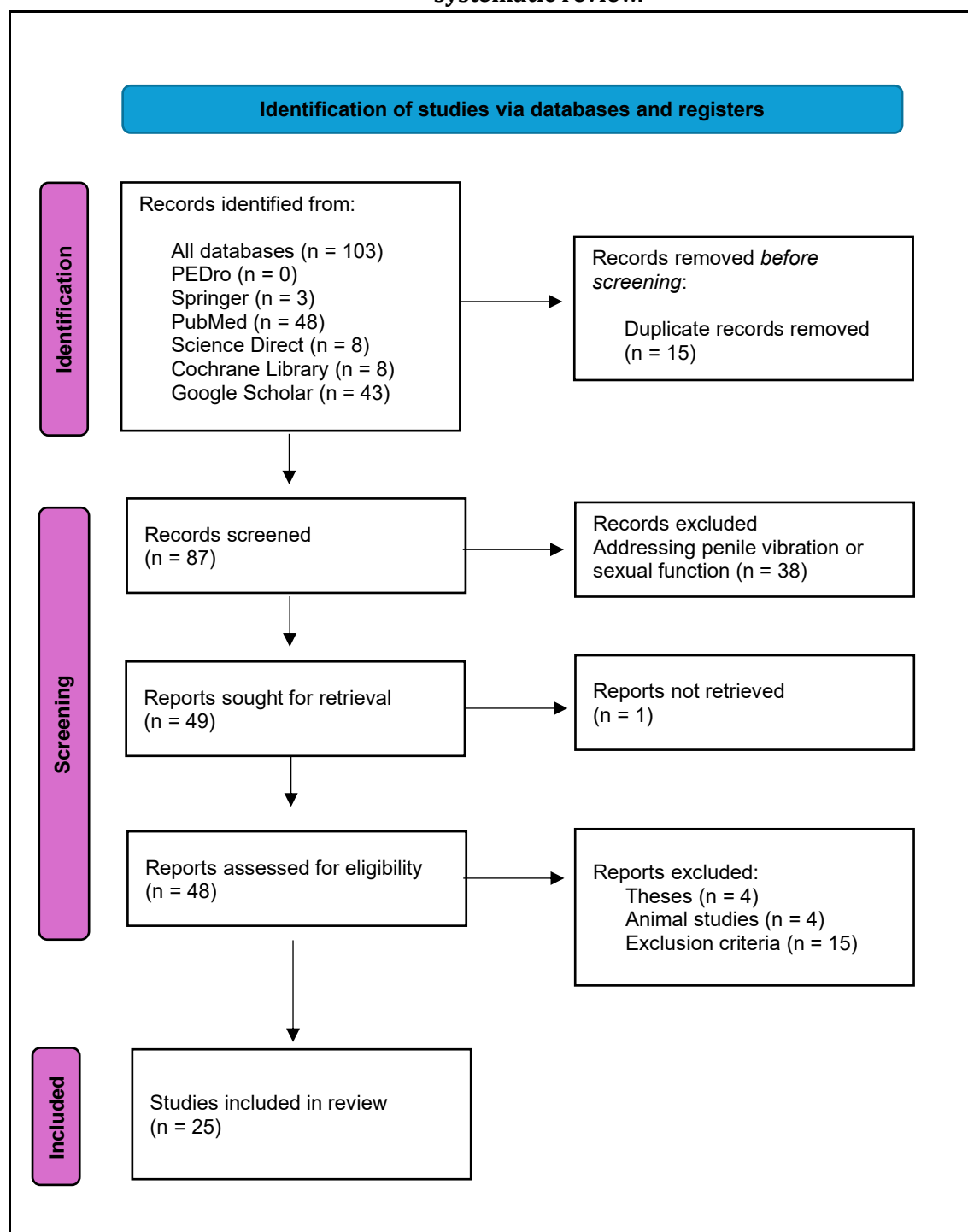
2.3.1.6 Methodological Quality Assessment

The Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) tool was applied to evaluate the methodological quality and the risk of bias of the included studies. The included studies were non-RCTs, and ROBINS-I tool is designed to assess the risk of bias in non-randomized intervention studies. The reason for choosing this tool is that the studies that were shortlisted after the inclusion criteria were mostly non-RCT, and we needed to choose a tool that can assess the methodological quality of these studies. ROBINS-I tool is designed to check the methodological quality of non-RCTs (Stern et al., 2016), hence it was used. It evaluates risks in seven domains including: confounding, participant selection, classification of intervention, deviation from the intervention, missing data, outcome measurements, and selection of reported results, to provide an overall risk of bias rating. Each domain received a risk rating (low, moderate, serious, critical), with overall bias determined by the highest risk level. For the methodological assessment one reviewer (MA) conducted the initial assessment, verified by a second (ANP), with discrepancies resolved consensually. The results of the risk assessment of this review are presented in table 4. Due to outcome heterogeneity, no meta-analysis was performed, prioritizing narrative synthesis to address the review’s exploratory aims.

2.3.2 Results

The systematic review identified 25 studies (see Table 2.4) meeting inclusion criteria, encompassing 427 SCI participants, that evaluated the effects of focal muscle vibration (FMV) on sensorimotor function, mobility, and strength up to February 2025. The literature search and screening process, detailed in Figure 1, yielded a diverse corpus spanning North America (14 studies: 11 US, 3 Canada), Europe (8 studies: 3 Italy, 2 Spain, 1 each from Netherlands, France, UK), Australia (1), and Japan (1). Participant demographics included a mean age of 38.45 years, with a gender distribution of 326 males, 87 females, and 14 unreported, reflecting the condition’s higher prevalence among males (Lee et al., 2014). Injury chronicity comprised 269 chronic, 27 acute, and 131 unreported cases, while severity included 95 complete, 174 incomplete, and 158 unreported, highlighting a bias toward chronic SCI in the evidence base. One study included multiple sclerosis patients alongside SCI, with only SCI-specific results extracted for this review (Verrier et al., 1975).

FIGURE 2.1B PRISMA flow diagram for papers identification and screening of the SCI systematic review.



Medication use, a potential confounder, was reported in 12 studies. Baclofen was the most common (51 participants), followed by diazepam (8 participants, 5 from a dedicated study), with smaller numbers using oxybutynin (2), clonazepam (1), dantrolene sodium (1), and single

instances of gabapentin, furosemide, 4-aminopyridine, and doxazosin. FMV delivery involved 15 distinct consumer devices (e.g., Vibrameter, Bosco system) and 7 custom devices, with one study unspecified, as listed in Table 2.2. Findings are presented separately for upper limb (UL) and lower limb (LL) applications due to SCI's differential impact (e.g., tetraplegia vs. paraplegia).

TABLE 2.2: FMV devices used for the identified SCI studies; NR: not related.

Sr. No.	Device Name	Type	Producer	Frequency and Amplitude	Size	Example Study
1	Vibrameter	Handheld	Somedic AB, Stockholm	50–120 Hz; 0.1–1.0 mm	Unknown	Herszkowicz et al., 1986
2	Zeniter TMT-18	Unknown	Heiwa Electronic, Japan	60–100 Hz; 0.5–2.0 mm	Unknown	Ribot-Ciscar et al., 2003
3	AMES Technology	Computerized system	AMES Tech, USA	60–80 Hz; 0.4–1.5 mm	Bulky computer system	Backus et al., 2014
4	CEN	Unknown	CEN, USA	60–120 Hz; NR	Unknown	Gomes-Osman et al., 2014
5	Bosco System	Handheld	Bosco, Italy	60–100 Hz; 0.5–4.0 mm	<5x10 cm ²	Etoom et al., 2015
6	CroSystem Nemoco	Handheld	Nemoco, Italy	80–120 Hz; 0.2–2.0 mm	<200x100 cm ²	Tazoe et al., 2021; Camerota et al. 2025
7	Thrive No. 91	Handheld	Thrive, Japan	60–80 Hz; NR	<15x5 cm ²	Calancie et al., 1993
8	4809 Vibrator	Unknown	Brüel & Kjær, Unknown	50–100 Hz; 0.5–1.5 mm	<15x15 cm ²	Hilgevoord et al., 1996
9	TNT-18 Vibrator	Unknown	Heiwa Denshi,	60–100 Hz; 0.5–2.0 mm	Unknown	Butler et al. 2006

			Japan			
10	Pro Massager USJ-301	Handheld	Unknown, Japan	60–80 Hz; NR	<20x10 cm ²	Field-Fote et al., 2012
11	Deep Muscle Stimulator	Handheld	DMS, USA	60–120 Hz; 0.5–7.0 mm	<20x5 cm ²	Bochkezanian et al., 2018
12	Jumbo Vibrator	Handheld	Wahl Clipper, USA	60–80 Hz; 0.3–1.0 mm	<20x10 cm ²	Ashby et al., 1974; Taylor et al., 1984
13	Model 4196 Sterling III	Handheld	Wahl Clipper, USA	60–80 Hz; 0.3–1.0 mm	<20x10 cm ²	Perez et al., 2004
14	Powersage 4300	Handheld	Wahl Clipper, USA	60–100 Hz; 0.5–2.0 mm	<20x10 cm ²	Murillo et al., 2011
15	Techo Concept	Handheld	Techo Concept, France	60–120 Hz; NR	<20x5 cm ²	Sabalette et al., 2024
16	Custom-Made Vibrators	Custom	Custom	60–120 Hz; 0.4–7.0 mm	custom	Takakura et al., 1996; Fusco et al., 2016; Vojinovic et al., 2019; Cotey et al., 2009; Onushko et al., 2013; Gómez-Soriano et al., 2018; DeForest et al., 2020
17	Detail Not Provided	Unknown	NR	NR; NR	<20x10 cm ²	Verrier et al., 1975

2.3.2.1 Quality of the included studies

The Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) assessment revealed varied methodological quality (Table 2.3). Seven studies exhibited low risk, five moderate, ten

serious, and three critical. Serious bias stemmed from absent control groups in multiple studies e.g., (Herszkowicz et al., 1986; Ribot-Ciscar et al., 2003), while confounding factors—e.g., prior functional tasks or stimulation—elevated risk in others e.g., (Gomes-Osman et al., 2014; Bochkezanian et al., 2018). Measurement bias in (Fusco et al., 2016) and missing data e.g., in (Gomes-Osman et al., 2014; Fusco et al. 2016) also introduced a risk of bias in some studies. Case reports e.g., (Etoum et al., 2015) were rated critical due to inherent limited methodological rigour and lack of comparative data. Low-risk studies e.g., (Calancie et al., 1993; Field-Fote et al., 2012) provided the most robust evidence, though overall variability underscores the need for rigorous designs, like including RCT designs and improving outcome comparability.

TABLE 2.3: Risk of Bias Assessment of Included Studies Using ROBINS-I

Included studies	ROBINS-I domains:								
	D1: confounding; D2: selection; D3: intervention; D4: deviation from intervention; D5: missing data; D6: outcomes; D7: reporting								
	Overall risk	D1	D2	D3	D4	D5	D6	D7	Notes
Herszkowicz et al., 1986	Serious	L	S	L	L	L	L	L	Lacks control group*
Takakura et al., 1996	Serious	L	S	L	L	L	L	L	Lacks control group*
Ribot-Ciscar et al., 2003	Serious	L	S	L	L	L	L	L	Lacks control group*
Backus et al., 2014	Serious	M	S	L	L	L	L	L	Functional task confounding**, lacks control group*
Gomes-Osman et al., 2014	Moderate	M	L	L	L	M	L	L	Functional task confounding**, some missing data
Etoum et al., 2015	Critical	L	C	L	L	L	L	L	Case report, high selection bias
Fusco et al., 2016	Moderate	L	L	L	L	M	M	L	Subjective measures, some missing data
Vojinovic et al., 2019	Critical	M	C	L	L	L	L	L	Case report, functional task confounding**

2.3.2.2 Use of FMV in the upper limb (UL)

Nine studies (n=145) explored the effects of focal muscle vibration (FMV) on the upper limbs in SCI, with six evaluating sensorimotor function (using: tonic vibration reflex (TVR), corticomotor excitability, sensation threshold, and transcranial magnetic stimulation (TMS)) and six assessing mobility and strength (using: grip force, torque, range of motion (ROM), EMG, modified Ashworth scale (MAS), 9 Hole Peg test, visuomotor tracking (Gomes-Osman et al., 2014), and mobility questionnaires). The literature reports FMV frequencies ranging from 60–120 Hz, most frequently 60–80 Hz, with amplitudes of 0.4–2 mm (four studies unreported) and durations from 9 seconds to 10 minutes across 1–25 sessions. Targeted muscles and tendons included biceps brachii, triceps brachii, flexor carpi radialis (FCR), and hand extensors (e.g., first dorsal interosseous (FDI)), with five studies applying FMV to tendons and four to muscles. Participants comprised 76 chronic SCI cases (levels C2–T2), 16 acute (levels C4–C7), and 53 unreported, indicating a predominance of chronic conditions.

Sensorimotor findings reveal diverse effects. The literature documents enhanced vibration sensation thresholds at the clavicle, correlating with injury level (Herszkowicz et al., 1986), and consistent TVR induction in biceps but only 50% in triceps after 9-second FMV (Ribot-Ciscar et al., 2003). A 10-minute FCR tendon vibration increased corticomotor excitability for 30 minutes, assessed via transcranial magnetic stimulation (TMS) and motor evoked potentials (Gomes-Osman et al., 2014), while FDI tendon FMV expanded TMS-derived motor maps (Tazoe et al., 2021). Mobility and strength outcomes include a 23% immediate grip-and-release test (GRT) improvement, with a 7% gain at three months after 25 sessions (Backus et al., 2014), and temporary pinch force gains post-10-minute FCR vibration (Gomes-Osman et al., 2014). Prolonged interventions (e.g., six 15-minute sessions) improved ROM and Modified Ashworth Scale (MAS) scores, with benefits lasting up to one month in some cases (Etoum et al., 2015). The literature highlights that sustained effects require multiple sessions, though long-term data and optimal parameters (e.g., tendon vs. muscle) remain underexplored, informing this thesis's focus on standardization.

2.3.2.3 Use of FMV in the lower limb (LL)

Sixteen studies (n=282) investigated the effects of focal muscle vibration (FMV) on the lower limbs in SCI, with eleven assessing sensorimotor function (using: H-reflex, TVR, tendon reflex, numerical rating scale (NRS) for pain and EMG) and seven evaluating mobility and strength (using: torque, EMG, MAS, ROM, trunk control test (TRT), ambulation and muscle strength

scales). The literature reports FMV frequencies predominantly at 60–80 Hz, with amplitudes ranging from 0.5–7 mm (nine studies specified) and durations varying from 1 second to 80 minutes across 1–30 sessions. Application targeted the Achilles tendon (six studies), tibialis anterior (TA), quadriceps (e.g., rectus femoris (RF)), and tensor fasciae latae (TFL), with ten studies focusing on tendons and six on muscles. Participants included 141 chronic SCI cases (levels C3–L3), 27 acute (levels C3–T6), and 114 unreported, with four studies mixing chronic and acute cases, reflecting a chronic-heavy sample.

Sensorimotor outcomes demonstrate significant neural modulation. The literature documents complete H-reflex suppression in acute SCI and reduced inhibition in chronic phases after Achilles tendon vibration, indicating phase-specific spinal excitability changes (Ashby et al., 1974; Calancie et al., 1993). Prolonged 10-minute quadriceps FMV decreased soleus H/M ratios, clonus frequency, and tendon reflex amplitude, with stronger effects in complete SCI (Murillo et al., 2011). A 5.5-minute thigh muscle vibration elicited step-like EMG responses in TFL, independent of SCI completeness or locomotor training (Field-Fote et al., 2012), while 10-second Achilles tendon FMV during hip flexion boosted TA and gastrocnemius medialis (GM) activity (Perez et al., 2004). Mobility and strength findings include enhanced proximal quadriceps activity and smoother gait phase transitions after 54-second RF vibration (Cotey et al., 2009), alongside improved range of motion (ROM) and Modified Ashworth Scale (MAS) scores following 10-minute quadriceps FMV (Murillo et al., 2011). A 30-session, 80-minute intervention increased MAS by 2 points, timed up-and-go (TRC) from 66 to 100, functional ambulation category (FAC) from 3/5 to 4/5, and walking speed in a chronic case (Camerota et al., 2024).

The literature suggests FMV's efficacy in LL is localized to stimulated muscles or synergists, with tendon applications often yielding robust reflex responses. However, inconsistent reporting of long-term effects and clinical outcomes (e.g., gait sustainability) limits broader conclusions, reinforcing this thesis's emphasis on longitudinal evaluation and standardized protocols.

TABLE 3.4: Characteristics of the SCI studies included in the systematic review.

Study	Measur- ement	Study Design	SCI details	Interven- tion	Muscle/ tendon	Location

<i>Upper Limb</i>						
Herszkowicz et al. 1986	Sensori-motor function	Case-series	(n=64, age=34) phase unclear severity unclear level: C2 & below AIS: NS	120 Hz, 1 session	NS	muscle
Takakura et al. 1996	Sensori-motor function	Crossover	(n=5, age=25) phase unclear complete level: C5,6 AIS: NS	60 Hz, 25 s, 1 session	finger	muscle agonist
Ribot-Ciscar et al. 2003	both	Case-series	(n=8, age=40) chronic, complete level: C4-7 AIS: A,C	80 Hz, 18 s, 1 session	biceps brachii triceps brachii	tendon both
Backus et al. 2014	both	Cohort	(n=10, age=40.5) chronic incomplete level: C2-7 AIS: NS	60 Hz, 30 minutes, 25 sessions	wrist flexors and extensors MCP	tendon, both
Gomes-Osman et al. 2014	both	Crossover	(n=20, age=43.7) chronic incomplete level: C4-7 AIS: C, D	80 Hz, 10 minutes 1 session	FCR	tendon, agonist
Etoum et al. 2015	mobility & strength	Case study	(n=1, age=35) chronic, incomplete level: C5 AIS: NS	100 Hz, 5 minutes, 10 sessions	triceps	muscle, anatomist
Fusco et al. 2016	mobility & strength	Case-control (controls=13)	(n=13, age=39.8) chronic, both severities level: C4-T1 AIS: A, B, D	70 Hz, 15 s, 3 sessions	biceps	tendon, agonist
Vojinovic et al. 2019	mobility & strength	Case study	(n=2, age=53) chronic	75 Hz, 15 s, 6 sessions	forearm flexors and extensors	muscle, both

			incomplete level: C2-T2 AIS: C			
Tazoe et al. 2021	Sensori- motor function	Case- control (controls= 17)	(n=22, age=54.4) chronic both severities level: C2-5,7,8 AIS: A, C, D	66 Hz, 10 minutes, 1 session	FDI	tendon, antagonist
Lower Limb						
Ashby et al. 1974	Sensori- motor function	Case- control (controls= 6)	(n=10, age=30.9) both phases both severities level: NS AIS: NS	60 Hz, TVR duration 1 session	Achilles	tendon, antagonist
Verrier et al. 1975	sensorimo- tor function		(n=5, age=27.6) phase unclear complete level: NS AIS: NS	60 Hz, duration of H-reflex, 1 session	Achilles	tendon, antagonist
Taylor et al. 1984	Sensori- motor function	Case- control (controls= 21)	(n=57, age=32) phase unclear severity unclear level: NS AIS: NS	60 Hz, duration of H-reflex, 1 session	Achilles	tendon, antagonist
Calancie et al. 1993	Sensori- motor function	Case- control (controls= 16)	(n=30, age=32) both phases both severities level: C1-7, T6,10 AIS: NS	110 Hz, duration of H-reflex, 1 session	Achilles	tendon, antagonist
Hilgevoord et al. 1995	Sensori- motor function	Case- control (controls= 30)	(n=33, age=44) chronic severity unclear level: NS AIS: NS	100 Hz, duration of H-reflex, 1 session	Achilles	tendon, antagonist

Perez et al. 2004	sensorimotor function	Crossover (controls=5)	(n=14, age=42.8) chronic incomplete level: C4-7, T1,2,5,8 AIS: C, D	80 Hz, 3 minutes 1 session	TA	tendon, antagonist
Butler et al. 2005	Sensorimotor function	Case-series	(n=8, age=37) chronic, complete level: C4-7, T6 AIS: A, B	60 Hz, 2 s, 1 session	TA	tendon, antagonist
Cotey et al. 2009	mobility & strength	Case-control (controls=5)	(n=11, age=32.3) both phases both severities level: C4-6,8, T2-4 AIS: A, B, C, D	80 Hz, 54 s, 1 session	RF	muscle, antagonist
Murillo et al. 2010	both	Case-control (controls=9)	(n=19, age=36) chronic both severities level: C3-7, T4,6,8,9,11 AIS: A, C, D	50 Hz, 10 minutes, 1 session	RF	muscle, antagonist
Field-Fote et al. 2012	mobility & strength	Case-control (controls=8)	(n=19, age=43.7) chronic both severities level: C4-7, T2-8,10 AIS: A, B, C, D	60 Hz, 5.5 minutes, 1 session	Quadriceps, Hamstring, TFL	muscle, both
Onushku et al. 2013	mobility & strength	Case-control (controls=8)	(n=9, age=43.1) chronic, complete level: C3-7, T5,6 AIS: A, B, C, D	80 Hz, 10 s, 1 session	Achilles	tendon, antagonist
Gomez-Sarriano et al. 2018	Sensorimotor function	Crossover	(n=28, age=39.3) both phases incomplete level: NS	80 Hz, 10 s, 1 session	foot	muscle, antagonist

			AIS: C, D			
Bochkezanian et al. 2018	mobility & strength	Crossover	(n=9, age=39.4) chronic both severities level: C6,7 T3,5-7,12 L3 AIS: A, B, D	55 Hz, during NMES, 1 session	patellar	tendon, antagonist
DeForest et al. 2020	Sensori-motor function	Case-series	(n=25, age=40.6) chronic both severities level: C2,4-7, T4-7,9,11 AIS: A, B, C, D	20, 40, 80, 120 Hz, 1s, 1 session	Achilles, TA	tendon, both
Camerota et al. 2025	both	Case study	(n=1, age=46) chronic severity unclear level: unclear AIS: NS	100 Hz, 80 minutes, 30 sessions	Quadriceps femoris, hamstrings, gastrocnemius, iliopsoas	muscle, both
Sabalette et al. 2024	Sensori-motor function	Case-series	(n=4, age=45.7) chronic both severities level: C6,7 AIS: A,B	10 minutes, 4 sessions	Hip, knee and ankle flexors and extensors	muscle, both
NS: not properly specified, SCM: sternocleidomastoid, MCP: metacarpophalanges and, FCR: flexor carpi radialis, FDI: first dorsal interosseous, TA: tibialis anterior, RF: rectus femoris, TFL: tensor fasciae latae, AIS: American spinal injury association impairment score						

2.3.3 Discussion of findings

The results presented in this study provide valuable insights into the use of FMV as a potential therapeutic approach for individuals with SCI. The discussion will address key findings, implications, and limitations of the reviewed studies. It will also shed light on the current state of knowledge on the use of FMV for improving sensory and motor function and mobility and strength in the upper and lower limbs in SCI population.

The included studies involved a total of 427 SCI patients. 76.4% of the SCI patients were male, reflecting the higher prevalence of research participation in SCI males, this is consistent with previous observations of higher occurrence rate (about 80%) in males (Raguindin et al., 2021). Chronic SCI cases were more prevalent in the studies, indicating a focus on individuals with

later phase of the injury. Interestingly, the majority of the studies did not specify the completeness of the SCI, which could significantly impact the interpretation of the results. In regard to the geographical distribution of the research, majority of studies were conducted in North America, which may be indicative of availability of resources and/or regional differences in research interest and priorities. It is important to note that there was a significant focus on chronic SCI cases in both upper and lower limb studies, while the representation of acute SCI cases was limited. This imbalance in participant demographics could affect the generalizability of the findings to acute SCI populations. Future research should aim to include a more diverse range of SCI types and durations to better understand the potential benefits of FMV across different phases of the injury. The studies reviewed primarily utilised vibration frequencies in the range of 60-80 Hz, with 60 Hz and 80 Hz being the most common choices. This consistency in frequency selection may indicate an established optimal range for FMV interventions. However, the vibration amplitudes and durations varied across studies, which could further influence the effectiveness of FMV. As underlying neurophysiological mechanisms determining the effects of FMV in SCI are still poorly understood with only handful of studies providing this mechanistic evidence (DeForest et al., 2020), further research is needed to determine the ideal parameters for FMV application in SCI rehabilitation.

2.3.3.1 Mobility and Strength

Upper limb (UL)

The use of FMV in ULs of SCIs present a mixed picture of its potential benefits on mobility. FMV applied to the biceps tendon in both complete and incomplete SCIs (level C4-T1) resulted in an illusion of arm movement, albeit smaller than in healthy individuals (Fusco et al., 2016), suggesting potential for sensory perception in SCIs, though the extent is unclear. In contrast, a single ten-minute FMV session at the FCR tendon area during a functional task had no immediate impact on mobility measures; incomplete SCI, level C4-C7 (Gomes-Osman et al., 2014). The effectiveness of FMV may depend on session duration, frequency and stimulation location. Case studies revealed promise in long-term effects. Six FMV sessions (duration: 15 minutes each) in forearm muscles alongside functional tasks improved the MAS and ROM; incomplete SCI, level C2-T2 (Vojinovic et al., 2019). Even shorter (duration: 5 minutes each), 10-session FMV interventions in the triceps brachii showed lasting benefits (up to a month) in the MAS; incomplete SCI, level C5 (Etoom et al., 2015). In a study involving 25 sessions of FMV in the hand region during functional tasks for 10 incomplete SCI patients (level C2-C7),

significant improvements were observed in grip and release performance as measured by the GRT and ROM (Backus et al., 2014). GRT showed a 23% improvement immediately after the sessions, with a 7% further improvement three months post-treatment. In summary, FMV's efficacy in SCIs is context-dependent – depending upon duration and length of intervention, and location of application, with potential for improvement in sensory perception and long-term benefits. The specific factors influencing its effectiveness, such as application location (tendon vs muscle), session duration, and combination with functional tasks require further exploration for optimal rehabilitation in SCIs.

FMV shows promise in improving upper limb strength in individuals with spinal cord injuries. However, its effects vary depending on factors such as muscle function and exposure duration. In complete SCIs who had injury sustained at C2-C7 level, 9 seconds of FMV improved elbow extension force generation in the biceps brachii but was inconsistent in the triceps brachii, highlighting the differences in its effects on antagonist and agonist muscles (Ribot-Ciscar et al., 2003). Long term effects were not studied. A 10-minute session of FMV at the FCR tendon enhanced pinch force but only temporarily, the improvements did not last 30 minutes post the session; incomplete SCI, level C4-C7 (Gomes-Osman et al., 2014). And 25 sessions of FMV for 30 minutes to the antagonist hand muscles (metacarpophalangeal joint and wrist) in incomplete SCIs (level C2-C7) while performing a functional task enhanced the muscle strength (Backus et al., 2014). Long term effects were again not studied. These findings suggest FMV's potential in enhancing upper limb strength, but further research is needed to understand the impact of vibration location (tendon vs muscle, agonist vs antagonist), long term effects and differences in its effects on complete and incomplete pathologies.

Lower limb (LL)

FMV presents opportunities for improving lower limb muscle activity and gait dynamics in spinal cord injuries. However, nuances and unexplored aspects deserve attention. In one study (Cotey et al., 2009), 54 seconds of FMV to the RF muscle boosted muscle activity in proximal quadriceps muscles during assisted gait but had no impact on distal leg muscles, suggesting the effects of FMV may be limited to stimulated muscle group(s) and its synergists/antagonists. In the same study, FMV also improved the transition between different phases of gait in SCI patients (both complete and incomplete; levels C4-6, 8, T2-4) that had pathological gait. Another study (Onushko et al., 2013) demonstrated that 10 seconds of Achilles tendon vibration during assisted hip movement increased muscle activity in the TA and GM muscles,

particularly during hip flexion and with voluntary assistance; complete SCI, level C3-C7, T5, 6. The effects of FMV with and without movement assistance, clinical outcomes, and long-term implications were however not studied in both these studies. A different study (Murillo et al., 2011) extended FMV to 10 minutes on quadriceps, enhancing range of motion and MAS scores in SCIs (both complete and incomplete; levels C3-7, T4, 6, 8, 9, 11), but it didn't assess muscle activity and had varied outcome measures. Surprisingly, 5.5 minutes of FMV to thigh muscles induced a step-like response in chronic complete and incomplete SCIs (levels C4-7, T4, 6, 8, 9, 11) (Field-Fote et al., 2012), independent of SCI completeness and unaffected by locomotor training. The TFL muscle showed the most robust response. Furthermore, a study explored the combination of FMV and neuromuscular electrical stimulation (Bochkezanian et al., 2018), revealing improved muscular work capability in some SCIs, while others experienced decreased capability. These were a mix of both complete and incomplete patients, at various levels: C6, 7 T3, 5-7, 12, L3. The underlying mechanisms here remain unclear. A longer dose of FMV – 30 sessions, 80 minutes each – in a chronic case study (level and severity unclear) reported promising results, with increases in MAS (by 2 points), TRC (from 66 to 100) and FAC (from 3/5 to 4/5) (Camerota et al., 2025). It also reported improvements in stride time and walking speed. In conclusion, FMV holds promise for enhancing mobility in SCIs, but location specificity, movement assistance, clinical outcomes, and long-term effects need further investigation to optimise its use in rehabilitation.

2.3.3.2 Sensorimotor Function

Upper limb (UL)

The presented findings provide valuable insights into sensory perception and motor function in the ULs of SCIs. Notably, individuals with SCIs at C2 and below (lower range not mentioned) have a reduced sensory threshold at the clavicle, directly correlating with the injury level (Herszkowicz et al., 1986). The level of completeness though was not mentioned. Furthermore, FMV interventions appear promising in restoring sensory perception, as demonstrated by significant improvements in finger digit sensation following a (30 minutes each) 25-session intervention; incomplete SCIs (levels C2-7) (Backus et al., 2014). 25 seconds of FMV to the middle finger resulted in a finger flexion reflex in complete SCIs (levels C5, 6), the amplitude of which was inhibited via acupuncture techniques (Takakura et al., 1996). Nine seconds of FMV always induces a TVR in the biceps brachii but only half the time in triceps brachii muscle; complete SCIs (levels C4-7) (Ribot-Ciscar et al., 2003). TVR is a sustained contraction of a

muscle after being subjected to vibration. Vibration excites muscle spindles, which in turn induce reflex contractions in the muscle being vibrated (Ribot-Ciscar et al., 2003). The inconsistent TVR response observed between the agonist and antagonist in upper arm muscles warrants investigation into its neurophysiological implications (Ribot-Ciscar et al., 2003). Additionally, the impact of vibration on motor function and neuroplasticity is evident, as 10 minutes of FCR tendon vibration increased long-term (30 minutes after intervention) corticomotor excitability; incomplete SCIs, level C4-C7 (Gomes-Osman et al., 2014). This corticomotor excitability was assessed with TMS and motor evoked potentials from the thenar muscle. A similar effect was observed with FMV at the FDI tendon, where motor maps generated by TMS expanded; both complete and incomplete SCIs, level C2-5, 7, 8 (Tazoe et al., 2021). The immediate corticomotor excitability in (Gomes-Osman et al., 2014) however did not change.

Lower limb (LL)

In the LL there is a larger number of studies investigating sensory and motor performance. The soleus H-reflex response to Achilles tendon vibration in the LL has been widely studied in literature and has offered valuable insights into neural mechanisms in the context of SCIs. The H-reflex is a monosynaptic reflex elicited by electrically stimulating sensory nerve fibers (Ia afferents), used to assess spinal motor neuron excitability and reflex pathways. Early studies by Ashby et al. (Ashby et al., 1974) and subsequent validations (Calancie et al., 1993; Hilgevoord et al., 1996) have shown that, in the acute phase of SCI for both complete and incomplete cases, vibration completely diminishes the soleus H-reflex, despite higher H-reflex amplitudes without vibration compared to healthy population. The level of SCIs is though not provided. In the chronic phase, the H-reflex response ratio between vibration and no vibration (H_{vib}/H) increases compared to healthy population, indicating reduced H-reflex inhibition in response to vibration (Ashby et al., 1974; Calancie et al., 1993; Hilgevoord et al., 1996). Additionally, the TVR for the soleus muscle elicited by Achilles tendon vibration is completely or almost completely diminished in acute SCI (both complete and incomplete, levels unknown), and this reduction persists in the chronic phase (Ashby et al., 1974). The H/M ratio is the ratio of the maximal H-reflex amplitude to the maximal M-wave amplitude, reflecting spinal motor neuron excitability. A higher ratio indicates increased excitability, while a lower ratio suggests reduced excitability or inhibition. Diazepam's influence on FMV action is also studied; the H_{vib}/H ratio in complete SCIs (levels unknown) does not change using Diazepam (Verrier et al., 1975).

However, Diazepam's effect on the H/M ratio is not known, which can provide further insights into the neural activity. Notably, as spasticity increases in SCI patients (unknown completeness and levels), the H_{vib}/H ratio also rises (Taylor et al., 1984), signifying reduced depression of the H reflex with vibration. The ratio increased with the duration of lesion for all patients and was unrelated to the level of lesion or the completeness of SCI (Taylor et al., 1984). Following neurophysiological implications are suggested by the author: a) mechanisms blocking the H-reflex become less effective as spasticity gains prominence, b) vibration produces greater background facilitation of motoneurons in spasticity conditions (Taylor et al., 1984).

Calancie (Calancie et al., 1993) noted that presynaptic inhibition is enhanced in complete and incomplete acute SCI (levels C1-7, T6, 10), contributing to hyporeflexia during spinal shock, while it is diminished in chronic SCI, contributing to hyperreflexia associated with spasticity. These studies laid the foundation for investigating complete H recruitment curves to better understand neurophysiological behaviour. Hilgervood (Hilgevoord et al., 1996) examined M-wave characteristics and H-reflex thresholds with and without vibration, finding that vibration lowered H-reflex thresholds but did not affect the maximum H-reflex thresholds, and the M-wave remains consistent between subjects and conditions (the completeness and levels were unknown). Reduction in H-reflex due to vibration is attributed to presynaptic inhibition and post-activation depression. (Murillo et al., 2011) extended vibration research to other muscle groups and with longer exposure time, applying 10 minutes of FMV to the quadriceps. This led to a decrease in the Soleus H/M ratio, with more prominent effects in complete SCIs. Vibration also reduced clonus frequency and duration and decreased the T-Reflex - a monosynaptic reflex triggered by mechanically tapping a tendon, stretching the muscle and activating muscle spindles. The heteronymous H-reflex response in complete and incomplete SCIs was attributed to mechanical spread of vibration and the 'busy line' phenomenon, making fibres unresponsive to other inputs during vibration.

(Perez et al., 2004) examined the effects of focal vibration on the TA tendon in chronic complete SCIs (levels C4-7, T1, 2, 5, 8), highlighting the H-reflex behaviour in reciprocal Ia and presynaptic D1 inhibition mechanisms in the Soleus muscle. Vibration inhibited H-reflex for reciprocal Ia inhibition (maintained up to 5 minutes) but did not have significant short or long-term effects on presynaptic D1 inhibition. The presynaptic Ia terminal and Ia interneuron were considered the possible sites of inhibition and presynaptic inhibition, post activation depression and robust spindle activation were attributed as the possible causes. Spasms are a

common consequence after SCI. (Butler et al., 2006) found that involuntary spasm-like EMG activity, evoked by superficial nerve stimulation in complete chronic SCIs (levels C4-7, T6), was reduced by vibrating Achilles tendon. The EMG activity depression was prominent in muscles proximal to the site of vibration but not in the distant ones. The vibration however did not affect the SOL H-reflex in SCIs. Persistent inward currents (PICs) were attributed to the long-lasting depression of the involuntary activity and not presynaptic terminal inhibition or motoneuron excitability. Cutaneous reflex responses were also explored. (Gómez-Soriano et al., 2018) showed that vibration inhibited the long latency TA cutaneous reflex during plantarflexions in incomplete SCIs (levels not available) with spasticity, with the extent of inhibition correlated to the Modified Ashworth Scale (MAS), indicating greater reflex inhibition in subjects with higher spasticity. In contrast, (DeForest et al., 2020) noted that tendon vibration at specific frequencies for complete and incomplete SCIs (levels C2, 4-7, T4-7, 9, 11) inhibited the long-lasting component of the cutaneous reflex in antagonist muscles but not in agonist muscles, offering insights into the suppression of PICs and the activation of interneurons involved in central pattern generator networks. (Camerota et al., 2025) showed that the pain threshold measured through NRC got alleviated by 30 sessions of 80 minutes each FMVs to a case of chronic SCI (level, severity unclear). It also reported improvements in EMG activation patterns and co-activations but failed to provide its empirical evidence. 4 sessions of 10 minutes of FMV combined with virtual reality also showed a decrease in NRC pain thresholds in chronic SCIs (levels C6, 7; both severities) (Sabalette et al., 2024).

In conclusion, these studies contribute significantly to our understanding of neural mechanisms affected by FMV in SCIs. They highlight the potential for vibration to induce plastic changes in neural circuitry and improve spasticity management. Future research should continue to explore the implications of different vibration frequencies, stimulation location (muscle Vs tendon, agonist Vs antagonist), with and without accompanying muscle contraction/activity and the potential for long-term neural modulation.

2.3.3.3 FMV devices used

Regarding the FMV devices employed in the reviewed SCI studies, the analysis reveals that more than 15 distinct devices have been utilized, reflecting a considerable diversity in instrumentation. Detailed specifications of these devices are presented in Table 2.2. The majority are handheld rather than wearable, and they typically rely on an external electrical power supply for operation. In terms of physical dimensions, most devices exceed $20 \times 10 \text{ cm}^2$.

Operationally, the devices predominantly operate within the 60-120 Hz frequency range as claimed by the manufactures. Even though these frequencies are claimed, however there is no characterization experiments detailed in literature that can confirm the validity of these frequencies. Notably, one study (Botter et al., 2020) has demonstrated that the claimed frequency output by FMV devices is not always consistent with output frequency measured in the real world. Hence raising confidence issues in the frequency and its association with the neurorehabilitation.

2.3.3.4 Study limitations

This systematic review has certain limitations to consider. The included studies exhibited substantial heterogeneity in design, FMV parameters, and participant characteristics, making direct comparisons and generalizability challenging. Small sample sizes, limited diversity in SCI severity and duration, and the absence of control groups in some studies raise questions about the robustness of the findings. Variation in vibration devices is another question. Regional bias and potential publication bias may affect the generalizability of results. Many studies focused on short-term outcomes, while long-term effects and underlying mechanisms were often underexplored. These limitations emphasize the need for diverse, and mechanistic research to better understand the potential and practical application of FMV in SCI rehabilitation.

2.4 Implications for study design

The literature review on FMV applications in SCI and CP, as detailed in Sections 2.2.3 and 2.3, underscores both the therapeutic promise and the critical limitations of current vibration therapy practices. These findings establish a compelling case for the development of a well-characterized FMV device and the integration of neurophysiological assessments, such as EEG and EMG, to advance vibration therapy's efficacy and mechanistic understanding. This section bridges the evidence from the literature to the objectives of subsequent chapters, highlighting the need for standardized technology and rigorous neurophysiological investigation.

The systematic reviews reveal that FMV can reduce spasticity, enhance motor function, and improve sensory feedback in SCI and CP populations (Ritzmann et al., 2018; Sadeghi et al., 2014) (Section 2.3). However, consumer-grade or inadequately characterized devices, often used in prior studies, fail to deliver precise, reproducible vibrations, undermining the ability to correlate specific parameters with clinical outcomes (Botter et al., 2020). This technological gap, evident across SCI and CP applications, necessitates the development of a wearable,

precisely calibrated FMV device capable of delivering controlled reproducible vibrations within the therapeutically optimal range of 60–120 Hz, as pursued in Chapter 4. Such a device would enable reliable comparisons across studies and populations.

Furthermore, the neurophysiological mechanisms underlying FMV's therapeutic effects remain inadequately characterized. While studies suggest that FMV modulates reflex pathways, enhances muscle spindle activation, and induces cortical reorganization (Jevtic et al., 2016; Marotta et al., 2025), the precise neural correlates, such as changes in cortical excitability or muscle co-contraction, require deeper exploration. The limited use of EEG and EMG in existing research restricts insights into supraspinal and neuromuscular responses, particularly in CP, where supraspinal changes are hypothesized but understudied (Ritzmann et al., 2018). Similarly, in SCI, H-reflex modulation is documented, but its linkage to cortical activation remains speculative (Gomes-Osman et al., 2014; Perez et al., 2004). Integrating EEG to measure cortical activity (e.g., sensorimotor cortex activation) and EMG to assess muscle responses (e.g., co-contraction patterns) is essential to elucidate these mechanisms, as proposed in Chapters 5, 6. These neurophysiological tools will provide quantitative data to refine FMV parameters and optimize therapeutic protocols, addressing the mechanistic gaps identified in the literature. In stroke FMV rehabilitation research is more mature, already addressing the problems with ideal vibration parameters and neurophysiological understanding. But there is a need to develop the device with a user-centric approach so that the technology can be transferred from clinic to home.

2.5 Research gaps in the literature

The literature review on FMV applications in SCI and CP, as detailed in Sections 2.2.3 and 2.3, identifies following four key research areas open for further investigation.

1. The devices used for FMV applications lack a coherency, i.e. a variable number of devices from varying manufacturers is utilised. Each having potentially different vibration dose characteristics.
2. There is a lack of neurophysiological studies that look into the mechanistic effects of FMV in CP and SCI patients. Particularly, its effect at the cortical level, and any possible plastic effects it can have. Longitudinal studies (e.g. > 1 month) are also in scarcity.

3. Even though there are studies that show FMV to improve strength and increased muscle activity (EMG) in CP, its effects on movement synergies like co-contraction are not widely studied.
4. Ideal dosage parameters (such as vibration frequency, dosage time, number of sessions, location on muscle) for best rehabilitation outcome is an open investigation problem for CP rehabilitation.
5. In stroke population, there is a lack of user-centric FMV device design, and the effectiveness of such designed devices for clinical rehabilitation.

This thesis will investigate these aspects of FMV rehabilitation. The research objectives and research questions of this thesis are laid down in the next chapter.

Chapter 3: Research Aims, Objectives and Strategy

3.1 Research Problem

Despite the growing interest in focal muscle vibration (FMV) as a non-invasive tool to neurorehabilitation, the extant literature on its application in SCI and CP reveals several critical and interrelated gaps that constrain both mechanistic understanding and clinical translation. Existing FMV devices lack consistency, employing heterogeneous hardware from multiple manufacturers that deliver inconsistent vibration-dose profiles, whereas a consistent trustable vibration frequency profile of FMV device is necessary for systematic dose-response investigations. Compounding this technological fragmentation is the near-absence of neurophysiological studies elucidating the cortical and subcortical mechanisms underpinning FMV-induced effects in SCI and CP populations, including potential experience-dependent plasticity; longitudinal designs exceeding one month remain particularly scarce. Although FMV has been shown to enhance volitional strength and EMG amplitude in CP, its influence on higher-order motor control features, such as pathological co-contraction and impaired movement synergies, has received minimal empirical attention. Optimal dosage parameters (vibration frequencies) for maximal functional gain in CP rehabilitation are similarly undefined. Parallel shortcomings exist in the stroke literature, where user-centred device design and subsequent clinical-effectiveness evaluations are notably absent. The present thesis therefore seeks to address these interconnected deficiencies through targeted device development, neurophysiological and behavioural experimentation, and parameter optimisation in SCI, CP, and user-centric device design in stroke cohorts. The specific research objectives and attendant questions are articulated in the following section.

3.2 Research Aim, Objectives and Questions

Thesis aim: The overall aim of this thesis was to progress the evidence on the effectiveness of FMV as a neurorehabilitation tool for CP, SCI and stroke, specifically by leveraging engineering development, electrophysiological outcomes and clinical outcomes

The research delineated in previous section address critical gaps in the application of FMV therapy for neurological rehabilitation. To guide the experimental design and data collection of this thesis, the study poses specific research objectives and questions that translate these objectives into testable inquiries. Each question targets a distinct aspect of FMV, ensuring a comprehensive evaluation across SCI, CP, and stroke.

OB1. Development of an FMV device capable of providing characterized, reproducible vibrations:

This thesis aims to design and construct a wearable FMV device delivering controlled reproducible vibrations to targeted muscles or tendons. The device will be characterized to ensure precision and reliability, establishing input-output relationships (e.g., voltage to frequency) critical for clinical applicability.

RQ1. *Engineering an FMV devices to deliver precise and reproducible vibrations suitable for neuromuscular and sensory rehabilitation*

OB2. Effectiveness of different frequencies of FMV on the cortical behaviour and muscular function and co-contraction in CP/ SCI:

This thesis will assess FMV's efficacy in improving motor function (e.g., strength, coordination), reducing spasticity, and enhancing sensory feedback in SCI and CP cohorts. Using EEG and EMG in clinical trials, the thesis will quantify neurophysiological changes, such as cortical activation, muscle activation, fatigue and muscle co-contraction, to link FMV with therapeutic outcomes. In this regard, the thesis will also assess the effects of using different vibration frequencies for FMV

RQ2. *What are the specific effects of long exposures of FMV on motor function, spasticity, and brain activity in individuals with SCI and CP, and how do these effects vary with different vibration frequencies?*

OB3. Investigating the usability and effectiveness of an FMV device co-designed with patients in stroke:

This study will evaluate FMV's feasibility and usability in a clinical setting for stroke survivors, focusing on device co-design with patients and clinicians, and then assessing its short-term effects on clinical measures of spasticity and upper limb function.

RQ3. *What is the feasibility, usability, and short-term clinical effects of a co-designed wearable FMV device on spasticity and upper limb function in stroke survivors?*

These objectives collectively aim to deliver innovative devices and actionable insights, positioning wearable FMV therapy as a scalable, evidence-based intervention for neurological rehabilitation.

3.3 Significance, Novelty and Strategy of the Research

This thesis addresses critical unmet needs in neurological rehabilitation by advancing wearable FMV therapy through technological innovation, mechanistic insight, and clinical validation. Its significance lies in five key contributions.

1. First, by developing an FMV device that provides accurate frequency vibrations this thesis aims to fill the gap in variability in the device output present in current literature. It also tries to achieve a wearable, cost-effective FMV device model, in turn potentially improving access to advanced neuromodulation tools, overcoming the limitations of existing bulky or expensive systems (e.g., Li et al., 2021). *This addresses the OB1 of the thesis that aims to develop vibration devices that deliver reproducible and accurate vibration frequencies and is investigated in Chapter 4.*
2. Second, the integration of EEG and EMG to probe cortical and muscular responses offers a novel framework for elucidating FMV therapy's neurophysiological mechanisms—such as cortical reorganization and muscle co-contraction modulation—beyond the descriptive accounts dominating current literature (e.g., Backus et al., 2014). This mechanistic clarity will inform FMV parameter optimization, enhancing therapeutic precision. *This addresses OB2 of the thesis which aims to investigate the*

neurophysiological mechanisms of FMV (in CP and SCI) – aspects studied in Chapters 5 and 6 of this thesis.

3. Third, by conducting a user-centric device design, this thesis aims to translate the research development from laboratory to the end-users directly and use that end-user designed device for checking potential clinical improvements. Hence bridging the gap in translation of healthcare medicine from laboratory to clinic/ home. *This ties up with OB3 of the thesis that aims to co-design an FMV device with users in the loop and use that device design for assessing clinical assessments. These are addressed in the Chapter 7 of this thesis.*
4. Fourth, this research bridges a critical evidence gap by systematically evaluating FMV across SCI, CP and stroke, conditions underrepresented in longitudinal vibration studies. Unlike prior work with small, heterogeneous cohorts (e.g., (Fusco et al., 2016), this thesis employs robust experimental designs to assess long-term efficacy, providing clinicians with robust, condition-specific protocols. *These are generally studied across the chapters of the thesis.*
5. Fifth, by improving motor function, reducing spasticity, and enhancing sensory feedback, this work promises tangible improvements in functional independence and quality of life for affected individuals. *These are also generally investigated through the thesis.*

Collectively, these contributions position this research as a transformative step toward integrating FMV therapy into mainstream rehabilitation practice, with implications for both clinical outcomes and neuroscientific understanding.

Chapter 4: Development of a Focal Muscle Vibration Device

The experiments in this chapter have been published as a book chapter in Springer, work was invited oral presentation at International Conference of Neurorehabilitation

Ashfaq, M., Pujari, A.N. (2025). "Developing and Characterizing a Low-Cost, Wearable Focal Muscle Vibration Device for Neurorehabilitation." In: Pons, J.L., Tornero, J., Akay, M. (eds) *Converging Clinical and Engineering Research on Neurorehabilitation V. ICNR 2024. Biosystems & Biorobotics*, vol 31. Springer, Cham. https://doi.org/10.1007/978-3-031-77588-8_117

4.1 Introduction

Focal muscle vibration (FMV) is a neurostimulation technique which has gained wide interest in neurorehabilitation over the past decade (Fattorini et al., 2021). It uses focused vibrations on muscles or tendons to activate the underlying afferent fibers (Rochi et al., 2018; Barss et al., 2021). It is extensively used for spasticity reduction, functional recovery, and muscle performance in healthy population and in neurological disorders – including stroke (Pietro et al., 2012), spinal injury (DeForest et al., 2018; Ashfaq et al., 2026), multiple sclerosis, cerebral palsy (Ritzmann et al., 2018). It is non-invasive and does not have a side effect profile which makes it a favourable option in administration over surgical and pharmaceutical interventions. The effectiveness of FMV intervention is directly linked with the frequency of vibration; varying frequencies can have a varying outcome effect (DeForest et al., 2020). It is therefore important to design a FMV device to deliver a precise vibrational profile, so that its effects can be properly quantified and compared across different research studies and different populations.

The devices currently used in literature are lack any proper vibration characterization, making it hard to know the real operating frequency of the device (Botter et al., 2020). Assessment outcomes from such uncharacterized devices can be misleading and result into inappropriate representation of the study outcomes.

Literature search on the current use of FMV devices revealed that more than 15 distinct devices have been used in literature, reflecting a considerable diversity in instrumentation. Detailed

specifications of these devices are presented in Table 4.1. Majority of the devices are handheld rather than wearable, and they typically rely on an external electrical power supply for operation. In terms of physical dimensions, most devices exceed $20 \times 10 \text{ cm}^2$. Operationally, the devices predominantly operate within the 60-120 Hz frequency range as claimed by the manufactures. Even though these frequencies are claimed, however there is no characterization experiments detailed in literature that can confirm the validity of these frequencies. Notably, one study (Botter et al., 2020) has demonstrated that the claimed frequency output by FMV devices is not always consistent with output frequency measured in the real world settings. Hence raising confidence issues in the frequency of the device and its association with the neurorehabilitation. One of the aims of the thesis (RQ2) is to check the effect of different vibration frequencies on the sensory and motor function in neurological individuals, hence it is imperative that the device used in experiments delivers a precise and accurate vibration frequency. This is important because it will help in correctly understanding the impact of different vibration frequencies on the functional/ neurophysiological performance.

Therefore, since the confidence in the precision of vibration frequency of the available FMV devices is low, in this study I design and characterize a wearable FMV device from scratch. Such that its frequency response is well quantified and can be used across different research studies and applications pertaining to this thesis, and beyond. To achieve this, I designed an experimental setup to quantify the frequency profile of our device. I designed an electronic circuitry to control and operate the device at different frequency settings, suitable for neurorehabilitation applications. Finally, I made a 3D printing to house the device, making it user-friendly and wearable for the user/ caregiver. Following section details the development and experimentation process. We aimed to make our device a wearable device, so it is easier for the user to don/doff, and make it cost-effective.

This chapter unfolds as follows: Section 4.2 outlines the experimental design methodology, detailing the selection of components and construction of the FMV device. Section 4.3 lays down the theoretical underpinnings of the mode of operation of the vibration motor used. Section 4.4 describes the experimental setup and characterization process, establishing the voltage-frequency relationship critical for therapeutic precision. Section 4.5 presents the characterization results, validating the device's performance and reliability. Section 4.6 summarizes the chapter and discusses the implications for clinical trials, which are further explored in Chapter 4. By addressing technological deficiencies through robust engineering,

this chapter lays the foundation for advancing FMV as a standardized, evidence-based intervention in neurological rehabilitation.

TABLE 4.1: FMV devices used for the SCI studies identified in the literature review; NR: not related.

Sr. No.	Device Name	Type	Producer	Frequency and Amplitude	Size	Example Study
1	Vibrameter	Handheld	Somedic AB, Stockholm	50–120 Hz; 0.1–1.0 mm	Unknown	Herszkowicz et al., 1986
2	Zeniter TMT-18	Unknown	Heiwa Electronic, Japan	60–100 Hz; 0.5–2.0 mm	Unknown	Ribot-Ciscar et al., 2003
3	AMES Technology	Computerized system	AMES Tech, USA	60–80 Hz; 0.4–1.5 mm	Bulky computer system	Backus et al., 2014
4	CEN	Unknown	CEN, USA	60–120 Hz; NR	Unknown	Gomes-Osman et al., 2014
5	Bosco System	Handheld	Bosco, Italy	60–100 Hz; 0.5–4.0 mm	<5x10 cm ²	Etoom et al., 2015
6	CroSystem Nemoco	Handheld	Nemoco, Italy	80–120 Hz; 0.2–2.0 mm	<200x100 cm ²	Tazoe et al., 2021; Camerota et al. 2025
7	Thrive No. 91	Handheld	Thrive, Japan	60–80 Hz; NR	<15x5 cm ²	Calancie et al., 1993
8	4809 Vibrator	Unknown	Brüel & Kjær, Unknown	50–100 Hz; 0.5–1.5 mm	<15x15 cm ²	Hilgevoord et al., 1996
9	TNT-18 Vibrator	Unknown	Heiwa Denshi, Japan	60–100 Hz; 0.5–2.0 mm	Unknown	Butler et al. 2006

10	Pro Massager USJ-301	Handheld	Unknown, Japan	60–80 Hz; NR	<20x10 cm ²	Field-Fote et al., 2012
11	Deep Muscle Stimulator	Handheld	DMS, USA	60–120 Hz; 0.5–7.0 mm	<20x5 cm ²	Bochkezanian et al., 2018
12	Jumbo Vibrator	Handheld	Wahl Clipper, USA	60–80 Hz; 0.3–1.0 mm	<20x10 cm ²	Ashby et al., 1974; Taylor et al., 1984
13	Model 4196 Sterling III	Handheld	Wahl Clipper, USA	60–80 Hz; 0.3–1.0 mm	<20x10 cm ²	Perez et al., 2004
14	Powersage 4300	Handheld	Wahl Clipper, USA	60–100 Hz; 0.5–2.0 mm	<20x10 cm ²	Murillo et al., 2011
15	Techo Concept	Handheld	Techo Concept, France	60–120 Hz; NR	<20x5 cm ²	Sabalette et al., 2024
16	Custom-Made Vibrators	Custom	Custom	60–120 Hz; 0.4–7.0 mm	custom	Takakura et al., 1996; Fusco et al., 2016; Vojinovic et al., 2019; Cotey et al., 2009; Onushko et al., 2013; Gómez-Soriano et al., 2018; DeForest et al., 2020
17	Detail Not Provided	Unknown	NR	NR; NR	<20x10 cm ²	Verrier et al., 1975

4.2 Experimental design

An FMV device was developed utilizing an eccentric rotation mass (ERM) motor to deliver targeted vibrations. The ERM motor was selected for its ability to generate consistent and controllable vibrations essential for therapeutic muscle stimulation. Precision Microdrives©

model 302-102 ERM was used because of its previous use in literature (DeForest et al., 2020). To ensure device's practicality and wearability, a custom casing was designed, and 3D printed. A three-dimensional computer-aided design (CAD) model for a motor casing was developed in SolidWorks® for encapsulating the motor before 3D printing. The casing was designed with a curved surface to ensure a good cushion and traction with the contacting muscle. The casing was crafted from polylactic acid due to its favourable properties, including biocompatibility, durability, and ease of fabrication. Velcro straps were used to aid strapping and wearability of device on to the body. To ensure uniform force delivery from the device to muscle, a pressure sensor (Flexiforce® A-201) was coupled with the device, it was calibrated to an equivalent of 1N weight to ensure uniform vibration delivery across muscles and users. LED lights were used as guidelines for the user to indicate if pressure falls within $\pm 0.1\text{N}$ range of 1N value. The device weighed 65g making it light weight and easy to use for patients and caregivers. The form factor is also small with the length of 58 mm in the longest device axis. Figure 4.1 shows the device.

It is well-known that different vibration frequencies can have a different impact on the neurological rehabilitation outcomes (DeForest et al., 2020). Therefore, we aimed to develop a device that can operate at various vibration frequencies. Hence a device characterization process was performed to establish a relationship between the vibration frequency of the motor with the battery voltage (detailed in the experimentation section). As a result, voltages corresponding to the desired frequency values were obtained.

From the literature review in Chapter 2 (Sections 2.2.3 and 2.3.2) 60-120 Hz was identified as the adopted range of frequencies for FMV delivery. Which underscores the potential of 60-120 Hz as frequency range responsible for stimulating the afferent neurons underlying the muscle surface. Therefore 60, 80, 100 and 120 Hz frequencies were selected as the device operational frequencies. Corresponding voltage values for these frequencies are in Table 3.1. After characterization process, an electronic circuitry was developed that can control the device operation. For this circuitry, a voltage regulator was used to provide a constant voltage of 2.85V which corresponded to the 120 Hz frequency value. A potential divider circuitry using 1 ohm power resistors was designed for operating the motor at voltages corresponding to the design voltages. User-controllable switches were installed in the circuit to manually control the device. A 3.7 V battery was used to power the circuit which in turn operates the motor. Device and

circuitry can be seen in Figure 4.1, while the electronic circuit diagram can be viewed in Figure 4.2.

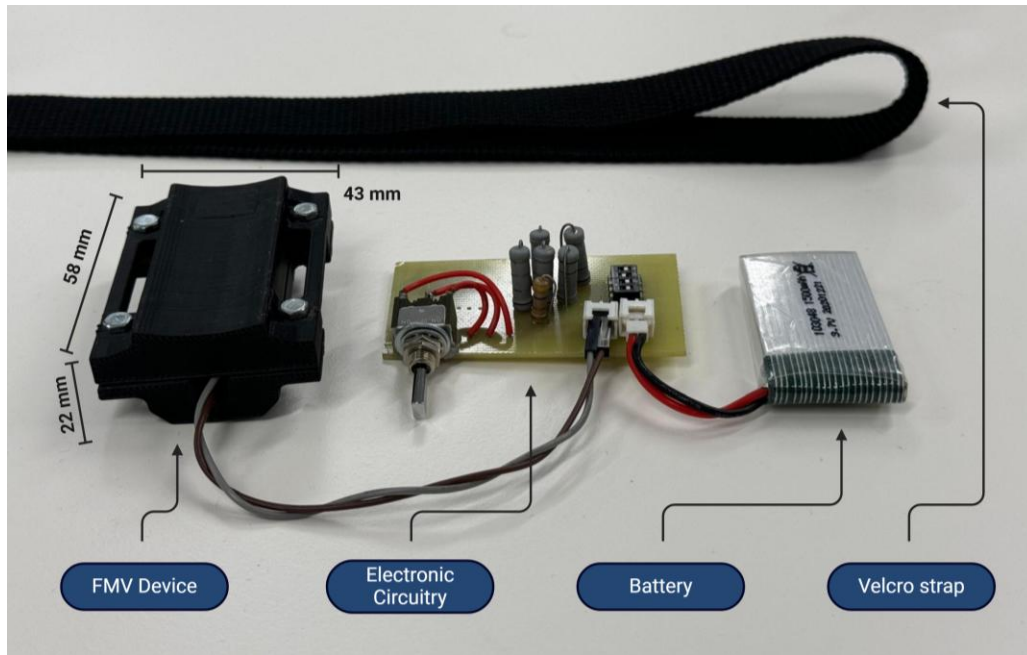


FIGURE 4.1. The developed FMV device with its different elements.

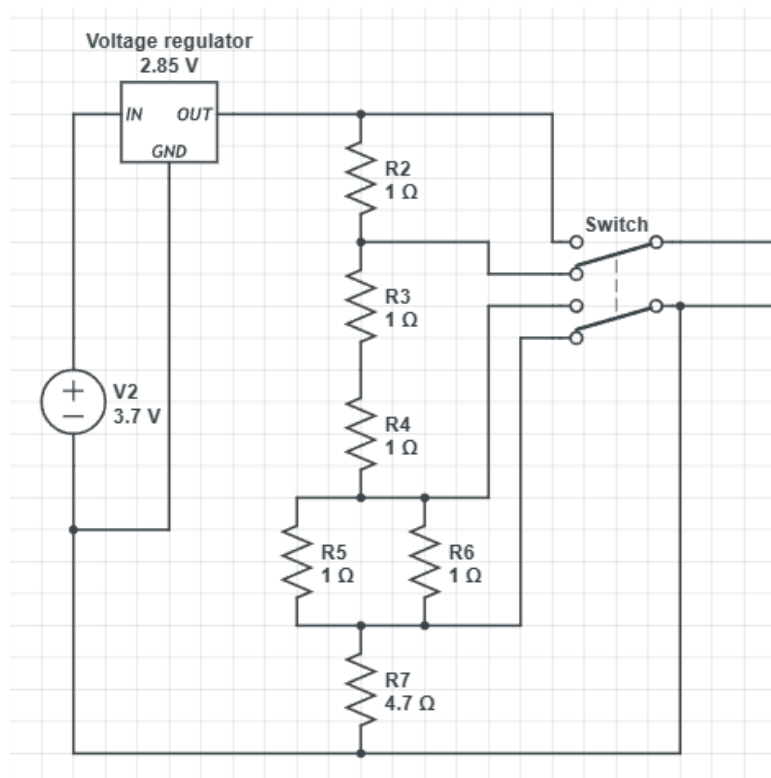


FIGURE 4.2. Circuit Diagram for device electronic circuitry

4.3 Eccentric rotating mass (ERM)

This study employed an ERM based motor for generating targeted and controllable vibrations. ERM is an offset mass attached to the output shaft of the motor creates a sinusoidal rotating movement. This rotating mass creates a reactional vibration on the motors body. Consequently, the motor's body can be used as a vibrating body. This phenomenon is usually termed as "Driven Harmonic Vibration". The frequency with which the motor vibrates is equal to the rotational speed of the eccentric mass, which is proportional to the motor's input voltage. The force generated by the motor is given as,

$$F = F \sin \omega t = mr\omega^2 \sin \omega t \quad \text{(Equation 4.1)}$$

And the equation of motion of the system is provided as,

$$(M - m) \frac{d^2x}{dx} + c \frac{dx}{dx} + kx = F_0 \sin \omega t \quad \text{(Equation 4.2)}$$

Where 'M' is mass of motor, 'm' is mass of eccentric mass, 'r' is distance from eccentric mass center to motor shaft, ' ω ' is rotating frequency, 'x' is displacement of the eccentric mass from the centre line of the motor, 'c' and 'k' are damping and spring constants. 'F0' is the maximum force amplitude generated by the motor.

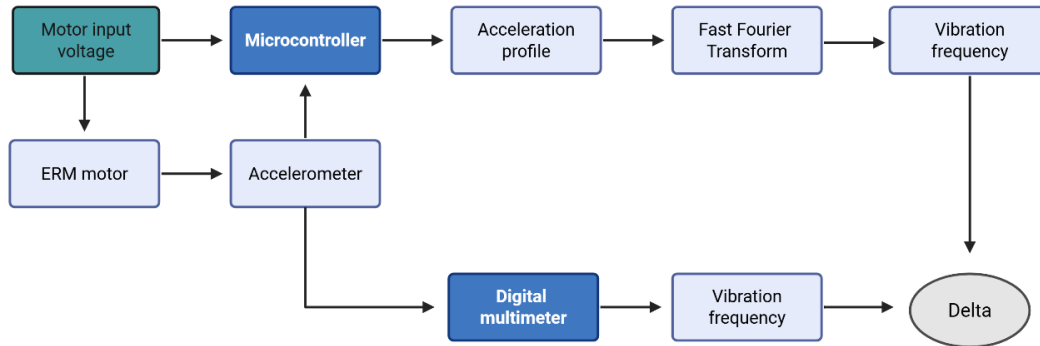


FIGURE 4.3 Process flowchart for vibration characterization

4.4 Device characterization

Establishing the relationship between the vibration frequency of the ERM motor and the input battery voltage is critical for an accurate control of the motor operation. To establish this relationship, acceleration profile of the motor was obtained. *ADXL 335* accelerometer and

Adafruit® *Feather Adalogger* microcontroller used to obtain the acceleration profiles. A special 3D printed casing was designed where accelerometers can be attached on to the motor.

The motor was connected to a power supply and was tightly fixed with a 10 cm³ foam using Velcro straps. 10 N weights were placed on all four sides of the foam to restrict any sideways movement that may be caused by the combined motion of the motor and the foam. The motor was then operated at a set voltage of 1 V for 1 minute and the acceleration profiles of motor were recorded and saved. The voltage value was then incrementally increased to 2.6 V (corresponding to the frequency range of interest) and the acceleration profiles were obtained and saved at each step. The increment voltage was set to 0.2 V for practical reasons. After the acceleration profiles were recorded, this data was imported to MATLAB and Fast Fourier transform was applied to it. This generated frequency plots of the data from which peak frequency values were extracted. This represented frequency of vibration. A digital multimeter was also used to confirm/ validate this frequency. Figure 4.4 shows the setup for the characterization experiments, while the stepwise flow diagram for the characterization process is presented in Figure 4.3.



FIGURE 4.4 Experimentation setup for vibration characterization

4.5 Results

We observed that there was a linear relationship between the input voltage and operating frequency of the motor. The relationship is displayed in Figure 4.4. Table 4.2 provides the results of the characterization process. To obtain values that were not recorded in the table, an interpolation procedure was adopted using the linear relationship between the voltage and the frequencies. 1.4, 1.8, 2.4 and 2.85V were identified as the voltages corresponding to the frequencies of 60, 80, 100 and 120 Hz respectively. These values were used for the design of the electronic circuit detailed in the experimental design section.

60-120 Hz is the range considered to be the frequencies which correspond to the activation of muscle fibres upon vibrating the muscles (Marotta et al., 2025). The literature review (Chapter 2) of this thesis also validates this since all the frequencies used for FMV applications are within this said range. This is the reason for choosing the 60-120 Hz frequency range for operating our designed device.

Since there is a small difference between the measured frequencies and the expected frequencies, we checked for the accuracy of our values to understand the performance of our device. The accuracy of these voltages were found by comparing the measured values against the expected values, using the following formula:

$$Accuracy = \frac{(measured\ value - expected\ value)}{expected\ value} \quad \textbf{(Equation 4.3)}$$

The accuracy of the device was calculated to be 96.83% and the results are given in Table 4.3. The cost factor of the device was low, with the components costing under £100 altogether. One limitation of the FMV device to be noted is heat dissipation from the voltage regulator. Although power resistors help limit this, prolonged use can still cause overheating. In the future, this issue could be mitigated by using alternative constant voltage sources, such as buck-boost converters. This device will now be used in the next chapter to study the neurophysiological (EEG and EMG) behaviour of CP and SCI populations as response to FMV applications.

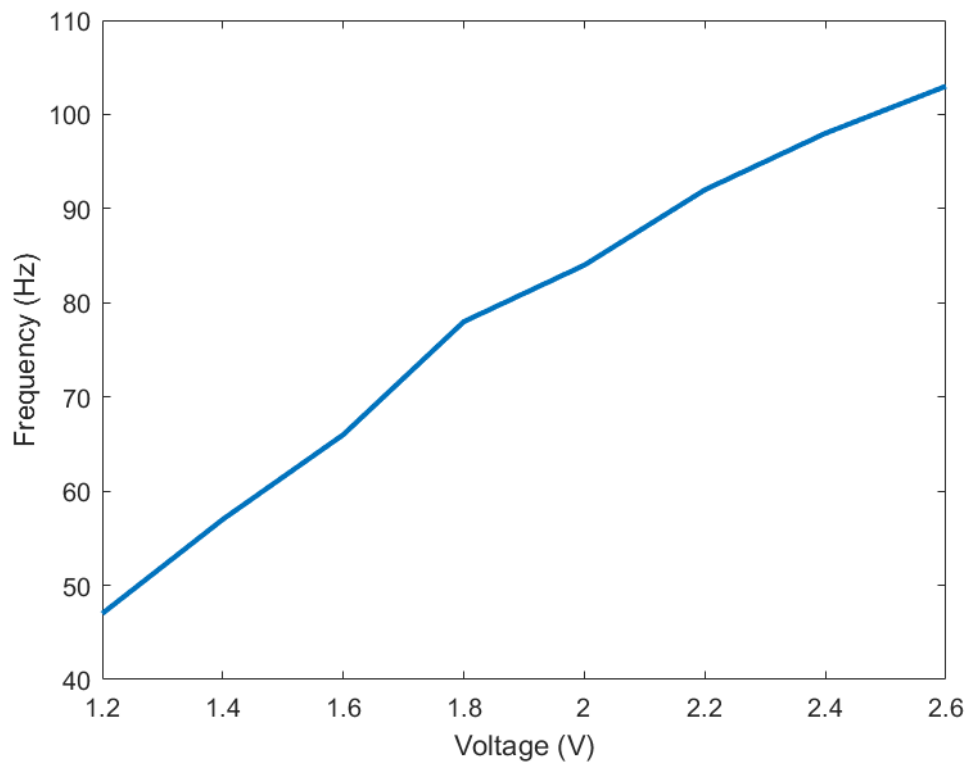


FIGURE 4.4 Relationship between the input voltage and output frequency of the designed FMV device

TABLE 4.2 Frequency-voltage characterization results of the ERM motor.

Voltage	Determined Frequency
1.2	47
1.4	57
1.6	66
1.8	78
2	84
2.2	92
2.4	98
2.6	103

TABLE 4.3 Accuracy table of the measured frequency values against ground truth

Ground truth	Measured Frequency	Accuracy
60	57	95
80	78	97.5
100	98	98
Mean		96.83

4.5.1 Comparison of the Developed FMV Device Against Existing Devices

Having established the characterisation results of the developed device, this section explicitly situates it within the landscape of existing FMV devices reviewed in Chapter 2 (Section 2.3.3.3) and presented in Table 4.1. Table 4.4 below provides a direct, structured comparison of the developed device against the key characteristics of representative existing FMV devices identified in the systematic review literature. This comparison is intended to highlight the specific engineering advances made and to justify the decision to develop a de novo device rather than adopting an existing commercial solution.

4.5.1.1 Device Selection Rationale

Table 4.1 in this chapter catalogued 17 distinct FMV devices identified through the systematic literature review. For the purposes of a structured comparative analysis, these 17 devices were grouped into four categories based on device type as reported in Table 4.1:

- **Category 1 — Handheld clinical/research devices** (10 devices):

Vibrameter, Bosco System, CroSystem Nemoco, Thrive No. 91, Pro Massager USJ-301, Deep Muscle Stimulator, Jumbo Vibrator, Model 4196 Sterling III, Powersage 4300, and Techo Concept.

- **Category 2 — Computerised/automated systems** (1 device):

AMES Technology.

- **Category 3 — Custom-built devices** (1 device):

Custom-Made Vibrators.

- **Category 4 — Unknown or unspecified device type** (5 devices):

Zeniter TMT-18, CEN, 4809 Vibrator (Brüel & Kjær), TNT-18 Vibrator, and the device with no detail provided. These five devices are *excluded* from the comparative table below, as insufficient information is available in the source literature to characterise their type, specifications, or clinical use, making meaningful comparison impossible.

One representative was selected from each included category (Categories 1–3). For Category 1, which contains 10 devices, two representatives were selected to capture the range within that group: the **Vibrameter (Somedic AB)**, the earliest and most established handheld device in the SCI FMV literature; and the **CroSystem Nemoco (Nemoco, Italy)**, the most frequently cited device in Table 4.1 within recent SCI studies (Tazoe et al., 2021; Camerota et al., 2025) and the only device from Table 4.1 with documented use across all three neurological populations addressed in this thesis (SCI, stroke, and CP). From Category 2, **AMES Technology** was selected as it is the sole computerised system in the list. From Category 3, collective information of the devices was selected for this device category. This selection rationale is summarised in Table 4.4.

TABLE 4.4. Structured comparison of the developed FMV device against representative existing devices from Table 4.1, organised by device-type category. Cat. 1 = Handheld clinical/research device; Cat. 2 = Computerised/automated system; Cat. 3 = Custom-built device. Five devices of unknown or unspecified type (Category 4) are excluded from the comparison (see text). All parameter values for existing devices are sourced directly from Table 4.1. NR = Not Reported in the source literature. The developed device column is shaded green for clarity.

Feature	Vibrameter (Somedic AB) [Cat. 1]	CroSystem Nemoco [Cat. 1]	AMES Technology [Cat. 2]	Custom-Made Vibrators [Cat. 3]	Developed Device (This Thesis)
A. General Properties					
Device Type	Handheld	Floor-mounted with mechanical arm	Computerised system	Custom (varied)	Wearable (strap-on)
Wearable?	No	No	No	Rarely	Yes
Power Source	Mains / external	Mains / external	Mains / external (computer-controlled)	Varied	3.7 V on-board battery (portable)
B. Technical Specifications (all values sourced directly from Table 4.1, Chapter 4)					
Frequency Range (Hz) [as claimed by manufacturer]	50–120 Hz	80–120 Hz	60–80 Hz	60–120 Hz	60–120 Hz (experimentally characterised; 96.83% mean accuracy)

Feature	Vibrometer (Somedic AB) [Cat. 1]	CroSystem Nemoco [Cat. 1]	AMES Technology [Cat. 2]	Custom- Made Vibrators [Cat. 3]	Developed Device (This Thesis)
Amplitude Range (mm)	0.1–1.0 mm	0.2–2.0 mm	0.4–1.5 mm	0.4–7.0 mm	0.4 mm
Size	NR	NR (floor- standing unit)	NR (bulky computer system)	Custom (varied)	58 mm (longest axis)
Weight (published data)	NR	NR	NR	NR	65 g
Cost (published data)	NR	NR	NR	NR	<£100 (components)
C. Validation and Feedback Features					
Frequency Characterisation Reported in Literature?	No	No	No	Rarely / No	Yes (96.83% mean accuracy; Table 4.3)
Integrated Pressure / Force Feedback	No	No	No	No	Yes (Flexiforce A-201; 1 N ± 0.1 N with LED indicators)
D. Neurological Populations Studied					
SCI	Yes	Yes	Yes (Backus et al., 2014)	Yes (multiple; Table 4.1)	Yes (Chapter 6, this thesis)
Stroke	No (sensory assess- ment tool only)	Yes (Wang et al., 2020)	NR	Yes (various)	Yes (Chapter 7, this thesis)
Cerebral Palsy	No (sensory assess- ment tool only)	Yes (Celletti & Camerota, 2011)	NR	Yes (various)	Yes (Chapter 5, this thesis)

Note on weight and cost data: A search of published academic literature and manufacturer sources was conducted to obtain weight and cost data for each representative device. Weight is not reported in the peer-reviewed literature for any of the 17 devices catalogued in Table 4.1, and manufacturer specifications are not publicly available for the majority of these research-era instruments (Vibrometer, CroSystem Nemoco, AMES Technology). Cost is similarly unreported in the academic literature for all devices. These fields are therefore marked NR (Not Reported) in Table 4.4 for existing devices. This absence itself constitutes a noteworthy finding, as it precludes cost-effectiveness comparisons in the existing literature — a gap directly addressed by the developed device, whose construction cost of under £100 is fully documented (Section 4.2).

4.5.1.2 Key Differentiating Features

The comparison in Table 4.4 reveals four principal respects in which the developed device advances the current state of FMV instrumentation.

Wearability and portability. All four representative existing devices, and the large majority of the 17 devices catalogued in Table 4.1, require external power sources and are not wearable. The CroSystem Nemoco, which Table 4.1 describes as handheld, is in fact a floor-mounted unit with a mechanical arm and dedicated electronic control module (Celletti & Camerota, 2011; Filippi et al., 2012), requiring a clinical setting. The AMES Technology device is a bulky computerised system (Backus et al., 2014). In contrast, the developed device is fully self-contained: wearable via Velcro straps, powered by a 3.7 V on-board battery, weighing 65 g with a longest axis of 58 mm (Section 4.2). This portability directly enables the home-based application explored in Chapter 7.

Experimentally verified frequency accuracy. The most critical differentiating feature is the complete absence of published frequency characterisation data for any of the 17 devices in Table 4.1. Botter et al. (2020), cited in Section 4.1, demonstrated that claimed and actual output frequencies of FMV devices can diverge meaningfully under real-world conditions, yet no device in the literature has addressed this directly. The characterisation experiments in Section 4.4 establish a linear voltage-frequency relationship and confirm a mean frequency accuracy of 96.83% across the four therapeutic frequencies (60, 80, 100, 120 Hz; Table 4.3). This metrological transparency is without precedent in the FMV neurorehabilitation literature, and it is what makes the frequency-dependent comparisons in Chapters 5 and 6 interpretable with confidence.

Integrated pressure feedback. None of the devices in Table 4.4, and none of the 17 devices in Table 4.1, incorporate any form of pressure or force feedback to standardise vibration delivery across users and sessions. This is a recognised methodological confound in the FMV literature (Botter et al., 2020). The developed device integrates a Flexiforce A-201 pressure sensor, calibrated to $1\text{ N} \pm 0.1\text{ N}$, with LED indicators guiding the user in real time, directly addressing this gap.

Cost. Cost is unreported for all existing devices in the academic literature (Table 4.4, NR). Research-grade clinical vibration equipment generally represents a significant financial barrier to adoption — a point reflected in the clinical literature's observation that the Vibrameter is

'expensive' without further specification (Brouwer & Ashby, 1992). The developed device was constructed for under £100 in components (Section 4.2), making it substantially more accessible for low-resource clinical environments and home-based use.

In summary, the developed device advances the field across four verifiable dimensions relative to the instrumentation catalogued in Table 4.1: (1) it is the only wearable, battery-powered device in the identified literature; (2) it provides the first published experimental frequency characterisation for a neurorehabilitation FMV device, confirming 96.83% mean accuracy; (3) it incorporates integrated pressure feedback absent from all catalogued devices; and (4) it has been validated across three distinct neurological populations within a single thesis, providing a unified and reproducible instrumentation platform. These properties collectively underpin the reliability of the experimental findings presented in Chapters 5, 6, and 7.

4.6 Main findings for the device development study

The main findings for this chapter is:

- A device was designed and developed that delivered vibration frequencies at four levels: 60, 80, 100 and 120 Hz with a mean accuracy of 96.83 %.

4.7 Summary

This chapter detailed the development and characterization of a wearable focal muscle vibration (FMV) device, designed to deliver precise, reproducible vibrations for neurological rehabilitation in spinal cord injury (SCI), cerebral palsy (CP) and stroke. Utilizing a Precision Microdrives 302-102 eccentric rotating mass (ERM) motor, the 65 g device achieves a therapeutic frequency range of 60–120 Hz, housed in a 3D-printed, user-friendly casing with Velcro straps for accessibility. The characterization process established a linear voltage-frequency relationship (1.4–2.85 V), confirmed uniform vibration output across the device, and validated its reliability through consistent performance testing. These results affirm the device's suitability for clinical applications, addressing the problem of delivering reproducible and precise vibration frequency identified in Chapter 2 (Section 2.2.5). A direct comparison of the developed device against existing FMV devices from the literature (Table 4.4, Section 4.5.1) confirms that the device advances the current state of the art in terms of wearability, verified frequency accuracy, integrated pressure feedback, and cost-effectiveness — properties that

collectively support its deployment in the subsequent clinical investigations. By providing a low-cost, wearable tool with precise control over vibration parameters, this work lays a robust foundation for subsequent clinical evaluations in Chapters 5 and 6, advancing FMV as an evidence-based intervention for motor and sensory rehabilitation.

Chapter 5: Focal Muscle Vibration Therapy in Cerebral Palsy Children

The experiments in this chapter are under review as two separate journal articles.

1. Ashfaque M, Khushnood K, Ghani U, Naizi I, Amjad I, Mehmood Q, Pujari A, “8 Weeks of Focal Muscle Vibration Alters Functional Connectivity and Cortical Potentials in Children with Cerebral Palsy”, under review in IEEE Transactions in Neural Systems and Rehabilitation Engineering

Preprint- <https://www.techrxiv.org/doi/full/10.36227/techrxiv.176238211.17782193>

2. Ashfaque M, Khushnood K, Ghani U, Naizi I, Amjad I, Mehmood Q, Pujari A, “8 Weeks of Focal Muscle Vibration Shows Improvements in Muscle Co-ordination and Co-contraction in Cerebral Palsy Children”, under review in IEEE Journal Journal of Translational Engineering in Health and Medicine

Preprint- <https://www.techrxiv.org/doi/full/10.36227/techrxiv.176127075.51166631>

5.1 Introduction

5.1.1 Aims of the CP experiments

Focal Muscle Vibration (FMV) has emerged as a promising non-invasive intervention for addressing sensorimotor impairments in neurological disorders such as CP. Building on the foundational work presented in Chapters 2 and 4, which outlined the therapeutic potential of FMV and the development of a wearable vibration device with a precise frequency profile, this chapter transitions from theoretical and technological frameworks to empirical validation. Here, we investigate the neurophysiological effects of FMV through EEG and EMG experiments in children with CP, addressing critical gaps in the understanding of FMV’s mechanistic underpinnings and clinical efficacy.

The therapeutic benefits of FMV are hypothesized to arise from its ability to modulate cortical and spinal neural circuits, enhance proprioceptive feedback, and reduce spasticity. However,

the literature lacks robust evidence linking specific vibration parameters (e.g., frequency, duration) to measurable neurophysiological changes, particularly in paediatric populations with CP. This chapter bridges that gap by systematically evaluating how FMV influences functional connectivity (FC) in the brain, movement-related cortical potentials (MRCPs), and muscle activation and co-contraction patterns.

For the CP experiments, first, we explore FC—a measure of synchronized neural activity across distributed brain regions—to assess whether FMV induces reorganization of sensorimotor networks. Prior studies suggest that FMV may enhance cortical plasticity in healthy and other neurological populations (Jevtic et al., 2016), but its effect in CP children, particularly the temporal dynamics and frequency-specific effects remain unclear. Second, we analyse MRCPs, slow cortical potentials associated with motor planning and execution, to determine whether FMV improves the efficiency of motor command generation. Finally, we employ EMG to quantify changes in muscle activation, co-contraction, and fatigue during dorsiflexion tasks, providing insights into the peripheral neuromuscular effects of FMV.

The experiments in this chapter are structured as randomized, double-blind controlled trials, comparing two FMV frequencies (80 Hz and 100 Hz) for CP children against a control group. By integrating EEG and EMG metrics, we aim to:

1. *Elucidate cortical mechanisms*: Determine how FMV modulates FC and MRCPs in CP children, with implications for neuroplasticity.
2. *Evaluate neuromuscular outcomes*: Assess changes in muscle activation, co-contraction, and fatigue resistance in CP population.
3. *Optimize therapeutic protocols*: Identify frequency-specific effects to guide clinical application.

Building on the development of a wearable FMV device (Chapter 4), this chapter investigates the therapeutic potential of a custom-designed FMV device in a clinical setting for individuals with CP. By employing neurophysiological assessments (EEG/EMG) and clinical outcome measures, the chapter aims to elucidate mechanisms such as cortical reorganization and reflex modulation, contributing to the thesis's goal of developing scalable, evidence-based neuromodulation tools. The findings will inform evidence-based rehabilitation strategies, ultimately improving functional outcomes for individuals with CP.

This chapter aligns with the thesis's objective (OB2) to evaluate FMV's efficacy in improving

motor function, reducing spasticity, and enhancing sensory feedback in CP, as outlined in Chapter 3. It addresses research question RQ2: *What are the specific effects of long exposure of FMV on motor function, spasticity, and brain activity in individuals with CP, and how do these effects vary with vibration parameters such as frequency and amplitude?* We anticipate that FMV, applied at controlled frequencies (e.g., 80–100 Hz), will improve motor coordination (e.g., 15% reduction in muscle co-contraction) and enhance sensory-motor brain activation in CP children, with sustained effects post-intervention, as measured by electroencephalography (EEG) and electromyography (EMG).

5.1.2 Background for the experiments

Recent studies on FMV in CP treatment have shown encouraging results, particularly in improving muscle tone, spasticity, and motor function (Reyes et al., 2011; Celletti et al., 2011; Hosbas et al., 2023). However, most studies have focused on the immediate and short-term functional effects of FMV, with little attention given to the underlying neurological mechanisms that drive these improvements. While some research has explored the effects of FMV on motor performance and spasticity reduction (Reyes et al., 2011; Celletti et al., 2011; Hosbas et al., 2023)), there is currently a clear gap in understanding of how FMV influences brain activity and connectivity, and muscular activation patterns in individuals with CP. This understanding could provide insight into how FMV facilitates motor rehabilitation, potentially inducing neuroplastic changes, and guide the development of more effective treatment protocols.

One key area of interest in understanding the brain's functioning is the concept of functional connectivity (FC) in the brain's electroencephalography (EEG) data. FC refers to the temporal correlation between spatially separated brain regions that work together as a network, reflecting how different parts of the brain communicate during rest and activity (Xie et al., 2022). In the context of CP, understanding changes in FC can reveal how motor and sensory networks are affected by FMV, offering a window into the cortical reorganization that may underlie functional improvements (Jacobs et al., 2023). Investigating FC in response to FMV could thus represent a novel approach to assessing the efficacy of FMV in CP rehabilitation, moving beyond traditional outcome measures like muscle tone and motor function.

Additionally, using EEG this chapter also explores changes in movement-related cortical potentials (MRCPPs) as a response to FMV intervention. MRCPPs are slow brain waves associated with the planning, initiation, and execution of voluntary movements (Shakeel et al., 2025). Analysing these potentials can provide further insight into how FMV might influence motor

preparation and execution at the cortical level, offering a more comprehensive understanding of the neurophysiological impacts of FMV in individuals with CP.

Crucially, the relationship between vibration stimulation parameters (e.g., frequency, duration) and long-term neuroplastic changes remains poorly characterized. While electromyography (EMG) offers a window into neuromuscular dynamics, few studies have employed EMG to quantify how FMV influences muscle activation, fatigue, or agonist-antagonist coordination over extended periods. Present EMG studies focus on using EMG as a biofeedback to guide the FMV delivery rather than understanding the effect of vibration on the neuromuscular underlay (Bloom et al., 2010). Addressing these gaps could refine FMV protocols, optimize outcomes, and unlock its full rehabilitative potential.

5.1.3 Objectives of the CP experiments

Therefore, this chapter aimed to investigate the efficacy of two FMV frequencies (80 Hz and 100 Hz) administered over 8 weeks, towards understanding the brain-related and muscle-related changes in children with spastic diplegic CP. The brain-related changes were performed using EEG experiments, while muscle-related changes were checked using EMG experiments. In this regard, the CP experiments are divided into two parts, first part presents the details of the EEG experiments while the second part gives the details of the EMG experiments.

EEG experiments: For the EEG experiment, the main aim was to investigate the efficacy of two FMV frequencies (80 Hz and 100 Hz), administered over 8 weeks, towards inducing functional changes at the cortical level in children with spastic diplegic CP. Using resting state EEG we examined the functional connectivity (FC) changes due to the 8-week intervention. A secondary aim was to explore if FMV had any effect on the cortical activity linked with movement. For this movement related cortical potentials (MRCPs) during dorsiflexion tasks were conducted and assessed. We hypothesized that FMV stimuli (80 Hz/100 Hz/both) would induce changes in FC, possibly at the sensorimotor level, when compared with Controls (no vibration), and it will result towards improvements in the MRCPs. By presenting the frequency-specific effects of FMV in the CP brain, this study thereby aims to enhance the mechanistic understanding of FMV's application, leading to reduce the gap between its clinical application and therapeutic potential.

EMG experiments: For the EMG experiment, using surface EMG (sEMG) during dorsiflexion tasks, we evaluated (1) time-dependent changes in muscle activation, (2) fatigue dynamics, and (3) co-contraction between the agonist and antagonist muscles in the lower limb. We

hypothesized that FMV stimuli (80 Hz/100 Hz/both) would elicit superior muscle activation patterns and exhibit greater fatigue resilience, compared to the Control (no vibration). By elucidating (stimulation) frequency-specific mechanisms, this work aims to advance FMV as a precision therapy for CP, bridging the gap between empirical application and mechanistic understanding. As per our knowledge, this is the first comprehensive study to systematically investigate the effects of wearable FMV on muscle activation, fatigue and co-contraction, in spastic diplegic CP children. This is also the first study to compare these effects, with two FMV stimulation frequencies (80 and 100Hz) over a longer (12 weeks) period, in CP children. Thus, the study aims to provide more comprehensive insight into the use of wearable FMV as an intervention technology in CP children.

As per our knowledge, this is the first comprehensive study to systematically investigate the effects of wearable FMV on brain functional connectivity and cortical potentials, and muscle activation and co-contraction in spastic diplegic CP children. This is also the first study to compare these effects, with two FMV stimulation frequencies (80 and 100Hz) over a longer (12 weeks) period, in children with CP. Thus, the study aims to provide better insight into the effects of wearable FMV as a rehabilitation technology in children with CP, as judged through its cortical and muscular effects. The remainder of this chapter is organised as following: Section 5.2 details the common experimental methods of both the EEG and EMG experiments, Section 5.3 presents details and findings of the EEG experiments, Section 5.4 details the EMG experiments. Sections 5.5 and 5.6 then discuss strengths, limitation and implications of the findings.

5.2 Common Methods for EEG and EMG experiments

Both the EEG and EMG experiments were conducted concurrently and on the same population, so they shared much of their protocol. This section details the common protocols and experimental methods for the EEG and EMG experiments. Sections 5.3 and 5.4 then provide experiment-specific details and protocols for the EEG and EMG study respectively.

5.2.1 Participants

The inclusion criteria were: age between 3 and 15 years, a clinical diagnosis of spastic diplegic CP, Gross Motor Function Classification Scale (GMFCS) levels II-IV, absence of severe cognitive, visual, or hearing impairments, no history of metabolic diseases, and no recent fractures. Additionally, individuals who had received botulinum toxin injections within the past year were

excluded. The study was designed as a double-blind, randomized, controlled trial with a three-group parallel structure. Participants were randomly assigned to one of three groups: a Control group and two intervention groups, labelled intervention-1a (80 Hz) and intervention-1b (100 Hz). Randomization was computer-generated. Groups were comparable in age, GMFCS level, and MAS scores at baseline. The participants and outcome assessor were kept blinded about the allocated groups. Due to the physical nature of vibration intervention, it was not possible to blind the control group from the intervention groups.

Sample size: The sample size for the main trial was calculated using G*Power, with an effect size of 0.25, a power of 80%, and three groups, resulting in a requirement of 96 participants. However, EEG assessments were only performed in a sub-cohort, as children with severe cognitive impairment, uncontrolled epilepsy, significant motor contractures, major visual or hearing deficits, or known skin sensitivity to electrode materials were excluded to ensure compliance, safety, and reliable data collection. Eligible participants for EEG data collection were randomly allocated into groups. Recruitment was open for a maximum of two months, during which we aimed to enroll as many eligible participants as possible. The two-month recruitment period was determined by the availability of researchers and equipment in Pakistan.

Total 65 participants (43 male, mean age: 12.45 +/- 4.27) were recruited for the study, 55 of which were retained by the 4-weeks assessment, 6 were lost to follow-up by the 8-weeks assessment. Therefore, a total of 49 participants completed the complete 8-week intervention treatment. Modified Ashworth scale scores of the participants were 1 (12), 1+ (18), 2 (25) and 3 (10). The gross motor function classification system (GMFCS) of the recruited participants was as follows: 9 subjects in level II, 33 in III, and 22 in level IV. The study was a double blinded randomized controlled trial with a three-group parallel design. The control group consisted of 20 participants, the Intervention-1a (80 Hz) group had 10, and the Intervention-1b (100 Hz) group had 19 participants. The 12-week assessments to check retention effects were conducted on half (27 participants) of the study population with the following population distribution: 9, 8 and 11 participants in the control, Intervention-1a, and Intervention-1b groups respectively. The CONSORT diagram for the study detailing the data collection procedures is visualized in Figure 5.1A. Of the participants with volitional control over their lower limbs, all were right leg dominant.

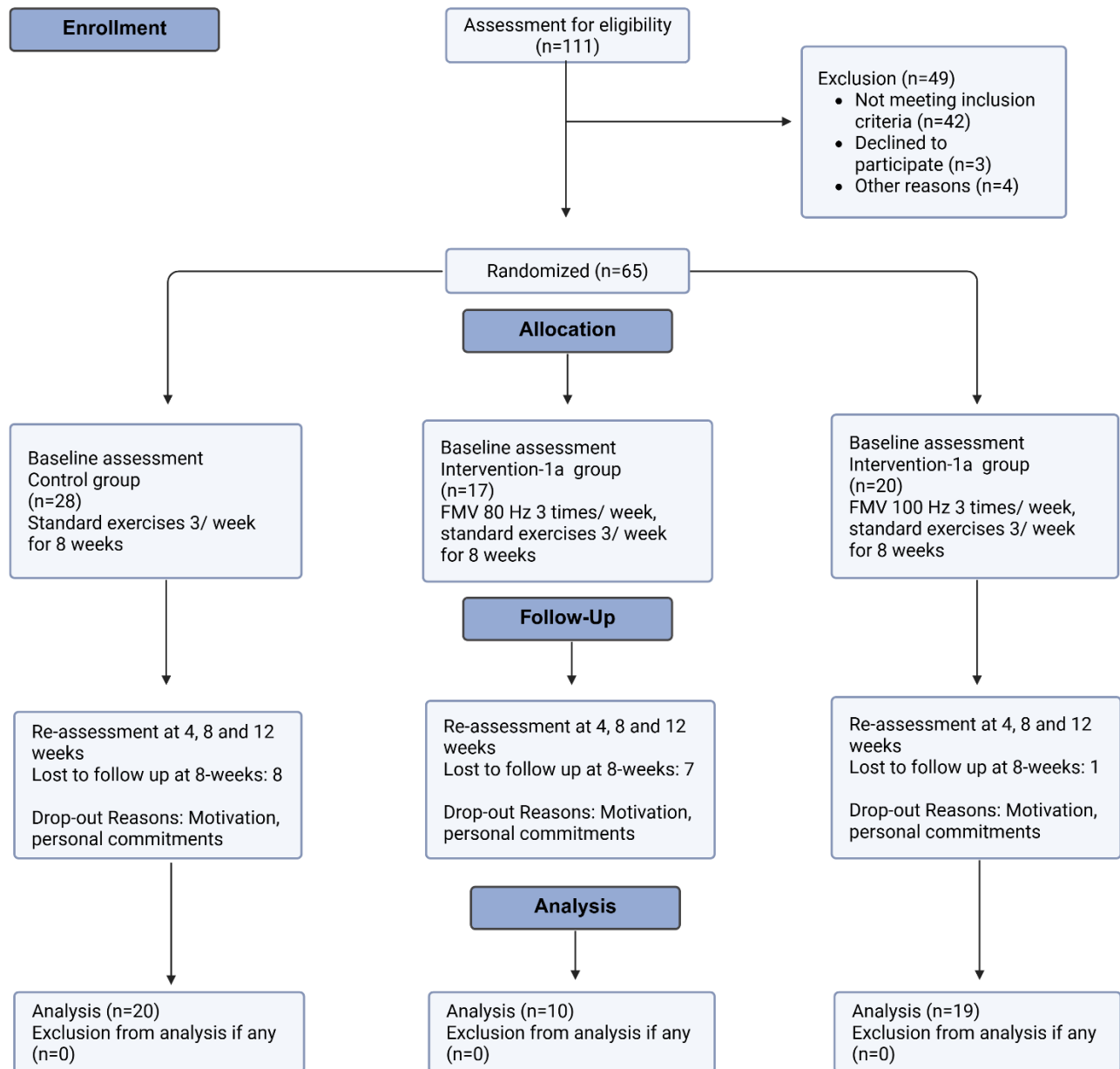


FIGURE 5.1A. CONSORT diagram for the experiments.

Data collection took place from March to August 2023 at Al-Farabi Special Education Centre and the National Institute of Rehabilitation Medicine, located in Islamabad, Pakistan. The trial was prospectively registered with United States clinical trial registry (clinicaltrials.gov) with trial ID: NCT05751135. The trial was prospectively registered with United States clinical trial registry (clinicaltrials.gov) with trial ID: NCT05751135. Before the trial commenced, our 40-channel EEG amplifier became non-functional. Given the pragmatic nature of the study, along with time and logistical constraints in procuring a

replacement, we proceeded using a 16-channel EEG amplifier to ensure timely completion of data collection within the available recruitment window. Prior to enrolment, detailed explanation of the experimental procedures were provided to the children and their parents. Written informed consent was obtained from the parents of the participating children. The study was carried out in compliance with the Declaration of Helsinki's ethical standards and with approval from ethical committee of Riphah International University, Islamabad, Pakistan (REC-01289).

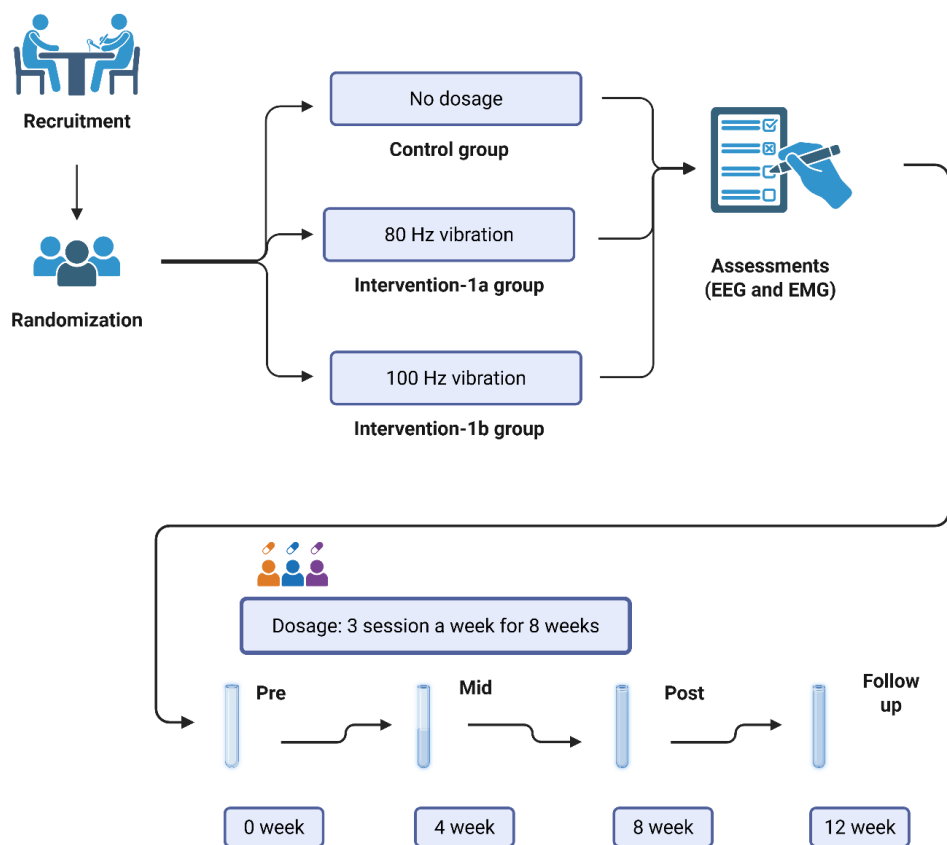


FIGURE 5.1B. Experimental protocol design for the study

5.2.2 Intervention protocol

The FMV intervention was delivered to participants using a custom-built device (Chapter 4). The population was divided into three groups: 1) Intervention-1a group received vibrations at a frequency of 80 Hz, 2) Intervention-1b group received vibrations at 100 Hz. The amplitude of the vibrations was set at 0.5 mm, 3) The control group did not receive any vibrational intervention, while all three groups received physical therapy (details below). Participants in the vibration groups were blinded to the specific frequency of vibration they received. However,

blinding was not possible for the control group, as the administration of vibration involved the use of a physical device. Stimulation frequencies were chosen based on previous evidence of their effectiveness (Celletti et al., 2011).

The FMV intervention targeted four muscles in each lower limb: the quadriceps, hamstrings, adductor longus, and vastus lateralis. The right leg was treated, followed by the left leg. These muscles were chosen as they are prone to weakness and develop spasticity in diplegic cerebral palsy (Seo et al., 2016; Rutovic et al., 2019; Darras et al., 2021). Each muscle received 3 x 30-second vibration sessions, with 10-second breaks between each session. Meaning each muscle received a total of 1.5 half minute vibration stimulation, leading to 6 minutes of vibration/leg/visit. A 30-second break was also taken when switching between muscles. The participants were instructed to lay down on a floor mat just before the intervention was given to have an inter-participant intervention consistency, and easier access to muscles while delivering the intervention. The FMV device was positioned on the belly of the targeted muscle and securely strapped using Velcro straps to minimize sideways movement of the device. The intervention lasted for 8 weeks, with three sessions administered per week (refer Figure 5.1B). To ensure consistency, a single physiotherapist conducted all FMV sessions, minimizing intra-participant variability in device placement and muscle tautness.

5.2.3 Physical therapy

All participants also received physical therapy sessions, with intervention-1a and intervention-1b groups receiving FMV intervention in addition to the physical therapy. These sessions were held three times a week throughout the eight-week intervention period: on the same days FMV intervention was administered. FMV intervention was administered prior to the physical therapy sessions. The standard physical therapy protocol included positioning, strengthening, and stretching exercises. For positioning, participants were seated on a block with their legs spread apart, feet flat on the floor, and backs straight to avoid posterior pelvic tilt. They also stood against a wall with their legs abducted and externally rotated for 15 minutes after each exercise session. Parents were advised to continue these positioning techniques at home. Spastic muscles were stretched to the point of mild discomfort and held for 20 seconds, with five repetitions per muscle. Weak muscles were identified and strengthened through targeted exercises, with each muscle group undergoing 10 repetitions (Mahmood et al., 2020).

5.3 Electroencephalography (EEG) experiments for CP study

5.3.1 Data recording

5.3.1.1 EEG Assessments

EEG data was recorded from all the participants to understand the effect of FMV on the underlying cortical changes in children with CP. To understand effects of FMV intervention on the cortical patterns of CP children following assessments were made: general cortical activity was assessed using resting-state EEG whereas action-dependent cortical changes were assessed through analysing MRCPs during dorsiflexion tasks. To. Assessments were made at baseline (before start of interventions), and at 4-, 8- and 12-week follow-ups after start of intervention (refer to Figure 5.1). The purpose of the 12-week follow-up was to check the retention effects of the intervention and was only assessed on half of the study population. Figure. 1 presents the experimental protocol of the study in detail.

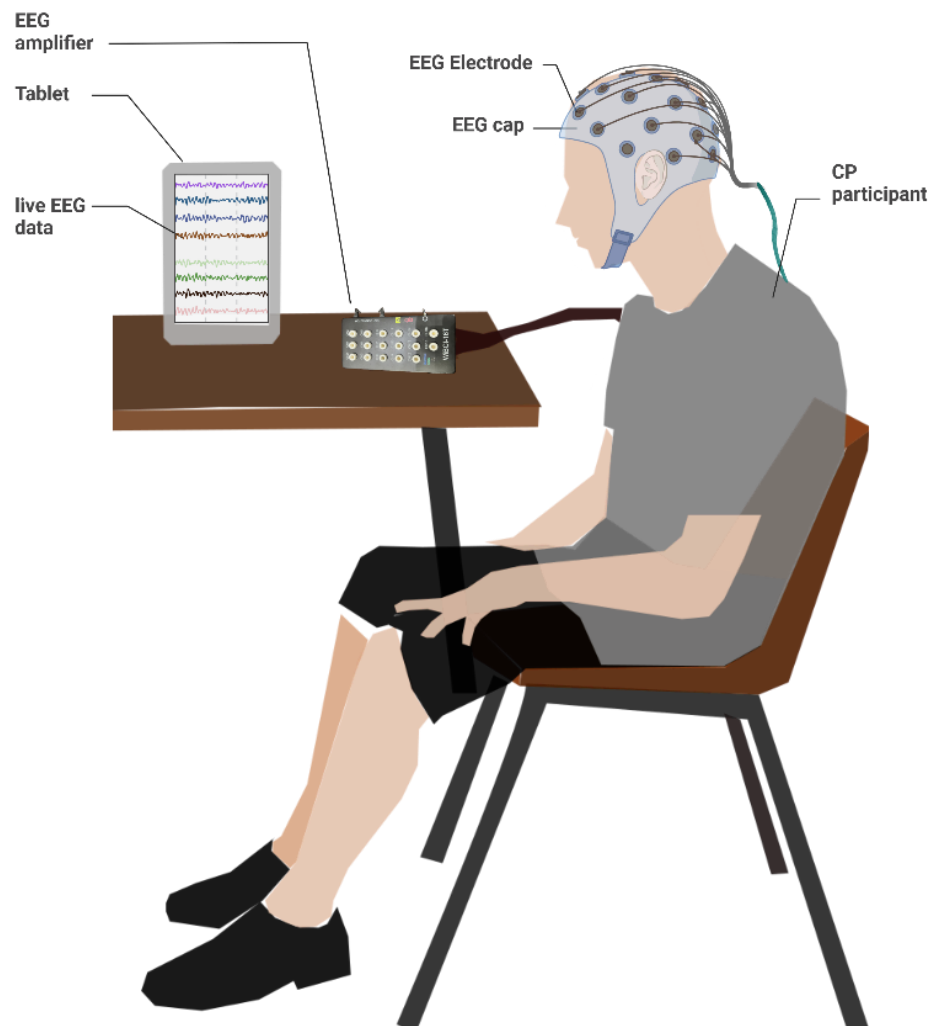


FIGURE 5.2A. Experimental setup and data collection scheme for the EEG assessments.

A saline-based 16-electrode EEG cap (GreenTek China[®]) was used for the EEG data capture (refer to Figure 5.2a). These 16-electrodes represented the following channels: FP1, FP2, F3, F4, FZ, C3, C4, CZ, T3, T4, P3, P4, PZ, O1, O2 and a reference electrode. The reference electrode was situated between CZ and FZ. The study utilized a Nortek Labs (<https://www.norteklabs.com/>) custom EEG system (WIBCI 16T), designed by combining two Texas Instruments ADS1299 8-channel analog-to-digital converters to enable 16-channel biopotential recording and acquisition (Aulenkamp et al., 2025; Ghani et al., 2023; Ghani et al., 2023; Liao et al., 2023; Rashid et al., 2018). Data was captured on a Samsung tablet (Galaxy Tab E) using a custom-built smartphone application (RISETech, 2025). that interfaced the EEG amplifier with the smartphone device. The application had visual interface for collecting and saving raw EEG data. The data was sampled at 250 Hz. It also included a separate electrode montage for recording MRCP data, which was used to collect in conjunction with dorsiflexion (DF) tasks (Jochumsen et al., 2018; Usama et al., 2006; Niazi et al., 2022). The app collected EEG from the following nine channels only: F3, F4, FZ, C3, C4, CZ, P3, P4 and PZ. Visual cues were displayed on the smartphone tablet screen for the MRCP, where the subject was instructed to start, hold and end DF tasks. The individual DF task cue was 3.5s long in the interface design with 2s rest and 1.5s lift and hold (more detail on MRCPs in the Section 5.3.1.3).

Two sessions of 2-minute resting state for both eyes-open (EO) and eyes-closed (EC) EEG data were recorded at each assessment. The order of these sessions was randomized. These two were then combined into a single file for each condition. During data collection, participants were instructed to sit straight on a chair with minimal body and head movements. They were asked to keep eyes on a target in front for EO, and keep eyes closed for EC state. Some participants were unable to close their eyes voluntarily, their eyes were passively closed either by their parents or by the assessor. Figure 5.2A shows the EEG data collection scheme for the participants and the experimental setup.

5.3.1.2 Functional connectivity (FC)

FC refers to the correlation between spatially separated brain regions that function together as a network. It describes how different areas of the brain interact and share information over time, even when there is no direct structural connection (Xie et al., 2022). It is based on the synchronization or coherence of neural activity across brain regions. We aimed to find out if there was a FC relation between the different EEG sensor locations during the resting state period in the CP population, and whether the FMV intervention had any influence over that FC.

5.3.1.3 Movement related cortical potential (MRCP)

Movement-related cortical potentials (MRCPs) are slow, negative shifts in scalp EEG activity that begin up to two seconds before voluntary movement onset and reflect the cortical processes underlying movement preparation and execution. MRCPs are characterized by several phases: the Bereitschafts potential (readiness potential), which starts approximately 1–2 seconds before movement and indicates early motor planning; the pre-movement potential, marking the transition from planning to action; and the motor potential, which peaks around movement onset and is directly linked to activation of the primary motor cortex. After movement, a positive rebound often called the post-movement potential—returns the signal to baseline, reflecting the resolution of movement-related activity. Collectively, these phases represent the cascade of neural events supporting voluntary motor actions. (Shakeel et al., 2015; Shibasaki et al., 2006; Nascimento et al., 1982).

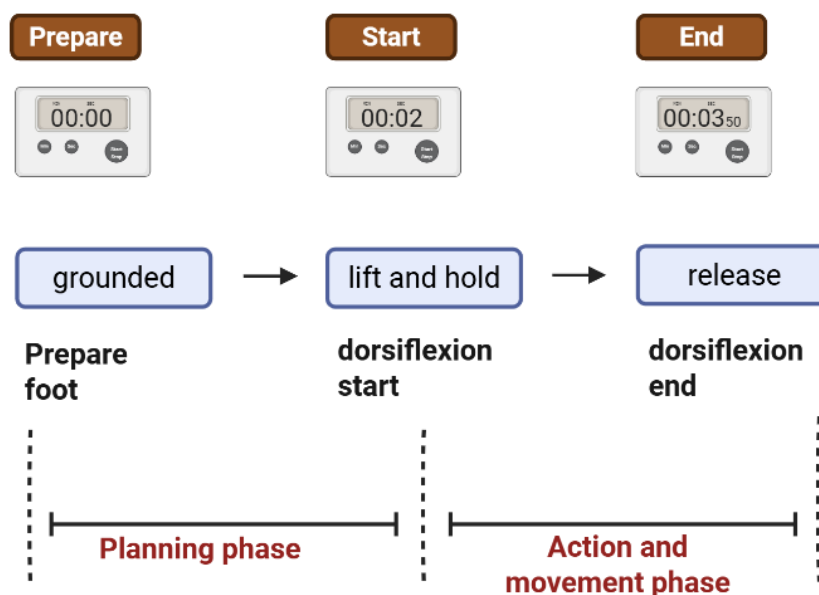


FIGURE 5.2B. Flowchart of the MRCP collection scheme.

MRCPs for DF tasks were captured from the study population at each assessment. Each participant performed 30 DFs following a visual cue on a smartphone screen whilst his/her EEG data was recorded. These were done for both the limbs. The total duration of an individual MRCP signal was set at 4 seconds, where the DF task started at 2 s and ended at 4 s. The first half (0-2 s) was attributed to planning and the second half (2-4 s) to movement and action. See Figure 5.2B for a schematic representation of the MRCP data collection scheme. Participants with active volition over their limbs performed the tasks themselves, while participants with

limited volition were helped passively to move their feet by a study clinician. The MRCP EEG graph follows a V-like shape with the depression at the time of decision making (which should be at the 2s timepoint in this experiment) (Shakeel et al., 2015).

5.3.2 Data processing

5.3.2.1 Data pre-processing

To preprocess/ clean the recorded EEG data a standard preprocessing pipeline was used (Pedroni et al., 2019). Firstly, any volume conduction and common noise between the EEG electrodes was removed from the raw data using common average referencing. The reference electrode was used for this averaging. The data was then band-pass-filtered at 0.5-45 Hz to extract the signal of interest and remove irrelevant and noisy data from the signal. Artifact subspace reconstruction (Pedroni et al., 2019; Mullen et al., 2015) was then used to remove bad burst of data in the EEG time series. The parameters used in artifact subspace reconstruction method were a standard deviation value of 20 and out-of-bound channels percentage of 25%. Independent component analysis (ICA) was then applied to the data to get the independent components of the EEG data. *ICLabel* (Pion-Tonachini et al., 2019) – a machine-learning based artifact prediction tool – was then used to label muscle, heart and eye artifacts and channel noise components from the data. Components exceeding 85% confidence were removed from the data. This cleaned data was then used to perform the FC analysis. All this preprocessing was performed using *EEGLAB* (Delorme & Makeig; 2004) in a *MATLAB* (R2023a, MathWorks) environment.

5.3.2.2 Phase locking value (PLV)

EEG functional connectivity was computed using the phase locking value (PLV) method because of its wide adoption in literature (Jian et al., 2017; Ghani et al., 2024). It finds the phase synchronization between two signals by calculating the difference in the instantaneous phase between them. If the brain regions are functionally connected, the phase difference should remain relatively constant. The following formula governs the PLV calculation:

$$PLV_{x,y} = \left| \frac{1}{N} \sum_{t=1}^N \text{sign}[\sin(\phi_x(t) - \phi_y(t))] \right| \quad \text{(Equation 5.1)}$$

Where $x(t)$ and $y(t)$ represent the two signals, and $\phi(t)$ is the phase of a signal, and N is the total number of samples. The PLV computation was performed between each EEG channel signal in a pair. The outcome of the computed PLV ranges in the interval from zero to one, with

zero indicating no connectivity, and one indicating maximum connectivity between signals. After PLV computation the results were stored in 15x15 adjacency matrices representing the connectivity values between all the 15 channels. Before the PLV computation the EEG data was sub-divided into the following EEG frequency bands using a 4th order Butterworth filter: alpha (7.5–12.5 Hz) and beta (12.5–30 Hz). PLV adjacency matrices were computed for both these EEG bands. The calculation of PLVs were performed using *Brainstorm*© software, and the results were imported back again to *MATLAB* for post processing.

5.3.2.3 MRCP processing

All the 30 individual MRCP signals of a single session for a participant were visually inspected to check for qualifying MRCPs that represented the V-like shape of cortical potential that is associated with dorsiflexion movement. A custom *MATLAB* code was written for this. MRCPs not qualifying were rejected from the data before average MRCP calculation, this came out to be usually 10 (+/- 4) rejections per participant. Average MRCP values of the 30 MRCP signals was calculated for all the participants. Then for each of the three groups (intervention-1a (80 Hz), -1b (100 Hz), and Control), the mean MRCP value for that were found using averaged MRCP values of the participants of that group. This was done for all the four assessments (baseline, 4, 8, 12 weeks). Separate mean MRCP plots were obtained for the left leg and the right leg. The graphs representing these results are presented in the result section (Section 5.3.3.3).

5.3.2.4 Statistical Analysis

To check the statistical significance in FC, a non-parametric cluster-based permutation test was employed. It addressed the multiple comparison problem and controlled the familywise error rate, following the methodology outlined in (Maris et al., 2007). This test was applied to a within-study design to compare PLV values within adjacency matrices across the assessments (baseline vs. follow-ups). The analysis was conducted using the *FieldTrip* toolbox, developed by the Donders Institute for Brain, Cognition, and Behavior, Nijmegen, the Netherlands (Oostenveld et al., 2011).

For each pairwise comparison (baseline vs. follow-up 1, 2 and 3), cluster-level statistics were calculated. The maximum cluster-level statistic served as the critical threshold for identifying significant clusters. To construct a null distribution, data labels were randomly shuffled 5000 times, and cluster-level statistics were recalculated for each permutation, representing the expected distribution of results under the null hypothesis of no differences in functional connectivity between conditions. This was done for all three study groups: control,

intervention-1a (80 Hz) and intervention-1b (100 Hz).

The p-value for each observed cluster was calculated as the proportion of permutations where the cluster-level statistic was more extreme than the observed cluster-level statistic. Significant positive clusters (+clusters) indicated increased functional connectivity, while significant negative clusters (-clusters) suggested decreased connectivity in one condition compared to another. This analytical approach enabled the identification of brain regions with significant changes in functional connectivity due to vibration, providing insights into the effects of vibration delivery on brain network interactions. Custom written algorithms in *MATLAB* that employed the use of *Field-Trip* libraries was used for this. The results were visualized on the scalp using Bio Render (created in <https://BioRender.com>). The electrodes represented different scalp sites, and the connecting lines represented statistically significant functional connectivity relationships.

To assess how FMV influenced MRCP values, a linear mixed-effects model (LMM) was used. The model included Group (control, intervention-1a, intervention-1b) as a between-subjects fixed factor and Time (0, 4, 8, 12 weeks) as a within-subjects fixed factor. A random intercept for participants was incorporated to adjust for repeated measures. This method extends traditional repeated measures analysis of variance (ANOVA) by handling missing data and unbalanced group sizes.

Significant interactions were further examined using post-hoc pairwise comparisons with Bonferroni correction. Model assumptions were checked, including variance homogeneity via Levene's test. If violations occurred, robust LMMs with Kenward-Roger approximation were utilized. All post-hoc tests applied Bonferroni-adjusted p-values.

5.3.3 Results for EEG experiments on CP children

5.3.3.1 Participant demographics

Total 65 participants were recruited for the study, 55 of which were retained by the 4-weeks assessment, 6 were lost to follow-up by the 8-weeks assessment. Therefore, a total of 49 participants completed the intervention treatment. The CONSORT diagram for the study detailing the data collection procedures can be visualized in Figure 5.1A. Of the participants with volitional control over their lower limbs, all were right leg dominated. The participant demographics for the experiment are already presented in section 5.2.1 which detail the recruitment and completion

details of the participants for the study. The results of the EEG analyses are presented in the following sections. These include results for the effect of vibration intervention on functional connectivity (FC) changes in the EEG and on the movement related cortical potentials (MRCPs).

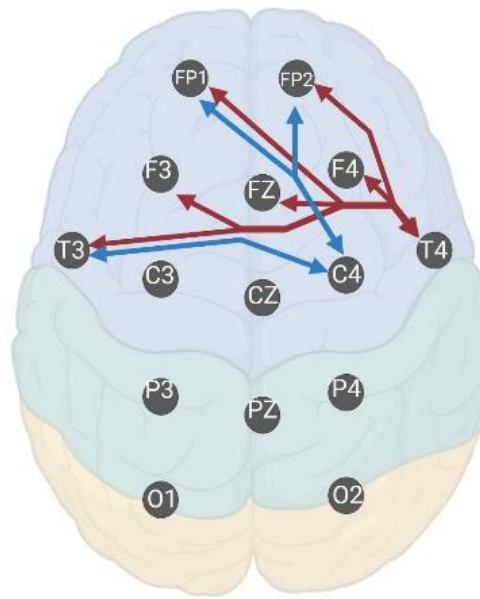
5.3.3.2 FC changes in the EEG

Our results demonstrated that in the absence of FMV intervention the resting state FC did not change for the tested CP population. For the control group, no significant FC was observed in any of the follow-up assessments (4-weeks, 8-weeks or 12-weeks) with respect to baseline. This was true for both the EC and EO EEG states and for both the alpha and beta EEG frequency bands. No significant FC change was observed in between the assessments either.

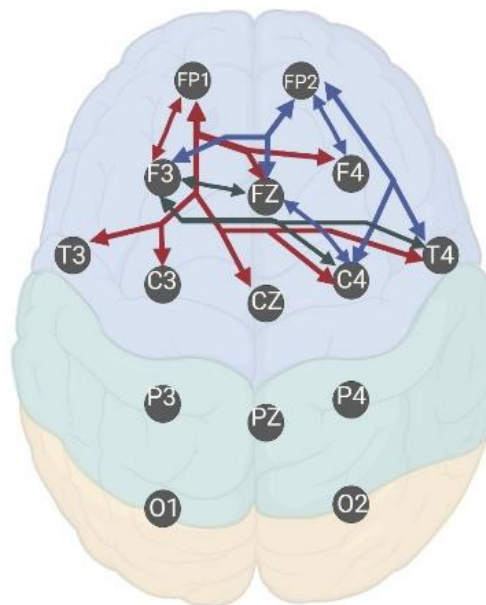
In the FMC, i.e., vibration intervention groups no significant FC change was observed for alpha band EEG for any of the groups or assessments. In the beta channel there were three conditions that showed significant FC changes, two for intervention-1a (EC and EO) and one for intervention-1a group (EC).

For intervention-1a (80 Hz) group, there was a statistically significant FC change observed at the 8-weeks assessment for the beta band EEG activity with respect to baseline for the EC state. This observed FC change included the following scalp locations: the C4, T4, FP1, FP2, F3, F4, FZ, and T3 channels that covered areas in the frontal, temporal and central lobe. This FC relation is shown in Figure 5.3(a) which shows connections between electrodes that displayed a FC. In the EO state, significant FC change was observed at the 12-weeks assessment compared to baseline for the beta band EEG activity. This FC relationship was observed between the FP1, FP2, F3, F4, FZ, C3, CZ, C4, T3 and T4 channels in the frontal, temporal and central lobe. This connectivity relationship diagram is shown in Figure 5.3(b). Detailed statistical results for both these conditions are presented in Table 5.1, where the t-value, p-value and the effect size of all the statistically significant observations are reported. There was no other significant change observed in intervention-1a group for any of the EC or EO state in any of the assessments or EEG frequency band.

For the intervention-1b (100 Hz) group, there was a significant FC observed at the 8-week assessment for the beta band EEG activity for the EC state when compared to baseline. This beta band FC was observed between the following EEG channel locations: FP1, FP2, F3, F4, FZ, C3, T3, P3 and PZ electrodes of the frontal, central, parietal and temporal lobe. The connectivity diagram for this relational activity is presented in Figure 5.4. The corresponding channels that have a FC relationship are shown in colour connected with arrow lines. For the statistical values for these results, Table 5.1 can be viewed.



(a)



(b)

FIGURE 5.3. Resting-state EEG FC in beta band for intervention-1a (80 Hz) group for (a) eyes closed (EC) at 8-week assessment, and (b) eyes open (EO) at 12-week assessment, compared to baseline

These results suggest that FMV may selectively modulate beta-band connectivity in cognitive networks, with effects emerging after sustained intervention. The absence of changes in the control group underscores the potential role of FMV intervention in inducing neuroplastic adaptations. Further research is warranted to explore the long-term implications of these FC changes and their relationship with functional motor improvements in CP.

TABLE 5.1 Results of the statistical analysis, presenting the combinations with statistically significant changes in the EEG FC.

Group and Assessment	Channels	p-value	Effect size	t-value
intervention-1b (100 Hz) at 8 weeks (EC)	P3-FZ	0.046	2.439	1.877
	P3-F4	0.046	3.568	2.565
	PZ-FP1	0.046	3.947	2.565
	PZ-FP2	0.046	4.379	2.482
	PZ-F3	0.046	2.900	2.214
	PZ-FZ	0.046	3.499	1.986
	PZ-F4	0.046	1.208	2.049
	PZ-T3	0.046	-5.587	2.183
	PZ-C3	0.046	-1.918	1.835
intervention-1b (100 Hz) at 12 weeks (EO)	F3-FP1	0.027	0.000	-4.335
	F3-FP2	0.027	0.000	-2.925
	FZ-FP1	0.027	0.000	-3.745
	FZ-FP2	0.027	0.000	-2.480
	FZ-F3	0.027	0.000	-3.299
	F4-FP1	0.027	0.000	-7.828
	F4-FP2	0.027	0.000	-2.759
	T3-FP1	0.027	0.000	-2.340
	C3-FP1	0.027	0.000	-2.161
	CZ-FP1	0.027	0.000	-2.153
	C4-FP1	0.027	0.000	-4.156
	C4-FP2	0.027	0.000	-3.084
	C4-F3	0.027	0.000	-2.444
	C4-FZ	0.027	0.000	-2.113

intervention-1a (80 Hz) at 8 weeks (EC)	T4-FP1	0.027	0.000	-2.875
	T4-FP2	0.027	0.000	-2.260
	T4-F3	0.027	0.000	-1.989
	F4-FP1	-3.5	0.6655	-7.226
	C4-FP1	-3.126	0.0324	-3.176
	T4-FP1	-3.442	0.0324	-4.656
	C4-T3	-2.134	0.0324	-1.282
	T4-T3	-2.784	0.0324	-1.594
	F4-FP2	-1.889	0.6655	-0.715
	C4-FP2	-2.595	0.0324	-1.59
	T4-FP2	-2.747	0.0324	1.359
	T4-F3	-2.131	0.0324	1.359
	O2-CZ	2.9639	0.7199	-0.054
	T4-FZ	-2.778	0.0324	1.252
	O2-C4	2.2682	0.7199	4.9951
	T4-F4	-2.736	0.0324	3.5248

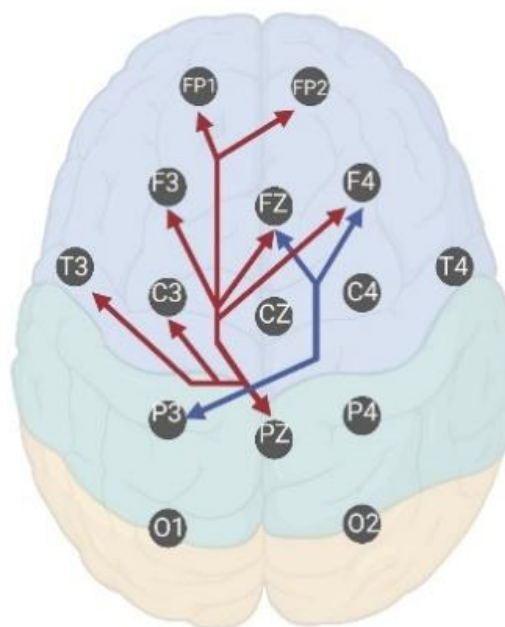


FIGURE 5.4. Resting-state EEG FC in beta band for intervention-1b (100 Hz) group for EC at 8-week assessment

5.3.3.3 MRCP Findings

The analysis of MRCPs revealed distinct temporal and group-specific patterns of cortical activation during motor tasks, with clear limb asymmetries and intervention-related effects. In the left limb, the linear mixed model did not show any significant main effects of Group ($F(2,173) = 0.10, p = 0.901$) or Time ($F(3,173) = 2.22, p = 0.088$), and no significant Group $\times$ Time interaction was detected ($F(6,173) = 0.51, p = 0.801$). However, post hoc analyses within the intervention-1b (100 Hz) group revealed significant reductions in MRCP amplitudes over time ($p = 0.0002$), with changes evident as early as four weeks post-intervention and sustained through twelve weeks.

Similar effects were also observed in the right limb. A significant Group $\times$ Time interaction was observed ($F(6,173) = 3.53, p = 0.003$). Clear and progressive significant reductions in MRCP amplitudes over time were again observed for intervention-1b group, with changes starting from 4- and maintaining through 12-weeks, indicating a consistent and durable neuromodulatory effect of the 100 Hz intervention. These statistical results are presented in detail in Table 5.2 presenting the LMM results and Tabel 5.3 presenting the post-hoc analysis results. Figures 5.5 and 5.6 present the visual representation of the average MRCPs for all the study groups and assessment timepoints for the left and the right leg.

TABLE 5.2 Linear mixed-effects model (LMM) results for MRCPs for both legs

Leg	Effect	F-value	DF (Num, Den)	p-value
Left	Group	0.10	2,173	0.901
	Time	2.22	3,173	0.088
	Group $\times$ Time	0.51	6,173	0.801
Right	Group	0.40	2,173	0.670
	Time	2.22	3,173	0.088
	Group $\times$ Time	3.53	6,173	0.003

TABLE 5.3 Significant movement-related cortical potential (MRCP) amplitude changes for intervention-1b group

Leg	Comparison	p-value
Left	Baseline vs. 4 weeks	0.006
	Baseline vs. 8 weeks	0.001
	Baseline vs. 12 weeks	0.024
Right	Baseline vs. 4 weeks	0.041
	Baseline vs. 8 weeks	0.019
	Baseline vs. 12 weeks	0.008

The sustained reductions in MRCP amplitudes suggest that the intervention-1b protocol exerts a robust neuromodulatory effect, potentially engaging mechanisms of cortical plasticity. The emergence of these changes by four weeks and their persistence through twelve weeks highlight the temporal stability of the intervention's impact.

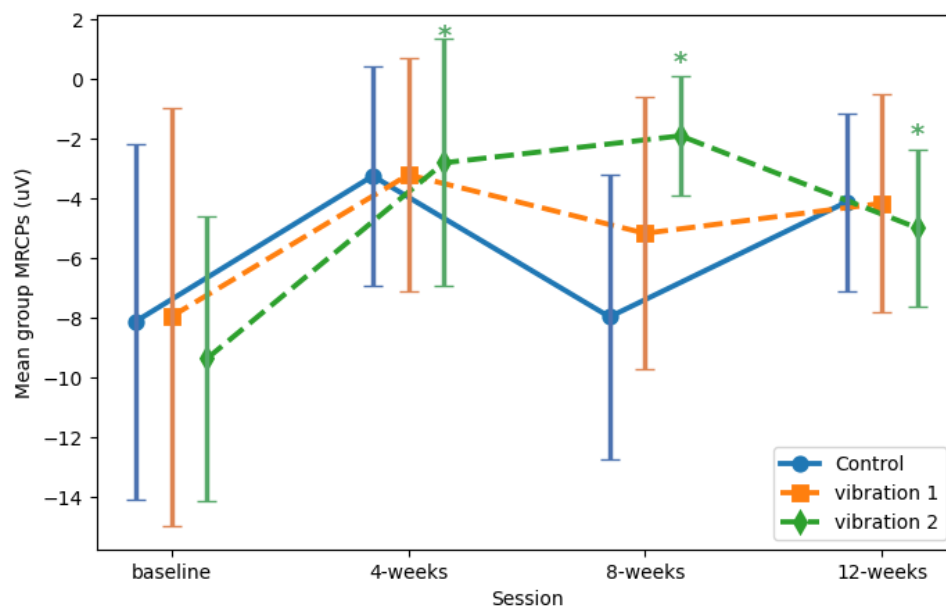


FIGURE 5.5. Average groupwise MRCPs of the left leg DFs at the four assessment timepoints

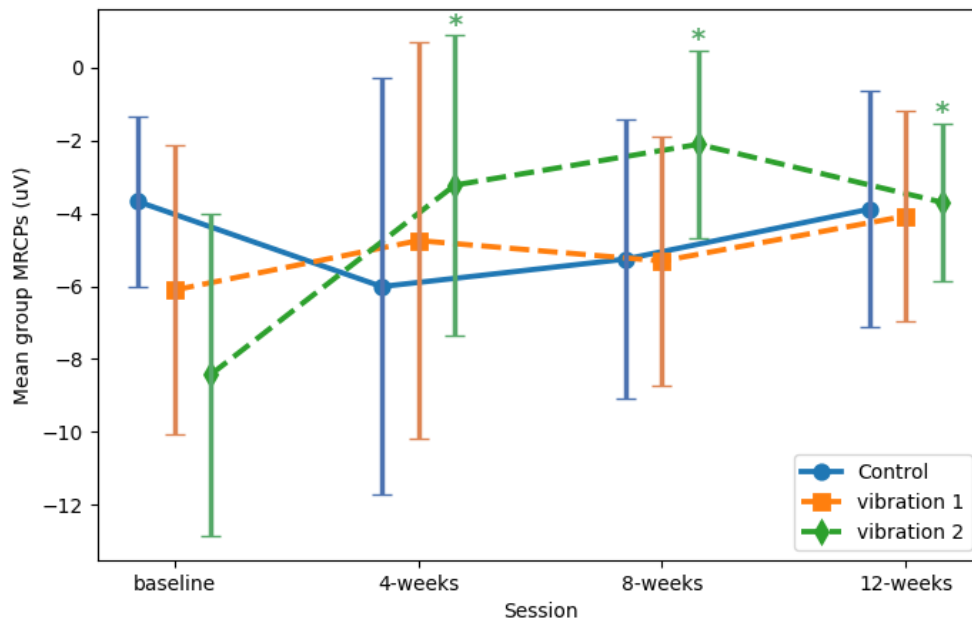


FIGURE 5.6. Average groupwise MRCPs of the right leg DFs at the four assessment timepoints

5.3.4 Discussion of EEG findings

This study investigated the effects of FMV on functional FC and MRCPs in children with cerebral palsy CP. The results demonstrate that FMV induces frequency-dependent neurophysiological changes, with distinct patterns observed in cortical connectivity and motor-related brain activity. Below, we discuss the implications of these findings and their potential impact on CP rehabilitation.

5.3.4.1 Impact of FMV on EEG functional connectivity (FC)

Our analysis revealed significant FC changes in the beta band for both FMV intervention groups (80 Hz and 100 Hz), while no such changes were observed in the Control group. These findings suggest that FMV selectively modulates beta-band connectivity, which is associated with motor control and cognitive processing. Notably, the 100 Hz intervention elicited broader FC alterations, extending to parietal and occipital regions, whereas the 80 Hz intervention primarily affected frontal, temporal, and central lobes.

The absence of FC changes in the alpha band suggests that FMV's effects are specific to networks involved in motor and cognitive functions. The observed beta-band synchronization may reflect enhanced sensorimotor integration, a critical mechanism for motor rehabilitation in CP. The delayed onset of FC changes (e.g., at 8- and 12-week follow-ups) further supports the

hypothesis that FMV induces neuroplastic adaptations over sustained/ longer intervention periods.

5.3.4.2 Modulation of MRCPs

The MRCP analysis revealed significant reductions in amplitude for the 100 Hz group, particularly in the right (dominant) limb, starting at 4 weeks and persisting through the 12-week follow-up. These reductions suggest improved efficiency in motor preparation and execution, as MRCP amplitudes are inversely correlated with movement automatization. The 80 Hz group showed no significant MRCP changes, highlighting the importance of frequency selection in FMV protocols. The 100 Hz intervention's stronger neuromodulatory effect could stem from its broader FC influence, potentially engaging additional cortical and subcortical networks involved in motor planning.

5.3.4.3 Clinical Implications

The combined FC and MRCP findings underscore FMV's potential as a non-invasive tool for CP rehabilitation. By enhancing beta-band connectivity and optimizing motor-related cortical activity, FMV may facilitate functional improvements in children with CP. The frequency-specific effects suggest that personalized FMV protocols (e.g., 100 Hz for broader cortical engagement) could optimize rehabilitation and functional outcomes.

These neurophysiological insights complement existing evidence of FMV's benefits for spasticity and motor function (Ritzman et al., 2018; Celletti et al., 2011). Future studies should explore whether FC and MRCP changes correlate with clinical measures (e.g., Gross Motor Function Measure) to validate their utility as biomarkers of recovery.

5.4 Electromyography (EMG) experiments for CP study

This section presents the methodological details and finding of the EMG experiments. Electromyography (EMG) data was collected from all participants to evaluate the effect of FMV on underlying muscle activation and its influence on co-contraction in children with CP. Assessments were conducted at baseline (prior to the start of interventions), and at 4-, 8-, and 12-week follow-up after the intervention began. The 12-week follow-up was specifically designed to examine the retention effects of the intervention after the 8-week dose had concluded and was performed on only half of the study population.

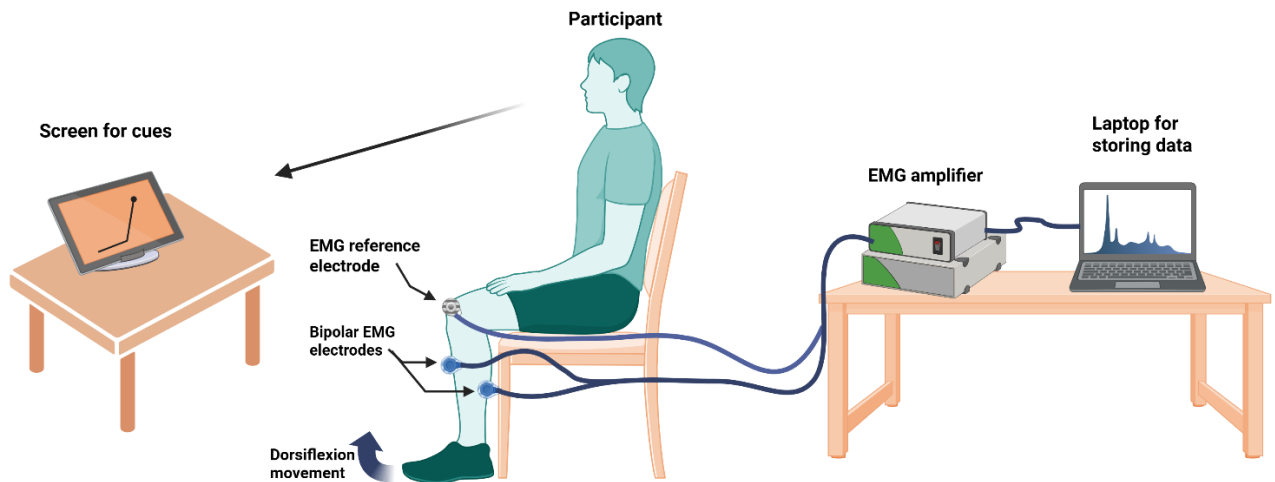


FIGURE 5.7. Experimental setup and data collection setup for the EMG assessments.

To analyse muscle activations and co-contraction effects, a dorsiflexion (DF) task was employed. Each participant performed 30 DF in response to a visual cue displayed on a smartphone tablet. The start of each DF was timestamped and synchronized with the recorded electromyography (EMG) data. Each DF task lasted 2 seconds, with a 4-second window (2 seconds before and 2 seconds after the task) used for analysis. EMG signals were recorded from the Tibialis Anterior (TA) and Soleus (Sol) muscles using bipolar electrodes (DelSys, Inc.; model: DE 2.1) with a 1 cm inter-electrode distance connected to the Bagnoli EMG data acquisition system from Delsys (DelSys, Inc.; model: Bagnoli-4). A reference electrode was placed on the knee of each participant. The SENIAM guidelines were followed for electrode placement and data recording (Hermens et al., 2000). Prior to data collection, the skin was cleaned with isopropyl alcohol or shaved if necessary to ensure optimal signal quality. The detailed protocol design is presented in in Figure. 5.1 and the experimental setup for the EMG experiments is shown in Figure. 5.7.

5.4.1 Data processing

5.4.1.1 EMG features

EMG data was detrended, rectified, and band-pass filtered to remove frequency noise using a Butterworth filter of 6th order (20-450 Hz). 50 Hz line noise and its harmonics at 100 and 150 Hz were removed using a notch Butterworth filter of the same order, the band of the filter was set at 1 Hz. All the 30 DF EMG epochs were averaged for each participant for the left and right

leg separately. These individual averages were then pooled across the three intervention groups (Intervention-1a (80 Hz), Intervention-1b (100 Hz) and control) to compute EMG features for comparative analysis. All data was processed in MATLAB.

To understand the effects of FMV on the muscular performance EMG signals were analysed and their Root Mean Square (RMS) values were calculated and compared across the study groups (Intervention-1a (80 Hz), Intervention-1b (100 Hz) and control) and assessments (baseline, 4-, 8-, 12-weeks). We also analysed the effect vibrations had on the fatigue in the study population, as prolong use of vibration may effect the fatigue characteristics. We checked how the fatigue behaved over time (baseline, 4-, 8-, 12-weeks). To assess the development of fatigue over time, median frequencies (MDF) of the EMG signal were calculated and compared for the study groups. These features (RMS and MDF) were calculated using source code from [29]. To study how FMV affects muscle synergy we calculated co-contraction between the TA and Sol muscles. We checked the behaviour of co-contraction over time, i.e. at the baseline, 4-, 8-, and 12-weeks assessment, in all three study groups to see how FMV might change the contraction patterns. The co-contraction was measured through the co-contraction index (CCI) [31], which is calculated as follows:

$$CCI = \frac{2I_{ant}}{I_{tot}} \times 100 \quad \text{(Equation 5.2)}$$

Where ' I_{ant} ' and ' I_{tot} ' represent the area under the EMG graph for the antagonist (TA) muscle and the common area for both muscles respectively. A CCI value of 100% represents total co-contraction, while a value of 0% represents pure agonist activation.

5.4.1.2 Statistical analysis

To analyze the effects of interventions on EMG RMS values, a linear mixed-effects model (LMM) was employed, with Group (Control, Intervention-1a (80 Hz), Intervention-1b (100 Hz)) as a fixed between-subjects factor, Time (0, 4, 8, 12 weeks) as a fixed within-subjects factor, and a random intercept for subjects to account for repeated measurements. This approach generalizes the classical two-way repeated measures ANOVA while accommodating missing data and unequal group sizes. Post-hoc pairwise comparisons with Bonferroni correction were conducted for significant interactions. Assumptions were verified as follows: homogeneity of variance via Levene's test. For violations, robust LMMs with Kenward-Roger approximation were applied. Post-hoc comparisons used Bonferroni-adjusted p-values. Analyses were performed in MATLAB (R2023a, MathWorks) using restricted maximum likelihood (REML)

estimation.

5.4.2 Results for EMG experiments on CP children

The participant demographics for the experiment are already presented in section 5.2.1. and Figure 5.1A, which detail the recruitment and completion details of the participants for the study. The results of the EMG analyses are presented in the following sections. These include results for the effect of vibration intervention on muscle activation (EMG root mean square), muscle fatigue (EMG median frequency) and muscle co-contraction.

5.4.2.1 EMG root mean square (RMS) analysis

This study investigated the effects of two interventions, 1) FMV Intervention-1a (at 80 Hz) and 2) FMV Intervention-1b (at 100 Hz), versus a Control group on normalized EMG RMS amplitudes of the TA and Sol muscles bilaterally across four timepoints: baseline, 4, 8, and 12 weeks.

For the right TA (dominant leg) muscle (Figure 5.8a), a general trend was observed: mean EMG RMS amplitudes increased at 4 weeks relative to baseline, followed by progressive declines at 8 and 12 weeks. The Intervention-1a group (80 Hz) demonstrated lower baseline amplitudes than controls, increased to exceed control levels by 4 weeks, maintained this elevation at 8 weeks, and returned to control-equivalent values by 12 weeks. In contrast, the Intervention-1b group (100 Hz) exhibited slightly higher baseline amplitudes than controls, further increased at 4 and 8 weeks, but decreased below control levels by 12 weeks. The left TA (non-dominant leg) muscle (Figure 5.8b) exhibited analogous trends with attenuated magnitude. The Intervention-1a group (80 Hz) consistently remained below control levels across all time points, suggesting limited efficacy of 80 Hz vibration on the non-dominant limb. Conversely, the Intervention-1b group (100 Hz) started below controls at baseline, increased at 4 and 8 weeks, and declined at 12 weeks while remaining above controls, indicating the potential benefits of 100 Hz vibration for non-dominant limb muscle activation.

Trends in Sol mirrored those of their agonist TA counterparts, albeit with reduced amplitude magnitudes. For the right (dominant) Sol (Figure 5.9a), both intervention groups began below controls at baseline. By 4 weeks, Intervention-1a (80 Hz) approached control levels, while Intervention-1b (100 Hz) slightly exceeded them. At 8 weeks, Intervention-1a (80 Hz) matched controls, whereas Intervention-1b (100 Hz) surpassed them. By 12 weeks, Intervention-1a (80 Hz) declined below controls, and Intervention-1b (100 Hz) returned to control-equivalent values. In

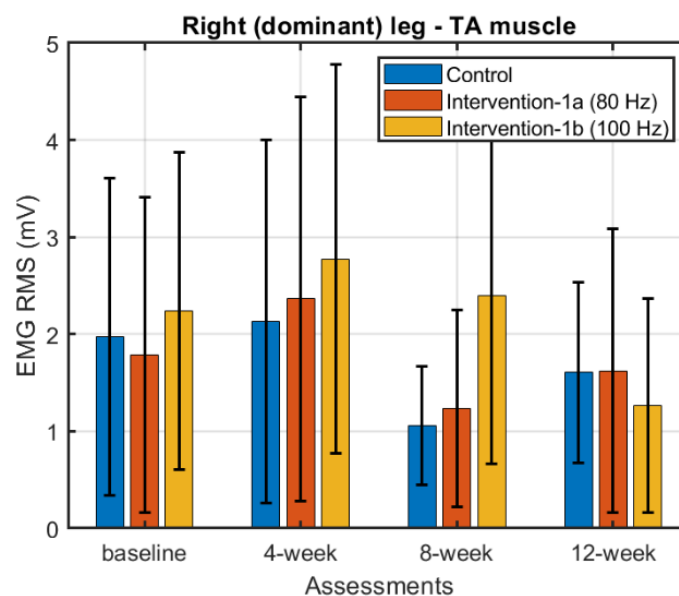
the left (non-dominant) Sol (Figure 5.9b), effects were less pronounced. Both intervention groups started below controls at baseline. At 4 weeks, Intervention-1a (80 Hz) transiently rose above controls, while Intervention-1b (100 Hz) approached control levels. By 8 weeks, Intervention-1a (80 Hz) dipped below controls, and Intervention-1b (100 Hz) marginally exceeded them. At 12 weeks, both groups registered slightly below control levels.

These findings underscore divergent time-dependent effects of vibration frequencies (80 Hz vs. 100 Hz) on neuromuscular activation, with sustained benefits observed for 100 Hz (Intervention-1b) in the non-dominant TA and transient efficacy in other muscle groups.

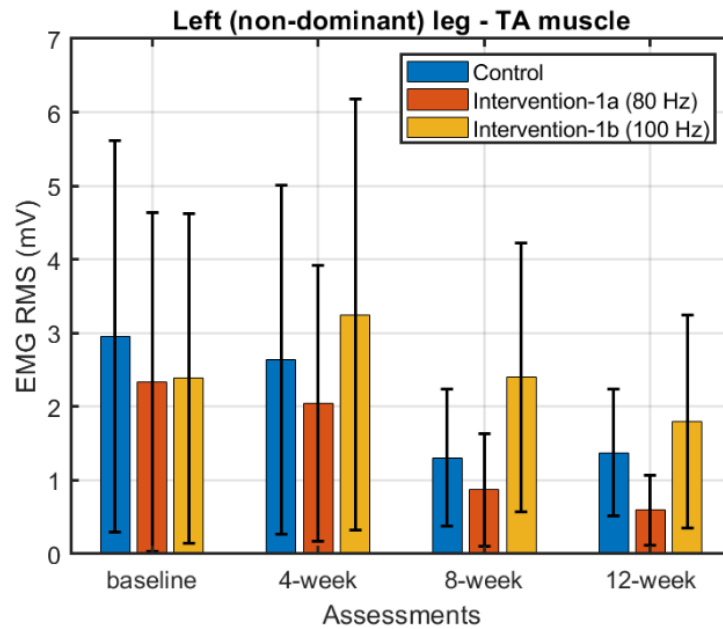
The statistical analysis revealed the following indications for the experimental findings:

Right (dominant) leg TA: A LMM revealed no significant main effects of Group ($F(2,163.45) = 2.87$, $p = 0.060$) or Time ($F(3,149.16) = 1.86$, $p = 0.139$), and no Group $\times$ Time interaction ($F(6,177.73) = 1.00$, $p = 0.429$). However, post-hoc analysis at 8 weeks showed a significant between-group difference ($p = 0.003$), with Intervention-1b (100 Hz) exhibiting lower higher EMG RMS than both Control ($p = 0.003$) and Intervention-1a (80 Hz) ($p = 0.045$).

Left (non-dominant) leg TA: Significant main effects were observed for Group ($F(2,192.36) = 5.84$, $p = 0.003$) and Time ($F(3,136.56) = 4.03$, $p = 0.009$), but no Group $\times$ Time interaction ($F(6,155.98) = 0.96$, $p = 0.455$). Post-hoc tests at 4 and 8 weeks demonstrated that Intervention-1b (100 Hz) had significantly lower higher EMG RMS than both Control (4 weeks: $p = 0.027$; 8 weeks: $p = 0.027$) and Intervention-1a (80 Hz) (4 weeks: $p = 0.045$; 8 weeks: $p = 0.008$).



(a)



(b)

FIGURE 5.8. Mean and standard deviation EMG root mean square (RMS) values of tibialis anterior (TA) muscle for the study participants across the intervention groups and the assessment timepoints, for the a) right and b) left leg dorsiflexion (DF) tasks.

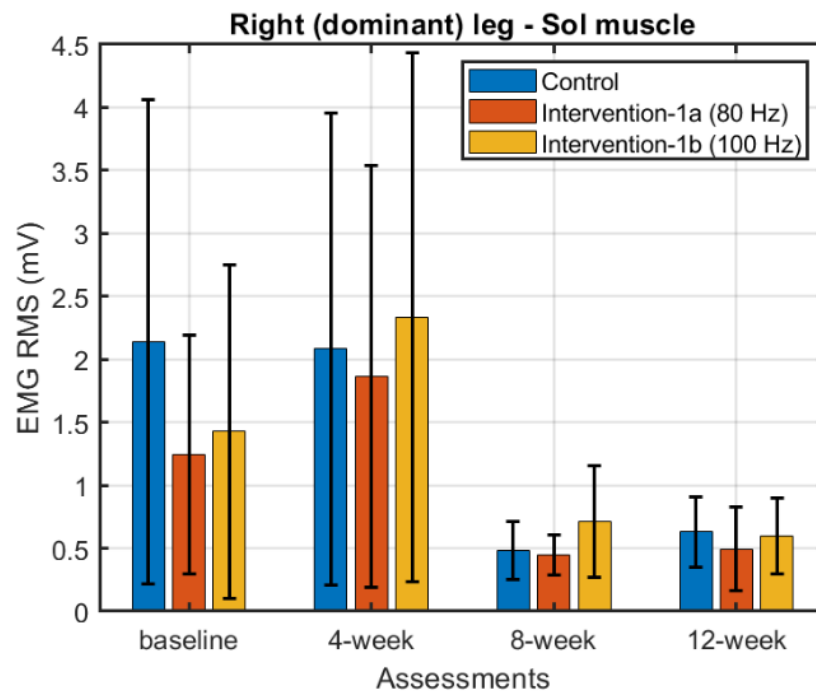
TABLE 5.4 Summary of LMM results for all conditions for EMG RMS

Muscle	Leg	Effect	F-value	DF (Num, Den)	p-value
TA	Right	Group	2.87	2, 163.45	0.060
		Time	1.86	3, 149.16	0.139
		Group × Time	1.00	6, 177.73	0.429
	Left	Group	5.84	2, 192.36	0.003
		Time	4.03	3, 136.56	0.009
		Group × Time	0.96	6, 155.98	0.455
Sol	Right	Group	1.15	2, 186.00	0.320
		Time	5.81	3, 186.00	0.001
		Group × Time	0.82	6, 186.00	0.559
	Left	Group	1.92	2, 132.61	0.151
		Time	5.73	3, 109.79	0.001
		Group × Time	1.59	6, 164.77	0.152

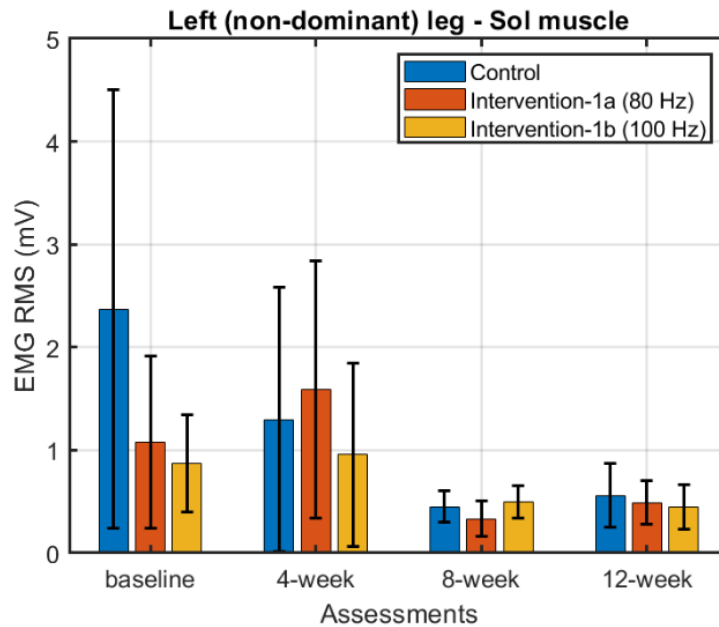
Right (dominant) leg Sol: A significant main effect of Time ($F(3,186) = 5.81$, $p = 0.001$) was found, but no effects for Group ($F(2,186) = 1.15$, $p = 0.320$) or Group $\times$ Time ($F(6,186) = 0.82$, $p = 0.559$). Post-hoc analysis at 8 weeks showed a marginal between-group effect ($p = 0.024$), but no pairwise differences survived correction. Within-group analyses revealed significant temporal changes in all groups (Control: $p = 0.046$; Intervention-1a (80 Hz): $p = 0.022$; Intervention-1b (100 Hz): $p = 0.017$), with Intervention-1b showing a notable Week 2 vs. Week 3 difference ($p = 0.035$, uncorrected).

Left (non-dominant) leg Sol: A significant Time effect ($F(3,109.79) = 5.73$, $p = 0.001$) was observed, but no Group ($F(2,132.61) = 1.92$, $p = 0.151$) or Group $\times$ Time ($F(6,164.77) = 1.59$, $p = 0.152$) effects. Post-hoc tests at 8 weeks indicated lower EMG RMS in Intervention-1a (80 Hz) compared to Intervention-1b (80 Hz) ($p = 0.020$). Within-group analyses demonstrated significant temporal changes in all groups (Control: $p = 0.018$; Intervention-1a (80 Hz): $p = 0.013$; Intervention-1b (100 Hz): $p = 0.005$), with Intervention-1b (100 Hz) exhibiting reduced activity at Weeks 8/12 versus baseline ($p = 0.015$, uncorrected).

All the statistical results for EMG RMS are presented in Table 5.4 for the LMM analyses and Table 5.5 for the post-hoc analyses.



(a)



(b)

FIGURE 5.9. Mean and standard deviation EMG RMS values of soleus (Sol) muscle for the study participants across the intervention groups and the assessment timepoints, for the a) right and b) left leg DF tasks.

TABLE 5.5 EMG RMS significant post-hoc comparisons ($p < 0.05$)

Muscle	Leg	Timepoint	Comparison	p-value
TA	Right	8 weeks	Control vs. Intervention-1b	0.003
			Intervention-1a vs. 1b	0.045
	Left	4 weeks	Control vs. Intervention-1b	0.027
			Intervention-1a vs. 1b	0.045
Sol	Left	8 weeks	Control vs. Intervention-1b	0.027
			Intervention-1a vs. 1b	0.008
	Right	8 weeks	Control vs. Intervention-1b	0.027
			Intervention-1a vs. 1b	0.020

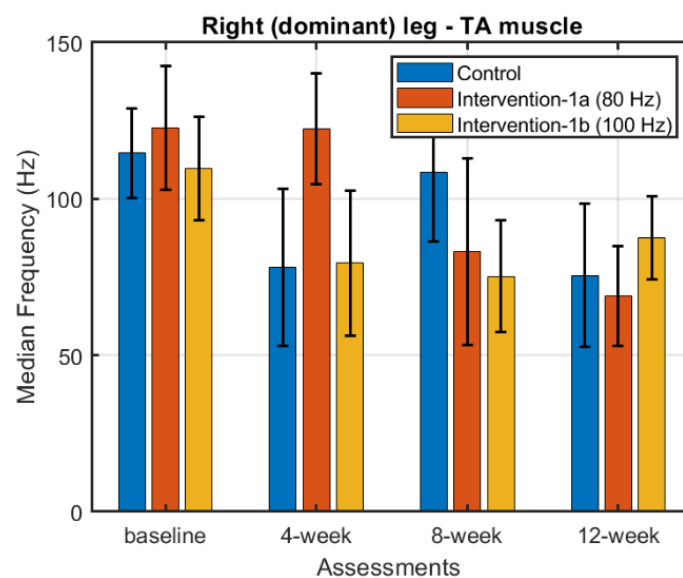
5.4.2.2 EMG median frequency (MDF) analysis

EMG median frequency (MDF) analysis revealed distinct fatigue and activation patterns across intervention groups and muscles. For the right (dominant) leg TA muscle (Figure 5.10a), the Intervention-1a (80 Hz) group exhibited marginally higher baseline MDF values than controls, which increased at 4 weeks before declining below control levels by 8 weeks. A modest rebound at 12 weeks restored values to near-control equivalence. In contrast, the Intervention-1b (100 Hz)

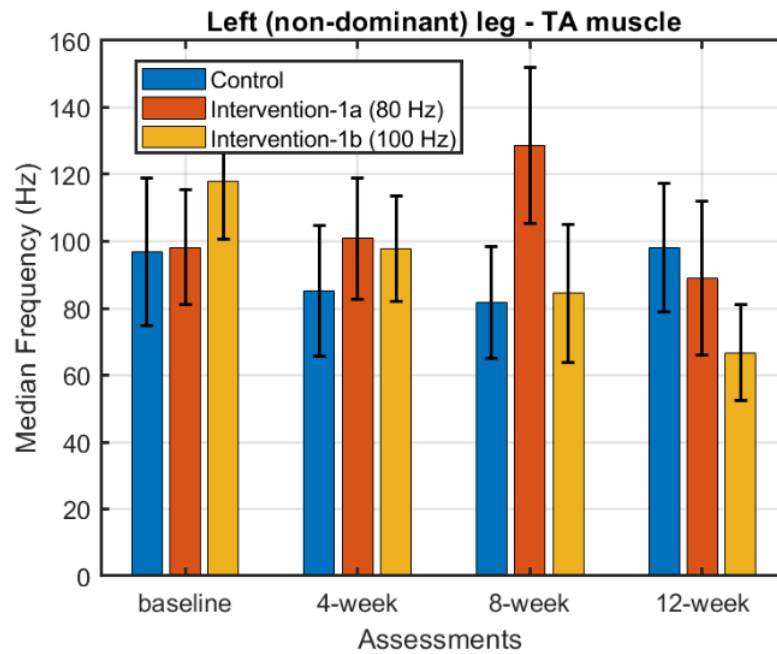
group demonstrated baseline MDF values slightly below controls, transiently increased at 4 weeks, sharply decreased at 8 weeks, and rebounded above controls by 12 weeks. In the left (non-dominant) leg TA muscle (Figure 5.10b), the Intervention-1a (80 Hz) group matched control MDF values at baseline, increased above controls at 4 and 8 weeks, but declined below controls by 12 weeks. The Intervention-1b (100 Hz) group began with higher baseline MDF than controls, maintained this elevation at 4 weeks, equilibrated with controls at 8 weeks, and dropped below controls by 12 weeks.

For the right (dominant) leg Sol muscle (Figure 5.11a), the Intervention-1a (80 Hz) group displayed elevated baseline MDF relative to controls, followed by progressive declines at 4, 8, and 12 weeks. Conversely, the Intervention-1b (100 Hz) group matched controls at baseline, increased at 4 weeks, and sustained elevated MDF through 12 weeks. In the left (non-dominant) Sol (Figure 5.11b), the Intervention-1a (80 Hz) group fluctuated dynamically: baseline values exceeded controls, dipped below at 4 weeks, rebounded above controls at 8 weeks, and declined below controls by 12 weeks. The Intervention-1b (100 Hz) group, initially higher than controls at baseline, normalized to control levels by 4 weeks and remained stable thereafter.

These MDF trajectories suggest frequency- and muscle-specific fatigue dynamics, with 100 Hz (Intervention-1b) eliciting more sustained activation in the right (dominant) Sol and transient resilience in the TA, while 80 Hz (Intervention-1a) induced progressive fatigue in the right (dominant) Sol and variable responses in the non-dominant limb. It should be noted that MDF EMG and fatigue have an inverse relation.

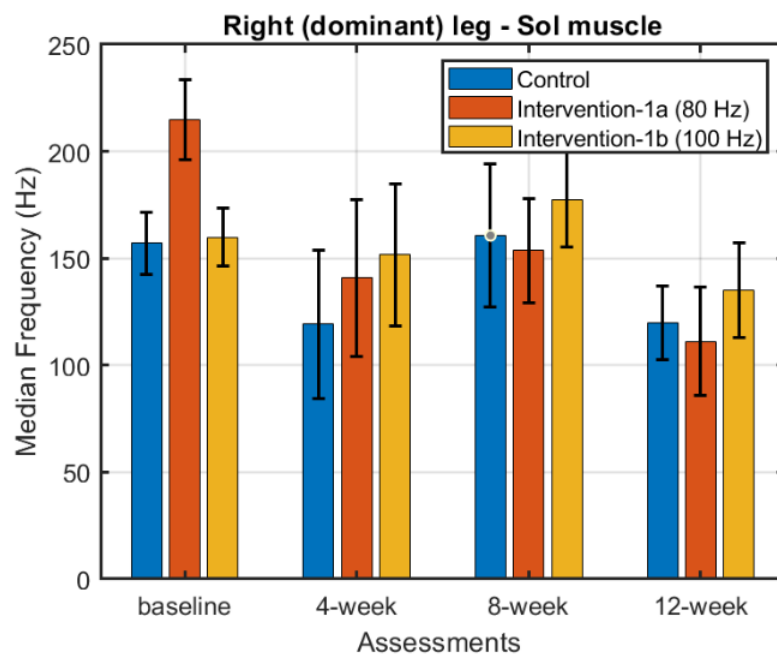


(a)

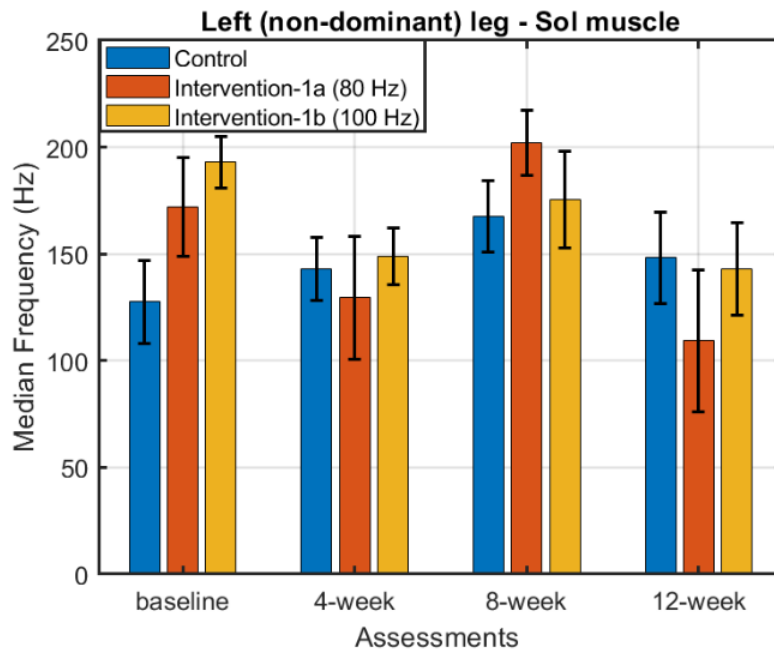


(b)

FIGURE 5.10. Mean and standard deviation EMG MDF values of TA muscle for the study participants across the intervention groups and the assessment timepoints, for the a) right and b) left leg DF tasks.



(a)



(b)

FIGURE 5.11. Mean and standard deviation EMG MDF values of Sol muscle for the study participants across the intervention groups and the assessment timepoints, for the a) right and b) left leg DF tasks

Statistical analysis revealed the following significance of the results:

TA: For both left and right tibialis anterior muscles, the LMM showed no significant group effects (Left: $F(2,195.14) = 0.35$, $p = 0.70$; Right: $F(2,194.09) = 0.38$, $p = 0.68$) or Group×Time interactions (Left: $F(6,174.4) = 1.13$, $p = 0.35$; Right: $F(6,177.83) = 0.91$, $p = 0.49$). The right tibialis anterior demonstrated a significant Time effect ($F(3,152.78) = 3.61$, $p = 0.015$), though post-hoc analyses failed to identify specific time points driving this effect. No significant post-hoc differences were found for either leg.

Sol: More pronounced effects were observed in the soleus muscles. Both left and right Sol showed significant Time effects (Left: $F(3,135.43) = 4.32$, $p = 0.006$; Right: $F(3,148.88) = 4.01$, $p = 0.009$), indicating temporal changes in median frequency. For the left (non-dominant) soleus: 1) baseline differences were found between Group 1 (Control) and Group 3 (Intervention-1b, 100Hz) ($p = 0.020$), 2) Intervention-1a (80 Hz) group showed significant Time effects ($p = 0.013$), with 8-week 3 vs 12-week differences ($p = 0.030$). The right (dominant) soleus demonstrated significant time effects in the Intervention-1a (80 Hz) group ($p = 0.030$), particularly between 4 weeks and 12 weeks ($p = 0.049$). ($p = 0.049$). These results are presented in Tables 5.8 and 5.9 in detail.

TABLE 5.8 Summary of LMM results for all conditions for Median Frequency

Muscle	Leg	Effect	F-value	DF (Num, Den)	p-value
TA	Left	Group	0.35	2, 195.14	0.703
		Time	0.78	3, 149.62	0.508
		Group × Time	1.13	6, 174.40	0.348
	Right	Group	0.38	2, 194.09	0.681
		Time	3.61	3, 152.78	0.015
		Group × Time	0.91	6, 177.83	0.492
Sol	Left	Group	1.02	2, 181.02	0.361
		Time	4.32	3, 135.43	0.006
		Group × Time	1.71	6, 163.23	0.122
	Right	Group	0.82	2, 171.81	0.441
		Time	4.01	3, 148.88	0.009
		Group × Time	0.93	6, 185.50	0.477

TABLE 5.9 Median frequency significant post-hoc comparisons (p < 0.05)

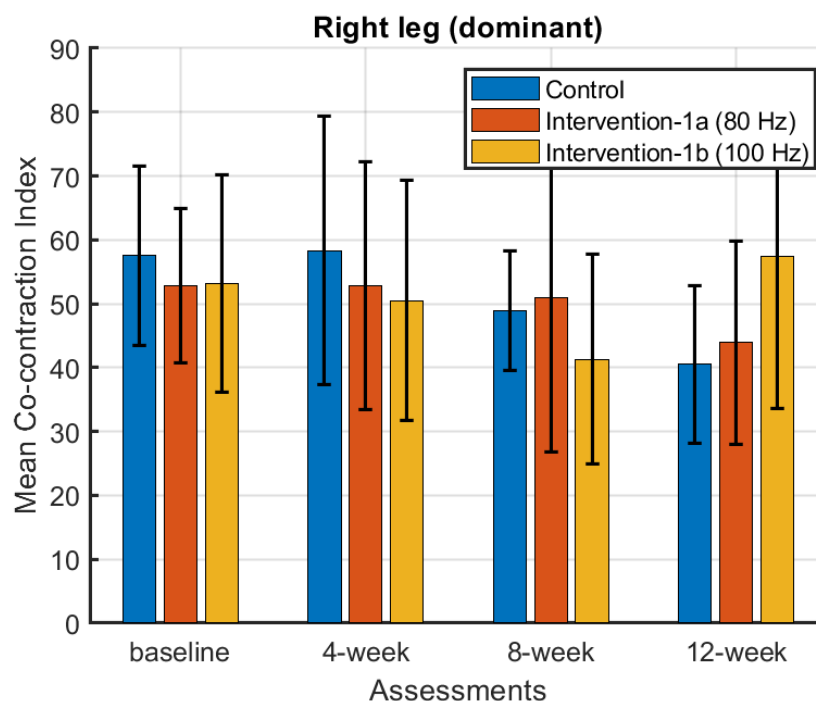
Muscle	Leg	Condition	Comparison	p-value
Sol	Left	Baseline	Control vs. Intervention-1b	0.020
		Intervention-1a	8- vs. 12-week	0.030
	Right	Intervention-1a	4- vs.12-week	0.049

5.4.2.3 EMG co-contraction index (CCI) analysis

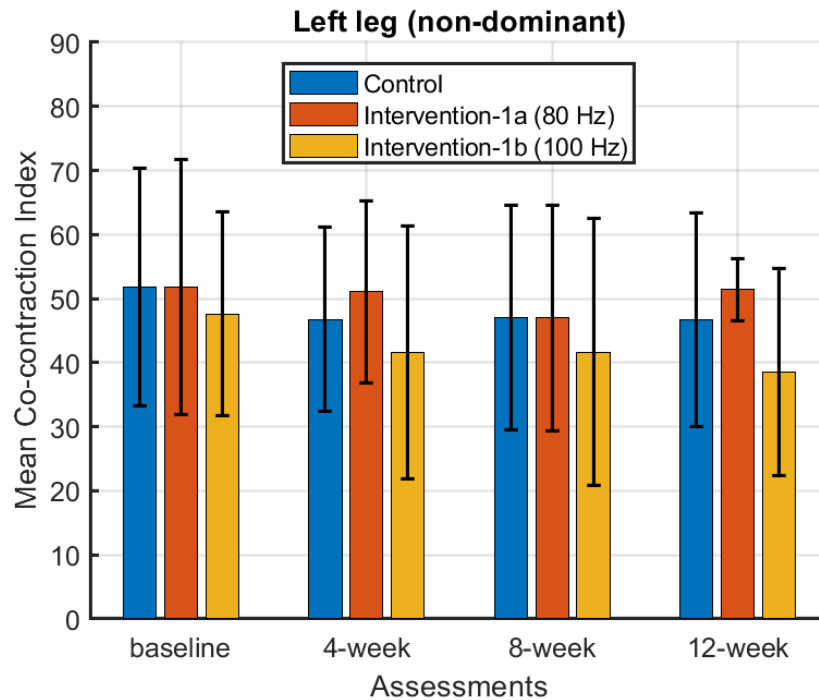
CCI analysis revealed distinct temporal and interventional patterns in agonist-antagonist coordination (Figure 5.12a–b). For the right (dominant) leg, both intervention groups exhibited lower baseline and 4-week CCI values compared to controls. The Intervention-1b (100 Hz) group remained below controls until 8 weeks but surpassed them by 12 weeks, whereas the Intervention-1a (80 Hz) group marginally exceeded controls at 8 weeks and stabilized at this elevated level through 12 weeks, indicative of a gradual, vibration-modulated increase in co-contraction activity.

In the left (non-dominant) leg, divergent trends emerged. The Intervention-1a (80 Hz) group demonstrated fluctuating CCI dynamics: baseline values matched controls, exceeded them at 4 weeks, settled back to control-level at 8 weeks, and rebounded above controls by 12 weeks; possibly showing an adaptation to intervention at 8 weeks point, but an improvement effect in the long-term (12 weeks). Conversely, the Intervention-1b (100 Hz) group exhibited persistently lower CCI values than controls across all time points, suggesting a minimal influence of 100 Hz vibration on co-contraction modulation in the non-dominant limb.

Lower CCI reflects reduced unwanted co-activation (improved control), whereas higher CCI may indicate compensatory stiffness. These findings highlight limb- and frequency-dependent disparities in neuromuscular coordination, with 80 Hz (Intervention-1a) eliciting progressive adaptation in the dominant leg and adaptive non-dominant responses. In comparison, 100 Hz (Intervention-1b) showed delayed dominance-leg efficacy and no detectable effects on non-dominant co-contraction. Low statistical significance of the results suggests interpreting these results with caution.



(a)



(b)

Figure 5.12. Mean and standard deviation co-contraction index (CCI) values between TA and Sol muscle across the intervention groups and the assessment timepoints, for the a) right and b) left leg DF tasks.

TABLE 5.10 Summary of LMM results for all conditions for CCIs

Leg	Effect	F-value	DF (Num, Den)	p-value
Left	Group	3.46	2, 192.57	0.034
	Time	1.37	3, 152.38	0.256
	Group×Time	0.35	6, 178.96	0.908
Right	Group	0.21	2, 183.48	0.808
	Time	3.14	3, 155.29	0.027
	Group×Time	1.34	6, 186.90	0.240

The right (dominant) leg showed different coordination patterns: a significant main effect of Time ($F(3,155.29) = 3.14, p=0.027$) was found, and no group effects ($p=0.808$) or interactions ($p=0.240$) effects were found. No post-hoc significant effects were identified. In the left (non-dominant) limb, a significant main effect of Group was observed ($F(2,192.57) = 3.46, p=0.034$), indicating

differences in co-contraction patterns between the control and intervention groups. However, post-hoc analyses failed to identify specific group differences. No significant time effects ($p=0.256$) or Group $\times$ Time interactions ($p=0.908$) were found. These are presented in Table 5.10.

5.4.3 Discussion of EMG findings

The study investigated effects of focal muscle vibration (FMV) at two frequencies (80 Hz and 100 Hz) on the neuromuscular activation, fatigue, and co-contraction patterns (between agonist-antagonist pair) in children with spastic diplegic cerebral palsy (CP). The findings revealed frequency-dependent, time-varying, and muscle-specific responses across EMG RMS (muscle activation), MDF (fatigue dynamics), and CCI (agonist-antagonist coordination). These results provide critical insights into the therapeutic potential of FMV for modulating motor control in CP while underscoring the complexity of neuromuscular adaptations to vibration interventions. Below, the thesis discusses the implications of these findings in the context of existing literature, clinical relevance, and methodological considerations.

5.4.3.1 Muscle activation

The normalized EMG RMS amplitudes demonstrated divergent trends between intervention groups and limbs. For the dominant (right) tibialis anterior (TA), the 100 Hz group (Intervention-1b) exhibited a transient increase in activation at 4 and 8 weeks, followed by a decline to baseline by 12 weeks. In contrast, the 80 Hz (Intervention-1a) group showed sustained activation in the dominant TA but limited efficacy in the non-dominant (left) TA. Similar trends were observed in the soleus (Sol), with 100 Hz eliciting transient activation peaks and 80 Hz showing progressive declines. These findings suggest that higher-frequency vibrations (≥ 100 Hz) may enhance acute neuromuscular recruitment potentially through increased muscle spindle modulation, while lower frequencies (≤ 80 Hz) may promote longer-term adaptations in muscle tone and stiffness. These observations are supported by earlier research which suggest, neuromuscular responses are dependent on vibration stimulation frequencies (Ritzman et al, 2018; Pujari et al, 2019).

The statistical analysis reinforced these observations. For the left TA, a significant main effect of Group ($p = 0.003$) highlighted the superiority of 100 Hz (Intervention-1b) in reducing increasing RMS amplitudes compared to controls and 80 Hz (Intervention-1a), particularly at 4 and 8 weeks. This suggests that 100 Hz may transiently improve muscle activation and/or inhibit spasticity in non-dominant limbs, potentially by modulating reflex pathways or

reducing co-contraction. However, the lack of significant Group×Time interactions in most muscles implies that the interventions' effects were consistent over time rather than progressively amplifying.

The transient nature of RMS changes, particularly the return to baseline by 12 weeks, underscores the need for a continual vibration dose to sustain therapeutic gains. The decline in RMS amplitudes at 12 weeks may reflect neural adaptation or habituation to vibration stimuli. Clinically, these results suggest that 100 Hz FMV could be prioritized for short-term muscle activation/ function improvement and/or spasticity management, while 80 Hz may require adjunct therapies (e.g., task-specific training) to prolong its effects.

5.4.3.2 Fatigue and Sustained Activation

Median frequency (MDF) analysis provided insights into fatigue dynamics, with lower MDF values indicating greater fatigue. The 100 Hz (Intervention-1b) group demonstrated resilience in the dominant Sol, sustaining elevated MDF through 12 weeks, while the 80 Hz (Intervention-1a) group exhibited progressive fatigue in the same muscle. Conversely, in the non-dominant TA, 80 Hz initially increased MDF (suggesting reduced fatigue) but declined sharply by 12 weeks. These frequency- and muscle-specific responses may stem from differences in muscle fiber recruitment: higher frequencies may preferentially activate the underlying fibers at a different rate than lower frequencies, thereby stemming the difference in behaviours (Burk et al., 1976; Bishop, 1974).

The significant Time effects in both Sol muscles ($p = 0.001$ – 0.009) indicate that fatigue accumulated universally across groups, likely due to the demanding intervention protocol (three weekly sessions). However, the 100 Hz (Intervention-1b) group's ability to sustain MDF in the dominant Sol suggests that this frequency may delay fatigue onset in postural muscles critical for gait—a finding directly relevant to CP rehabilitation, where fatigue resistance is a key therapeutic target. The transient MDF rebound in the 100 Hz (Intervention-1b) group's dominant TA at 12 weeks further implies that intermittent "rest periods" in vibration dosing could potentially enhance performance-related outcomes.

Notably, the lack of significant Group×Time interactions for MDF suggests that both frequencies induced comparable fatigue trajectories, differing only in magnitude, potentially due to variability in motor unit recruitment thresholds or spasticity severity. Future studies should explore personalized vibration parameters tailored to individual muscle characteristics (e.g., spasticity grade).

5.4.3.3 Agonist/ antagonist co-contraction

CCI analysis revealed limb- and frequency-dependent disparities in agonist-antagonist coordination with higher CCI values meaning high co-contraction. In the dominant leg, 100 Hz (Intervention-1b) FMV reduced CCI initially but surpassed control levels by 12 weeks, indicating a delayed shift toward co-activation. In contrast, 80 Hz (Intervention-1a) elicited gradual CCI increases, suggesting progressive adaptation. For the non-dominant leg, 100 Hz had minimal impact on CCI, while 80 Hz induced adaptive patterns, first exceeding control levels, coming back to control levels by 8 weeks (the end of intervention period), but again surpassed at 12 weeks follow-up; again hinting towards a delayed co-activation. These results show limb specificity in the FMV action and suggest a different rate of adaption for different frequencies.

The significant Group effect for the left leg CCI ($p = 0.034$) highlights 80 Hz FMV's ability to reduce co-contraction in non-dominant limbs, potentially by normalizing reciprocal inhibition disrupted in CP. However, the absence of post-hoc differences limits definitive conclusions.

Clinically, these findings advocate for combining FMV with activities that reinforce optimal co-contraction patterns (e.g., balance training). The limb-specific responses also emphasize the need for bilateral assessments in CP rehabilitation, as the both the limbs in CP are known to show a different behaviour in task completion, and display a varying compensatory mechanism (Lott and Johnson, 2016; Sylvia et al, 2018).

5.5 Study Limitations and Future Directions

This section provides the combined study limitations for both the EEG and the EMG studies that are detailed in the previous sections (Sections 5.3 and 5.4)

While these electrophysiological studies provide novel insights into the underlying neural mechanisms, several limitations warrant acknowledgment. First, the attrition rate (16 participants lost by 8 weeks) and uneven group sizes (Control: 19, Intervention-1a: 11) may have reduced statistical power, particularly for interaction effects. Second, the inability to blind the control group (due to the visible absence of vibration devices) introduces potential performance bias. Third, the use of 16 EEG channels restricted FC analysis to the sensor level; high-density EEG or source localization could provide deeper insights. Fourth, the 12-week follow-up assessed only half the cohort, limiting generalizability of retention effects. Fifth, the

short-term follow-up precludes conclusions about long-term sustainability. Additionally, focusing on lower-limb muscles excludes potential systemic or upper-limb effects of FMV. Using a single physiotherapist for all sessions minimized intra-participant variability but may limit reproducibility across clinicians. Further, FMV dosage of 1.5 minutes/per muscle and 6 minutes/session in total, could be considered low to induce meaningful functional changes. For example, earlier FMV studies in stroke population, which have reported significant benefits in spasticity reduction and functional improvement have delivered a 10 minutes/muscle/visit FMV dose (Imran et al., 2024; Marconi et al., 2010). Future studies with larger FMV dosage (10 minutes or more/muscle/visit) in CP population could further explain dose response mechanisms.

Future research should: investigate larger cohorts with longer follow-ups to assess durability; combine FMV with other therapies (e.g., electrical stimulations) to evaluate synergistic effects; explore correlations between neurophysiological changes and functional outcomes; explore vibration to upper and lower limbs and its interplay with functional tasks (e.g., walking, stair climbing).

The combined FC and MRCP findings underscore FMV's potential as a non-invasive tool for CP rehabilitation. By enhancing beta-band connectivity and optimizing motor-related cortical activity, FMV may facilitate functional improvements in children with CP. The frequency-specific effects suggest that personalized FMV protocols (e.g., 100 Hz for broader cortical engagement) could optimize outcomes. These neurophysiological insights complement existing evidence of FMV's benefits for spasticity and motor function (Ritzmann et al., 2018; Celetti et al., 2011). Future studies should explore whether FC and MRCP changes correlate with clinical measures (e.g., Gross Motor Function Measure) to validate their utility as biomarkers of recovery.

The frequency-specific effects of FMV on the EMG-related measures highlight its potential as a precision therapy tool in CP management. Clinically, these findings suggest distinct applications for different vibration parameters: 100 Hz FMV appears optimal for short-term spasticity reduction and delaying fatigue in dominant limbs, offering immediate therapeutic benefits. In contrast, 80 Hz FMV, with its progressive activation patterns, may synergize effectively with strength training programs to enhance neuromuscular adaptation over time. Furthermore, combining protocols, such as alternating frequencies, could balance acute relief with sustained improvements, addressing both immediate and long-term rehabilitation goals.

To advance these applications, future research should prioritize three key areas. First, extending intervention durations beyond 8 weeks and defining optimal maintenance dosing regimens could clarify FMV's long term effects and clinical scalability. Second, mechanistic studies using neuroimaging (e.g., functional magnetic resonance imaging (fMRI)) and neurophysiological tools (e.g., transcranial magnetic stimulations (TMS), electroencephalography (EEG)) are critical to unravelling the neural mechanisms underlying frequency-specific responses, such as cortical reorganization or spinal reflex modulation. Finally, developing personalized FMV protocols tailored to individual factors, including spasticity severity, motor function, or limb dominance, may maximize therapeutic precision and outcomes. Together, these insights could refine FMV as a targeted, adaptable intervention in CP care.

5.6 Main findings for the CP study

The main findings for the CP study are:

- 8-weeks of FMV therapy (at both 80 and 100 Hz) resulted in an increased beta-band EEG FC, predominantly in the frontal and central regions
- 8 weeks of FMV therapy resulted in increased muscle activations and decreased fatigue for the TA and Soleus muscles in the lower limb.

5.7 Conclusion for CP study

The studies explored the differential effects of focal muscle vibration (FMV) at 80 Hz and 100 Hz on the brain-level function (EEG) through connectivity pattern and cortical potentials, and muscle- level function (EMG) through neuromuscular activation, fatigue dynamics, and co-contraction patterns in children with spastic diplegic cerebral palsy (CP). The findings underscore the potential of FMV as a targeted therapeutic intervention while highlighting the nuanced, frequency-dependent neurophysiological responses in this population.

EEG Findings demonstrated that FMV modulates functional connectivity and movement-related cortical potentials in children with CP, with frequency-dependent effects. The 100 Hz intervention induced broader FC changes and more pronounced MRCP reductions, suggesting its superior potential for motor rehabilitation.

Key EMG results revealed that 100 Hz FMV elicited transient improvements in muscle activation (EMG RMS) and delayed fatigue (higher MDF) in the dominant limb, particularly in the soleus muscle, suggesting its utility for short-term spasticity management and fatigue mitigation. In contrast, 80 Hz FMV demonstrated progressive adaptations in neuromuscular coordination (CCI), indicating its potential for fostering longer-term improvements in agonist-antagonist synergy. The time-dependent nature of these effects—evidenced by the return of RMS and MDF values to baseline by the 12-week follow-up—emphasizes the need for longer FMV intervention protocols to sustain therapeutic gains.

Our findings suggest 100 Hz FMV may provide short-term spasticity relief, while 80 Hz may support longer-term coordination. These interpretations are based on EMG outcomes and require confirmation in studies measuring functional and clinical endpoints. The limb-specific disparities in co-contraction patterns further highlight the importance of bilateral assessments and interventions in CP rehabilitation, as both the limbs in CP are known to show a different behaviour in task completion and display a varying compensatory mechanism (Lott et al, 2016; Sylvia et al., 2018).

As per our knowledge, this is the first comprehensive study to systematically investigate the effects of wearable FMV on brain functional connectivity, muscle activation, fatigue and co-contraction, in spastic diplegic CP children, expanding on a recent case study hinting at the relevance of co-contraction in CP (Boulay et al., 2025). This is also the first study to compare these effects, with two FMV stimulation frequencies (80 and 100Hz) over a longer (12 weeks) period, in children with CP. Thus, providing improved insight into the use of wearable FMV as an intervention technology in CP children.

While the study provides valuable insights, limitations such as attrition, uneven group sizes, and partial follow-up data necessitate cautious interpretation. Future research should investigate longitudinal protocols (>12 weeks) to assess sustained benefits, investigate higher FMV dosage (>10 minutes/per muscle/visit), incorporate functional outcome measures (e.g., gait analysis), and explore mechanistic correlates (e.g., cortical excitability via TMS/ EEG) to unravel the neural underpinnings of frequency-specific effects. Integrating FMV with task-specific training or alternating vibration frequencies may also optimize functional outcomes.

In conclusion, this work advances the understanding of FMV as a precision tool in CP rehabilitation, offering a foundation for evidence-based, individualized intervention strategies.

By bridging neurophysiological insights with clinical practice, it paves the way for innovative approaches to enhance motor function in children with CP.

Chapter 6: Focal Muscle Vibration Therapy in Spinal Cord Injury Individuals

The experiments in this chapter will be submitted to in IEEE Journal of Translational Engineering in Health Medicine.

6.1 Introduction

Focal muscle vibration (FMV) has emerged as a promising non-invasive neuromodulation technique for addressing sensorimotor impairments in neurological disorders, including spinal cord injury (SCI), by delivering targeted mechanical oscillations (50–120 Hz) to stimulate neuromuscular pathways and modulate reflex activity (DeForest et al., 2020; Murillo et al., 2011). As established in Chapter 2, SCI presents significant rehabilitation challenges due to motor deficits, spasticity, and sensory impairments, which conventional therapies like physiotherapy and pharmacotherapy often address inadequately due to their limited focus on sensory restoration (Fattorini et al., 2023). The therapeutic benefits of FMV are hypothesized to arise from its ability to modulate cortical and spinal neural circuits, enhance proprioceptive feedback, and reduce spasticity. However, as discussed in Chapter 2, the literature lacks evidence linking FMV therapy to measurable neurophysiological changes at the cortex (e.g., EEG-related functional connectivity (FC)), in SCI population.

This chapter bridges that gap by systematically evaluating how FMV (delivered at 80 Hz) influences functional connectivity (FC) in the brain of SCI individuals. In this regard, this chapter explores how 3 weeks of FMV therapy would affect the FC measured through pre-post EEG assessments in 10 SCI individuals. In the context of SCI, understanding changes in FC can reveal how motor and sensory networks are affected by FMV, offering a window into the cortical reorganization that may underlie functional improvements (Kaushal et al., 2017). Investigating FC in response to FMV could thus represent a novel approach to assessing the efficacy of FMV in SCI rehabilitation, moving beyond traditional outcome measures like muscle tone and motor function.

For the EEG experiment, the main aim was to investigate the efficacy of 80 Hz FMV, administered over 3 weeks, towards inducing functional changes at the cortical level in individuals with SCI. Using resting state EEG, we examined the functional connectivity (FC) changes effected by the 8-week intervention. We hypothesized that FMV stimuli would induce changes in FC, possibly at the sensorimotor level, when compared with Controls (no vibration), this study thereby aims to enhance the mechanistic understanding of FMV's application, leading to reduce the gap between its clinical application and therapeutic potential.

This chapter also examines how FMV affects clinical outcomes in individuals with SCI over a 3-week intervention period. Specifically, it evaluates two clinical measures: the Modified Ashworth Scale (MAS) to assess changes in muscle spasticity, and the Penn Spasm Frequency Scale (PENN) to measure the frequency and severity of muscle spasms. Both of which (frequency and severity) are prominent issues in people living with SCI,

This chapter aligns with the thesis's objective (OB3) to evaluate FMV's efficacy in improving motor function, reducing spasticity, and enhancing sensory feedback in SCI, as outlined in Chapter 1. It addresses research question RQ3: *What are the specific effects of FMV on motor function, spasticity, and brain activity in individuals with SCI?* The experiments test hypothesis H2, which posits that FMV therapy, applied at a controlled frequency (e.g., 80 Hz), will significantly reduce spasticity (e.g., a 1-point reduction on the Modified Ashworth Scale (MAS)) and enhance sensorimotor cortex activation, as measured by electroencephalography (EEG).

Building on the systematic review of FMV applications (Chapter 2) and the development and characterization of a wearable FMV device (Chapter 4), this chapter investigates the therapeutic potential of a custom-designed FMV device in a clinical setting for individuals with SCI. By employing neurophysiological assessments (EEG) and clinical outcome measures, such as the MAS, the study aims to elucidate the mechanisms underlying FMV's effects, including reflex modulation and cortical reorganization. The findings contribute to the thesis's broader aim of developing scalable, evidence-based neuromodulation tools for neurological rehabilitation, complementing the evaluations of FMV in cerebral palsy (Chapter 5) and stroke (Chapter 7). This chapter seeks to establish FMV's feasibility as a rehabilitation aid for SCI, informing parameter optimization and future interventions to enhance functional outcomes.

6.1 Methods

6.1.1 Participants and intervention

A total of 11 SCI participants were recruited (3 male) for the study. The participants had a mean age of 34.64 ± 13.4 years. The inclusion criteria were: age between 18 and 85 years, a clinical diagnosis of SCI, more than one year since injury, ASIA scales A, B, C and D, and injury level on the spinal cord above L5. Following exclusion criteria were considered while recruiting. No uncontrolled medical problems including pulmonary, cardiovascular or orthopaedic disease; no debilitating disease prior to the SCI that caused exercise intolerance; premorbid, ongoing major depression or psychosis, altered cognitive status; history of head injury or stroke, metal plate in skull; receiving drugs acting primarily on the central nervous system, which lower the seizure threshold such as antipsychotic drugs (chlorpromazine, clozapine) or tricyclic antidepressants; and pregnant females. One participant was excluded due to psychosis leaving a total of 10 participants for the study.

The study was designed as a double-blind, randomized, controlled trial with a two-group parallel structure. Participants were randomly assigned to one of two groups: a control group and a vibration intervention group. Both the participants and the outcome assessors were blinded to the group allocations. Intervention was given for three weeks (5 sessions a week) for 10 minutes each, targeting the Achilles tendon. Vibration frequency was set at 80 Hz (amplitude 0.5 mm). This frequency and muscle setting was selected based on previous studies (Deforest et al., 2018) that show its effectiveness over a single session, we here extend it to a three-week long experiment. The initial intent was to conduct a 4-week long experiment as it has shown improvements in the functional performance of stroke population (Constantino et al. 2014; Constantino et al. 2016; Choi et al. 2017) but due to limitations in the availability of all the SCI participants the study had to be restricted to 3 weeks.

Right leg followed the left leg. Participants were seated on a chair or a wheelchair while intervention delivery. The control group did not receive any intervention. Data collection took place in July-August 2023 at the National Institute of Rehabilitation Medicine, located in Islamabad, Pakistan. Prior to enrolment, detailed explanations of the experimental procedures were provided to the participants and written informed consent was obtained. The study was carried out in compliance with the Declaration of Helsinki's ethical standards and with approval from ethical committee of Riphah International University, Islamabad, Pakistan (REC-01289).

6.1.2 Physical therapy

Physical therapy was also administered to the participants alongside the vibration intervention. The standard physical therapy protocol for SCI patients included stretching performed 5 days a week to prevent tightness and contractures. Strengthening that target preserved muscles using resistance bands, weights, or functional activities. Postural alignment training performed in sitting and during transfers to prevent deformities i.e. scoliosis, kyphosis. Orthotic devices such as ankle foot orthosis/ knee ankle foot orthosis were used. Thrice a week gait training exercises were performed using parallel bars, walker, or crutches, and standing frame or tilt table were used to promote bone health and circulation. To promote cardiovascular health deep breathing and diaphragmatic breathing exercises were performed. Physical therapy was delivered by experienced and registered physiotherapist.

6.1.3 EEG Assessments

EEG data was recorded from all the participants to understand the impact on the associated cortical changes, particularly understand the FC changes. Assessments were conducted at baseline (pre) and after the three-week intervention (post). Changes in the resting-state functional connectivity in the EEG activity was accessed to understand the impact vibration intervention has on the behaviour of cortical patterns. The setup and protocol of the EEG resting state data collection and then data processing was kept the same as was for the CP experiments detailed in Sections 4.3.1 and 4.3.2 in Chapter 4. Statistical analysis was also the same as for the CP experiments (Section 4.3.2.4); statistical analysis comparisons were made between pre and post for control and vibration groups.

6.1.4 Clinical evaluations

To understand FMV's impact in clinical application, clinical measurements were also conducted for the SCI cohort pre and post intervention. These included the Penn frequency scale (PENN) for measuring the spasm frequency and severity, and modified Ashworth scale (MAS) readings for spasticity measurements. MAS assessments were carried out for the knee and ankle joints of both the legs. These clinical measurements were conducted by an experienced and registered physiotherapist.

6.3 Results

6.3.1 Participant demographics

Total 11 participants were recruited for the study, 10 of which were retained for the experiments. One participant was excluded from the population due to not adhering to the inclusion criteria. All ten participants completed the experiment. Five were included into the control group and five into intervention group. All the participants were paraplegic, 6 of which were incomplete and 4 were complete. The disease characteristics of the study population is presented in Table 6.1.

TABLE 6.1: Disease characteristics of the recruited SCI population.

ID	Age	Years since injury	Gender	Level	Severity	Cause	ASIA scale
1	30	17	female	paraplegia	incomplete	Earthquake	ASIA C level: T11
2	60	5	male	paraplegia	complete	Fall	ASIA A level: T10
3	46	17	female	paraplegia	incomplete	Earthquake	ASIA C level: T10
4	32	17	female	paraplegia	complete	Earthquake	ASIA A level: T12
5	30	17	female	paraplegia	complete	Earthquake	ASIA A level: T1
6	31	17	female	paraplegia	complete	Earthquake	ASIA A level: T10
7	50	1	male	paraplegia	incomplete	Compression	ASIA B level: T1
8	17	2	female	paraplegia	incomplete	gunshot wound	ASIA D level: T1
9	19	2	male	paraplegia	incomplete	motor vehicle accident	ASIA C level: T1
10	24	2	female	paraplegia	incomplete	Compression	ASIA B level: T1

6.3.2 Clinical outcomes

The clinical measures did not show any noticeable change due the application of FMV. The PENN values were 0 (no spasm) for seven participants, 1 (mild) for one, and 4 (severe spasms) for two participants pre intervention, which remained same for all participants post intervention. Similarly, MAS did not show a clear changing trend either, with MAS values ranging from 1+ to 4 pre-intervention, showing a prevalent spasticity profile in the study population. No change in MAS scores was recorded post-intervention for the control group. In the intervention group, only one participant (participant-6) showed a one-point decrease in the MAS score for the ankle, while two participants showed a one-point MAS decrease for the knee spasticity measures. Due to no or minimal change recorded, no statistical analysis was conducted. These results show that FMV to the Achilles tendon do not contribute to spasm reduction and can, in some participants, decrease spasticity. The clinical measure results are shown in detail in Table 6.2.

TABLE 6.2: Pre- and post-intervention clinical outcome measures for the SCI study population—modified Ashworth scale (MAS) and Penn frequency scale (PENN) readings.

ID	Group	pre MAS right leg	post MAS left leg	pre MAS right leg	post MAS left leg	pre PENN	post PENN
1	intervention	Knee 2 Ankle 4	Knee 2 Ankle 4	Knee 2 Ankle 4	Knee 2 Ankle 4	No spasm (0)	No spasm (0)
2	control	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	No spasm (0)	No spasm (0)
3	control	Knee 3 Ankle 3	Knee 3 Ankle 3	Knee 3 Ankle 3	Knee 3 Ankle 3	Severe (4)	Severe (4)
4	intervention	Knee 4 Ankle 2	Knee 4 Ankle 2	Knee 4 Ankle 2	Knee 4 Ankle 2	No spasm (0)	No spasm (0)
5	control	Knee 2 Ankle 1+	Knee 4 Ankle 4	Knee 2 Ankle 1+	Knee 4 Ankle 4	No spasm (0)	No spasm (0)
6	intervention	Knee 2 Ankle 4	Knee 2 Ankle 4	Knee 1+ Ankle 4	Knee 1+ Ankle 4	Severe (4)	Severe (4)
7	control	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	No spasm (0)	No spasm (0)

8	intervention	Knee 2 Ankle 4	Knee 2 Ankle 4	Knee 2 Ankle 4	Knee 2 Ankle 4	Mild (1)	Mild (1)
9	control	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 4 Ankle 4	Severe (4)	Severe (4)
10	intervention	Knee 4 Ankle 4	Knee 4 Ankle 4	Knee 3 Ankle 3	Knee 3 Ankle 3	No spasm (0)	No spasm (0)

6.3.3 FC changes in the EEG

Results demonstrated that in the absence of FMV intervention the resting state FC did not change for the tested SCI population. This was true for both the EC and EO EEG states and for both the alpha and beta EEG frequency bands. In the vibration intervention group however, the EC condition resting-state EEG showed significant changes in FC for both alpha and beta EEG bands. Surprisingly, the pattern of the FC observed was exactly similar in both the bands, with central, parietal and the right temporal lobe being involved in the FC change. CZ, C4, T4, P3 PZ and P4 were the identified electrodes that participated in the contribution towards the functional change. The visual representation of the FC graph is presented in Figures 6.1 and 6.2 for the alpha and beta bands, and the statistical results are presented in Tables 6.3 and 6.4 respectively. No other statistically significant change was observed.

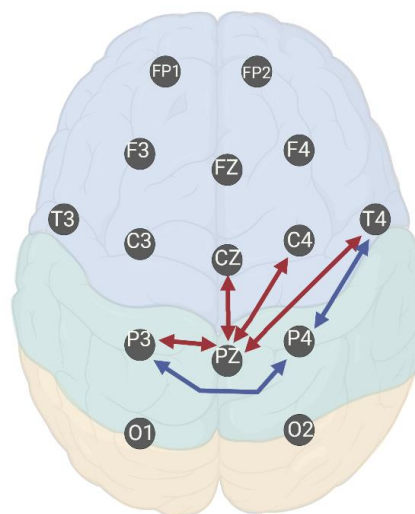


FIGURE 6.1. Resting-state EEG FC in alpha band for 80 Hz vibration group for the EC condition. Post-intervention vs pre-intervention comparison.

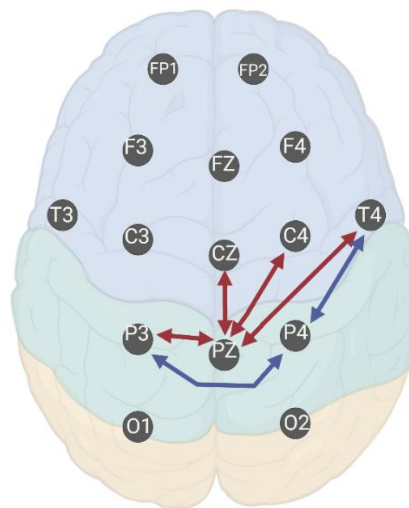


FIGURE 6.2. Resting-state EEG FC in beta band for 80 Hz vibration group for the EC condition. Post-intervention vs pre-intervention comparison.

These results suggest that FMV may selectively modulate brain activity at the parietal lobe, with similar effects between EEG bands (alpha, beta). The absence of changes in the control group underscores the potential role of vibration therapy in inducing neuroplastic adaptations. Further research is warranted to explore the long-term implications of these FC changes and their relationship with functional motor improvements in SCI.

TABLE 6.3 Results of the statistical analysis for EC alpha band comparisons, presenting the combinations with statistically significant changes in the EEG FC.

Region	p-value	t-value	Effect size
PZ-CZ	0.0004	-3.62957	1.552509
PZ-C4	0.0004	-3.31333	-0.96682
PZ-T4	0.0004	-2.87771	-0.02664
PZ-P3	0.0004	-2.71698	-4.01481
P4-T4	0.0004	-2.46692	-0.05746
P4-P3	0.0004	-7.69291	-5.37362

TABLE 6.4 Results of the statistical analysis for EC beta band comparisons, presenting the combinations with statistically significant changes in the EEG FC.

Region	p-value	t-value	Effect size
PZ-CZ	0.0004	-3.62957	-0.95699
PZ-C4	0.0004	-3.31333	-5.56794
PZ-T4	0.0004	-2.87771	0.498471
PZ-P3	0.0004	-2.71698	-7.26489
P4-T4	0.0004	-2.46692	-2.05E+15
P4-P3	0.0004	-7.69291	7.77E+14

6.4 Discussion

The present study investigated the effects of 3-week long FMV on 10 SCI participants, focusing on clinical outcomes and cortical FC changes measured via EEG. The results revealed limited clinical improvements in spasticity and spasm frequency but demonstrated significant alterations in resting-state FC following vibration intervention, particularly in the alpha and beta frequency bands.

6.4.1 Clinical Outcomes

The clinical measures, including the PENN and MAS, showed minimal changes post-intervention. Only a few of participants (1/5) in the vibration group exhibited slight reductions in spasticity, as evidenced by one-point decreases in MAS scores for the knee and ankle joints. These findings suggest that FMV applied to the Achilles tendon may have a modest effect on spasticity in some individuals but does not significantly impact spasm frequency or severity. The lack of pronounced clinical improvements could be attributed to location of application, as (Murillo et al., 2011) and (Camerota et al., 2024) have shown MAS improvements in the lower limb from FMV applied to quadriceps. The results will depend on the intactness of the neural connections and the interplay between agonist, antagonist activities. Another factor that could contribute to the lack of pronounced clinical improvements is the duration of FMV. Maybe a 6/8 weeks dosage of FMV could provide better results as shown in other stroke studies (Calabro et al. 2017), and 3 weeks may not be sufficient for a meaningful effect, dose of vibration could also

be increased up to 20 minutes instead of 10. Future research could explore effect of different muscle locations, FMV duration, FMV dose to determine their potential for eliciting more robust clinical benefits.

6.4.2 Functional Connectivity Changes

In contrast to the clinical outcomes, the EEG data revealed significant FC changes in the vibration group, particularly in the eyes-closed (EC) condition. These changes were localized to central, parietal, and right temporal regions, with notable involvement of electrodes CZ, C4, T4, P3, PZ, and P4. These changes imply possible improvements by FMV in the sensory and motor processing in the SCI brain. The similarity in FC patterns between the alpha and beta bands suggests that FMV may induce synchronized neuroplastic adaptations across multiple frequency bands. The absence of FC changes in the control group further supports the specificity of the vibration intervention in driving these neural adaptations.

6.4.3 Implications and Future Directions

The observed FC changes underscore the potential of FMV as a non-invasive tool for promoting neuroplasticity in SCI patients. While the clinical benefits were limited, the EEG results suggest that FMV may influence cortical networks involved in motor control and sensory processing. This dissociation between clinical and neural outcomes highlights the need for multimodal assessments in future studies to comprehensively evaluate the therapeutic potential of FMV. Additionally, investigating the long-term effects of vibration therapy and its correlation with functional motor recovery could provide deeper insights into its clinical applicability.

Several limitations should be acknowledged. The small sample size ($n=10$) limits the generalizability of the findings, and the heterogeneous nature of SCI (e.g., varying injury levels and completeness) could introduce variability in responses. Furthermore, the study focused solely on the Achilles tendon, and the effects of FMV on other muscle groups or combined with other rehabilitation techniques remain unexplored. Future studies with larger cohorts and diverse intervention protocols are warranted to validate and extend these findings.

In summary, this study demonstrated that FMV can induce significant changes in cortical FC in SCI participants, particularly in the parietal and central regions, without corresponding pronounced clinical improvements. These results suggest that FMV may serve as a promising adjunct therapy for modulating neural activity in SCI rehabilitation. Further research is needed

to optimize vibration parameters, explore long-term effects, and establish the translational potential of these FC changes for functional recovery.

6.5 Main findings of the SCI study

The main finding of this study is that:

- Three weeks of 100 Hz FMV to the Achilles tendon results in an increase in alpha and beta-band FC predominantly in the central and parietal region of the cortex.

Chapter 6: Usability of Focal Muscle Device in Stroke Patients

The experiments in this chapter have been published as a journal article in IEEE Journal of Translational Engineering in Health Medicine

M. Ashfaque et al., "Wearable Focal Muscle Vibration Device for Reducing Spasticity and Improving Upper Limb Function: Device Co-Design and Results From a Feasibility Study in People With Stroke," in IEEE Journal of Translational Engineering in Health and Medicine, vol. 13, pp. 354-364, 2025, doi: 10.1109/JTEHM.2025.3590582.

7.1 Introduction

Focal muscle vibration (FMV) has gained much attention in stroke rehabilitation, particularly for spasticity management. Building on Chapter 2 which lays the foundation of FMV in neurorehabilitation, and extending on the device development and testing laid out in Chapters 4, 5 and 6, this chapter addresses a key issue in adaptability of FMV as a rehabilitation technology in people with neurological disorders. Here, we investigate the usability of a commercial wearable FMV device for home-based application in stroke population by patient or carer. It also measures how self-usage of the device affects spasticity treatment in the stroke population. This chapter transitions from theoretical and mechanistic frameworks to practical user-centric validation, addressing critical gaps in the adaptation of FMV beyond laboratory and clinical settings.

Spasticity, a common and disabling complication in stroke and other neurological conditions, affects 30% to 80% of stroke survivors and ranges from mild tightness to severe joint immobility (Kuo and Hu, 2018), often impairing upper limb function and daily activities like eating and dressing (Doan et al., 2012; Walker and Lincoln, 1991). If left untreated, it can lead to pain, stiffness, contractures, joint subluxation, and increased care needs (Koman, Smith and Shilt, 2004). Clinically defined as a velocity-dependent increase in muscle tone due to hyperexcitability of the stretch reflex, spasticity may be alleviated by neuromodulatory

interventions. Particularly FMV stimuli has shown to reduce H-reflex drive and thereby decrease reflex hyperexcitability (Barss et al., 2021; DeForest, Bohorquez and Perez, 2020). Indeed, a number of studies have shown that Focal Muscle Vibration (FMV), can reduce spasticity and improve limb (upper/lower) function and balance in people with stroke (Moggio et al., 2021; Avvantaggiato et al., 2021; Fattorini et al., 2025; Giorgi et al., 2024; Wang et al., 2020; Sambe et al., 2022). However, in its current form it is not mobile and require expert/clinical supervision, limiting its access and potential. For example, an influential study, and one of the first to report sustained effects of FMV in reducing spasticity and improving upper limb function in chronic stroke patients, used a stationary machine with pins to provide stimulation (Marconi et al., 2011). As opposed to the stationary machine requiring expert supervision, an easy to use to wearable FMV device can: 1) improve access to vibration therapy by removing barriers of visiting the clinic, 2) allow longer term use of the vibration therapy, in patients' homes, potentially resulting in increased patient benefits, 3) allow vibration therapy to be used while: doing activities of daily living (ADL), physiotherapy or while out socializing. Indeed, the positive effects of longer therapy (duration/intensity) on rehabilitation outcomes is well recognized (Teasell et al., 2005; Kwakkel, 2006; Jette, Warren and Wirtalla, 2005). For example, when studies employed vibration therapy for longer durations (3-7 days/week for up to 4 weeks), the results were encouraging, both in reducing spasticity (Marconi et al., 2011), (Caliandro et al., 2012; Noma et al., 2009; Casale et al., 2014) and improving upper limb function (Paoloni et al., 2010; Zankel, 1969). However, in these studies, participants had to visit the laboratory to receive the intervention, making this approach impractical for the wider use. Further, it is known that spasticity and reduced upper limb function (in the affected limb) can inhibit activities such as eating, personal hygiene and dressing (Binder, Kaya and Liepert, 2009; Avvantaggiato et al., 2021).

Hence, the aim of this study was to take first step towards addressing the limitations of the current FMV stimulation devices by co-developing (with patients and clinicians) a wearable FMV device. With a vision that, such a wearable device, once fully developed, can: 1) improve access to vibration therapy by removing barriers of visiting the clinic, 2) allow longer term use of the FMV therapy, in patients' homes, 3) allow FMV therapy to be used while: doing activities of daily living, therapy or while out socializing. As a first step crucial step in achieving the above aim, this study co-developed a wearable FMV device with patients and clinicians and tested its

feasibility as a rehabilitation tool in reducing spasticity and improving upper limb function, in clinic setting.

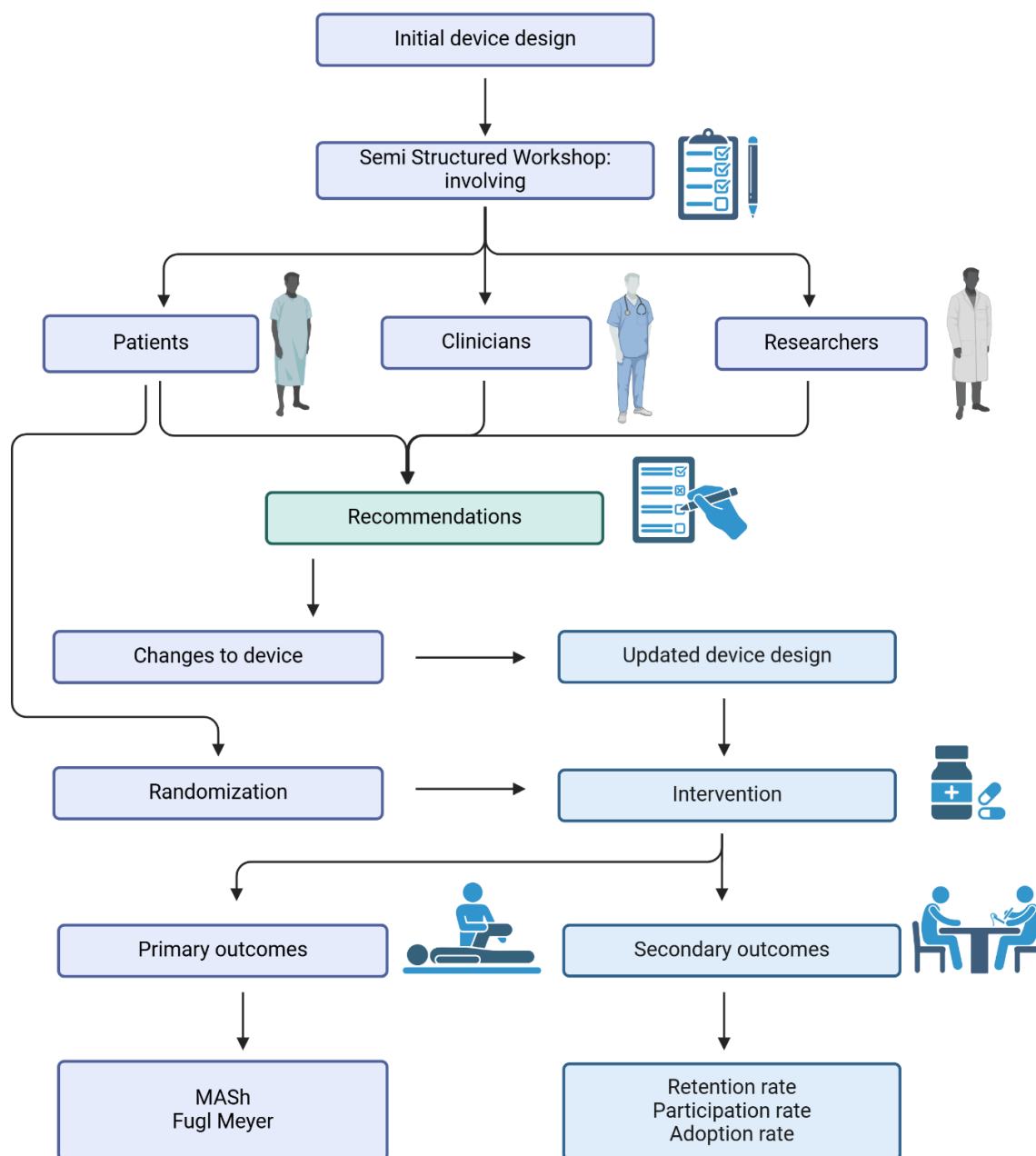


FIGURE 7.1. Flow chart depicting various stages of the design of the study.

This chapter aligns with the thesis's objective (OB4) to investigate FMV's feasibility and feasibility and usability in a clinical setting for stroke survivors, focusing on device co-design with patients and clinicians, and assessing short-term effects on spasticity and upper limb

function. as outlined in Chapter 1. It addresses research question RQ3: *What are the feasibility, usability, and short-term clinical effects of a co-designed wearable FMV device on spasticity and upper limb function in stroke survivors??* The experiments test hypothesis H3, which predicts that a co-designed wearable FMV device, applied in a clinical setting for stroke survivors, will demonstrate high feasibility and usability (e.g., positive participant feedback on ease of use and comfort) and yield significant improvements in upper limb function (e.g., increased Fugl-Meyer Upper Extremity scores) supporting its potential as a practical rehabilitation tool.

7.2 Methods

7.2.1 Study Phases

This study consisted of multiple chronological phases. As shown in Figure 7.1, the chronological phases involved: 1) Semi structured workshop: involving patients, clinicians and researchers, 2) Changes to the device design based on patient and clinician feedback from the workshop, 3) Device feasibility study in clinical setting to assess device's effect on spasticity and upper limb function, 4) Primary and secondary outcome measures through quantitative and qualitative assessments.

Below subsections describe each of these chronological phases in detail. Results of each of these phases are then described in Results section (Section 7.3).

7.2.1.1 Semi Structured Workshop: involving Patients, Clinicians and Researchers

To obtain systematic user feedback, from patients and clinicians a semi structured workshop was organized. The main aim of the workshop was to obtain user feedback; so that this feedback could be used to adapt the 'wearable FMV device' design, to make it suitable and effective (rehabilitation tool) for stroke users.

The one-day workshop involved 3 chronic (1-year > post-stroke) stroke volunteers, 5 clinicians (4 physiotherapists and 1 occupational therapist, all specialist in neurorehabilitation) and 1 (biomedical engineering) researcher. Stroke volunteers had clinically diagnosed spasticity and diminished upper limb function in their paretic (i.e. affected) limb.

On the day of the workshop, each stroke volunteer was first introduced to the wearable FMV device by the researcher and clinician. The device's intended function, its operation (how to: don, doff and operate) was described to the stroke volunteer. Following the device introduction, each volunteer was then asked to, don the device on their affected limb using their able limb, use the device (with stimulation on) on their affected limb for 10 minutes and, doff the device. Following this, the volunteers were asked a series of questions, and their answers were recorded in writing. The above process was followed with one stroke volunteer at a time. The questions were constructed by clinicians and researchers together, to specifically identify issues and aspects most relevant to stroke people when using the wearable FMV device.

Specific questions presented to the stroke volunteers included:

- a) comfort in wearing the device,
- b) ability/ease to don and doff the device,
- c) device material, size and fit,
- d) weight of the device,
- e) aesthetics/style,
- f) stimulation sensation (in response to 0.5 mm amplitude and 100 Hz frequency),
- g) size/appropriateness of device ON/OFF switch,
- h) any adverse reactions.

7.2.1.2 Changes to the Device Design Based on Patient and Clinician Feedback from the Workshop

At the workshop, stroke volunteers identified some key difficulties and challenges, while also quoted on salient and good features of the wearable FMV device, when using the device without any assistance from clinician. Key issues identified by all the volunteers pertained to only one specific aspect: 'ability/ease to don and doff the device'. These issues were then addressed by making changes to the device design. The identified issues and how they were resolved by making changes to the device design is described in the results section (Section 7.3) below.

The device design (see Figure 7.3a) used by stroke volunteers at the workshop was '*Myovolt arm*' version of the device developed by *Myovolt*TM. The device works by delivering sinusoidal vibration stimulation (at 100 Hz and 0.5 mm), generated by one neodymium mechanical motor

that is incorporated in the device strap (Figure 7.3). The motor allows for precise focal (mechanical) vibration stimulation, at a set frequency (100 Hz for this study), to be delivered to the desired muscle.

7.3.1.3 Device Feasibility Study in Clinical Setting to Assess Device's effect on Spasticity and Upper Limb Function

Aims of the Feasibility Study

Main aim of this feasibility study was to establish feasibility of using this newly adapted (following the changes made to the device design based on the above-mentioned feedback) wearable FMV device in a clinical setting, to treat spasticity and upper limb function in stroke population. A secondary aim was to establish whether a smaller dose (40 minutes) of wearable FMV intervention can be effective in reducing muscle spasticity and/or improving upper limb function in stroke population.

Feasibility Study Design and Setting

The study was a cross over randomized controlled study conducted at Hobbs Rehabilitation, UK. The Ethical Review Committee of the University of Hertfordshire approved the study (Reference: SPECS/SF/UH/05488). All procedures performed involving human participants followed the ethical standards of the institutional review committee and adhered to the declaration of Helsinki. An information sheet was given to the participants, and all the participants signed a 'written consent form' in presence of the clinician before the experiment.

7.3.2 Participants

Participants were recruited from the outpatient stroke database of Hobbs Rehabilitation, UK, by contacting the potential participants via telephone and inviting them to participate. Participants were included if they were aged between 18 and 80 years, had sustained stroke > 1 year ago, had less than 53 on a upper extremity Fugl-Meyer Assessment (FMUE) of motor function (i.e., they had significant motor impairment) and the spasticity score for Bicep Brachialis and Extensor Carpi Radialis muscle of affected side was <3 on Modified Ashworth scale (MAS), were able to hold isometric contraction of wrist and elbow. Participants were excluded if they had any other neurological deficit, diabetic ulcer, infection or amputation of the limb, serious cardiovascular disease or unstable angina, serious orthopedic problem, epilepsy, CNS active drug or botulinum toxin in the 12 weeks prior to intervention, change in spasticity medication in the last 4 weeks or had cognitive or severe language impairment.

Participant characteristics are detailed in Table 7.1 below.

7.3.3 Intervention

10 chronic stroke participants took part in the study, following a 30-minute screening and virtual consent appointment. To minimise the order effect, as a cross-over randomised study, these 10 participants were randomly divided into two groups of 5 volunteers each. One group completed intervention part of the study, followed by control part of the study whereas the other group completed control part of the study first, followed by intervention part of the study. Meaning all 10 participants completed both the control and intervention treatments.

TABLE 7.1. Characteristics of the stroke population for the FMV device feasibility study.

ID	Age	Stroke Lesion Side	Gender	Years since injury	Medication
1	55	Right	Female	05	Baclofen
2	49	Right	Male	10	None
3	38	Left	Male	02	None
4	31	Left	Female	07	Baclofen, Botox 3-monthly (no dose in last 3 months)
5	60	Left	Female	01	None
6	77	Left	Male	03	None
7	75	Left	Male	01	Baclofen
8	70	Right	Female	04	None
9	59	Left	Female	17	None
10	77	Left	Female	10	None

To minimise any aftereffects, all the participants had a washout period of one week, when transitioning from intervention to control part of the study and vice versa. Each participant attended the clinic (at Hobbs Rehabilitation) twice for the study. Once for receiving control therapy session and once for receiving intervention therapy session. Please refer to Figure 7.2 for schematic representation of the feasibility study protocol. Additionally, both groups, i.e. all 10 volunteers, were prescribed a home exercise programme to be completed 2 days prior to their (both) control and intervention sessions at the clinic.

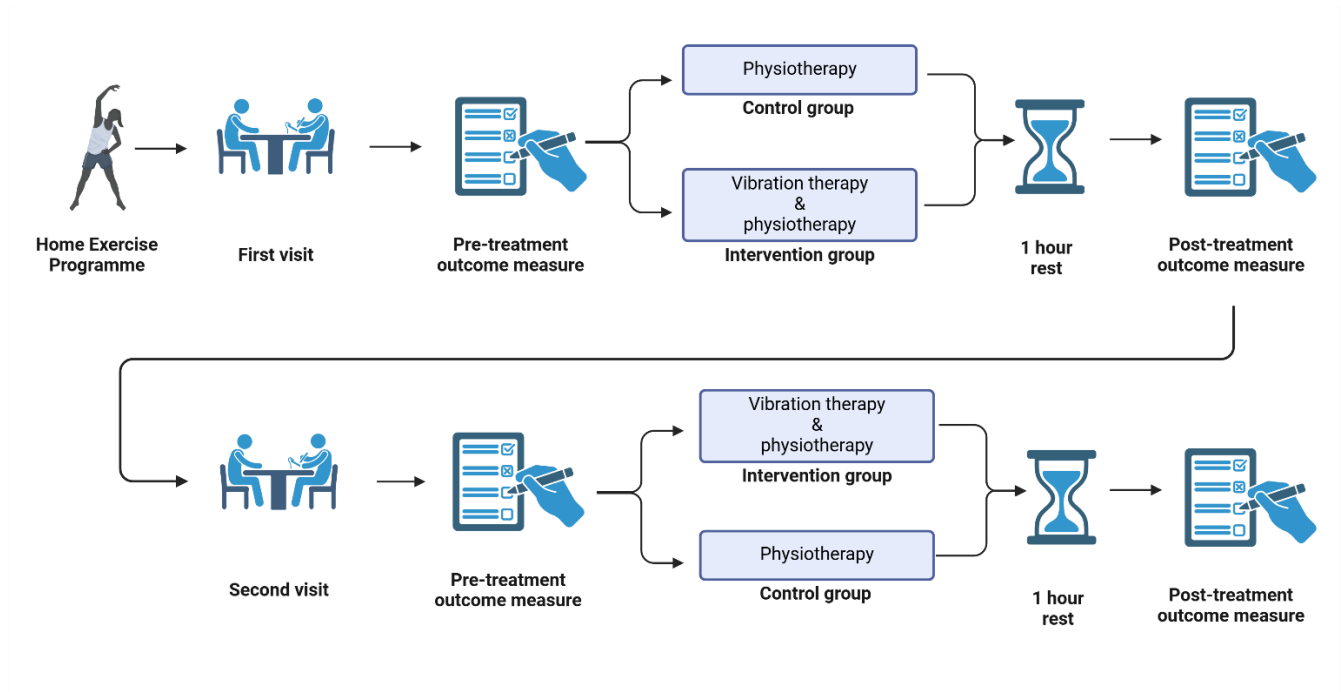


FIGURE 7.2. Study protocol for delivering the FMV intervention.

7.3.3.1 Home Exercise program

All 10 participants completed home exercise programme, which they completed 2 days prior to their experimental session. Participants' level of participation, in the exercise programme was high and was recorded through the verbal feedback gathered by clinician and post study questionnaire (please refer to the outcome measures section for further details). The home exercise programme, mainly consisting of 'upper limb stretching and range of movement exercises' involved: 1) shoulder elevation, 2) shoulder flexion, 3) elbow flexion and extension, 4) wrist extension, 5) forearm pronation/supination, 6) finger flexion and extension, and 7) thumb stretch.

7.3.3.2 Control i.e. Conventional Therapy Group

Participants in the control, i.e. conventional therapy group received 45 minutes of conventional/standardized therapy consisting of: 1) Passive stretches/ Proprioceptive neuromuscular facilitation (PNF) hold relax (15 minutes): Shoulder abduction / external rotation, elbow extension, elbow/wrist pronation / supination in 90 degrees flexion, and elbow extension, wrist extension, finger flexors. 2) Active / active assisted movement/PNF combined movements (15 minutes): shoulder flexion / extension, elbow flexion / extension, pronation / supination, wrist flexion / extension, finger flexion / extension. 3) Functional tasks (15 minutes): Grasp / release work with item, stabilizing item - jar / bottle, reach and grasp work, bringing to mouth with item, wiping table.

7.3.3.3 Intervention i.e. Wearable Focal Muscle Vibration (FMV) Group

Participants in the vibration therapy group also received 45 minutes of conventional/standardized therapy described above, in addition they received *Wearable FMV* therapy. FMV therapy consisted of 4 bouts x 10 minutes focal vibration stimulation each, delivered via the wearable device. 5 minutes rest period was included between two FMV therapy bouts. Participants wore FMV device so as to receive vibration stimulation on their antagonist muscles of elbow and wrist flexion. Thus, the vibration stimulation was delivered to the elbow and wrist extensor muscles, i.e. triceps brachii and extensor carpi radialis, simultaneously, during the FMV therapy, by placing one wearable strap on triceps brachii and extensor carpi radialis muscle each. Each strap had one motor to deliver the FMV. Vibration stimulation delivered was of sinusoidal profile, 100 Hz frequency and 0.5 mm peak to peak amplitude, while participants maintained low level (approximately 5% of their maximum voluntary contraction) isometric contraction of wrist and elbow.

The above FMV location (antagonist muscles), characteristics (frequency and amplitude) and muscle contraction were chosen as they have been shown to reduce spasticity and improve upper limb function in stroke patients (Marconi et al., 2011; Sanford et al., 1993; Harb and Kishner, 2023).

7.3.4 Primary Outcome Measures (Device Feasibility Study)

Primary outcome measures were Fugl Meyer Upper Extremity (FMUE) and Modified Ashworth Scale (MAS) to quantify changes in upper limb function and spasticity respectively. Motor domain of the FMUE was used to assess changes in the upper limb motor function pre and post treatments. FMUE is subscale of Fugl-Meyer assessment scale which is a reliable performance-

based impairment scale recommended to quantify recovery after stroke (Jacques et al., 2022). FMUE consists of 33 items that include assessment of movement ability, coordination, speed, control and reflex activity. The scoring ranges from 0 to 66 such that higher FMUE score indicates less impairment of the affected upper limb. MAS is the most widely used tool to assess muscle tone and has greater reliability for the upper limb (Lenze et al., 2004). It is 5-point scale where participants are scored from 0 (no increase in muscle tone) to 4 (affected part rigid in flexion or extension) with scores given as 0, 1, 1+, 2, 3, 4.

Both FMUE and MAS were measured at the baseline (pre-treatment outcome measure) i.e. before the start of the control or intervention session and after (1 hour rest period after post-treatment outcome measure) completion of the control or intervention treatment.



FIGURE 7.3a. Inside of the wearable strap consisting of sleeve before (top part) and after (bottom part) after the design changes

7.3.5 Statistical Analysis

Linear mixed effect models (LMM) were employed to assess the effect of treatment on the study outcomes. The model included post intervention values as the dependent variable, with baseline values at baseline as a continuous covariate. Fixed factors in the model included treatment (Levels: [FMV, Control]), period (Levels: [first, second]), and sequence (Levels: [FMV

then Control, Control then FMV]). Participants were specified as a random intercept, and a variance components covariance structure was utilized. The sequence effect within the LMM served as the primary test for potential carryover effects (Sinclair et al., 2022). A two-sided significance level of $P \leq 0.05$ was adopted for all tests. All statistical analyses were conducted using IBM SPSS Statistics (Version 29.0.0.2). It is important to note that, there was no carry over effect between the first session post treatment and second session pre-treatment. This was true, irrespective of whether participants completed conventional therapy first and vibration second or vice versa. This was likely due to the small duration of the conventional therapy and vibration (FMV) intervention.



FIGURE 7.3b. Outside of the wearable strap consisting of circular housing to accommodate the actuator, before (top part) and after (bottom part) after the design changes.

7.3.6 Outcome Measures (for the Entire Study)

7.3.6.1 Recruitment and Retention Rate

The recruitment rate quantifies the percentage of individuals who were approached to participate in the study over how many agreed to participate (Jones and Kenward, 2014). The retention rate quantifies the proportion of participants who completed the study over the initially enrolled number of participants. Both rates were quantified for this study.

7.3.6.2 Volunteer Participation Rate

Stroke volunteer's participation rate in the device feasibility study was assessed through the number of sessions they attended and using Pittsburgh Rehabilitation Participation Scale (PRPS) (Sinclair et al., 2022). PRPS is scored on a 6-point scale that takes into account the patient's engagement in an intervention (1: none, patient refused entire session to 6: excellent-patient participated in all activities of the session). PRPS score was obtained through the post study questionnaire.

7.3.6.3 Participant's Perception on Adoption of Technology

To evaluate the wearable FMV technology's feasibility and acceptability, stroke volunteers were asked to complete in-depth questionnaire, at the end of the study. Verbal feedback was also gathered by clinicians, when carrying out in-person FMV therapy experiments.

The questionnaire specifically focused on the participants' experiences during the FMV therapy session, including the device setup (don/doff), and perceived usability of the device as a rehabilitation tool. The participants were asked to rate their experiences, about the above aspects of technology, on a scale of 1 to 5 (1: very difficult, 2: difficult, 3: normal, 4: easy, and 5: very easy). The participant answered the following specific questions:

- 1) How easy or difficult did you find the setup (donning/doffing) of the wearable FMV therapy equipment?
- 2) How easy or difficult did you find the use of the wearable FMV therapy, as a tool for rehabilitation?
- 3) How easy or difficult did you find wearing (comfort) the wearable FMV therapy equipment?

The participants were also asked if they would recommend the wearable FMV therapy equipment to other stroke patients. Further, they were asked to comment on 'anything about the wearable FMV technology that they believe needs to be improved'.

7.3 Results

7.3.1 Semi Structured Workshop: involving Patients, Clinicians and Researchers

For brevity, succinct summary of the feedback from all stroke volunteers on each of the questions (please refer section 7.2.1.1 in Materials and Methods) is presented here, whereas

detailed feedback can be found in Tables 7.5 and 7.6 in the Appendix section of the thesis. Feedback summary: a) Comfort in wearing the device: all volunteers reported comfort in wearing the device with no major concerns. b) Ability/ease to don and doff the device: all volunteers were successfully able to don the device strap on the forearm but struggled with positioning the strap on the biceps. Specifically, the inside of the strap consists of a sleeve which the user needs to slide their limb through and then need to adjust and tighten the strap, housing vibration actuator so that it is positioned correctly on top of the biceps or forearm muscle. Please refer to Figure 7.3 for clarification. The volunteers reported wearing the device through the sleeve was manageable but had difficulty in adjusting the vibration actuator on correct muscle location. They also added that the sleeve could crease instead of sliding when donning, making it somewhat difficult put the device on. c) Device material, size and fit: overall volunteers commented that the device fabric material was soft and well designed. However, added that straps to tighten the device around the biceps/arm were too long making it difficult for them to create appropriate tension/fit around the limb. d) Weight of the device: overall, volunteers felt the device was light on the arm and did not feel heavy to wear. e) Aesthetics/style: volunteers were happy with how the device looked and would not mind it wearing out in public/social places. f) Stimulation sensation: volunteers were comfortable with light (0.5 mm, 100 Hz) 'vibration sensation' which caused no pain. g) Size/appropriateness of device ON/OFF switch: volunteers were easily able find the ON/OFF switch and press it without any issue. h) Any adverse reactions: volunteers reported no worries or adverse reactions with some superficial markings over skin, which disappeared soon, after removing the device strap.

7.3.2 Changes in device design based on patient and clinician feedback from workshop

Ability/ease to don and doff the device: Volunteers reported that they struggled with positioning the device on biceps and commented that they found it difficult to adjust the vibration actuator on correct muscle location. They also added that the sleeve could crease instead of sliding when donning the device. Through deliberation between researchers and clinicians, it was realized that all the above issues could be addressed by reducing the strap width of the device, see Figure 7.3. Reducing the strap size made it easier for the users to don the device on biceps muscle (as indicated through the subsequent feedback from the volunteers following this change), as volunteers earlier commented that the strap size was bigger. Reduced strap width also gave the users better view of the device (vibration) actuator enabling them to better position the actuator on appropriate muscle location (as indicated through the

subsequent feedback from the volunteers following this change). In line with the reduction in strap width, inside sleeve width was also reduced, minimizing the creasing of sleeve reported by the volunteers. As judged from participant feedback from the workshop, none of the other aspects of device design impacted on the device usability and/or comfort; with the above-mentioned changes in the device design, the improved device was then used to complete the feasibility study, results of which are described below.

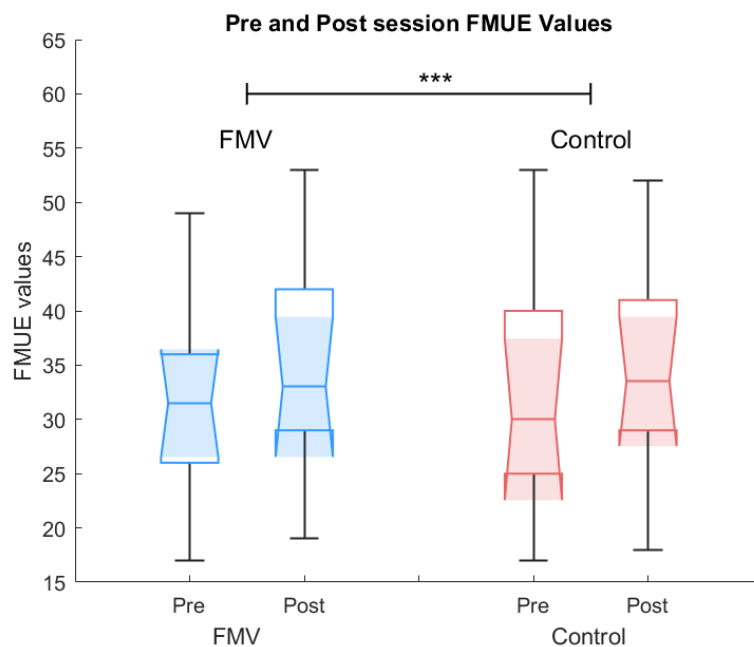


FIGURE 7.4. Mean difference in pre and post FMUE values in both the study groups (FMV and Control). Box and whisker plot representing median value in center and data distribution in four quartiles.

7.3.3 Device Feasibility Study in Clinical Setting to Assess Device's effect on Spasticity and Upper Limb Function

Primary Outcome Measure for the Upper Limb Function: Fugl Meyer Upper Extremity (FMUE)

The results of FMUE before (baseline) and after the control or FMV intervention are presented in the Table 7.2 below. The LMM model revealed a highly significant main effect of treatment, $F=64.848$, $P<0.001$. Adjusted for baseline values, FMV treatment resulted in significantly greater improvements in FMUE scores compared to Control. A significant main effect was also observed for Period, $F=7.143$, $P=0.017$. FMUE scores were significantly higher in first Period

than in second Period. The main effect of sequence was not statistically significant, $F=0.164$, $P=0.691$. This finding suggests no evidence of a significant carryover effect for FMUE. The results are also visualized in Figure 7.4 which presents the mean FMUE difference between pre and post for both the FMV and control group.

TABLE 7.2. FMUE scores pre and post study for the FMV and control group.

ID	FMV		Control	
	Pre FMUE	Post FMUE	Pre FMUE	Post FMUE
1	36	41	38	41
2	24	29	28	32
3	31	34	28	31
4	35	42	40	40
5	32	32	32	35
6	49	53	53	52
7	17	19	17	18
8	26	26	25	29
9	26	29	25	29
10	48	52	44	46

Primary Outcome Measure for Spasticity: Modified Ashworth Scale (MAS)

The results of MAS before (baseline) and after the control or FMV intervention are presented in Table 7.3 and visualized in Figure 7.5 below.

LMM results of MAS scores for individual muscles are described below. The model revealed no statistically significant main effect of treatment for the *Elbow flexor* ($F=0.177$, $P=0.686$), *Elbow extensor* ($F=0.180$, $P=0.678$), *Wrist flexor* ($F=2.395$, $P=0.171$), *Wrist extensor* ($F=0.023$, $P=0.884$) and *Finger flexor* ($F=4.883$, $P=0.059$). Adjusted for baseline values, neither treatment

resulted in significantly greater improvements in MAS. Similarly, no statistically significant main effect was observed for Period, *Elbow flexor* ($F=0.230$, $P=0.645$), *Elbow extensor* ($F=0.180$, $P=0.678$), *Wrist flexor* ($F=0.424$, $P=0.538$), *Wrist extensor* ($F=3.430$, $P=0.108$) and *Finger flexor* ($F=0.134$, $P=0.723$). The main effect of Sequence was also not statistically significant, *Elbow flexor* ($F=0.019$, $P=0.895$), *Elbow extensor* ($F=0.055$, $P=0.818$), *Wrist flexor* ($F=1.888$, $P=0.210$), *Wrist extensor* ($F=0.114$, $P=0.746$) and *Finger flexor* ($F=0.032$, $P=0.862$). This finding suggests no evidence of a significant carryover effect for MAS.

TABLE 7.3. MAS scores pre and post treatment for the FMV and Control group.

ID		1	2	3	4	5	6	7	8	9	10
FMV	Pre MAS	1+	2	2	2	1	1+	1	1+	2	0
		0	1	2	2	1	0	2	1+	1+	0
		2	1+	2	1+	1	1	1+	1	1+	1
		0	0	1	1	0	0	1	0	0	0
		2	1+	3	2	1	1	2	1	1+	1
	Post MAS	1+	2	1+	1+	0	1	1	1	2	0
		0	1	1+	2	1	0	1+	1+	1+	0
		1+	1	2	1	1	1	0	1	1+	0
		0	0	1	0	0	0	0	0	0	0
		1	1	1+	2	1	1	1+	1	1+	1
Control	Pre MAS	2	2	2	2	1	1+	1	1+	2	1
		1	0	2	2	1	0	2	1+	1+	0
		1+	1+	2	1	1	1	1	1+	1+	1
		0	0	2	0	0	0	0	0	1	0
		3	1+	3	2	1	1	2	1+	1+	1

	Post MAS	1+	2	2	1+	1	1	1	1+	2	0
		1	0	2	1	1	0	2	1	1+	0
		1+	1	2	1	1	1	1	1	1+	0
		0	0	2	0	0	0	0	0	1	0
		2	1	2	2	1	1	1+	1	1+	0

TABLE 7.4. Statistical significance values of the LMM for the MAS scores of the five muscles tested.

Group	Stats	Elbow	Elbow	Wrist	Wrist	Finger
		flexor	extensor	flexor	extensor	flexor
Treatment	F-values	0.177	0.180	2.395	0.023	4.883
	P-values	0.686	0.678	0.171	0.884	0.059
Period	F-values	0.230	0.180	0.424	3.430	0.134
	P-values	0.645	0.678	0.538	0.108	0.723
Sequence	F-values	0.019	0.055	1.888	0.114	0.032
	P-values	0.895	0.818	0.210	0.746	0.862

The results of the LMM analysis results on the pre and post treatment MAS outcomes are presented in Table 7.4 above.

7.3.4 Outcome Measures (for the Entire Study)

Recruitment and Retention Rate

Thirteen stroke patients were invited to participate in the study, of which ten agreed to take part, resulting in a recruitment rate of 83.3%. In total, ten stroke volunteers took part in the

study, and all ten participants completed all therapy sessions (FMV + conventional therapy sessions), resulting in the retention rate of 100%.

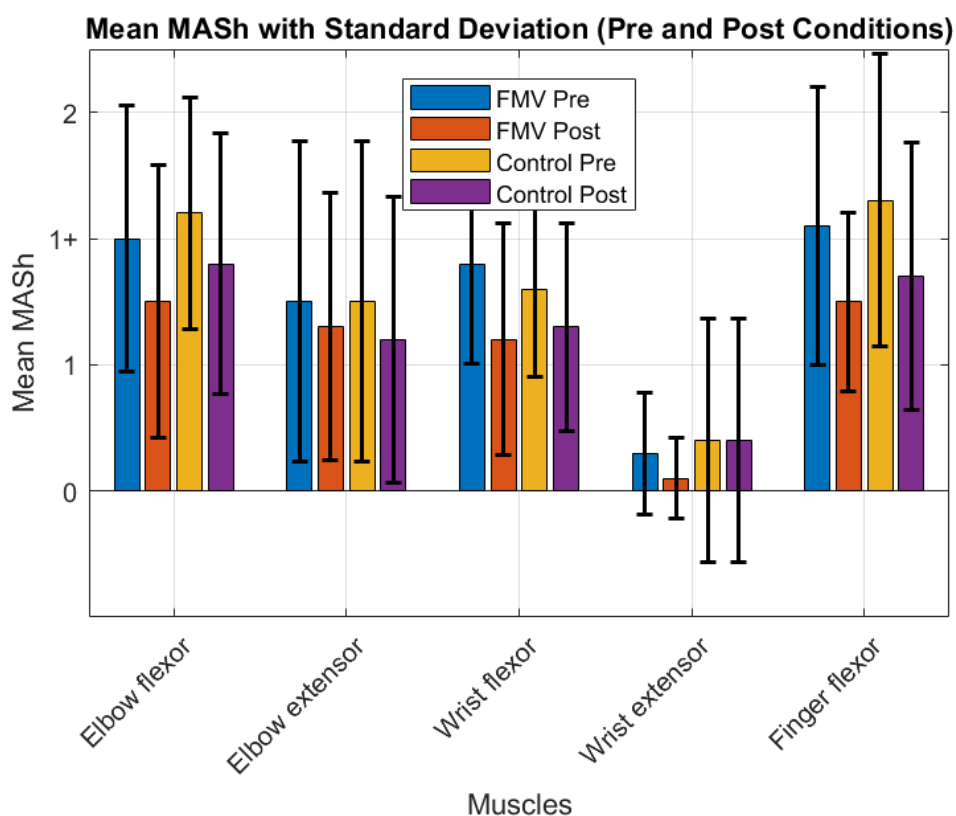


FIGURE 7.5. MAS values for the study groups pre (before) and post (after) the intervention.

For the home exercise sessions, excluding one participant, all nine participants completed assigned 2 home exercise sessions before their first clinic appointment, resulting in retention rate of > 90%. For the home exercise sessions assigned before their second clinic visit, 2 participants did not complete home exercise, 1 participant cited injury, while other participant chose not to complete, resulting in retention rate of 80%. Thus, average retention rate was 85% for all the home exercise sessions assigned.

Volunteer Participation Rate

The participation rate of the stroke volunteers in the FMV device feasibility study was excellent, as assessed by the PRPS. Ten out of ten participants attended all intervention sessions (in person Control + FMV interventions). The mean PRPS score for participants was 6 out of 6, indicating a very high level of engagement in the (feasibility) intervention study.

Participant's Perception on Adoption of Technology

For brevity only key elements of participant feedback are discussed below, whereas detailed feedback can be found in Tables 7.5 and 7.6 in the Appendix section of the thesis. Based on the feedback received from the questionnaire at the end of the study, overall, participants reported positive experience of using the wearable FMV device.

More specifically, when asked about the ease of set-up, i.e. donning and doffing of the wearable device, most participants said the device was easy to don/doff. Interestingly, none of the participants categorized the device set-up (don/doff) as difficult or very difficult. When asked about the ease of device use, as a rehabilitation tool, most participants said, as a wearable rehabilitation tool, the device was easy to use. Similarly, all participants agreed that the device was 'comfortable' to wear, with majority participant rating 'high' for comfort. Participants also made some valuable suggestions regarding device design improvement, this included "changing the device strap (size) so that one can easily slide ones hand through", "ON/OFF button should be simple with only ON/OFF options (i.e. without options for changing stimulation setting etc.)". Encouragingly, when asked 'would you use this wearable vibration therapy if it was available to you' and 'would you recommend this technology to other stroke patients', all patients responded saying 'yes' to both questions.

7.4 Discussion

7.4.1 Device Co-design via Workshop Involving Patients, Clinicians and Researchers, and Changes to the Device Design to meet Patient Requirements

The aim of the semi-structured workshop was to gather systematic feedback from stroke participants on the design of the wearable FMV device. Based on participants' feedback, of all the aspects of device design investigated, i.e. a) comfort in wearing the device, b) ability/ease to don and doff the device, c) device material, size and fit, d) weight of the device, e) aesthetics/style, f) stimulation sensation, g) size/appropriateness of device ON/OFF switch, h) any adverse reactions; participants thought the device design matched or exceeded their requirements in all the above aspects with the exception of b) ability/ease to don and doff the device.

Hence, participants specific comments and suggestions on this aspect 'b) ability/ease to don and doff the device', were used to adapt and improve the device design to facilitate easier don/doff/device set-up, thus meeting the user's requirements.

7.4.2 Feasibility Study in a Clinical Setting to Assess Device's effect on Spasticity and Upper Limb Function

The aim of the feasibility study was to establish feasibility of using this newly adapted wearable FMV device in a clinical setting, to treat spasticity and upper limb function in stroke population. Following changes to the device design, newly adapted device was successfully used to complete clinic-based rehabilitation intervention. Overall, participants reported their satisfaction with the new design (as indicated in verbal feedback received by clinicians during the intervention and feedback gathered through questionnaire, at the end of the study) and completed the intervention (i.e. feasibility study) using the newly adapted device design. Based on participants' verbal and written (questionnaire) feedback, the new design improved the ease of use and did not result in any complications, contraindication or issues with device use or comfort.

Secondary aim of the feasibility study was to establish whether smaller, one-off dose of (40 minutes) wearable FMV intervention can be effective in reducing muscle spasticity and/or improving upper limb function in stroke population. Based on primary outcome measures recorded for the upper limb function (FMUE) and spasticity (MAS), measures show that 40 minutes of wearable FMV intervention combined with conventional therapy improves upper limb function but did not reduce spasticity, in chronic stroke patients. The reduction in spasticity is not significant when compared to conventional therapy; this may indicate, for more clinically meaningful improvements in spasticity reduction, FMV therapy should be delivered for longer durations and that shorter durations (~30-40 minutes) may be beneficial but are not sufficient to induce clinical benefits. See also (Paoloni et al., 2010; Marconi et al., 2011).

Further, as mentioned above, the site (elbow extensor muscles) and frequency (100 Hz) of stimulation was chosen based on previous neurophysiological (Sanford et al., 1993; Harb and Kishner, 2023) and clinical (Marconi et al., 2011) evidence of their effectiveness in targeting underlying neural mechanisms in reducing spasticity and improving motor function. Previous studies have reported that delivering wearable FMV stimulation to the antagonist (extensor) muscles, alters spasticity and function in agonist muscles (DeForest, Bohorquez and Perez, 2020; Sanford et al., 1993). This effect is believed to be achieved via reciprocal inhibition mechanism. However, our study found that, delivering wearable FMV stimulation to the antagonist, the changes observed in agonist muscle spasticity are non-significant. This is likely due to the small population and duration of FMV intervention in our study. As this study only

investigated short-term effects of FMV, the results may not be extrapolated. Further, other studies have reported that FMV stimulation delivered to flexor muscles can also reduce spasticity and improve function in flexor muscles in chronic stroke patients (Marconi et al., 2011). Thus, mechanisms underlying these effects are not exactly clear and the most effective stimulation location (agonist/antagonist of the spastic muscle) in FMV intervention is still an open question (Harb and Kishner, 2023).

7.4.3 Outcome Measures (for the entire study)

Based on the combined feedback received from the participants, i.e., received through a) semi-structured workshop at the start of the study, b) verbal feedback received throughout the feasibility study and c) questionnaire at the end of the study, overall participants reported positive experience of using the wearable FMV device.

Both recruitment and retention rate were high (>80%) in this study, indicating participant found ‘the need of spasticity reduction and upper limb function improvement’ important to address and worthwhile to engage in, to resolve. This is further supported by excellent PRPS score of the study indicating high level of participant engagement throughout this study. It cannot be stressed highly enough that user’s perception of the problem (i.e. patient/clinical need) and early feedback on technological solution to address this problem are extremely important to develop and translate a user centric and effective technological solution that satisfies unmet clinical need and avoids later problems of technology abandonment.

Further, participants’ perception on adoption of wearable FMV technology was positive. Participants found technology: 1) easy to set up (don/doff/operate), 2) comfortable, 3) easy and useful as a rehabilitation aid. Participants also expressed ‘they would use such a technology if it were available to them’ and ‘that they would be happy to recommend such a technology to other stroke patients. Again, these findings are encouraging and indicative of the potential of wearable FMV technology as a rehabilitation aid.

7.4.4 Limitations of the Study

Main limitation was with the feasibility part of this study. As a feasibility study, the participant numbers were smaller and FMV intervention dosage (duration in days/weeks and frequency in how many hours/day) was smaller. Whilst patients found the FMV intervention helpful and were very engaged in the study, a higher-powered study with suitable outcome measures will be required to better establish clinical relevance of the intervention.

7.5 Main finding of the device usability study

The main findings of this study are:

- A device was co-developed using patient feedback and a co-designing workshop showing high usability and participation.
- A single 45-minute session of FMV from the co-developed device to the arm resulted in improvements in FMUE score.

7.6 Conclusion

To the best of our knowledge this is the first study to systematically investigate a wearable FMV device to reduce spasticity and/or improve upper limb function in stroke patients, from co-designing a device with patients and clinicians to carrying out a feasibility study.

We co-developed a bespoke device with stroke patients and clinicians, and patients found the device to be acceptable and beneficial (as a rehabilitation aid) in reducing their spasticity and improving their upper limb function.

Despite the perceived acceptability and benefits of the wearable FMV technology found in this study, the fact remains that the technology was tested in a clinical setting, under clinical guidance and over shorter intervention duration (40 minutes). To bring about true translational benefits, i.e. clinically meaningful and long-term benefits to stroke patients in their limb function, this technology needs to be tested and shown effective: 1) without/with limited clinical supervision, 2) in patients' home and 3) with longer intervention durations. We plan to address these questions in our future work.

Once fully developed and tested further in real world settings, i.e. in patients' homes over longer use/durations, this technology has significant potential to be used as a wearable, easy to use, rehabilitation aid, to enable and improve upper limb function in stroke patients

Chapter 8: Discussion

8.1 Introduction

The application of vibration therapy as a non-invasive rehabilitation strategy for neurological diseases, including CP, SCI and stroke, represents a promising intersection of biomedical engineering and clinical neuroscience. This thesis investigates the efficacy of focal muscle vibration (FMV) in addressing motor, spasticity, and sensory deficits in these conditions and understanding the potential underlying neurological mechanisms. The thesis can be broadly divided into three distinct parts, with the first part systematically reviewing FMV application in SCI, stroke and CP, leading to development of a device with precise and reproducible vibration frequencies helping in comparable experimental investigations. By conducting EEG and EMG experiments on SCI and CP, the second part investigates the effect of vibration therapy on motor and sensory improvements in the neurological disease population. Then by conducting a user-centric usability study of the FMV device for stroke, the third part investigates the translation of FMV device from laboratory and clinical setups to home-based use.

By integrating findings from Chapters 2 and 3, which critically reviewed the literature landscape and progressed it towards development of FMV device with precise reproducible vibrations, this discussion chapter debates the relevance of FMV therapy as a rehabilitation tool and its impact. By integrating findings from Chapters 4, 5 and 6, which evaluated FMV for CP, SCI and for stroke, respectively, this discussion chapter synthesizes the results, interprets their significance, and contextualizes them within the broader scientific literature. It also addresses the study's limitations, outlines implications for clinical practice and biomedical engineering, and proposes directions for future research to advance the field.

The discussion is structured comprising the following sections:

- I. **Summary of Key Findings:** A concise overview of the findings from the systematic reviews and main results from the experimental chapters and the development of a wearable FMV device.

- II. **Interpretation of Results:** An analysis of the findings' significance, focusing on neurophysiological mechanisms and their alignment with the research hypotheses.
- III. **Comparison with Existing Literature:** A contextualization of the results within the current body of research on vibration therapy.
- IV. **Limitations:** A critical acknowledgment of the study's constraints and their potential impact on the interpretation of results.
- V. **Implications for Clinical Practice and Biomedical Engineering:** A discussion of the practical and theoretical contributions of the research.
- VI. **Future Research Directions:** Recommendations for further studies to address gaps and build on the current findings.
- VII. **Conclusion:** A synthesis of the thesis's contributions and its broader impact on neurological rehabilitation.

8.2 Summary of Key Findings

The thesis investigated the efficacy of vibration therapy, specifically FMV, in improving sensory and motor performance in individuals with CP, SCI, and stroke. Systematic reviews (Chapter 2) revealed the therapeutic potential of FMV in CP and SCI populations but revealing certain shortcomings—lack of vibration devices with characterised vibration frequencies, longitudinal studies and neurophysiological research. A meaningful engineering contribution (Chapter 4) was the development of a wearable, low-cost FMV device, addressing the critical issue of frequency characterization in vibration therapy. The experimental chapters (Chapters 5 and 6) provided detailed insights into the therapeutic effects, supported by neurophysiological assessments using EEG and EMG. The usability chapter (Chapter 7) provided the translational journey for FMV therapy for laboratories to home-base use.

Systematic reviews for CP and SCI in Chapter 2 reveal that FMV reduce spasticity and improve motor function, though methodological limitations persist. Findings for CP report significant spasticity reduction and enhanced GMFM scores with FMV (30–200 Hz) usually delivered in single doses (with exception of two studies), but sparse longitudinal studies, variable vibration frequencies used, and limited neurophysiological data (e.g., sparse EEG/EMG) restrict generalizability. Results in SCI found that FMV (50–120 Hz) decreases spasticity and improve

mobility, with some evidence of neuroplasticity via corticospinal excitability, yet small cohorts, device heterogeneity, and lack of long-term follow-ups limit conclusions. In stroke, FMV device has shown user- adaptability for home-based use, while also improving FMUE scores.

This thesis addresses these gaps by employing a wearable FMV device with accurate reproducible vibrations and providing novel EEG (e.g., increased beta-band connectivity in CP, alpha/beta changes in SCI) and EMG (improved muscle activation) insights in cohorts of 65 CP and 10 SCI participants, offering frequency-specific (100 Hz for CP, 80 Hz for SCI) and neurophysiological advancements to enhance clinical applicability and mechanistic understanding.

TABLE 8.1 Key findings of the thesis.

Chapter	Disease	Vibration Frequency	Main Finding
04	-	60, 80, 100, 120 Hz	• A device was designed and developed that delivered vibration frequencies at four levels: 60, 80, 100 and 120 Hz with a mean accuracy of 96.83 %.
05	Cerebral Palsy (CP)	80, 100 Hz	• 8-weeks of FMV therapy (at both 80 and 100 Hz) resulted in an increased beta-band EEG FC, predominantly in the frontal and central brain regions • 8 weeks of FMV therapy resulted in increased muscle activations and decreased fatigue for the TA and Soleus muscles in the lower limb.
06	Spinal Cord Injury (SCI)	80 Hz	• Three weeks of 100 Hz FMV to the Achilles tendon results in an increase in alpha and beta-band FC predominantly in the central and parietal region of the cortex.
07	Stroke	100 Hz	• A device was co-developed using patient feedback and a co-designing workshop showing high usability and participation. • A single 45-minute session of FMV from the co-developed device to the arm resulted in improvements FMUE score.

To address the frequency characterization gap Chapter 4 develops a wearable, low-cost FMV device (65g, 60–120 Hz) was developed with precise frequency control, improving the reproducibility and accessibility of vibration therapy. The summary of the key findings from Chapters 4,5,6 and 7 are presented in Table 8.1. For CP, FMV at 100 Hz showed significant improvements in motor function compared to 80 Hz. EEG revealed increased beta-band FC and reduced MRCPs, while EMG indicated improved muscle activation and delayed fatigue in dominant limbs, leading to enhanced motor performance and neuromuscular coordination. In SCI, FMV at 80 Hz resulted in modest reductions in spasticity (measured by MAS scores) for some participants. EEG showed significant alpha and beta band connectivity changes in central, parietal, and right temporal regions, suggesting cortical reorganization, though functional gains were limited. For stroke, use of a commercially available FMV device demonstrated high usability in stroke patients, with ease of application, comfort during sessions, and seamless integration into rehabilitation routines. Preliminary reductions in the FMUE scores were observed, supporting FMV as an effective adjunct for stroke motor rehabilitation.

These findings demonstrate that FMV therapy can modulate cortical and neuromuscular activity, with varying degrees of clinical efficacy depending on the condition and vibration modality. The development of a characterized FMV device enhances the potential for scalable and reproducible therapeutic interventions.

8.3 Interpretation of Results

The experimental results provide significant insights into the neurophysiological mechanisms and potential clinical applications of FMV therapy for neurological diseases, supporting the hypotheses outlined in Chapter 3 and highlighting the importance of tailored therapeutic parameters. The development of a wearable, low-cost FMV device (65g, 60–120 Hz) addresses a critical gap in the characterization of vibration therapy. The device's precise frequency and amplitude control ensure reproducibility, overcoming limitations of previous studies with variable vibration parameters. This engineering advancement facilitates the translation of vibration therapy into clinical and community settings, particularly in resource-limited environments. The disease specific interpretations for the thesis' findings are presented below.

CP:

The superior efficacy of FMV at 100 Hz compared to 80 Hz in improving motor function suggests that higher vibration frequencies optimize motor unit recruitment and sensorimotor integration. But better co-contraction modulation at 80 Hz shows its potential for long-term adaptation. The EEG findings of increased beta-band functional connectivity and reduced MRCPs indicate enhanced efficiency in motor planning and execution, which is critical for functional improvements in CP. The EMG data, showing improved muscle activation and delayed fatigue, further corroborate the therapy's role in enhancing neuromuscular coordination. The frequency-specific effect suggests that 100 Hz may be ideal for acute motor improvements, while lower frequencies (e.g., 80 Hz) could support long-term coordination, providing a basis for personalized rehabilitation protocols.

SCI:

The modest clinical outcomes in SCI patients, such as slight reductions in spasticity, contrast with significant EEG changes in alpha and beta band functional connectivity across central, parietal, and right temporal regions. This dissociation suggests that FMV induces neuroplasticity at the cortical level, potentially laying the groundwork for functional improvements with extended interventions. The limited clinical impact may be attributed to the small sample size (n=10), the focus on a single muscle group (Achilles tendon), and the short intervention duration (3–8 weeks). These findings underscore the complexity of SCI rehabilitation and the need for longitudinal studies to evaluate cumulative therapeutic effects.

Stroke:

The stroke study's objectives diverge from the CP and SCI investigations by focusing primarily on usability and short-term clinical feasibility rather than neurophysiological mechanisms. The high usability scores, positive participant feedback on comfort and ease of use, and excellent retention and participation rates strongly support the hypothesis that a co-designed wearable FMV device is feasible and acceptable for stroke survivors in a clinical setting. This successful translation of the device from a laboratory prototype to a user-accepted clinical tool is a significant outcome. The preliminary improvement in upper limb function (FMUE scores) following a single, combined session of FMV and conventional therapy, compared to conventional therapy alone, suggests an immediate beneficial effect. However, the absence of

significant changes in spasticity (MAS scores) indicates that a short-term, 40-minute dose of FMV may be sufficient to modulate motor function but not to produce clinically meaningful reductions in muscle tone. This dissociation between functional improvement and spasticity reduction highlights that FMV's therapeutic benefits may be mediated through mechanisms other than, or in addition to, spasticity reduction in the short term, such as enhanced sensorimotor integration or improved motor planning. These results lay a crucial foundation for the device's potential use in longer-term, home-based rehabilitation trials.

These findings collectively support the hypothesis that FMV therapy can enhance sensory and motor functions through neurophysiological mechanisms, with implications for personalized rehabilitation strategies. The frequency-specific effects provide a foundation for advancing both clinical practice and research in neurological rehabilitation.

8.4 Comparison with Existing Literature

The findings of this thesis contribute significantly to the growing body of research on vibration therapy for neurological diseases, aligning with and extending previous studies while addressing critical gaps in device characterization, mechanistic understanding, and novel applications.

CP:

Previous studies, as reviewed in Chapter 2, have demonstrated that FMV can reduce spasticity and improve motor function in CP (Ritzmann et al., 2018). However, these studies often lacked detailed neurophysiological evidence. This thesis advances the field by providing EEG and EMG data that link clinical outcomes to cortical and neuromuscular changes. The frequency-specific effects (100 Hz vs. 80 Hz) offer new insights into optimal vibration parameters, addressing inconsistencies in earlier studies that used a wide range of frequencies (30–200 Hz). These findings align with previous research indicating short-term applications results reductions in spasticity and coordination deficits post-vibration therapy (Ritzmann et al., 2018) but extend the evidence by linking clinical outcomes to cortical and neuromuscular changes.

SCI:

Existing research on FMV for SCI shows variable outcomes due to differences in vibration parameters, application sites, and devices (Chapter 2). This thesis addresses these gaps by

assessing both clinical and neurophysiological outcomes. The modest clinical improvements (e.g., slight reductions in MAS scores) contradicts previous literature potentially due to difference in muscle group, while the significant EEG changes in alpha and beta band functional connectivity support findings that vibration therapy induces neuroplasticity. This dissociation between neural and clinical outcomes emphasizes the need for longer-term interventions and longer follow-up periods. These SCI findings extend the previous literature that highlight FMV's potential in inducing neuroplastic changes in muscle activations/ co-contractions (Sabalette et al., 2024) and the cortex (Gomes-Osman et al., 2014)

Stroke:

The stroke feasibility study (Chapter 7) aligns with the literature's evidence from systematic reviews and meta-analyses (Section 2.2.4) for FMV's potential to improve upper limb function by reducing spasticity and improving motor function post-stroke. While directly addressing its most significant translational gap: the heterogeneity of protocols and reliance on bulky, clinic-bound devices. This thesis confronted this limitation through a user-centric co-design process, resulting in a wearable FMV device that demonstrated high feasibility, acceptability, and excellent participant engagement, thereby successfully transitioning FMV from a stationary concept to a practical tool. In terms of outcomes, the significant improvement in Fugl-Meyer Upper Extremity (FMUE) scores after a single session supports the functional gains reported in the literature. However, the absence of a significant reduction in spasticity (MAS) refines this understanding, suggesting that the single-session dosage, while sufficient for functional benefits, was likely insufficient to modulate muscle tone, thereby corroborating the literature's emphasis that sustained, repetitive protocols are required for robust spasticity reduction. Previous literature had strong evidence of FMV reducing spasticity (Moggio et al., 2021) but the administered FMV doses were generally higher than a single session. Perhaps future studies can concentrate on increasing FMV dosage to see better effects.

Overall, this thesis fills critical gaps in the literature by providing neurophysiological insights via EEG and EMG, and novel applications, and translating clinic-bound FMV devices towards home-based use. It also underscores the need for larger, more standardized studies to confirm and expand upon these findings, ensuring greater generalizability and clinical applicability.

8.5 Limitations

While this thesis provides valuable insights into the application of FMV therapy for neurological diseases, several limitations must be acknowledged to ensure a balanced and critical evaluation of the research.

Small Sample Sizes: The studies involved relatively small cohorts, particularly for SCI (n=10) and stroke (n=10), limiting the generalizability of the findings. Additionally, the high attrition rate in the CP study (16 participants lost out of 65) could introduce selection bias. Larger, more diverse cohorts are needed to enhance the robustness and applicability of the findings.

Intervention durations and follow-up periods: The intervention periods ranged from 3 to 8 weeks, which may be insufficient to observe long-term effects, particularly in conditions like SCI where recovery can be protracted due to the complexity of neural repair. Furthermore, the follow-up periods post intervention were limited – 2 weeks for CP, and just post intervention for SCI and stroke, limiting the understanding of long-term impact. The short duration limits the ability to assess the sustainability (long-term ness) of benefits, such as motor improvements in CP or cortical changes in SCI and stroke, necessitating longer follow-up periods in future studies.

Focus on specific muscle Groups: The experiments targeted specific muscle groups, such as the lower limbs (quadriceps and Achilles tendon) in CP and SCI, and the triceps brachii and extensor carpi radialis of upper limb in stroke. This focus restricts the applicability of the findings to other muscle groups or more comprehensive functional outcomes, such as whole-body mobility or upper limb function. Exploring multi-site vibration applications could provide a more holistic understanding of therapeutic potential.

Technical Limitations of the FMV Device: The wearable FMV device developed in Chapter 3 is a significant advancement, offering precise frequency and amplitude control (60–120 Hz). However, its heat dissipation issues during prolonged use could compromise patient comfort and clinical applicability. Addressing this technical limitation is critical for ensuring the device's suitability for extended therapeutic sessions.

Reliance on EEG and EMG: While EEG and EMG provided valuable neurophysiological insights into cortical connectivity and muscle activation, these methods lack the spatial resolution of advanced neuroimaging techniques like functional magnetic resonance imaging

(fMRI). This limitation restricts the ability to pinpoint specific brain regions involved in the observed changes, which could enhance mechanistic understanding in future studies.

Methodological Constraints: Blinding was challenging due to the sensory nature of vibration therapy, which participants could perceive. This could introduce biases in the assessment of clinical outcomes, despite efforts to mitigate this through randomization and double-blind designs where feasible. Future studies should incorporate alternative blinding strategies to strengthen methodological rigor.

These limitations highlight areas for improvement in future research and underscore the need for cautious interpretation of the current findings. They also provide a roadmap for refining study designs and expanding the scope of vibration therapy research to maximize its clinical impact.

8.6 Implications for Clinical Practice and Biomedical Engineering

The findings of this thesis have significant implications for clinical practice and biomedical engineering, offering practical and theoretical contributions that bridge neuroscience, engineering, and rehabilitation science.

8.6.1 Clinical Implications:

CP:

The demonstrated efficacy of FMV at 100 Hz in improving motor function and reducing spasticity in CP suggests that it could be integrated into standard rehabilitation protocols, particularly for children with spastic CP. The wearable FMV device's lightweight design (65g) and ease of use make it suitable for home-based therapy, potentially increasing patient adherence and accessibility, especially in resource-limited settings. This could enhance functional outcomes and quality of life for individuals with CP, aligning with findings from studies like (Rutović et al., 2019) and (Boulay et al., 2025).

SCI:

Although clinical improvements in SCI were modest (e.g., slight reductions in spasticity), the significant cortical changes observed via EEG suggest that FMV could play a role in promoting neuroplasticity. This makes it a promising adjunct therapy within a broader rehabilitation strategy, potentially combined with physical therapy or pharmacological interventions to

enhance long-term functional recovery. The findings align with research indicating that vibration therapy may support neural reorganization in SCI (Gomes-Osman et al., 2014; Tazoe et al., 2021).

Stroke:

The high usability and positive patient acceptance of the co-designed wearable FMV device are its most immediate clinical implications. The device's design, refined through direct patient feedback, demonstrates that wearable neuromodulation tools can be comfortable, easy to use, and seamlessly integrated into clinical therapy sessions. This paves the way for its adoption as a practical adjunct to conventional upper limb therapy in stroke rehabilitation. The preliminary improvement in FMUE scores suggests that even short-term use may boost the efficacy of standard therapy, potentially leading to more efficient recovery of motor function. For clinicians, this offers a new, non-invasive tool to enhance treatment sessions. However, the lack of significant change in spasticity underscores that short-duration FMV should be viewed primarily as a functional adjunct rather than a direct spasticity-reduction treatment, guiding realistic clinical expectations and application.

8.6.2 Biomedical Engineering Implications:

Characterized device development:

The development of a wearable, low-cost FMV device (65g, 60–120 Hz) addresses a critical gap in the characterization of vibration therapy, overcoming the variability in devices that has hindered prior research. The device's precise frequency and amplitude control, validated through accelerometer-based characterization, ensures reproducibility and scalability. Future iterations could incorporate features like temperature regulation to address heat dissipation issues, enhancing clinical applicability.

Optimizing vibration parameters:

The neurophysiological insights from EEG (e.g., alpha and beta band connectivity changes) and EMG (e.g., improved muscle activation) provide a foundation for optimizing vibration therapy protocols. For instance, the frequency-specific effects (100 Hz for acute motor improvements in CP) can guide the design of adaptive devices that tailor parameters to individual patient needs, improving therapeutic outcomes.

Integration with adjunct technologies:

The thesis highlights the potential for combining FMV therapy with other technologies, such as robotics, virtual reality, or wearable sensors, to create comprehensive rehabilitation systems. For example, integrating FMV with robotic exoskeletons could enhance motor rehabilitation in neurological patients.

8.6.3 Broader Impact:

Democratizing Rehabilitation:

Vibration therapy's non-invasive and low-cost nature, coupled with the wearable FMV device, has the potential to democratize rehabilitation, particularly in resource-limited settings where access to advanced technologies is restricted. This could significantly impact global health by making effective rehabilitation more accessible to underserved populations.

Interdisciplinary Collaboration:

The thesis exemplifies the power of interdisciplinary research, bridging biomedical engineering, neuroscience, and clinical practice. This approach sets a precedent for future collaborative efforts to develop innovative, evidence-based rehabilitation solutions that address both technical and clinical challenges.

In summary, this thesis advances the understanding of FMV therapy's mechanisms and applications, paving the way for its integration into clinical practice and further technological development. By addressing gaps in mechanistic understanding, and clinical applicability, it lays a robust foundation for improving rehabilitation outcomes in neurological diseases.

8.7 Future Research Directions

To build upon the findings of this thesis, several avenues for future research are recommended:

1. **Larger, multicentred trials:** Conduct larger, multicentred trials with extended follow-up periods (6–12 months) to assess long-term effects and generalizability across diverse populations.
2. **Personalized protocols:** Develop personalized FMV therapy protocols based on patient characteristics, such as age, disease severity, and specific deficits, to optimize therapeutic outcomes.

3. **Combined therapies:** Investigate the integration of FMV therapy with other rehabilitation modalities, such as robotics, virtual reality, or pharmacological interventions, to enhance efficacy.
4. **Advanced neuroimaging:** Use advanced neuroimaging techniques like fMRI to further elucidate the neural mechanisms underlying vibration therapy's effects, complementing EEG and EMG findings.
5. **Upper limb applications:** Extend research to a wide muscle group, e.g., upper limb applications for CP/ SCI, which are often more functionally limiting in conditions like SCI, to broaden the therapeutic scope.
6. **Device optimization:** Address technical limitations of the FMV device, such as heat dissipation, to improve usability and patient comfort for prolonged therapeutic sessions.
7. **Functional outcomes:** Assess broader functional outcomes, such as quality of life, activities of daily living, and gait analysis, to provide a more comprehensive evaluation of therapeutic benefits.

8.8 Conclusion

In conclusion, this thesis provides robust evidence for the potential of FMV therapy in rehabilitating individuals with neurological diseases such as CP, SCI, and stroke. The development of a wearable FMV device and the neurophysiological insights gained from EEG and EMG analyses represent significant advancements in the field. While clinical outcomes varied across conditions, the findings underscore the therapy's ability to modulate cortical and neuromuscular activity, offering a foundation for future research and clinical applications.

Key findings of this thesis are listed below:

- FMV therapy administered to CP children for 8 week (at both 80 and 100 Hz frequencies) resulted in an improved cortical functional connectivity (FC); and it resulted in increased muscle activations and decreased fatigue in the lower limb (for the TA and Soleus muscles)
- FMV therapy administered to SCI patients for 8 weeks at 100 Hz to the Achilles tendon results in an increase in alpha and beta-band cortical FC
- An FMV device for stroke patients was co-developed using patient feedback and a co-designing workshop showing high usability and participation. A single 45-minute session of FMV from the co-developed device to the arm resulted in improvements in FMUE score.

This thesis paves the way for more effective, accessible, and personalized rehabilitation strategies, ultimately improving the quality of life for individuals with neurological conditions.

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Appendix

PARTICIPANT FEEDBACK			
Questions	Patient 1	Patient 2	Patient 3
Patient observations	F, 73, Stroke Aug 2022, right side UL affected. Tone into finger flexors, most present when using arm functionally. No change in sensation on affected size. Previously right hand dominant. Device fitted to FCR	M, 67, Stroke 2019, right sided UL affected. Increased tone biceps / FCR. Aphasic	M, 60, stroke 2019, left hand affected, significantly reduced sensation in left arm and reduced coordination Device applied to left biceps
1. Comfort/ discomfort?	No discomfort from the device. Feels loose at the bottom but tight at the top	Comfortable to wear but aware that it is there. 10/10 when wearing it at rest but would find the noise irritating after a while	Not uncomfortable, not too constricting/painful when placed on biceps (patient usually finds if something is too tight then he cannot tolerate this) With the device on the forearm feels more uncomfortable, gets an intense stinging/tingly than it did on upper arm even without the haptics turned on. Vibration doesn't make it more intense therefore more related to tightness of sleeve (This is a usual feeling that the patient would get with wearing something tight on his arm) Thinks noise would get irritating after a while to both himself and people around him
2a. Ability to don/doff device? 2b. Remove and insert haptic into the cuff?	Managed to get onto arm independently, but difficult to reposition to correct place on arm. Struggled to reposition around arm as initially put it on the wrong way. Sleeve not gliding smoothly Patient reported OK to put on but would have been easier to do the right way round. self-reported 5/10 to install. Didn't feel like it took a significant amount of time to install "Easy" to take off 2nd attempt prompted to put onto arm facing correct way. Appeared easier from observation and reported to be slightly easier. Patient found it easier to install to forearm without the sleeve present. Able to remove insert from cuff easily and inserted it back in using unaffected arm well. Patient anticipates that to use for upper arm would be very difficult to put on	Observation: Managed to don independently. Some difficulty to get over affected hand but managed. Able to pull sleeve up to bicep, but patient reported this to be difficult. Haptics on triceps on initial application, had to twist to put onto biceps - achieved independently. Some prompting to find correct position. Finding it difficult to reposition the device on his arm. Patient try to move the device using outer material, and inner material and haptics not moving with it. Able to take the device off easily - independently undid Velcro straps and pulled off arm Fitting without the inner sleeve: (demonstrated to patient firstly) - Able to hold the device between	Observation: Able to get arm through sleeve and pull sleeve up to bicep, able to tighten the straps. On initial application placed the cuff too low down on his arm. Due to reduced sensation finds it difficult to get it into the right position without a mirror. Struggling to twist device - and repeat issue of the sleeve creasing rather than sliding. Able to doff with no concerns Self-reported - no problems doing the velcro straps up, more difficult as cuff got higher up the arm. Could perceive that finding the vibration insert over the muscle bulk may be difficult Able to don to forearm Donning without the sleeve: Patient reports that he would find this much more difficult but was able to don independently. Not able to get the straps as tight as when he had the sleeve on. Doesn't feel

		arm and torso to stabilise. Independently did Velcro straps up. Needed to be repositioned as fitted over elbow crease but able to glide to move it back up the arm. Not fitted quite as tightly as when fitted using the sleeve Did not find one technique particularly easier than the other Patient also independently fitted to forearm - found this easier than biceps Able to remove and insert haptic device into the cuff with minimal difficulty	like it has as much contact with the skin. Comes off much easier. Able to remove and re-insert the haptic insert but with mild difficulty (using both hands bilaterally to complete task)
3. Material, size and fit?	Material feels quite smooth. Device did not fit over biceps due to size of band and patients' arm "Well designed" and "Sleeve wasn't necessary" Robustness - couldn't comment.	Sleeve able to fit over bicep bulk. Sleeve material creasing rather than sliding nicely to facilitate movement, therefore sleeve restrictive and difficult to move. Once in correct position, and straps tightened feels like it is a good fit Observed some difficulty in getting the device tight enough using the Velcro straps Patient would choose to use device without sleeve rather than with sleeve Patient reported would be easier if it was shorter as felt too long on bicep area	Material feels soft to unaffected arm. Unable to feel material on affected side Sleeve fits well. Cuff too long for biceps Happy with fastening mechanism Prefers the device with the sleeve than without the sleeve and fits better with sleeve on. Patient reports need to be made from a material that will not roll up / bunch up and will slide more easily
4. What's an acceptable force, tension, pulling velcro, sliding sheet?	Needs quite a lot of force in order to reposition around forearm as sheet wouldn't slide particularly well. Difficult to get tension right on the straps at the top and bottom one handed as needs to stabilise the bottom part of material. Upper part more difficult to do.	Reasonable force and tension for applying tightness to the Velcro Needed significant force to reposition the sliding sheet	Able to get accurate tension the Velcro to do the device up. Some difficulty with the sleeve sliding and creasing but patient able to problem solve
5. Weight?	Arm usually feels heavy due to stroke, but doesn't feel heavier with it on and not heavy to put on	Device does not feel heavy on arm	Feels pretty light to put on / off. Can't feel the weight of it on arm
6. Aesthetics, stylish?	Looks like a device. Understands the device is "not for fashion". "Not ugly". Not bothered by the colour of the device, as long as it is not a bright device. Orange band colour help identify where the straps are Wouldn't have any problems with wearing it outside, if it were proved to be useful. Wouldn't feel	Does not mind the colour of the device Responded "Yes" to would he wear out to lunch. No reason why he would not - but later in session reported he would probably not wear it out. Particularly when the vibration is more intense.	"I'm happy with black" - reported it would be better if it was all black rather than the orange stripes, particularly if he was to wear it out and about Fairly unobtrusive When asked if he would wear out and about reported it wouldn't be a problem. Used to wear devices out. Also suggested he would wear a

	embarrassed. Not a problem with it being obvious that it is being worn under clothing / without clothing covering	Wouldn't wear it out because you can hear it	coat or jacket over it if he could Reports it does look like a medical device
7. What do they think about the stimulation sensation?	Doesn't feel like it does much in terms of hand which she expected to feel, sensation feels reduced compared to wearing on non-affected arm. (feels 80%) Quite a nice feeling. No particular difference over time in how the vibration feels "Reasonably comfortable"	Can feel the vibration, comfortable. No pain. Arm feels the same having it on - no change. Can hear the vibration but noise not an issue Bicep 4/10 intensity forearm 6/10 intensity (? if got tighter to arm on forearm)	Non affected arm - feels tickly, not unpleasant. Placed on biceps of affected arm - can feel some sensation/tingling at elbow but nothing more proximally. Not a concerning feeling at elbow Vibration can be felt with it on his forearm. again can feel this more at his elbow rather than forearm
8. Size of switch, usability?	"Easy" to press button and find switch on 1st device (single mode device). No problems with locating button or pressing down on the button Needed some promoting with different press types for 2nd device - to turn on and switch modes. Patient reported "awkward"	Able to find the switch easily and press to turn both on and off Patient reported "Easy" Still able to find button when device placed on forearm - but due to supination tone/ tightness more difficult to find.	Able to find switch and press button with no concerns once found where the button is, can turn back off with no problems. Patient reported button could be a different colour to make it more obvious. Also expected the button to be raised to make it easier to feel
9. Any adverse reactions?	Superficial markings, nil redness. Felt no difference in arm after removing 20 minutes after wearing and removing - feeling a bit tingly now	Reports a little bit of tingling on forearm where device was - expects it would settle in 5-10 minutes Arm feels the same before and after device	twitching/tingling in hand, feels like the hand is becoming overactive. Patient concerned that it makes the fingers more tight and reduce function. Immediately resolves when turning the device off. Feels like coordination when completing task is worse - "more jerky" immediately after taking off bicep. Some redness over where the device was. Taking it off relieves restrictive feeling immediately and tingling back to baseline
Additional comments	Can't see the therapeutic benefit after removal of device. "wasn't a nuisance but didn't do any good" Patient reports that using a previous device designed for hand ROM, this had a long term effect and was aware of "good movement" after use. Therapist highlighted that initially patient did not report immediate effect until the next day.	Would use it if it was shown to be helpful and beneficial. Considerations to fitting it in to usual routine	If it was useful then he would likely wear it Interested to see if he would put it on with clothes over the top of it and still be able to turn it on and off Summary - OK to put on, more robust material for sleeve, size wise too big for arm. Two straps are fine and adjusted easily.

THERAPIST QUESTIONS

Type of population - disability in both the upper limbs?	Observed that can be easily fit by the patient independently when only affected on one side.
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Different versions for different levels of disability?			
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TABLE 6.5. Usability feedback for Semi Structured Workshop: involving Patients, Clinicians and Researchers

Q1	Q1a	Q2	Q2a	Q3	Q4	Q5	Q6	Q7	Q8	Q9
2 times		2 times		5. Very good: I participated in all exercises and activities with maximal effort and finished all of them	3. Normal	3. Normal	3. Normal	Yes	Yes	Unknown as I don't know the results of the study
2 times		2 times		3. Fair: I participated in most or all of exercises and activities in the sessions	3. Normal	3. Normal	3. Normal	Yes	Yes	No
2 times		2 times		4. Good: I participated in all exercises and activities with good effort and finished most of them	4. Easy	4. Easy	4. Easy	Yes	Yes	The cuff could be eased a bit so you could easily slide your hand through.
2 times		2 times		4. Good: I participated in all exercises and activities with good effort and finished most of them	3. Normal	3. Normal	4. Easy	Yes	Yes	Not that I can think of
1 time	Yes	2 times		6. Excellent: I participated in all exercises and activities with maximal effort, I finished all exercises, with active interest in the exercises and activities	5. Very Easy	5. Very Easy	5. Very Easy	Yes	Yes	Suite are often.
2 times		Did not finish	Injury	6. Excellent: I participated in all exercises and activities with maximal effort, I finished all exercises, with	3. Normal	3. Normal	3. Normal	Yes	Yes	I felt that the vibration could have been more intense or variable in intensity, so that it would be better suited to the individual. The

				active interest in the exercises and activities						concept is excellent, and I definitely found a benefit from the use of the device. I would be happy to participate in any further experiments regarding the development of this therapy.
Questions: Q1. How many times did you complete the home exercise programme before your first session at Hobbs? Q1a. If you did not complete the home exercise programme twice (before first session), why not? Q2. How many times did you complete the home exercise programme before your second session at Hobbs? Q2a. If you did not complete the home exercise programme twice (before second session), why not? Q3. Please rate your level of participation in the therapy exercises/activities in your clinic visits: Q4. How difficult or easy did you find the setup (donning/doffing) of the wearable vibration therapy equipment? Q5. How difficult or easy did you find the use of the wearable vibration therapy, as a tool for rehabilitation? Q6. How easy or difficult did you find wearing (comfort) the vibration therapy equipment? Q7. Would you use the vibration therapy equipment if it was available to you? Q8. Would you recommend the vibration therapy equipment to other patients with stroke? Q9. Is there anything about the vibration therapy equipment that you think could be improved?										

TABLE 6.6. Participant feedback to Questionnaire about the device, to understand Participant's Perception on Adoption of Technology