Investigation of the feasibility of using focal vibratory stimulation with robotic aided therapy for spasticity rehabilitation in spinal cord injury

by

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Student number: M00471499

A thesis submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

at the

School of Science and Technology

Middlesex University London

August 2018

Declaration of authorship

I certify that to the best of my knowledge the content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged. This thesis has not been submitted for any other degree or purposes.

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Supervised by Dr Rui Loureiro and Dr Aleksandar Zivanovic
Submitted to the School of Science and Technology
on February 26, 2019, in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

Dedicated to Mr and Mrs Dragan and Živodarka Jevtić who guided me to have a head full of knowladge and a heart full of love
and to loving memory of Mr and Mrs Boško and Milojka Erčević who showed me the importance of having an ear to listen and a hand to help

Abstract

The occurrence of a traumatic spinal cord injury is in hundreds of thousands of people every year. Survivors are left with loss of many bodily functions, loss of sensation below the point of injury and many more painful and uncomfortable repercussions which interfere with activities of daily living. Over 70% of people with SCI develop spasticity: abnormally increased muscle tone and connected joint stiffness that interfere with residual volitional control of the limbs. Treatments for spasticity include many pharmacological and non-pharmacological techniques, however many of them have severe sideeffects. Evidence suggest the use of vibratory stimulation to relieve repercussions of spasticity, despite not agreeing on the most advantageous protocol.

This thesis evaluated effects that focal vibratory stimulation have on the muscle performance. Within two studies, focal muscle vibration is compared against different application conditions such as timing and location. The results suggests that if focal vibrations are applied to the relaxed muscle, the increase in muscle's force is observed. Analysis of the cortical waves indicates minimal cortical involvement in vibratory stimulation modulation. On the other hand, FV applied of the connected tendon/bone imposed to a contraction seems to have a potential to increase muscle's activation. There is evidence that motor cortex is responding to this stimulation to stabilise the muscle in order to perform the contraction.

Within clinical trial, focal muscle vibratory stimulation is employed in total of 6 interventional sessions while a joint's spastic flexor and extensor muscles were relaxed. Spasticity appears to be reduced as a consequence of the stimulation. Moreover, engaging the joint into robotic-aided therapy increase volitional control of the wrist, according to the analysis of the active range of motion, joint stiffness and kinematic parameters associated to the movement. The measurement and movement facilitation device used in the clinical trial was designed and developed in accordance to the spasticity and spinal cord injury repercussions consideration.

The studies conducted for this thesis demonstrated feasibility and potential for the use of focal muscle vibratory stimulation to enhance muscle power in healthy muscles but also relieve consequences of spasticity. Vibrations combined with movement robotic-aided therapy have a prospects to enhance motor control.

Acknowledgements

The path towards this dissertation was circuitous and challenging but the most gratifying experience so far. Many people along the way helped build and complete this thesis and to all of them I am mostly grateful. However a few of them deserve special consideration and attention.

To my Director of Studies, Dr Rui Loureiro, thank you for being you. Your words full of solace, your thought filled with knowledge and hands of skills helped me to develop my own ideas into reality. You gave me strength to always go forward even if a high brick wall was on sight. Thank you for scientific support and guide throughout my studies.

To my second supervisor, Dr Aleksandar Zivanovic, thank you for always finding the time to be there for me and this adventure. I have learned a lot from you, from your knowledge in designing, experience in technical consideration and skilfulness in practical implementation. The time spent with you building my thesis, but also encourage my restless spirit is stamped into my heart.

To Middlesex University, thank you for providing me with this once in a lifetime opportunity to fulfil my dreams and for supporting me throughout. Prof Mehmet Karamanoglu, without your consideration in my times of need, I wouldn't have endure a challenging life in London. I never thought I will have such a delight and pleasure to teach extraordinary minds, and you made that possible for me. I will always cherish all resources and experiences you made possible and shared with me. Thank you Prof Richard Comley for guiding me with administration sides of my PhD. A special thanks to all members of Design Workshop at Middlesex University, the great Spike but also Collin, Cecil and everyone, for making my time with you productive, brilliant and smashing.

To Aspire CREATe Lab, you made every day of my PhD exceptional. Growing with you, shaping my research personality and striving to greatness architect my mind to be fearless. On a rainy day you were my rainbow. Peter, Ha, Elliott, Chi, Nayereh, Reni, Nadia, Sean, Ali, Yazi, Sarah, Kylie, Irvin, Fjodor, Anne, Lynsey, Steve and all others current and past members, you guys are my stars. Big thanks to Dr Tom Carlson for all help and support with EEG system.

To all colleagues from Royal National Orthopaedic Hospital at Stanmore, Ms Emma Linley and the team from Occupational and PhysioTherapy, team from Research and Development, and many others for assisting me with the clinical trial. Many thanks to all people who found the time to participate in the studies of this thesis, especially those from the clinical trial.

At the end of every day, I am blessed to have my family as a safe harbour. My sister Nevena, my mum and dad Jasmina and Zoran, my aunty Svetlana, and grandparents, you packed my suitcases with beliefs and sent me to this odyssey knowing I have you as winds into my sails. And my superhusband Uros, your hugs and words of encouragement are my charging station, where all worries vanish and energy and motivation full-fill my heart.

Svoj familiji, prijateljima, kolegama i poznanicima, hvala od srca.

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Glossary of Abbreviations

ANOVA	Analysis of Variance
AROM	Active Range Of Motion
ASIA	American Spinal Injury Association
BCI	Brain Computer Interface
BMI	Brain Machine Interface
CNS	Central Nervous System
EEG	Electroencephalography
EMD	Empirical Mode Decomposition
EMG	Electromyography
ERD	Event Related Desynchronisation
ERP	Event Related Potentials
ERS	Event Related Synchronisation
ES	Electrical Stimulation
mFDI	First Dorsal Interosseous muscle
FES	Functional Electrical Stimulation
FV	Focal Vibrations or Focal Vibro-Tactile Stimulation
GABA	Gamma Aminobutyric Acid
GTO	Golgi Tendon Organ
HAVS	Hand-arm vibration syndrome
IMF	Intrinsic Mode Functions
IMNF	Instantaneous Mean Frequency
ISNCSCI	International Standards for Neurological Classification of Spinal Cord Injury
JS	Joint Stiffness
MAS	Modified Ashworth Scale
MEP	Motor Evoked Potentials
MVC	Maximal Voluntary Contraction

NS	Nervous System
PID	Proportional Integral Derivative controller
PNS	Peripheral Nervous System
PROM	Passive Range Of Motion
PSD	Power Spectral Density
PVD	Post-Vibration Depression
RMS	Root Mean Square
RMT	Robot Mediated Therapy
ROM	Range Of Motion
rpm	Rotations Per Minute
SCI	Spinal Cord Injury
SV	Segmental Vibrations
TENS	Transcutaneous Electrical Nerve Stimulation
TES	Transcranial Electrical Stimulation
TMS	Transmagnetic Stimulation
TVR	Tonic Vibration Reflex
UMN	Upper Motor Neuron
WBV	Whole Body Vibrations

CHAPTER 1

Thesis overview

The first chapter introduces the research topic and the research problem. It defines the research questions, presents the methodology and gives an overview of the results. An outline of this thesis can be found at the end of this chapter.

1.1 Problem statement

Spinal cord injury (SCI) has a major impact on the human body's ability to perform everyday life activities. Although mortality caused by SCI is less than 5% (Grundy & Swain 2002) survivors are left with loss of many bodily functions, loss of sensation below the point of injury and many more painful and uncomfortable repercussions which interfere with daily life. It is estimated that worldwide there are over 2.5 million people living with SCI with 180,000 new cases every year caused by trauma to the spinal cord (Lee et al. 2013, Thuret et al. 2006). The incidence of SCI in United Kingdom is estimated to be between 12 and 16 per million with the majority of cases caused by trauma (*National Health Society* 2016). Most traumatic SCI statistics showed a bimodal age distribution. The first peak was found in young adults between 15 and 29 years and a second peak in the older adults (mostly $\geq$ 65 years) (van den Berg et al. 2010).

Injury can be classified as complete or incomplete depending on the level of sensation remaining in the area below the point of injury. In contrast to complete SCI, incomplete injury often refers to the ability of the spinal cord to convey messages between the brain and peripheral body parts. As the absence of the motor and/or sensory functions below the area of injury does not necessarily mean that there are no remaining neural communication, but that these pathways needs to be reinforced and rehabilitated (Zaaimi et al. 2012). It is estimated that approximately 65% of SCIs are incomplete, i.e. injuries where there is some muscle function and sensation below the level of injury (*Spinal Injuries Association* 2014).

SCI affects the perception of pain and has a significant impact on the regulation of bladder and lung function and sexual activity (Grundy & Swain 2002). People with SCI are left with residual disabilities weakening the performance of voluntary movements and ability to sense the environment (e.g. through tactile means) (Lam et al. 2007). Spasticity is a common repercussion contributing to the development of contractures, pressure ulcers, infections and degradation in posture, sitting and the ability of to use wheelchairs. The percentage of people affected by spasticity after hospital discharge is between 67% and 78% (Maynard et al. 1990).

Currently, there are a variety of both invasive and non-invasive rehabilitation procedures practiced in healthcare facilities or at home for treatment of disabilities and health complications caused by SCI. Treatment options include surgical repair and implants, tendon transfer, electrical stimu-

lation, adaptive equipment and environmental control devices (Bradbury & McMahon 2006, McDonald & Sadowsky 2002, Thuret et al. 2006). Although over 40% of SCI patients have incomplete lesions affecting the body from the neck down, the majority of SCI research focuses on enabling locomotion, stepping and walking (DeVivo 2012). Current clinical rehabilitation protocols mostly target the restoration of motor function, bowel and bladder and sexual function (Simpson et al. 2012). Motor function rehabilitation includes rehabilitation of the arms and hands, or mobility of the legs for individuals who have lost leg function. Unfortunately, there are no uniform nor worldwide recognised protocols for rehabilitation. Occupational and physio-rehabilitation therapies are mostly based on current rehabilitation achievements, staff experience and equipment availability. For example, functional electrical stimulation is used for the restoration of hand movements and standard gym exercises for muscle atrophy prevention. A small number of hospitals who are able to afford commercially available rehabilitation robots (such as ARMEO or HAPTIC MASTER or similar) are using them with success for motor function restoration (Calabrò et al. 2017, Loureiro & Smith 2011). Spasticity is usually treated with anti-spasticity medications, despite any latent side-effects they may have.

Because of the high incidence of spasticity among the SCI population, the first thing a therapist must undertake is to reduce high spastic muscle tone in order to continue with a traditional motor restoration therapies. Anti-spasticity medications are used to prevent spasticity but recent research studies recommend use of vibration therapy in clinical practice as a means of achieving an instant effect (Yelnik et al. 2009). Depending on the type of vibration actuator and area of application, whole body (WBV), segmental (SV) or focal vibrations (FV) are used. While the anti-spasticity effect of focal vibrations might last up to 6 hours, WBV can, in some cases prolong this effect up to 6-8 days (Sadeghi & Sawatzky 2014). Even though the effects of vibrations on spasticity are evident, the further effects they have on muscle strength and performance are unclear due to the limited number of studies and the lack of clinical trials investigating the underlying effects it has on the body. Furthermore, it is not clear why vibrations are helpful at decreasing spasticity and why some modalities are more effective than the others (Hsieh et al. 2012).

Instead of creating a novel approach towards SCI and spasticity rehabilitation, this thesis proposes combining existing rehabilitation paradigms to reinforce their effectiveness in tackling spasticity and residual volitional movements. To this end, a robotic system combined with focal

muscle vibration is used for upper limb movement control and muscle performance evaluation while neuro-imaging techniques are used to observe and record internal processes during and after targeted movements. While observing spastic movements, sensory and motor pathways, and cerebral responses can be identified and described with a model for both healthy participants and those with SCI. By comparing these models, between healthy and SCI study participants, a better understanding of the impact of focal vibration on the human body and its response can be determined: is it muscular, spinal or cerebral? Furthermore, the analysis of the data from electromyography (EMG), electroencephalography (EEG) and kinematic movement tracking recorded during interventional sessions, could give an insight into the physiological state of the body before, during and after robotic-vibration interaction sessions. The results and conclusions can be then translated from one neurological trauma or disease to the other to develop a generalised approach to spasticity rehabilitation with least side-effects and major effectiveness.

1.2 Thesis objective, method and hypothesis tested

1.2.1 Methodology and objectives

The aim of this thesis is to assess combination of two rehabilitation methods, focal muscle vibration and robot-mediated therapy on people with spasticity as a sequela of the spinal cord injury. Our vision is to integrate multiple approaches to tackle several SCI impairments such as spasticity and volitional motor control, and to propose a complementary rehabilitation paradigm for clinical management and self-management. Integration of multiple approaches couples focal vibrations to amortise spasticity and robotic-aided rehabilitation to enhance residual volitional control in upper limbs. Robotic-aided device is also proposed to be used as a progress evaluation tool.

Literature research was performed to build an understanding and clarity for the use of focal vibration in rehabilitation. There are two main focuses: one is concerning the effects FV have on rehabilitation outcome measures and the second's the clarification of underlying mechanisms behind changes in outcome measures. Although the majority of the reported studies agree on the mechanisms of action, some differs and propose alternatives. Nonetheless, the consensus is

that focal vibrations applied on the muscle have a potent predisposition to enhance functional performance of the muscles and executed movement. These claims are of special interest for its use in rehabilitation treatments. There is a considerable amount of research addressing focal vibrations effect on spasticity in different diseases (e.g. Multiple sclerosis, Parkinson's disease) and medical conditions (e.g. spinal cord injury, stroke) (Murillo et al. 2014). Four recent studies have been identified to combination of focal vibrations with robotic-aided rehabilitation for spasticity due to stroke (Calabrò et al. 2017, Casale et al. 2014, Cordo et al. 2008, 2013*a*) and only one for spasticity due to spinal cord injury (Backus et al. 2014). Furthermore this thesis proposes supplementary use of the robotic approach for quantification of change in the outcome measures.

To achieve the aim of this thesis defined at the beginning of this section, three studies were performed during the course of research reported in this thesis: two with able-bodied participants and one with participants with SCI. The first study was designed to evaluate the effects of FV on a single healthy muscle. The second study was performed to observe the cortical responses to FV when applied on a healthy muscle. It was divided in two parts: a single case study and an investigational study. The single case study protocol was the same as the first study but focusing on evaluating recordings from the brain. The results were used to adapt and sculpt the protocol for a larger population investigational second study. Third study was designed as a single case pilot clinical trial for participants with spasticity due to spinal cord injury.

To summarise, the objectives of this thesis are to:

- identify and review rehabilitation methods with clinical features of spasticity
- develop comprehensive understanding of effects focal vibrations applied on a healthy muscle have on a strength, muscle and brain activity
- characterise the impact of focal vibration on a joint stiffness and volitional controll affected by related muscle's spasticity
- design and develop a simple robotic device for performing and evaluating wrist movements
- investigate changes in functional recovery and controll due to focal muscle vibration combined with robotic-aided therapy

1.2.2 Hypotheses

Central Hypothesis: Focal muscle vibration can enhance muscle's performance and associated joint function.

Vibratory stimulation seems to be an affordable easy-to-use rehabilitation tool (Saggini et al. 2017). Literature suggests a variety of applications ranging from enhancing muscle performance, decreasing spasticity to degrading proprioceptive channels (Bock et al. 2007, Sadeghi & Sawatzky 2014). However very little is known about the most appropriate vibration parameters (such as position, duration, amplitude, frequency, etc) for the desired outcome. Therefore this hypothesis will be tested under three different experimental setup inclusive of healthy people and those with a lesion to central nervous system, and a variety of vibratory parameters. Outcome measures are reflected in those assessing changes in muscle's strength, volitional and functional control. The experimental protocols are presented in chapters 5, 6 and 8 and results from each of them contribute to the central hypothesis being proven. To complement this evaluation in more details, the central hypothesis is devised to three sub-hypotheses listed below:

Hypothesis 1: Focal muscle vibration applied to the relaxed muscle belly is a beneficial tool for muscle strength enhancement.

This hypothesis is tested in a study with non-impaired able-bodied participants presented in chapters 5 and 6. Exerted force from vibrated muscle, muscle activity (EMG) and brain signals (EEG) are measured to assess the effects of short focal vibrations applied on a single muscle. The results strongly support this hypothesis.

Hypothesis 2: Focal vibration applied on a relaxed muscle with abnormally increased tone (spasticity) can reduce related joint stiffness (tightness) and increase range of motion of the connected joint for a short period of time.

Spasticity is often treated with a range of medications with possible side effects (Bavikatte & Gaber 2009). Given the beneficial effects of vibrations on healthy muscles (Jevtic et al. 2015), focal vibrations could potentially be used in various treatments and therapies. This hypothesis will be tested on an abnormally increased tone of flexors/extensors muscles in the forearm controlling flexion-extension of the wrist joint. Biomechanical measure of the related joint stiffness and active and passive range of motion will be used to determine the changes pre and post vibratory

stimulation application to the muscle. In addition, neuromuscular assessment will be conducted to compare benefits to the muscle strength enhancement. Strong evidence found towards this hypothesis are presented in chapter 8.

Hypothesis 3: The combination of focal muscle vibrations with subsequent robotic-assisted movement of the wrist joint can reduce spasticity and enhance functional recovery by improving strength and volitional control of the targeted muscles. Spasticity deprives the affected muscle of its ability to perform a wide range of movements due to high muscle tone and joint stiffness (joint tightness with subsequently reduced range of motion). There is evidence suggesting robotic-aided task-oriented therapy can minimize neurological impairments (Andrade et al. 2014). After reducing muscle tone, the use of robotic therapy is expected attribute to functional recovery. To test this hypothesis in chapter 8, a study is designed to employ focal vibration of the forearm muscles with the aim of reducing spasticity prior to engaging wrist movements in a robotic-aided game throughout the course of several sessions. Clinical (Modified Ashworth Scale) and engineering biomechanical (active and passive range of motion, joint stiffness) measures are obtained to track progress of through each session and for the duration of the study. Movement analysis is performed to establish movement performance after the game and compared in-between sessions. All results are supporting this hypothesis but more evidence is needed.

1.3 Summary of results and key contributions

The author's specific contributions in this thesis and to the scientific community are fundamentally practical contributions as opposed to theoretical (clinical and physiological principles). Hypothesis 1 was addressed in two studies performed on able-bodied volunteers, written in chapters 5 and 6. Hypotheses 2 and 3 are assessed based on the the results from the third study: a pilot case study clinical trial presented in chapter 8. The key results arising from these studies are as follows:

- Muscles can be preconditioned to achieve greater output force by applying focal vibratory stimulus to the relaxed muscle before the contraction.
- Focal vibrations applied to the bone or tendon connected to the targeted muscle can amplify the amplitude of EMG signals which are interpreted as the presence of tonic vibration reflex.

- The underlying mechanisms of this vibratory preconditiong of the muscle seems not to be depended on the cortical control but rather supraspinal, spinal or even muscular responses.

- Sensorimotor cortex appears to be sensitive to the onset and offset of the muscle focal vibrations, but not responsive to the prolonged stimulation.

- Coupling muscle focal vibration with robot mediated therapy appears to decrease spasticity in participants with spinal cord injury.

- After relieving hypertonicity with the muscle focal vibration, participants who engaged in robot mediate therapy are able to improve volitional control of the joint controlled by the targeted muscles.

1.4 Publications

- Vojinovic Jevtic T., Zivanovic A., Carlson T., Loureiro R.C.V. (2017). VIBROfocus: Design of a focal vibro-tactile robotic-assistive system for spasticity rehabilitation. Proceedings of IEEE International Conference In Rehabilitation Robotics (ICORR) 2017, pp. 783-788.

- Jevtic T., Zivanovic A., Loureiro R.C.V. (2017). Cortical and Muscle Response to Focal Vibro-Tactile Stimuli. Converging Clinical and Engineering Research on Neurorehabilitation II. Biosystems & Biorobotics, vol 15. Springer.

- Jevtic T., Zivanovic A., Loureiro R.C.V. (2016). Brain Response to Focal Vibro-Tactile Stimulation Prior to Muscle Contraction. Proceedings of IEEE 12th International Conference on Intelligent Environments (IE) pp. 182-185.

- Jevtic T., Zivanovic A., Loureiro R.C.V. (2015). Focal vibro-tactile stimulation as a preconditioner to enhance muscle performance in robot-mediated neurorehabilitation. Proceedings of IEEE International Conference In Rehabilitation Robotics (ICORR) 2015, pp. 696-701.

1.5 Thesis outline

The work presented in this thesis is organised in nine chapters. This, the first chapter introduces the motivation and objectives, summarised in three hypothesis. This introduction chapter ends with a summary of the results and a list of publications.

Chapters two, three and four are reviewing the literature relevant for this research. Chapter two considers the main anatomical and physiological aspects important for understanding the focus of this research: spasticity in spinal cord injury presented in chapter three. Readers with sufficient physiological knowledge can progress to the chapter 3 without reading chapter 2. Chapter 3 lists spasticity definitions and assessment approaches with reflection on challenges from scientific and clinical point of view. It also includes current trends in spasticity rehabilitation methods and their effectiveness reflected in ability to diminish spasticity with minimal side-effects.

The use of vibratory stimulation in rehabilitation with the state of the art is introduced in chapter four followed by the rationale for further investigation. The chapter is divided in three different sections depending on the application of the vibratory stimulation: whole body stimulation, segmental stimulations and focal vibration. The latter sections of the chapter summarise the application of focal vibration in rehabilitation and tally papers where FV is used for spasticity rehabilitation with vibration parameters and outcomes highlighted. Five papers implementing similar approach to this thesis: use of focal vibration with robotic-aided therapy, are discussed in detail in section 4.4.2 with pinpointing main differences and changes in protocol to be incorporated as a part of research conducted in this thesis.

Methodology used to test the three hypothesis defined in previous section of this chapter, results and discussions are organised in chapters five, six and eight. Each chapter presents different approach towards understanding best rehabilitation employment of focal vibratory stimulation. Chapter 5 addresses application site and timing in respect to the stimulated muscle. Force and muscle activity were recorded in chapter 5 within two phases: vibrations applied to the muscle versus applied on the bone but also conditions: no FV applied, FV applied when the muscle is relaxed and when it is contracted. Results indicated instantaneous increase in force produced after the muscle was vibrated during relaxation as compared to all other phases and conditions. The discussion section referred to this as preconditioning the muscle to enhance the strength as a

consequence of muscle fibres reorganisation during vibratory stimulation. Analysis of the muscle's electrical activity revealed second important finding: the muscle seems to be more fatiguing when vibrations are exerted to the bone as compared to the muscle.

Brain responses to focal vibrations are analysed in chapter 6. The first part of the chapter 6 discuss results from a single case study identifying key features from the brain electrical activity. The protocol used for this study is the same as the one presented in chapter 5. The results indicate presence of the specific brain waves observed when the body is in the relaxed state and whilst the vibrations are applied to the muscle. The same patters are discerned within application of the vibrations while the muscle is contracting. These observations alluded to the correlation between focal vibrations and this type of the waves (in literature referred to as mu waves, further explained in chapter 2, section 2.6.2). This is interpreted as no motor response from the brain towards the vibrations if applied to the relaxed muscle prior to the contraction. If FV is applied simultaneously to the contracting muscle, then perhaps the muscle and the brain are working together to stabilise affected muscle fibres in order to achieve muscle contraction. These theories are then further explored with second study and adapted protocol tapping into association of the side of application of the vibrations and exertion of the contraction. Distinctive presence of the mu waves associated to the vibrations are observed from the sensorimotor part of the brain, contralateral to the side of application. Finding from the chapters 5 and 6 drive the considerations for the most favourable FV application protocol for rehabilitation purposes.

the results from the previous two chapters are adapted and consolidated with a chapters 2 and 3 for creation of a work-plan and design requirements for FV application in rehabilitation. Hence, chapter 7 as a stand alone chapter presents design of the measurement and treatment system to accommodate several aspects of FV outcomes. The apparatus is inclusive of engineering measures of wrist joint abilities reflected in active and passive range of joint and joint stiffness. Additionally, it can deliver repetitive movement therapy by engaging the user in game playing, whilst recording kinematic movement profiles such as index of performance, movement accuracy, movement smoothness and similar listed in chapters 7 and 8. Aside from design perspective, the guide towards all necessary calculations, considerations and equipment selection are commented upon in chapter 7. Lastly, the selection and design of the vibratory equipment used in clinical trial is presented as a part of the system.

As chapters 5 and 6 recognize the effects focal vibrations have on able body participants, pilot single case clinical trial findings can be found in chapter eight equating effects FV have on spasticity, abnormally increased muscle tone and associated joint stiffness. The clinical trial consisted of one initial assessment session and 6 interventional sessions dispersed in 2 weeks: 3 sessions per week. In addition to engineering measures of joint stiffness, electrophysiological and clinical measures are included in this clinical trial as a part of the assessment. Initial data from 2 case studies demonstrate an instantaneous short-term increase of active range of motion after the application of the FV as well as decrease of joint stiffness. Repetitive robotic movement therapy is improving these results by tapping into volitional control and abilities of the participants. Perusal of the kinematic parameters during game playing suggest gradual improvement through 6 interventional sessions. As a part of qualitative analysis of the questionnaires, participants highlighted subjective feeling of improvement, decrease of spasticity associated repercussions and advancement in performing activities of a daily living. Discussion section referred to the advantageous increase in muscle performance observed in chapters 5, with minimal brain involvement as showed in chapter 6 and links analysis of the observed results from the 2 case studies to muscular and spinal involvement in diminishing spasticity symptoms using focal vibratory stimulation applied to the relaxed muscle.

Chapter nine summarises the thesis with the consideration of the key contributions to the body of knowledge. This thesis ends with outline of the limitation and suggestions for future work. The flowchart illustrating the thesis layout can be found in Figure 1.1.

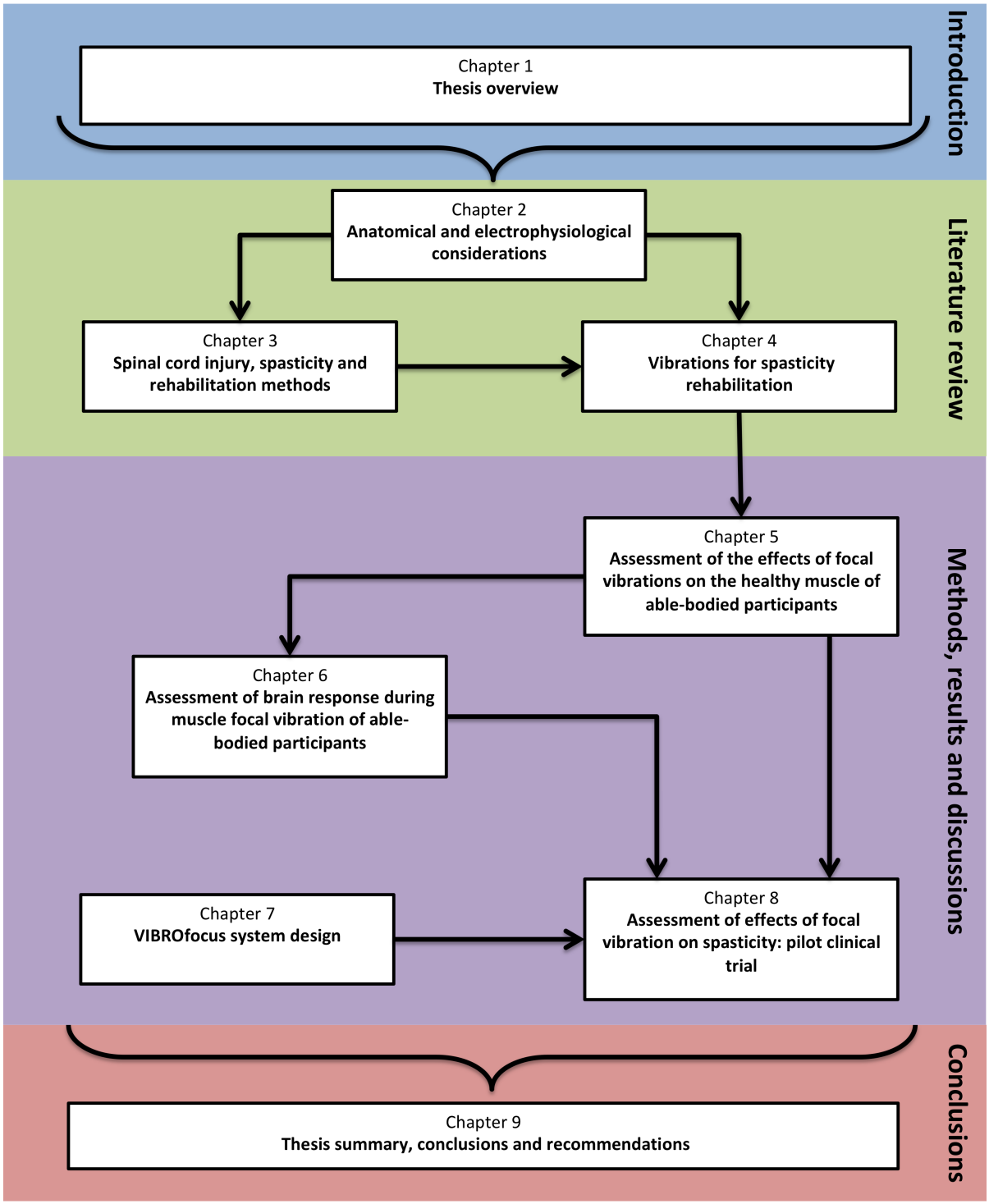


Figure 1.1: Flowchart illustrating the structure of this thesis.

CHAPTER 2

Anatomical and electrophysiological considerations

This chapter is an overview of upper limb anatomy, nervous system organisation and electrophysiological signals derived from the body. It is to provide a reader with a simplification of the terminology used in this thesis and enhance understanding of physiological mechanisms of a muscle contraction. The material for this chapter was mainly sourced from anatomy, neuroscience and biomechanical books. Readers with sufficient physiological knowledge can progress to Chapter 3.

2.1 Organisation of the nervous system

Human movement is controlled and monitored by the nervous system. The nervous system observes the internal and external environment, integrates sensory information and then coordinates voluntary and involuntary responses of different organ systems (Martini & Bartholomew 2012). The nervous system (NS) consists of two parts presented in Figure 2.1:

- The central nervous system (CNS) − the brain and the spinal cord (both are the means by which human movement is initiated, controlled and monitored)
- The peripheral nervous system (PNS) − all the branches of nerves that lie outside the spinal cord and are intermediate in the execution of movement:
  - Somatic nervous system (including 12 cranial nerves from the brain) − transmits somatic and sensory information and consists of :
    - Somatic nerves − responsible for voluntary movements by transmitting information from the CNS to the end organs (such as muscles)
    - Sensory nerves − providing information from the sensors to the CNS
  - Autonomic nervous system − controls involuntary responses to regulate physiological functions (Laight 2013) and consists of:
    - Sympathetic nervous system − activated during "fight or flight" situations where great level of energy and high responsiveness are needed.
    - Parasympathetic nervous system − activated in "rest and digest" state where relaxation is allowed.

In the body, both the CNS and PNS communicate information between each other as one system to control voluntary and involuntary movement execution and use internal models driving sensorimotor integration of both feedback and feedforward mechanisms. In addition to generating and controlling involuntary movements, the CNS is also responsible for planning and correcting voluntary movements. Different parts of the brain have been mapped to different roles. For example, sensory and motor areas of the brain are activated during movement and correlated sensory

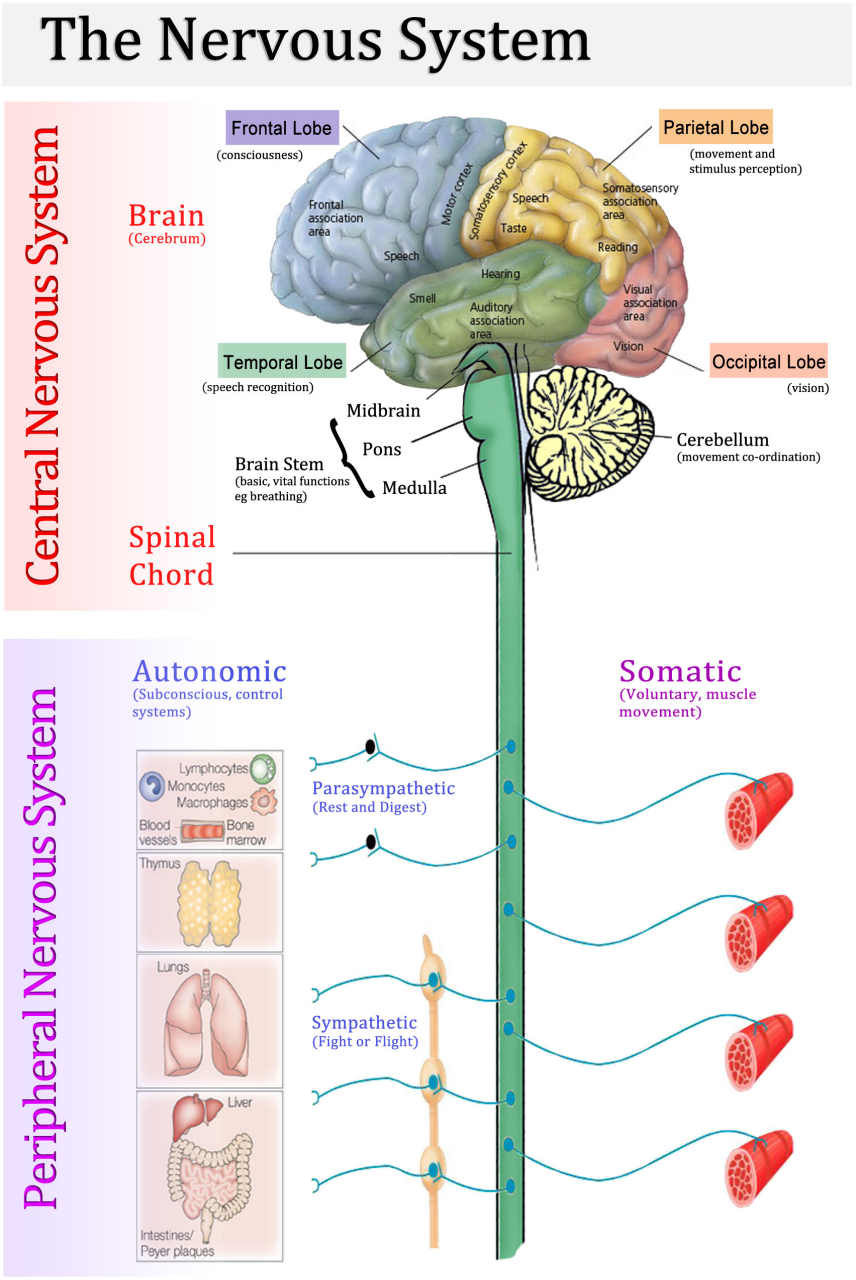


Figure 2.1: Nervous system organisation and division into the central nervous system (the brain and the spinal cord) and the peripheral nervous system (all other branches of the nerves) (*The Nervous System* 2011).

facilitation. The activation of these areas corresponding to different body parts is graphically presented by Penfields homunculus in Figure 2.2.

It can be observed that one of the largest anatomical representations within the homunculus is that of the hands, the reason being the range and complexity of movements which can be performed

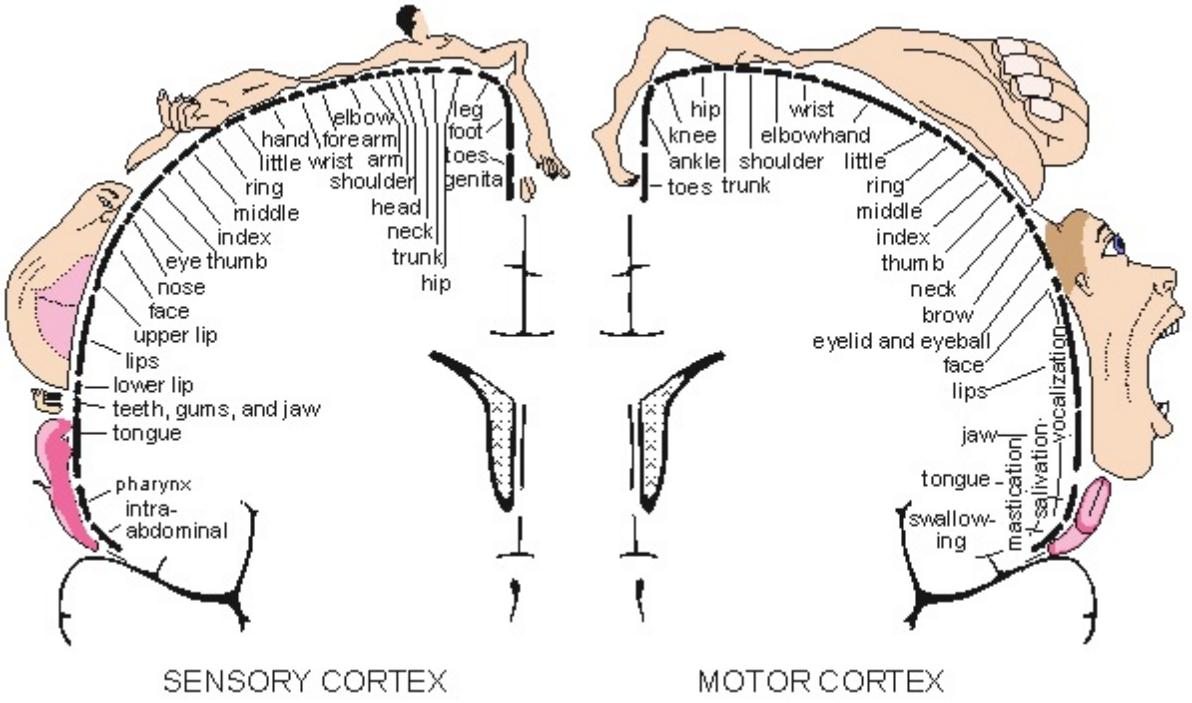


Figure 2.2: Penfields homunculus maps sensory and motor areas of the brain to different body parts according to their movement and sensory complexity (Penfield & Rasmussen 1950).

by the hand as opposed to the foot. Movement of the hand and general motor tasks can either be voluntary, as in the case of reaching and grasping, or involuntary (reflex based) such as moving the hand out to prevent injury or breathing. However, recent work by Courtine et al. (2009) and colleagues have demonstrated the spinal cords importance in facilitating movement (coordinated muscle recruitment and locomotion (Rosenzweig et al. 2010)) in rats and have proposed strategies by which individuals suffering from spinal cord injuries could regain a tangible level of motor control (van den Brand et al. 2012).

2.1.1 Nerve cells

There are approximately 10^{11} neurons in the brain.

A neuron is the essential cellular element of the NS. All neurological processes depend on complex intracellular interaction among single cells as well as groups of related neurons. Morphologically, in a typical neuron, three major regions can be defined (Squire 2013) as seen in Figure 2.3:

- the cell body *soma*, which contains the nucleus and the major cytoplasmic organelles.

- a variable number of dendrites, which emanate from the soma and spread over a certain volume of grey matter and which differ in size and shape, depending on the neuronal type.
- a single axon, which extends, in most cases, much farther from the cell body than the dendritic arbor.

Another kind of cell is found in CNS and PNS whose main function is to support neurons, *glia cells*. Glia cells are non-neural cells that surround neurons to hold, protect and feed them. In vertebrates, many axons are surrounded by an insulating myelin sheath, which facilitates rapid impulse conduction, called *action potentials*. In the axon, the terminal region is where the contacts with other cells are made, and these connections points are called *synapses*. These connections display a wide range of morphological specialisations depending on their target area in the CNS or PNS. Two types of synapses are

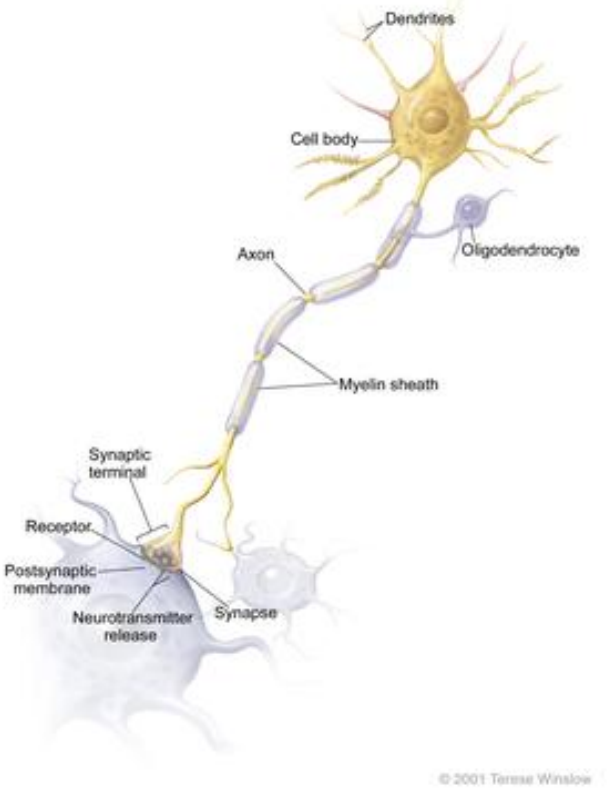


Figure 2.3: Neuron cell with a chemical synapse

- electrical synapse - forms a link between two neighbouring neurons that conducts nerve impulses very fast
- chemical synapse - is a conductive junction found between neurons and other target tissues (e.g. muscles)

In resting conditions the concentration of positive ions (Potassium K^+ and Sodium Na^+) inside and outside of the axon membrane is in equilibrium of -70mV. Exchange of the intra- and extracellular positive ions causes the change in the electricity to +30mV therefore causing depolarisation of the axon membrane, and the action potential propagation though the neuron cell (Figure 2.4). Once the action potential has passed onto the next part of the axon, the repolarisation of the

membrane brings back the equilibrium and the resting potential. Action potential passes onto the other neuron via the *gap junction tunnels* located in the electrical synapses (e.g. neural communication in the brain). On the other hand, when the action potential reaches the chemical synapse, it releases the neurotransmitter which triggers processes within the targeted tissues for subsequent biochemical cascades (e.g. muscle contraction).

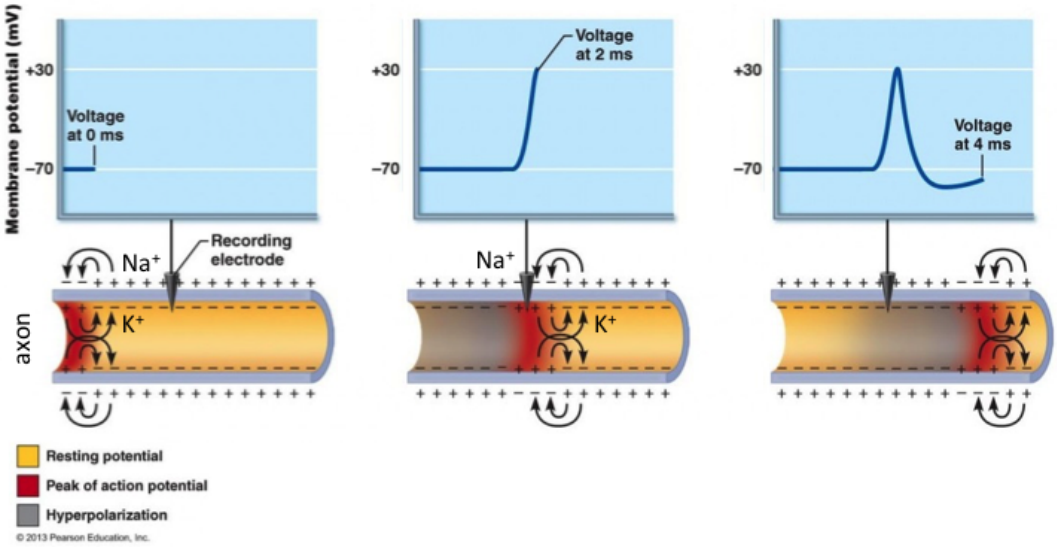


Figure 2.4: Action potential propagation through the axon

2.2 Physiology of the brain

The brain is one of the most important, complex and largely unknown parts of the body. This fascinating structure located in the head below the skull (i.e. cranium), is suspended in the cerebrospinal fluid. The brain consists of four main structures (as seen in Figure 2.5):

- the cerebrum - is the distal part of the brain made by the two hemispheres divided by the central sagittal plane to a right and left one. The outer layer of the Cerebrum is called the *the grey matter* (mostly made of stomas and dendrites) while the inner is *the white matter* (mostly made of cortical layers of axons). The two hemispheres are divided into four functional regions:
  - Frontal lobe - the most anterior part considered to be responsible for thinking, planning, decision-making and conscious emotions. The posterior part of the frontal lobe

is considered to be the sensorimotor cortex in charge of motor movements and sensory perception and responses.

  - Parietal lobe - leaning on the sensorimotor cortes of the frontal lobe, this part of the brain mainly focuses its actions on spatial orientation, proprioception and attention.
  - Temporal lobe - extends laterally onto the parietal lobe to the left and the right side of the head and is excited during hearing, speech, language and memory.
  - Occipital lobe - posterior to the temporal and parietal lobe, is mainly responsible for visual processing.

- the cerebellum - is part of the brain between the brainstem and the proximal parts of the cerebrum. It appears to have a role in planning and conducting complex motor movements, and maintaining balance of the body.

- the pons - is considered to be a part of the brainstem lying superior to the medulla and anterior to the cerebellum. It has a role in sleeping, dreaming and tasting.

- the medulla - is a part of the brainstem between the pons and spinal cord and it is believed to control breathing, heart beating and vomiting.

The basal ganglia are a cluster of structures in the centre of the brain that coordinate information flow between different parts of the brain. The brainstem connects the brain and the spinal cord.

As previously mentioned, the cerebrum facilitates volitional motor and sensory functions of the body. Motor function originates in the motor cortex but is not limited to it. The motor system is organised hierarchically (Squire 2013) starting from:

1. Premotor cortex areas - The highest level of motor control is identifying target spaces, choosing a course of actions and programming the movement (Popovic & Sinkjaer 2012). The premotor cortex lies on the lateral surface of the cerebral hemispheres.

2. Primary motor cortex - the next highest level is posterior to the premotor cortex and generates neural impulses that control the execution of the movement.

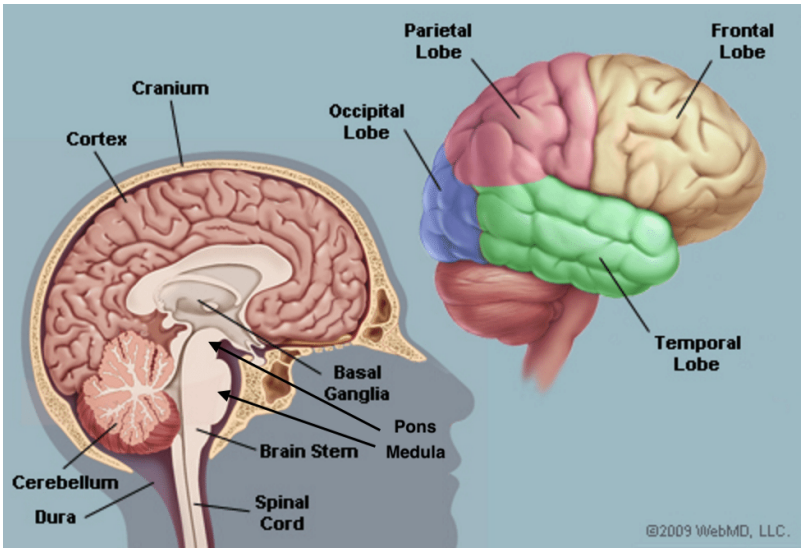


Figure 2.5: (Left) Sectional anatomy of the brain and (right) parts of the cerebrum (*Brain (Human Anatomy): Picture, Function, Parts, Conditions, and More* 2014).

3. Brainstem - integrates motor commands descending from the higher levels and ascending from the lower levels of the motor control. It is believed that this is where the messages are processed and conveyed into corresponding areas of the brain.

4. Spinal cord - the lowest level which is responsible for most autonomous movements due to stimuli (i.e. reflexes). Additionally, this is where the *central pattern generator* is located, an important feature in the process of walking.

5. Peripheral nerves - motoneurons transmitting signals to the targeted actuators to perform movement.

2.3 Physiology of the spinal cord

The spinal vertebral column, also known as the spine, is a bony structure found in vertebrates. The human vertebral column usually consists of 24 articulating vertebrae and 9 fused vertebrae. It can be divided into several regions:

- Cervical region − 7 vertebrae, referred as C1 through C7 in order from the closest to the skull to furthest from it. Anatomically covers regions from the skull to the neck.

- Thoracic region − the next 12 vertebrae, designated T1 or Th1 through T12 or Th12. It covers the anatomic region of the rib cage and the chest.
- Lumbar region − the last 5 individual vertebrae, designated L1 through L5, the vertebrae of the lower back above the pelvis.
- Sacral region − 5 vertebrae that are fused to form the sacrum and 4 coccygeal bones, which form the tailbone.

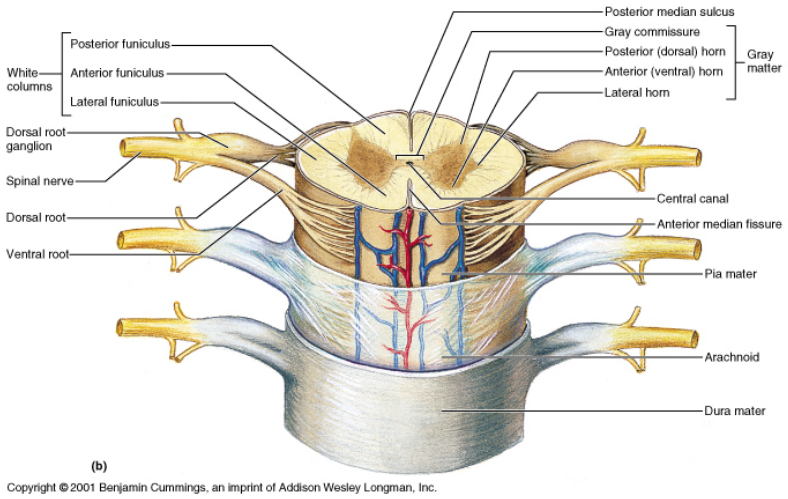


Figure 2.6: Sectional anatomy of the spinal cord that labels anatomical landmarks and the major regions of white and grey matter (Cummings 2004*a*).

The *spinal cord* extends from the base of the skull to the first lumbar vertebra inside the spine (i.e. from C1 to L1). The spinal cord receives sensory information from the skin, joints, muscles of the trunk and limbs, and contains the motor neurons responsible for both voluntary and reflex movements. It is divided into a core of central grey matter and surrounding white matter as presented in Figure 2.6. The grey matter, which contains nerve cell bodies, is typically divided into dorsal and ventral horns (so-called because the grey matter appears H-shaped in transverse sections). The dorsal horn contains an orderly arrangement of sensory relay neurons that receive input from the periphery, whereas the ventral horn contains groups of motor neurons and interneurons that regulate motor neuronal firing patterns. The axons of motor neurons innervate specific muscles.

The white matter is made up of longitudinal ascending and descending tracts of myelinated axons. The nerve fibres to and from the spinal cord are bundled into 31 spinal nerves, each of

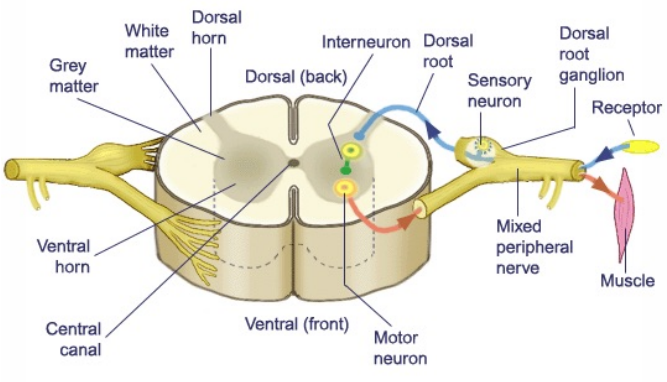


Figure 2.7: Conduits of spinal nerves. Sensory information is received through sensory neurons emerging from spinal dorsal root, marked in blue, while muscles are activated through motor neurons emerging from the spinal ventral root, represented in red (Cummings 2004*b*).

which has a sensory and a motor division. The sensory division (the dorsal root) carries information from muscles and skin to the spinal cord and terminates in the dorsal aspect of the cord, as shown in Figure 2.7. Different classes of axons within the dorsal roots convey pain, temperature, touch, and visceral sensory information. The motor division (the ventral root) emerges from the ventral aspect of the cord and comprises the axons of motor neurons that innervate muscles (Figure 2.7). Ventral roots from certain levels of the spinal cord also include sympathetic and parasympathetic axons. The motor neurons of the spinal cord comprise the final common pathway through which all higher brain levels controlling motor activity must act (Kandel et al. 2013).

2.4 Physiology of muscles and muscle contraction

Muscle tissue is a soft tissue, and is one of the four fundamental types of tissue present in animals (the other three being epithelial, connective and nervous tissue). There are three types of muscle tissue recognized in vertebrates:

- Skeletal muscle or "voluntary muscle" − anchored by tendons to bone, is used to effect skeletal movement such as locomotion and maintaining posture.
- Smooth muscle or "involuntary muscle" − found within the walls or as a part of the organs. Unlike skeletal muscles, smooth muscles are not under conscious control.
- Cardiac muscle (myocardium), also an "involuntary muscle" − more akin in structure to

skeletal muscle, and is found only in the heart, and completely controlled by the autonomic (involuntary) nervous system.

The smallest functional unit to describe the neural control of the muscular contraction process is called a motor unit showed in Figure 2.8. It is defined as "...the cell body and dendrites of a motor neuron, the multiple branches of its axon, and the muscle fibers that innervates it" (Enoka 1994). The term unit outlines the behavior of all muscle fibres acting simultaneously as a unit within the muscle activation process (Konrad 2005).

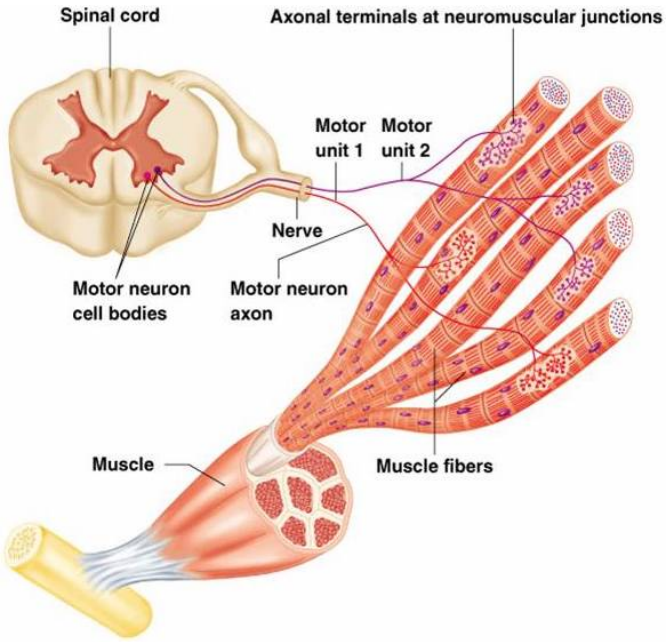


Figure 2.8: The muscle unit is the smallest functional unit to describe the neural control of the muscular contraction process and it is the place where the nerve enters the muscle (Cummings & P 2004).

A tough layer of connective tissue called the epimysium sheaths skeletal muscles. Within the epimysium are multiple bundles called fascicles, each of which contains 10 to 100 or more muscle fibres collectively sheathed by a perimysium. Besides surrounding each fascicle, the perimysium is a pathway for nerves and the flow of blood within the muscle. The threadlike muscle fibres are individual muscle cells called myocytes, and each cell is encased within its own endomysium of collagen fibres. Thus, the overall muscle consists of fibres (cells) that are bundled into fascicles, which are grouped together to form a muscle.

Scattered throughout the muscles are the muscle spindles that provide sensory feedback information to the CNS about the changes in the muscle length (see Figure 2.9). Muscle spindles

contain small muscle fibres called intrafusal fibres laying in parallel to the large-diameter muscle fibres called extrafusal fibres connected to the bone via tendon. A sensory nerve, the Ia afferent, surrounds the spindle and intrafusal fibres transmitting the signal to the spinal cord about the changes in the muscle length. Another sensory fibre, the group II afferent, is responsible for notifying the spine when the extrafusal fibres contract relative to the intrafusal ones, meaning the non-contractile part of the muscle is changing position or length.

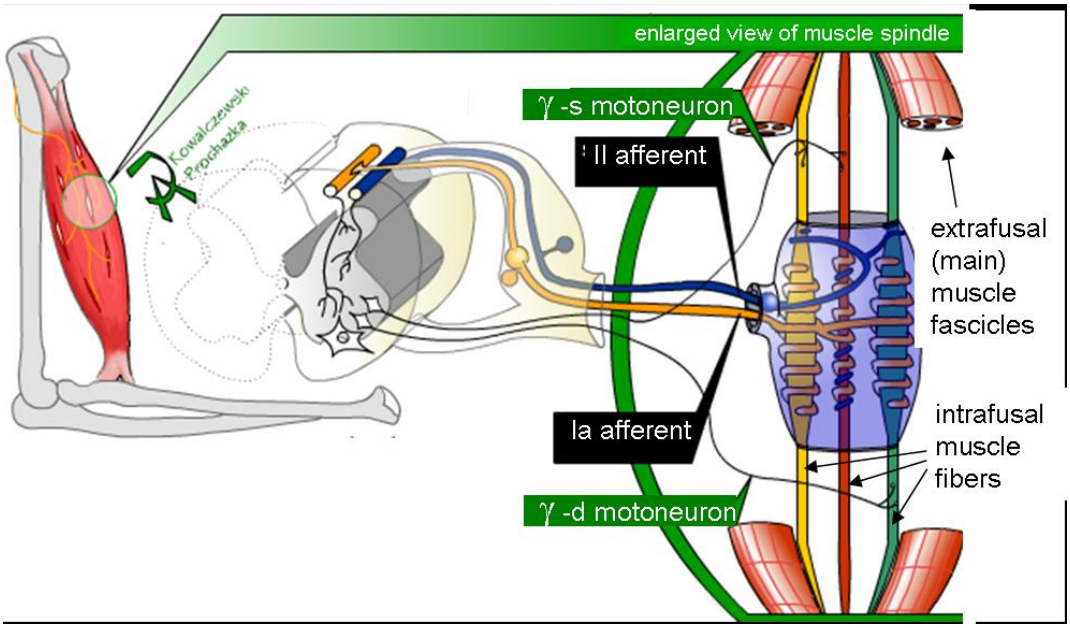


Figure 2.9: Physiology of the muscle elements responsible for sensory feedback and proprioceptive control. Ia, Ib and II afferents sense changes on muscle spindles and Golgi tendon organs in order to generate spinal stretch reflexes and supraspinal responses that control the muscle contraction (Rosenbaum 2009).

The brain generates the intention of movement and sends an electrical signal (the action potential) down the spine and the motoneurons. The action potential is the fast polarization of the neural or muscle fibre membrane from -80mV to +30mV (see Figure 2.4). When the action potential from the neuron reaches the muscle through the chemical synapse, it triggers the process of muscle contraction, which contributes to the movement. If there is a response to the movement, muscle spindles in synergy with the cutaneous sensory excitation provide feedback information to the brain. By shortening its length, the muscle flexes and by prolonging its length it extends. The antagonistic muscle pairs work in synergy to protect the muscles and support the movement. The synergetic reaction consist of agonist muscle flexing (shortening flexing muscle length and it achieved by the flexor's muscle contraction) while the antagonist extends (lengthening of extensor

muscle due to agonist's contraction).

Nerve impulses are passed along the muscle cells by nerve endings on the muscle cells called neuromuscular synapses (Rosenbaum 2009). The neurotransmitter is released and when received by the muscle cell membrane, the muscle cell becomes permeable to ions and the membrane develops an action potential similar to the same signal sent by neurons in the brain (Martini & Bartholomew 2012). This action potential is passed into the cell along the muscle fibres. The chemical chain reaction causes sliding of the thin and tick fibres in the sarcomere. The actual movement within the sarcomere is produced by heads or knobs of thick filaments (myosin) attaching to thin filaments (actin) and bending in order to past one another, causing the entire muscle to contract and shorten its length.

Muscles attach to other anatomical structures (such as bones or skin) through tendons. Within tendons are sensory receptors called Golgi tendon organs (GTO). Golgi tendon organs are quite sensitive to the muscle tension, delivering information about its changes to the brain through type Ib afferent fibres. Moreover, Ib afferents actually respond to the induced muscle tension of a tenth of a gram or less (Binder et al. 1977).

The Ia, Ib and II afferent fibres generate spinal stretch reflexes and supraspinal responses (i.e. sensory-motor feedback loop), which assist with the control of the muscle contraction. Whenever a muscle is stretched, the excited spindles cause reflex contraction of the same muscle and also the synergistic muscles. The dynamic response is over within a fraction of a second while a weaker static stretch reflex continues for a prolonged period. The information about the position and motion of the limbs is called propriocetion and it is provided both by the overt consequences of humans actions perceived through the eyes and ears, and the sensory receptors (Rosenbaum 2009).

Muscle tone is generated by the muscle spindles acting through the stretch reflex. Muscle tone is the constant muscular activation as a background to an actual movement in order to maintain the basic posture of the body, particularly against the force of gravity. As tone opposes the movement and tends to keep muscles at preset lengths, it has to be changed in steps during a movement. Muscle tone passing a threshold of a comfortable common state is diagnosed as a *hypertonic muscle*, meaning that the muscle has "too much tone".

The stretch of a muscle activates Ia afferent fibres to produce excitation of α motoneurons. In addition to the inhibition of the α motoneurons, there are innervating antagonist muscles

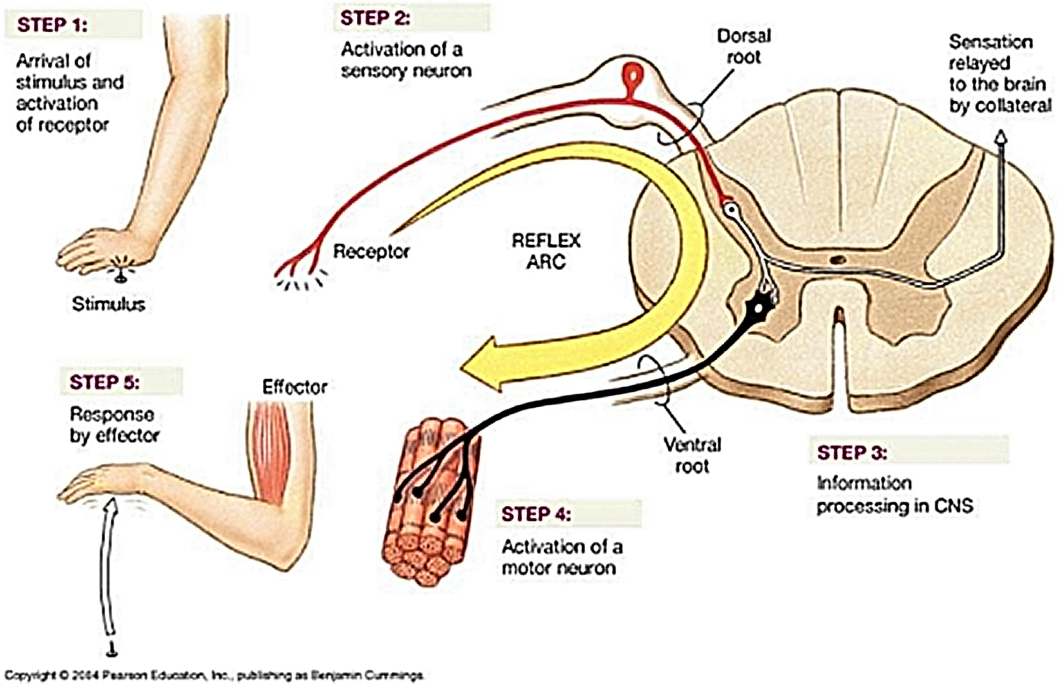


Figure 2.10: Spinal stretch arc reflex is a closed loop reaction to an external stimulus. As the stimulus is perceived by the sensory system and information transmitted to the spine, the spine generates a motor response to protect the body in a form of a corresponding muscle contraction (i.e. movement) (*The Reflex Arc and Selected Reflexes* 2015).

(reciprocal inhibitors). As well as the established role of group II fibres, these fibres are known to produce a flexion reflex by exciting the flexors α motoneurons and inhibiting the extensors motoneurons. Ib afferent fibers from Golgi tendon organs also receive diverse segmental and supraspinal inputs, such as Ia afferents. Therefore, Ib inhibition is not a simple autogenic inhibitory safety mechanism to regulate muscle tension only. It is a part of complex system regulating muscle tension to control muscle tone, posture and movement (Mukherjee & Chakravarty 2010). The excitatory and inhibitory actions of muscle efferent fibres caused by the segmental and supraspinal responses to afferent sensory stimulation is called spinal stretch arc reflex (presented in Figure 2.10) and one of its main roles is to protect the contracting muscle from damage. Reflexes can be:

- monosynaptic reflex - mediated by a connection between one sensory neurone and one motoneuron. Depending on the sensory signal charge, motoneuron generated a reciprocical response.

- polysynaptic reflex - mediated by one or more spinal interneurons between afferent and

efferent pathways. With interneurones involvement, sensory signal strength can be altered to consider several muscles responses and accordingly excite one or more motoneurons.

A sudden, involuntary, usually short term muscle contraction is called a spasm. Spasms in skeletal muscles often occur when the muscle is fatigued, dehydrated or chemically (electrolyte) imbalanced. Spasms in smooth muscle tissues can cause significant pain. Spasms of the heart muscles are the most dangerous as they can lead to heart lesions and even death.

The upper motor neuron UMN syndrome is when the motor control changes in skeletal muscles following lesion of the upper motoneurons, usually after SCI, CP, MS, stroke or similar CNS injuries. Among others, the UMN syndrome can cause muscles to weaken or alter the muscle tone, leading to a decrease in motor control, accuracy and dexterity. Spasms continuous over longer period of time are called tonic muscle spasms and have to be investigated immediately by medical experts as they can be caused by the deadly bacterial infection *Clostridium Tetani*. The term *spasm* must be distinguished from the term *spasticity* even though some of the symptoms are similar.

2.5 Upper Limb anatomy

The human skeleton can be divided into two parts:

- Axial skeleton − bones of the central core of the body which includes the head, vertebral column and rib cage. It is derived from the word *axis* to represent its proximity to the central axis of the body.
- Appendicular skeleton − bones of the extremities: hands and legs. Derived from the noun *appendage* which means a part that is attached to something larger.

The superior appendicular skeleton (or the upper limbs) consists of 64 bones and 45 muscles. The upper limbs are divided into four main regions by the shoulder, elbow and wrist joints (Figure 2.11):

- Shoulder − proximal segment of the limb which connects the arm with the trunk. Muscles and tendons attached to the sholder can control the arm's movements.

- Arm (*L. brachium*) – the first mobile segment of the upper limb that can move independently from the trunk. It extends between the shoulder and the elbow via the *humerus*bone. Muscles in the arm control movements of the elbow joint and subsequently the forearm.

- Forearm (*L. antebrachium*) – the second longest segment of the upper limb which extends between the elbow and the wrist via two bones: *ulnar* and *radial*. Muscles in the forearm are responsible for the flexion and extension of the wrist.

- Hand (*L. manus*) – the most distal part of the upper limb and mostly used to manipulate objects. It extends from the forearm via the wrist and consists of the wrist, palm, dorsum of hand and fingers. This part of the body is richly supplied with sensors for touch, pain and temperature.

The upper limbs are highly mobile for positioning their different parts and, most importantly, the hands in space, some of which are presented in Figure 2.12a). Range of motion is a maximal angular distance that a joint can travel in a certain direction. The shoulder joint allows the arm to move around three axes with a wide range of motion. Movements of the arm about this joint are flexion and extension, abduction and adduction, medial rotation (internal rotation), lateral rotation (external rotation), and circumduction, all presented in Figure 2.12b). The major movements of the forearm are flexion and extension above the elbow joint and pronation and supination. At the wrist joint, the hand can be abducted, adducted, flexed, extended, and circumducted. The hand has five digits: four fingers and one thumb. The fingers consist of three phalanges each, that can be flexed and extended and abducted and adducted. The thumb has only two phalanges. However it has more

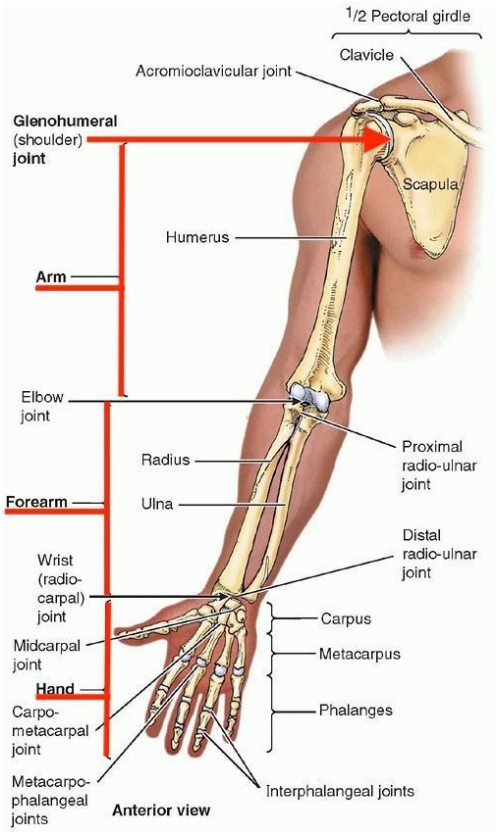


Figure 2.11: Bones of the upper limb divide the superior appendicular skeleton (i.e. the upper limb) into four main segments: shoulder, arm, forearm and hand (*Bones of the upper limb* 2018).

movement than the fingers: flexion, extension, abduction, adduction and opposition and reposition.

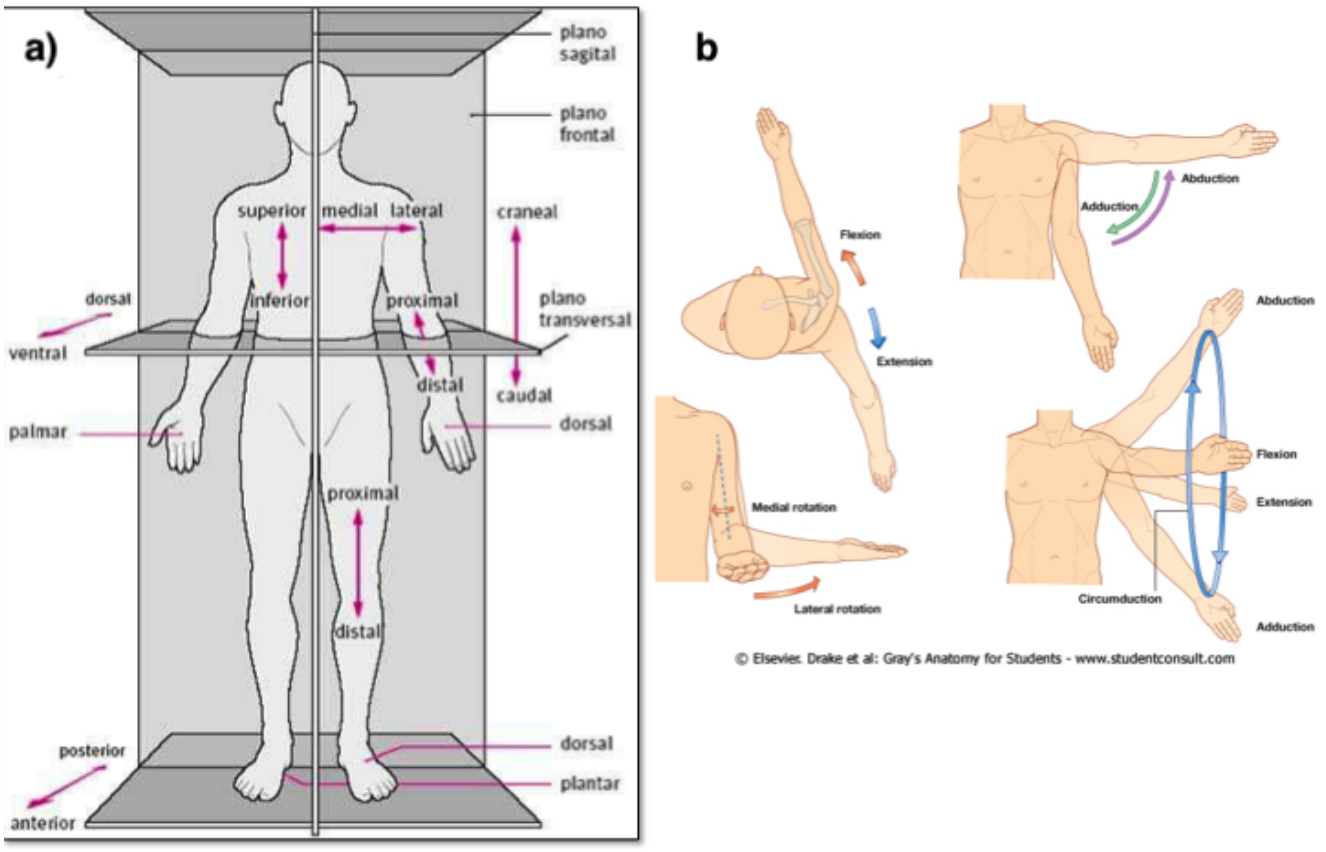


Figure 2.12: a) Planes of the body b) Upper limb movements in different planes (Drake et al. 2009).

2.5.1 Forearm

The forearm extends between the elbow and wrist joints. It provides additional functionality and more movement abilities to the upper limb and the hand. A total of 20 muscles are localised in the forearm and divided into two fascial compartments (Figure 2.13). The posterior compartment (represented in pink in Figure 2.13c) is supplied by the radial nerve and contains the extensors of the hand and wrist joint. The anterior compartment (represented in gold in the same figure) contains flexor muscles that are supplied by median and ulnar nerves. The flexor muscles are bigger in mass than the extensors, because they work against gravity to act as an anti-gravity support. Other forearm functionalities include flexion and extension of the fingers, flexion of the elbow, pronation and supination of the hand.

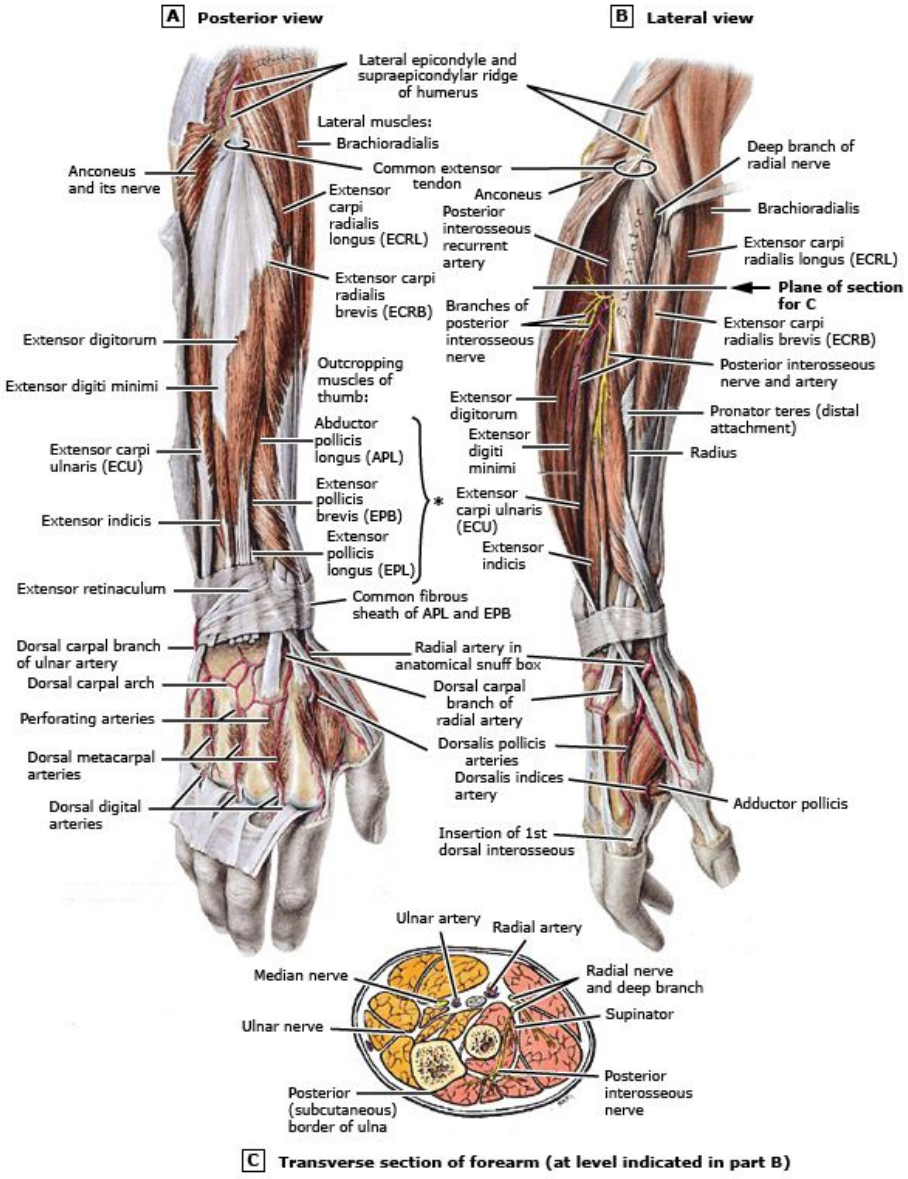


Figure 2.13: Muscles of the forearm are presented in A) posterior view of the superficial extensor muscles, B) lateral view of the deep extensor muscles and C) transversal view of both superficial and deep flexors (in gold colour) and extensors (in pink colour) (*Forearm muscles* 2018).

Dependent pairs of movements which allow the forearm and the hand to rotate in order to "face down" or "face up" are called *pronation* and *supination*, respectively (Figure 2.14). These movements occur when the radius pivots around the static ulna using the proximal and distal radio-ulnar joints. Due to the appearance of the angular displacement of the hand around its long axis, it is often mistakingly assumed that the movements are produced by the wrist.

Muscles of a special interest for chapter 7 are the wrist flexor and extensor muscles, presented

in respect to the location in the forearm:

- parts of the superficial posterior compartment
  - Extensor carpi radialis longus
  - Extensor carpi radialis brevis
  - Extensor digitorum
  - Extensor digiti minimi
  - Extensor carpi ulnaris
- parts of a deep posterior compartment
  - Extensor indicis
  - Extensor pollicis longus
  - Extensor pollicis brevis
  - Abductor pollicis longus
- superficial anterior compartment
  - Flexor Carpi Radialis
  - Palmaris Longus
  - Flexor Carpi Ulnaris
- intermediate anterior compartment
  - Flexor Digitorum Superficialis
- deep anterior compartment
  - Flexor Digitorum Profundus
  - Flexor Pollicis Longus

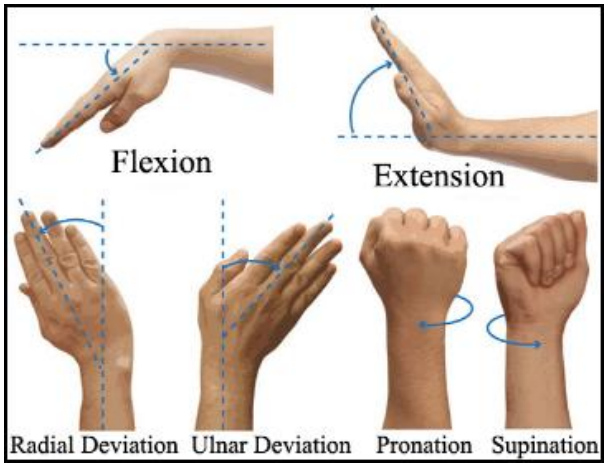


Figure 2.14: Hand movements. The wrist has 6 degrees of movement for the rotation and translation. Except for the pronation and supination which occur in the forearm, the wrist can flex or extend the hand, or position it in radial or ulnar deviation (*Is pronation/supination a movement part of the wrist or the...* 2013).

2.5.2 Hand

According to the Encyclopaedia Britannica, "the hand is a grasping organ at the end of the forelimb of certain vertebrates that exhibits great mobility and flexibility in the digits and in the whole organ. The major function of the hand in all vertebrates except human beings is locomotion; bipedal locomotion in humans frees the hands for a largely manipulative function" (*Hand anatomy* 2018). The hand has total of 27 degrees of freedom: 4 in each finger; the thumb is has 5 DOF, leaving 6 DOF for the wrist (ElKoura & Sing 2003). Parts of the hand and the wrist are controlled by muscles in the forearm via tendons extending to the actuators, and parts are controlled by the hand's internal muscles to achieve all the movements listed in the beginning of this section.

The muscle of the hand that is of most interest for this thesis is a first dorsal interosseous muscle mFDI, see Figure 2.15. The main role of the mFDI is to abduct the index finger, meaning to move it away from the finger's middle line. This muscle is used in experiments described in Chapters 5 and 6. The reason behind the selection of this muscle is its position in respect to the other muscles of the hand: this muscle is a superficial autonomous muscle within the range from the base of the thumb to the base of the index finger.

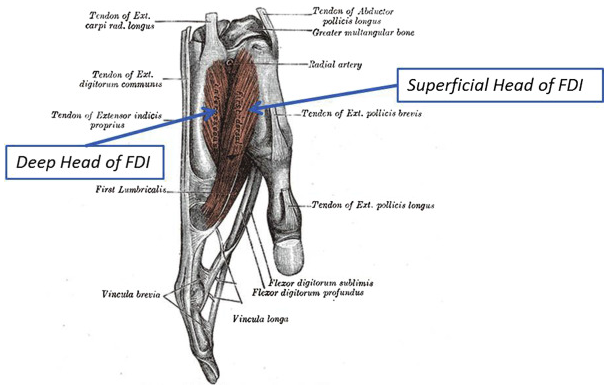


Figure 2.15: The first interroseous muscle is responsible for the index finger abduction and adduction (*Dorsal Interossei of the hand* 2018).

2.6 Electrophysiological Signals

Since the discovery of current and the flow of ions, scientists and medics have tried to exploit its properties for healing. Coupled with technological advances, nowadays there are many diagnostical tools, treatments, rehabilitation paradigms and many other medical means used to provide the best care. *Electrophysiology* is a branch of science dedicated to the study of the electrical and magnetic properties of biological cells and tissues. Recordings of electrical and magnetic signals from the body are widely used to monitor and diagnose, the most well-known being ECG or electrocardiography, the recording of electrical activity of the heart. As many as there are, only a few of importance for this thesis will be introduced in this section.

Electrophysiological signals are usually recorded using *electrodes*, an electrical conductor that can make contact with nonmetallic parts of a electrical circuit. A variety of different electrode types are used depending on the tool.

2.6.1 Electromyography

"Electromyography EMG is an experimental technique concerned with the development, recording and analysis of myoelectric signals. Myoelectric signals are formed by physiological variations in the state of muscle fibre membranes" (Basmajian 1962). An alternative definition is "the neuromuscular activation of muscles within postural tasks, functional movements, work conditions and treatment/training regimes" (Konrad 2005).

EMG can be recorded invasively using needle electrodes inserted into the muscle tissue. However, to avoid potential damage to the muscle and skin, surface EMG recording is preferred. Surface electrodes are easily positioned to the skin above the muscle using adhesive, hypoallergenic and easily removable gels. Depending on the position of the electrodes against the muscle of interest, the recording can be:

- monopolar recording - one electrode is positioned over the muscle and the other on the neutral tissue such as bone.
- bipolar recording - both electrodes are positioned on the muscle with a few centimetres apart.

Typical charge of the surface EMS is only a few millivolts, typically 1-3mV. That is why these signals are usually amplified. Thus EMG is susceptible to noise accumulation. Many hardware and software techniques are used to filter the noise and analyse the properties of EMG, some of which are used in this thesis.

EMG is used in medical diagnosis, rehabilitation therapies, sports science and ergonomics design and analysis.

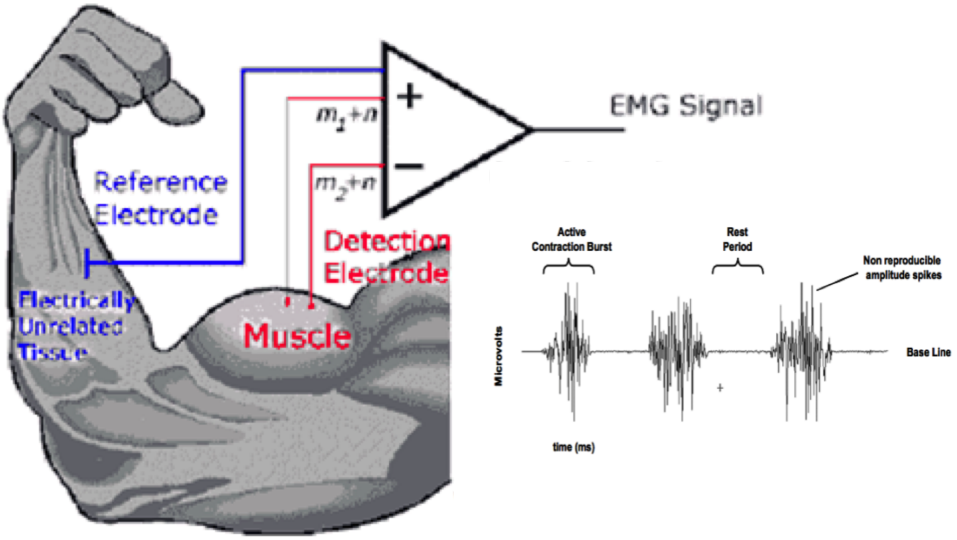


Figure 2.16: Typical EMG bipolar recording setup with the generated EMG signal (*Electromyography* 2016).

EMG signals have a great feature of easily (even visually) distinguishing between times when the muscle is contracting and when it's resting, as seen on the signal from the Figure 2.16. More signal analysis can determine the level of muscle fatigue during or after continuous contraction.

2.6.2 Electroencephalography

"An electroencephalography EEG signal is a measurement of the electricity that flows during synaptic excitations of the dendrites of neurons in the cerebral cortex. When brain cells are activated, the synaptic currents are produced within the dendrites. This current generates a magnetic field and a secondary electrical field over the scalp measurable by an EEG system" (Chambers & Jonathan 2007). These signals are only 10-100 microvolts in amplitude when measured from the scalp because of the layers of bone (skull), and non-neural tissues protecting the brain.

There are two main ways of measuring EEG signals: invasive and superficial. The invasive method implies implantation of arrays of needle electrodes deep in the cerebrum. Aside from the exposure of the brain to the pathogenic outside world, these needles are very likely to hurt neurons and cause disruption in communication, leading to the brain damage and serious consequences to the body. Nonetheless, information recorded via this method is very helpful in deciphering the information from the depths of the brain and individual cell firings, unlike superficial EEG recording. Superficial EEG records a summary of the neural activity over the entire cortex, at least those signals reaching the electrodes.

EEG caps are used for superficial EEG recording. Electrodes, whose number can be as little as 16 to as many as 256 or more, are spatially arranged corresponding to different areas of the brain (frontal, central, parietal, occipital, temporal). To ensure contact with the scalp and suppression of hair interference, water based, easily washable gels, are used to ensure better conductivity. Amplifiers and hardware filters are used to suppress noise. Still, these signals need to be processed in order to extract the most useful information.

When processing EEG signals, one would look to extract features correlated to the specific task in question. For example, these features can be changed in signal frequencies or amplitudes. It is noted that brain signals have different frequency bands depending on the state of the body:

- delta δ waves - lies within a range of 0.5 to 4Hz and are related to very deep sleep.
- theta θ waves - ranging between 4 and 7.5Hz are associated with conscious sleeping, dreaming, deep meditation. Abnormal theta waves are very important in detecting pathologies.
- alpha α waves - are usually observed over the posterior part of the head, especially the

occipital part of the cortex. Frequency ranges between 8 and 13Hz are commonly sinusoidal shaped and correlated to relaxed continuous awarenesses with no attention or concentration. It is observed that alpha waves are usually produced when the eyes are closed, disappearing once the eyes are opened or when auditory or other distractions occur. This is why it has been claimed that it is nothing but a waiting or scanning pattern produced by the visual regions of the brain.

- mu μ waves - have a similar range as alpha waves (between 7.5 to 12Hz) however they are observed over the anterior parts of the brain, over frontal, primary motor and sensory cortex. The mu rhythm is observed during relaxed states of the body with no intention to move, while suppression of these waves are observed during motor tasks or even imaginary motor tasks.

- beta β waves - cover the ranges of 14 to 26Hz, sometimes up to 35Hz. They are characteristic during motor movements such as hand movements or walking, as well as focused states during thinking, problem solving, learning, and similar activities.

- gamma γ waves - frequencies above 30Hz having very low amplitude are rare signals and can occur during certain pathologies.

Besides frequency analysis and correlation to certain tasks, signals observed before, during or after specific events such as sensory, affective or cognitive events, are called *evoked potentials*. Among many of them some are *event related potentials* (ERP) and *event related desynchronisation/synchronisation* (ERD/ERS, respectively) (Pfurtscheller & da Silva 1999). ERPs have a smaller amplitude from 1 to 30uV relative to the background EEG activity because they are a time-dependent summarised action potentials response to sensory, motor or cognitive events. There are a variety of individual signals related to certain stimuli and recorded either during or with a specific latency in respect to the stimuli; one example is a visual N1 signal detected after a visual stimuli recorded about 150-200ms post-stimulus. In contrast, ERD and ERS are observed changes in amplitude of certain wave bands. Event related desynchronization (ERD) is "a short-lasting and localized amplitude decrease of rhythmic activity" (Dujardin et al. 1993), while the amplitude enhancement is called event related synchronisation (ERS). These observations are widely

used in brain computer interfaces BCI to link brain signals for producing an action. Another type of evoked potential is a *somatosensory evoked potentials* observed during tactile or electrical stimulation, even possibly vibration stimulation.

2.7 Chapter summary

This chapter has introduced a background to a human anatomy and electrophysiological considerations. A special appreciation is given to the upper limb muscle and bone structure, muscle contraction and voluntary control. The last section briefly comment on two main measurements of the electrophysiological signals from the body. This thesis relies on the the principles and terminology presented in this chapter.

CHAPTER 3

Spinal cord injury, spasticity and rehabilitation methods

With chapter 3, a familiarisation with a spinal cord injury and an adverse repercussion spasticity is made. This chapter epitomise spasticity physiology, quantification contrivances and treatment resources.

3.1 Spinal cord injury

A spinal cord injury SCI can be traumatic and non-traumatic. Non-traumatic SCI can be caused by genetic, metabolic, degenerative CNS disorders, infections, tumours and all other disease related states. Traumatic SCI results after mechanical injury to the vertebra column.

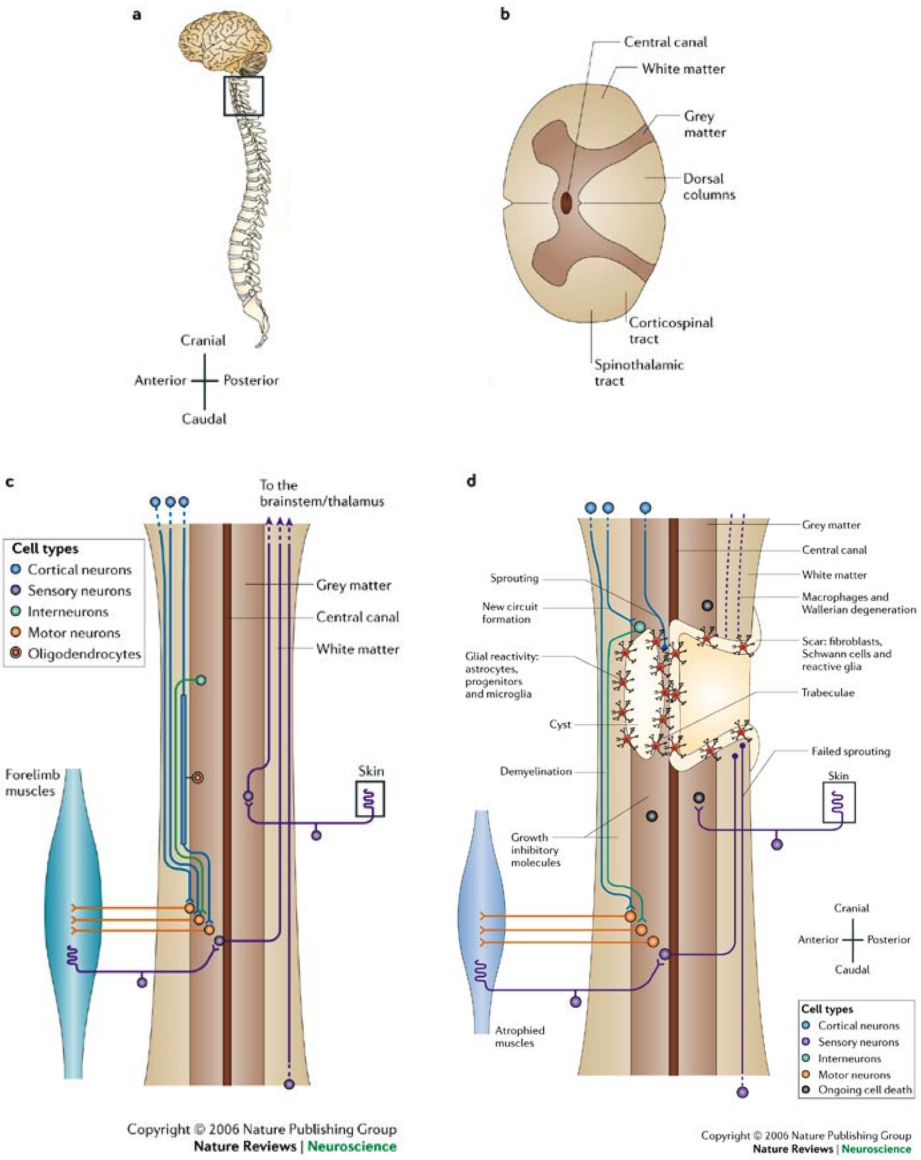


Figure 3.1: (top) a) Sagittal view of the CNS with cervical spine selected. b) Transversal view of the spinal cord. (bottom) Schematic representation of spinal cord injury from sagittal view. Picture c) represents intact spinal cord. Picture d) demonstrate penetrating injury, cells from the PNS often invade the injury site to form a connective tissue scar. Many ascending and descending axons are interrupted and fail to regenerate over long distances. Some axons form new circuits with motor neurons via interneurons (Thuret et al. 2006).

Direct compression of the neural elements by fractured and displaced bone fragments, disc material, and ligaments injures both the central and peripheral nervous systems. Blood vessels are damaged, axons disrupted, and neural-cell membranes broken, as shown on the d) part of the Figure 3.1 (bottom right). Within minutes, the spinal cord swells to occupy the entire diameter of the spinal canal at the injury level. Auto-regulation of blood flow ceases. Ischaemia, release of toxic chemicals from disrupted neural membranes, substantially compounds initial mechanical damage by harming or killing neighbouring cells (McDonald & Sadowsky 2002). Any resulting cavities and cysts may interrupt descending and ascending axonal tracts, although the white matter is often spared. After the initial insult to the spinal cord, additional structure and function are lost through active secondary processes. Demyelinated axons are observed up to a decade after human SCI, and the extent to which these axons survive unmyelinated or become remyelinated by central or peripheral myelin (Guest et al. 2005, Totoiu & Keirstead 2005). SCI culminates in glial scarring. While healthy glial cells surround, protect, supply nutrients and support for both neurons and insulation between them, scarred glial cells can no longer perform some or all of those tasks. Progressive expansion of the injury across more than one segment (syringomyelia) can also occur over months or years, sometimes proving fatal (Thuret et al. 2006).

All above-mentioned processes occur moments after the injury and it is therefore referred as primary injury causing an irreversible damage. Secondary injuries are not precisely classified by time, but are rather considered as long-term changes and reorganisation within the spine, NS and the entire body as a response to the injury. Some of those repercussions are spasticity, brain and neural reorganisation, muscle atrophy, organs dysfunction and/or failure etc.

The American Spinal Injury Association ASIA first published an international classification of spinal cord injury in 1982, called the International Standards for Neurological and Functional Classification of Spinal Cord Injury. Now there are several editions know as International Standards for Neurological Classification of Spinal Cord Injury ISNCSCI (Kirshblum et al. 2011). One classification is based on the remaining abilities below the point of injury due to SCI and are categorised as (Kirshblum et al. 2011):

- Complete − there is an absence of sensory and motor function in the lowest sacral segments (S4-S5)

- Incomplete − there is a preservation of any sensory and/or motor function below the neurological level that includes the lowest sacral segments S4−S5

Based on the types of paralysis caused by SCI, the classification is (Kirshblum et al. 2011):

- Tetraplegia (also called quadriplegia) − impairment or loss of motor and/or sensory function in the cervical segments of the spinal cord due to damage of neural elements within the spinal canal. Tetraplegia results in impairment of function in the arms as well as typically in the trunk, legs and pelvic organs, i.e. including the four extremities.

- Paraplegia − impairment or loss of motor and/or sensory function in the thoracic, lumbar or sacral (but not cervical) segments of the spinal cord, secondary to damage of neural elements within the spinal canal. With paraplegia, arm functioning is spared, but, depending on the level of injury, the trunk, legs and pelvic organs may be affected.

Taking into consideration the locations of injury within spinal column, SCI can be divided into (*Spinal Injuries Association* 2014):

- Cervical − injuries within the cervical region, usually resulting in tetraplegia. However, depending on the specific location and severity of trauma, limited function may be retained.

- Thoracic − injuries at or below the thoracic region result in paraplegia. Functions of the hands, arms, neck, and breathing are usually not affected.

- Lumbosacral − injuries resulting with decreased control of the legs, hips, urinary system, anus and sexual dysfunction

These classifications are sometimes fused together to form a complete physiological understanding of the SCI type. For example *traumatic incomplete cervical C3 tetraplegia* means the traumatic injury in a neck area around cervical vertebra C3 which caused partial loss of motor and sensory functions from the neck down.

Acute SCI is consider to be a timeframe in the first six months post injury. Additionally subacute phase of the SCI is the time between hospital discharge until 3 months post-discharge. Chronic SCI is after six months post injury where the injury is mostly healed, stabilization of the spinal vertebra reinforced and the person achieved a level of independence.

3.2 SCI motor function rehabilitation

The anatomical impact of SCI on the body is significant, with outcomes depends on the nature, severity and level of injury. There are several approaches to SCI management and rehabilitation mainly concerning the application in acute or chronic phase. The stabilization of the spinal vertebra and surgical approaches of repercussions minimisation take place in a few days post injury. McDonald & Sadowsky (2002) summarised the aspects of SCI management in table 3.1. Rehabilitative methods are targeting restoration of the function of the respiration, bowel and bladder functions, prevention or management of musculoskeletal complications and a restoration of functional participation in a daily living.

Table 3.1: Overview of the traditional management of the spinal cord injury (McDonald & Sadowsky 2002).

Medical	Surgical	Rehabilitative
Spinal stabilisation: spine immobilisation during transport and resuscitation	Internal fusion/instrumentation; external orthoses	
Cardiovascular: haemodynamic instability; autonomic dysfunction; thromboembolism		Management of chronic haemodynamic issues; autonomic dysreflexia
Respiratory system: respiratory failure; atelectasis; pneumonia; vent-dependent care	Tracheostomy	Preventive respiratory care; respiratory conditioning programme
Gastrointestinal system: ileus; impaction, constipation; gastric and duodenal ulcers; GORD, cholelithiasis		Establish predictable bowel continence programme; preventive gastrointestinal care
Genitourinary system: urinary-tract infection; hydronephrosis; cycto/nephrolethiasis	Urinary system augmentation; diversion procedures; penile implants; lithotripsy; sphincterotomy	Programme to establish bladder continence; preventive genitourinary care; sexual dysfunction programme
Dermatological: pressure ulcers	Pressure ulcer repair	Establish skin integrity programme; prevent and manage pressure ulcers
Musculoskeletal system: osteoporosis; heterotopic ossification; fractures; overuse syndromes; acute and chronic pain	Treatment of delayed neurological and spine complications: syringomyelia; focal nerve entrapments; central pain, spasticity; spinal instability; implantation of intrathecal drug-delivery systems	Prevent/manage musculoskeletal complications: contractures; spasticity; postural abnormalities; skeletal deformities; long-term intrathecal drug treatment
		Functional retraining in self-care; mobility; psychosocial adaptation; vocational and recreational skills; adaptive equipment and orthotic devices

GORD=gastro-oesophageal reflux disease.

Considering the limited level of knowledge about anatomical and physiological processes reflecting CNS functioning after the injury, the diversity of symptoms underlying lesions and the unavailability of research resources, there are no universal rehabilitation packages, medical treat-

ments or other approaches for treating SCI (Whiteneck et al. 2009). However, over the past 20 years, in parallel with technological development, numerous research groups throughout the world have started investigating different methods and possibilities to, primarily, enhance locomotor movements for SCI patients. The first breakthroughs were the results of experiments with cats and treadmills, when it was established that after intense training, cats could support their full weight body but couldnt properly step on the treadmill (De Leon et al. 1998, Tillakaratne et al. 2002). From then on there are several directions of engineering approaches for overcoming walking disabilities: brain computer and machine interfaces (BCI and BMI, respectively), pharmaceutical and/or neuroprosthesis, robot mediated therapy and neurorehabilitation, various forms of electric stimulation (ES) etc.

Challenges of the motor rehabilitation after the injury include the inability of the spine to reconnect damaged sensorimotor pathways and the inability to reorganize the NS to adapt to the change. Because the restoration of movement is important goal of SCI rehabilitation, inducing reconnection of descending motor pathways is crucial. Lemon (2008) reported that even though different descending pathways are in charge of different operations within motor control, functionality that one may have can be diverse, concluding that even small amount of connectivity may serve some special functionalities within adaptive motor behaviour (Lemon 2008). De Leon et al claim that treadmill exercises in cats reinforce the functionality of existing motor pathways rather than recreating new ones (De Leon et al. 1998). While some studies carried out on adult rats insist that spinal cords spontaneously remodel and form new intraspinal circuits (Bareyre et al. 2004), others have demonstrated that functional recovery can occur simply by the reorganization of descending pathway connections (Courtine et al. 2008). Studies on macaque monkeys showed that even after changes within motor pathways occur towards the functional restoration of movements, some muscle groups have greater bias towards recovery while some, innervated by the same neurons, remains paralyzed (Zaaimi et al. 2012). Edgerton et al. (2008) emphasize that, after SCI, sensory information can be used by the spinal circuitry to actually control and not just modulate locomotion therefore proving the importance of preservation of sensory pathways. This finding demonstrates that sensory input plays a significant if not the most important part in driving stepping activity in rodents. However, many of these findings from animal studies may be important, Lemon states that there is a significant difference within descending pathways within mammal

species (Lemon 2008). Post mortem human spinal cord tissue analysis has revealed anatomical changes in the motor pathways markedly different from those found in animal models (Oudega & Perez 2012). The lack of more comparison studies is directly proportional to the invasiveness of neural recording that subjects have to undergo in order to obtain comparable data. Even non-invasive methods such as CT or fMRI demand special preparation of subjects, especially animals, and cannot be applied with conventional robotic movement assistance, because of the limitations of these devices.

A brain-computer interface BCI, sometime referred to as a brain-machine interface BMI, is a hardware and software system that helps navigate and interact with the surroundings using electrophysiological signals from the brain. BCI systems first acquire signals from the brain using neuroimaging methodology. Signals are then preprocessed, cleared of any artefacts and noise, and amplified to obtain a distinct features. Feature extraction algorithms find discriminative information from recorded signals and classify user's intentions using patter recognition methods. This act intention is transferred to a control signal that helps the user perform an action using supporting hardware or output devices. The hardwares used to deliver an action are diverse. Some research groups use wheelchairs (Carlson & del R Millán 2013, Rebsamen et al. 2010) while others are more focused on robotics for restoring grasping abilities (Hayashi et al. 2012, Kaiser et al. 2011, L Collinger et al. 2013) or use of functional electrical stimulation (Pfurtscheller et al. 2005). There has been a particular focus on robots driven with EEG. They are widely used for rehabilitation. Hayashi et al. (2012) proposed an EEG-driven assistive robot for upper limb rehabilitation after strokes, (Müller-Putz et al. 2005) Kaiser et al. (2011) similar approach after SCI and L Collinger et al. (2013) EEG controlled prosthetic limb. BCI, as non-invasive approach for SCI rehabilitation, is being investigated profoundly to optimise the method. This means that there is a lot of effort that SCI patients need to undergo to generate a control signal, while hardware systems and robotic platforms are still in an experimental stage and are too expensive for mass production. But the main disadvantage of this method is that users with SCI have to focus their brain waves for BCI and cannot perform any other tasks whatsoever during BCI control.

Electrical stimulation ES delivers current to the nerve or muscles in order to evoke an action potential in the nerve fibers that induces muscle contraction. ES can be delivered through electrodes from the surface of the skin (surface, transcutaneous ES), from just under the skin (percutaneous)

or electrodes that can be implanted. Functional electrical stimulation FES restores or achieves function of a paralyzed muscle. FES is commonly used for improving motor function in patients with SCI. Lynch & Popovic (2012) used FES to control knee movements, de N Donaldson & Yu (1996), Donaldson et al. (1997)for standing, Bajd et al. (2000), Guiraud et al. (1999), Kobetic et al. (1997, 1999) for walking and Perret et al. (2010) for cycling. FES is also used for upper limb rehabilitation for individuals with SCI (Ethier et al. 2012, Hasnan et al. 2013, Pfurtscheller et al. 2005). However, the justification of the use of FES as a rehabilitation tool is questionable because different research groups report different success rates, questioning the repeatability of this method for a prolonged period of time (Bersch et al. 2013, Hamid & Hayek 2008, Martin et al. 2012, Ragnarsson 2007).

A new concept, combining electronic and pharmaceutical approaches, is giving promising results regarding SCI rehabilitation (Borton et al. 2014, Musienko et al. 2012, 2009). Corticospinal neuroprostheses use implantable electrodes and pharmaceutical compounds in order to regain control of the information delivery within the spine after SCI. Implanted electrodes deliver specific current pattern to the lesion while pharmaceutical agents are injected prior to the stimulation intraperitoneally or subcutaneously in order to induce electrical and chemical reaction. This results in descending pathways reconnecting, thus regaining information delivery through damaged spinal pathways. Courtine et al. (2009) showed that this method induced the stepping of hind paws in mice with SCI. Harkema et al. (2011) performed a case study on a human with complete motor SCI. Results showed that 7 months after the implantation, the subject regained certain leg movements but only with FES. The physiological mechanisms supporting these results remain unknown. However, these findings opened the door for several research groups to approach this problem from a variety of angles: using computational models to better understand FES (Capogrosso et al. 2013) or creating a closed loop control system for rehabilitation (van den Brand et al. 2012, Zimmermann & Jackson 2014). ES and corticospinal neuroprostheses gave promising results for SCI locomotion restoration. However, this method is quite invasive and demands a lot of medical care.

The development of electrical stimulation and the diversity of the stimulation parameters brought the need for development of surface electrodes made of different materials, with a variety of shapes, pad numbers and stimulation framework. Multi-pad surface electrodes gave functional grasping movements in stroke patients (Jevtic et al. 2013, Popovic-Maneski et al. 2013). On the other

hand, electrical stimulation applied through the skin can induce only the simple sensation of touching or stinging (Stevanovic-Karic et al. 2013), evoking sensory ascending pathways. Melzack & Wall (1967) reported the effect of neuromodulation for chronic pain relief back in 1965, giving a scientific basis for transcutaneous electrical neurostimulation (TENS) used for pain treatment. Moreno-Duarte et al. (2014) reported several clinical trials where different stimulation paradigms were tested on SCI patients. These findings imply that there is an effect of TENS on CNS and that CNS is responding to this input. Applying TENS on the spinal cord induces changes in the H-reflex at the soleus muscle (Lamy et al. 2012, Winkler et al. 2010), changes of evoked potentials at the tibial nerve (Cogiamanian et al. 2008, Hubli et al. 2013) and has inconsistent effects on the bodys blood flow (Visocchi et al. 2011). Cogiamanian et al. (2012) presented evidence that TENS induces changes in spinal cord functionality, however mechanisms underlying these changes need further investigation.

Since the industrial revolution there is a tendency to replace humans with robots for specific tasks. Considering that rehabilitation is a long-term process that demands repeatability, automation and precision, it is only natural to employ robotic assistance or complete independency in performing rehabilitation models. Although physiotherapeutic assistance and decision-making abilities are irrepressible, greater autonomy for people with SCI is required, especially if rehabilitation paradigms can be carried out at home with no need for hospitalization. The main types of robot for rehabilitating upper extremities, are shown on Figure 3.2:

- End effectors provide a single interaction point with a subjects forearm. Combining multiple end effector systems, several robots can be used for bilateral or multiple site hand manipulation. Examples of these robots are MIT/IMT-Manus (Hogan et al. 1992), MIME (Lum et al. 1999), BI-Manu-Track (Hesse et al. 2003) Gentle/S (Loureiro et al. 2003), ARMEO (Calabrò et al. 2017).

- Exoskeletons confine the arm within a robot mechanical skeleton in order to gain maximal control over joints. Some provide full and some partial arm support and control. Examples are MPL (L Collinger et al. 2013) T-WREX (Sanchez et al. 2006)[92].

- Combination combine both end effector and exoskeleton approaches in order to obtain more accurate control and greater manipulation possibilities as ROBIN (Loureiro & Smith 2011).

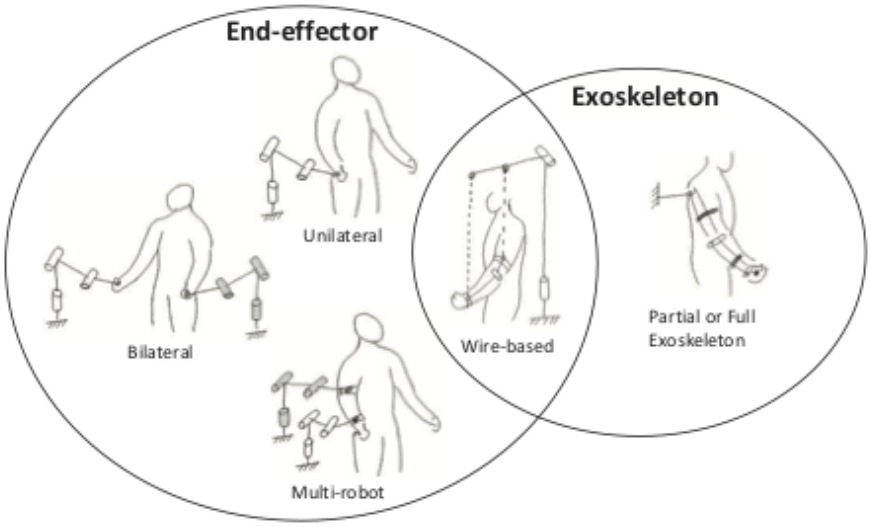


Figure 3.2: Graphical representation of different robot configuration (Loureiro & Smith 2011).

All of these robots are reporting a remarkable results in motor function enhancement. However one remark for these systems is a lack of measurement of rehabilitation progress or any specific rehabilitation outcome. The need of more inclusive robotic devices is commented in following sections. To further the discussion on the overall SCI rehabilitation, the need of inclusiveness in different rehabilitation methods is an imperative for moving forward. This is because, as observed from this section, different up-mentioned methods elicit different neural and motor structures which, in fact, are working together to obtain motor control. With deep appreciation of individual evaluation in clinical settings, perhaps the focus should shift to designing or combining existing approaches to a single one, tailored for addressing the symptoms and desired outcomes for each participant independently.

3.3 Spasticity

The term *spasticity* is inconsistently defined and measured (Malhotra et al. 2009). The most commonly used definition is that of Lance where spasticity is "a motor disorder, characterised by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex as one component of the upper motor neurone UMN syndrome" (Lance 1980). The broader definition is proposed by the EU-SPASM

consortium: "Assuming that all involuntary activity involves reflexes, then spasticity is intermittent or sustained involuntary hyperactivity of the skeletal muscle associated with an UMN lesion". Clinical spasticity manifests as an increased resistance during passive stretching of the muscle, sometimes accompanied with increased tendon reflexes, muscle spasms and clonus.

Most broadly speaking, spasticity is caused by an imbalance of signals from the NS to the muscles and vice versa, due to NS injury or disease. In another words, the lose of control of the reflexes (Sheean 2002). Similar to the upper motor neurone UMN syndrome, this imbalance is therefore mostly found in people with cerebral palsy, traumatic brain injury, stroke, multiple sclerosis, Parkinsons disease, SCI, and similar.

In the early 1950s, the scientific community was introduced to the muscle anatomy and spindles, tendon organs, afferent nerves etc. Interestingly, the spasticity mechanisms were widely explored using vibrations during late 1950s and 1960s because it was found that in healthy body with no disorders nor diseases, vibration stimuli to the muscle or tendon induces only activation of the Ia afferent nerves (Hagbarth & Eklund 1966*a*).

Since then, general opinion appears to be divided by two schools of thought (Ibuki & Bernhardt 2007):

- one that correlates spasticity with hypertonic muscles. Physiological changes in the muscle structures such as fibres, spindles and GTO could be the cause of the mechanical resistance during velocity dependent passive movements of the limbs. The changes in the spindles' and GTOs' thresholds can affect type Ia, Ib and type II afferents and alter presynaptic and postsynaptic firing rate. Interestingly the presynaptic inhibition of the Ia afferents is reduced in spasticity associated with multiple sclerosis and spinal cord injuries but not in hemiplegia after stroke (Burke & Ashby 1972, Faist, Mazevet, Dietz & Pierrot-Deseilligny 1994). Additionally the GTO afferent reflexes are unaltered after SCI in humans (Brown et al. 1967).

- the other proposing it as a combination of positive and negative symptoms of the upper motor neurone UMN lesion. Upper motor neurons are those pathways above the anterior horn of the spinal cord, originating in the cortex. Loss of the motor control of the spinal reflexes due to UMN miss-communication seems to contribute to the development of the spasticity.

Mass reflex in flexion spasticity in acute paraplegia is correlated to the supersensitivity of the synapses and sprouting of the axons after spinal shock (Ashby et al. 1974). The upper motor neuron lesion overview is presented in figure 3.3.

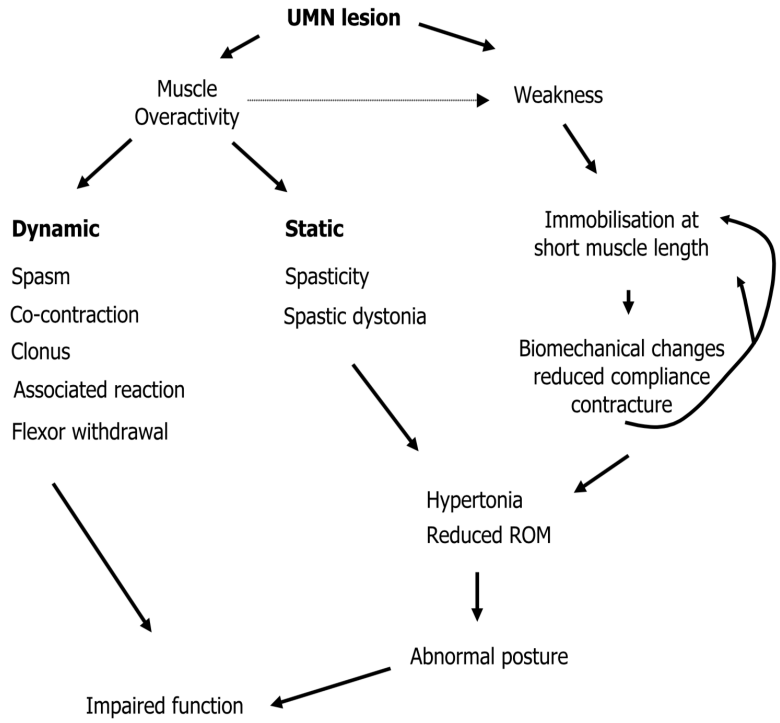


Figure 3.3: An overview of positive and negative features of the upper motor neurone lesion (Sheean 2002).

It is believed that spasticity contains both a neural and non-neural elements that develop due to abnormal stretch arc reflexes (Bavikatte & Gaber 2009). The type of plasticity, spinal and cortical rearrangement after the development of NS disease or injury is believed to highly impact the difference in spasticity manifestation. The variability in correlation of severity, lesion and symptoms has been delaying comprehensive understanding or spasticity mechanisms. However the main agreements on spasticity are that (Sheean 2002):

- it causes a sustained stretch reflex
- is mediated by Ia afferents predominantly by muscle spindles
- its triggering is velocity dependent

- excitability is dependent on the length of the stretch
- is a dynamic in symptoms and manifestations

Spasticity results in increased tone, overstressed tendon jerks, sharp uncoordinated reflexes and weakness, representing one component of the upper motor neurone syndrome (Burke 1988). Further symptoms can cause involuntary movements or spasms, pain, bone, joint deformities and abnormal posture, all of which leads to contracture, difficulties with mobility and activities of daily living. Depending on the combination and severity of the repercussions, spasticity is descriptively categorised in mild, moderate and severe. This classification is subjective to the assessor.

3.3.1 Outcome measures

A recent literature review of spasticity definitions and measurements suggests that 71% of researchers use biomechanical measures/assessments to indirectly quantify spasticity (e.g. measuring joint stiffness during manual passive or controlled motorized perturbations) and 15% using elecctrophysiological measurememts (e.g. EMG or H, M and/or F reflexes) (Malhotra et al. 2009). The most commonly used clinical assessment of spasticity are the Ashworth Scale (Ashworth 1964) and the Modified Ashworth Scale MAS (Bohannon & Smith 1987, Johnson 2004). The resistance is graded with a number between 0 and 4 as presented in table 3.2. These scales use an assessment of a resistance to a stretch when a limb is passively moved. Their reliability is questioned by the subjectivity required by the observer to carry out the test and by the fact that it measures multiple aspects of the limb stretch (Pandyan et al. 2016). Furthermore it is believed that this stretch induces a treatment or a trigger of spasticity causing further changes in the state. Fleuren et al. (2010) evaluated repeatability and reliability of AS and concluded that it is unsatisfactory related to an assessment of a reflex muscle activity.

Johnson (2004) summarised different scales used to quantify spasticity in correlation with different electro-physiological symptoms and responses to numerical values. Total of 24 scales are identified for measurement of spasticity and associated clinical phenomena: 10 scales for volitional "active" function, and 3 scales for "passive" function with a documented association with spasticity. The main issues with all these scales are a substandard repeatability and lack of clinical validation. Additionally, many authors proposed use of the scientific electrophysiological methods

Table 3.2: Ashworth Scale and Modified Ashworth Scale assessment as a score to a resistance to a stretch of a limb during passive movement.

Score	**Ashworth Scale**	**Modified Ashworth Scale**
0	No increase in tone	No increase in tone
1	Slight increase in tone giving a catch when the limb is moved in flexion/ extension	Slight increase in tone giving a catch, release and minimal resistance at the end of range of motion (ROM) when the limb is moved in flexion/extension
1+		Slight increase in tone giving a catch, release and minimal resistance throughout the remainder (less than half) of ROM
2	More marked increase in tone, but the limb is easily moved through its full ROM	More marked increased in tone through most of the ROM, but limb is easily moved
3	Considerable increase in tone passive movement difficult and ROM decreased	Considerable increase in tone passive movement difficult
4	Limb rigid in flexion and extension	Limb rigid in flexion and extension

coupled with MAS such as:

- Responses to electrical stimuli (H-reflex, F-wave)
- Responses to mechanical stimuli (vibrations, Tendon reflex, Polysynaptic responses)
- Passive movements (Stretch reflex, Pendulum test, joint stiffness)
- Active movements (residual volitional movements)
- Evoked potentials analysis (Transcranial magnetic stimulation, Lumbosacral Potentials)

However not of these used independently managed to accurately and in full represent spasticity to be adopted in clinical practice. Moreover, there is a notable lack of biomechanical spasticity measurement research having in mind technological achievements at the time. For example, methods concerning EMG, and reflex waves as a response to the stretch reflexes depend on a background activity, thresholds and reflex gains and it can not be standardised to fit an unified scale. Evoked potentials analysis can introduce a treatment during the measurement therefore not being fit for objectivity because every participant might respond to the measure differently.

Wood et al. (2005) classified spasticity outcome measures proposed by researchers to seven categories:

- manual - passive manual stretch by pulling a limb to cause a rotation and elicit tonic stretch reflex (Pandyan et al. 2001).
- controlled displacement - response to a passive movement where movement/displacement parameters (velocity, amplitude, angle, movement type) are controlled (Becher et al. 1998, Pisano et al. 2000).
- controlled torque - similar to controlled displacement but the response to prescribed torque is measured (Yeh et al. 2000).
- gravitational methods - lifting a limb against the gravity with or without the load and assessed based on reached position, time, weight etc (Katz et al. 1992, Lin et al. 2003).
- tendon tap - some types of stimuli (e.g. vibrations, mechanical force impact) to the tendon can elicit muscle contraction causing a joint displacement (Vattanasilp & Ada 1999).
- voluntary methods - analysis of the residual volitional movements during spasticity (Da Vies et al. 2009, Dewald et al. 1995).
- functional methods - assessment of predetermined set of activities of daily living such as walking, writing, using cutlery and similar (Krawetz & Nance 1996).

In addition to this list there is an effort to quantify joint stiffness by correlating a torque and resistance against passive limb movement to the spasticity (Akman et al. 1999, Franzoi et al. 1999, Perell et al. 1996).

Unfortunately, only a few of these or their adaptations are found to be used in clinical practice, mainly dependent on the association of the clinical environment to the university and research facilities. Alongside already mentioned AS and MAS, two are for assessment of lower limb spasticity Wartenberg Pendulum Test (adaptation of gravitation method where the responsiveness of the spinal stretch reflex to a muscle stretch is assessed) and the Spinal Cord Assessment Tool for Spastic reflexes (adaptation of the manual method where clonus and/or spasms due to a passive joint flexion/extension is assessed), and the last two are self-assessment questionnaires Visual Analogue

Scale and Penn Spasm Frequency Scale (available in appendix B as a part of questionnaire B-12). It is obvious that the only widely used upper limb spasticity measured are either subjective to the observer or to the affected.

Within the literature, majority of papers concern knee, elbow or ankle joints with the devices being in a state of the art or experimental testing phase. Limitations are specialist approach and inability for easy and affordable amatherous use, repeatability, no integrations with other measurements, restriction to only one joint assessment. There is a safety component to the problem of scientific approaches, especially those taking advantage of the motorised movements. It is essential to consider physical constrains and limitations, joint physiology, limb structure and other factors. Selection of parameters such as torque, velocities and ranges of motion, following the participant assessment to address these concerns and limitations (Price 1990). Malhotra et al. (2009) stated, quoting: "The solution to the spasticity measurement problem is fairly simple: both researchers and clinicians will need to ensure that any outcome measures used in spasticity-related research is valid and congruent to the definition" and Biering-Sørensen et al. (2006) continued, quoting "For the daily clinical routine, simple instruments will be very much appreciated". To summarise, a clinically accepted spasticity assessment needs to assimilate volitional and passive movements, multiple joints, electrophysiological measurement related to the UMN as well as stimuli, and need of repeatability and ease-of-use approach (Abbruzzese 2002, Burridge et al. 2009).

3.4 Rehabilitation of spasticity in SCI

Maynard et al. (1990) detected a very high percentage 65-78% of spasticity indices in chronic spinal cord injury. At least 40% reported pain associated with spasticity (Adams & Hicks 2005). Cervical SCI is responsible for 60% of spasticity in the upper limbs (Sköld et al. 1999). Furthermore it seems that level of injury and type of injury have a strong correlation to the occurrence of spasticity in SCI as presented in table 3.3:

Rehabilitation of spasticity in SCI depends on the location and the degree of the SCI lesion. Primary outcome goal of the clinical treatment of spasticity is based on recipients' personal goals (these may include walking, sexual activity, use of hands etc...) translated to the functional recovery of volitional movements and abilities to participate in active daily living. Therefore

Table 3.3: Occurrence of spasticity in SCI depending on level and type of injury (Sköld et al. 1999).

Level of injury	**Type of injury**	**Spasticity occurrence**
cervical SCI	ASIA-A	93%
cervical SCI	ASIA-B,C,D	78%
thoracic SCI	ASIA-A	72%
thoracic SCI	ASIA-B,C,D	73%

the emphasis is on the individualisation in treatment choices which may include several cost-effective options (Abbruzzese 2002). Physical therapy, surgery, pharmacotherapy and neurolysis (i.e. application of physical agents such as hot or cold or chemicals such as phenol or alcohol to nerves in order to interrupt the transmission of nerve signals) are most commonly used spasticity treatments in SCI (Hsieh et al. 2012). Table 3.4 summarise the treatments and level of evidence of the effectiveness. It has been reported that between 26 to 37% of people with spasticity in SCI receive anti-spasticity medications at hospital discharge and this number increases to 49% after one year follow-up (Maynard et al. 1990).

Block diagram in Figure 3.4 illustrates the flow of events following a spinal cord injury. The site of action and the nature of effect of the various drugs and interventions used for the management of spasticity after SCI are illustrated. Red colour indicates a increase in action/activation, whereas a blue colour indicates a reduction followed by a description of the effect of each treatment method.

It seems that pharmaceutical medications assessed in randomised controlled studies and meta analysis (Level evidence 1) hold a strong position to claim the effectiveness in spasticity reduction. Baclofen is the most commonly used in oral and intrathecal form (implanted programable pump) as a derivative of gamma aminobutyric acid (GABA) (Ward 2003). The benefits of Baclofen are reported to be more notable in the lower limbs and trunk affecting posture, personal independence, reduction in pain (Yelnik et al. 2009). Additionally it provides a better sleep and bladder function (Bensmail et al. 2006, Parke et al. 1989). Intrathecal pumps provide a short term efficacy with reduction in spasms and spasticity with no infections. However in long term Baclofen can have severe detrimental consequences. Pump failure with the need to perform intervention to remove and implant another one is one big stress for the body. Moreover, a failed pump can introduce overdose to the medicine causing migraines, respiratory and cardiac problems (Stempien & Tsai 2000). Baclofen withdrawal seems to trigger even worse spasticity symptoms therefore causing

a form of an addition with effectiveness lessen as the dose increase in long term usage (Yelnik et al. 2009). Tizanidine and Clonidine have short lasting effectiveness, starting from 1 to 2 hours following oral administration lasting up to 5 hours. The most common adverse events observed during administration are sedation, drowsiness, hypotension, dizziness, muscle weakness and insomnia (Gracies et al. 1997). Other medicaments mentioned in Table 3.4 are mostly used to treat spasticity in other disorders and diseases, while the influence on spasticity is a side effect. However, adaptation of these drugs is needed in order to enhance efficacy for spasticity and eliminate adverseness for other neurological structures.

In the past 20 years the increased use of Botulin Toxin type A seems to have a major breakthrough in spasticity repercussions elimination and restoration of functional abilities. Botulin Toxin clinical potency for spasticity reduction gradually increases over the first 7 days after the administration. Spasticity remains diminished for 12-16 weeks, sometime longer (Simon & Yelnik 2010). Unfortunately, there is a lack of above Level 4 evidence (case reports) studies to confirm botulin toxin effectiveness, long-lasting effects on spasticity within SCI population (Hsieh et al. 2012). The invasiveness of administration is very limiting factor for botulin toxin use. Targeted muscle or muscle group have to be investigated in depth for its location, injection sites and injection invasiveness. It is a painful process and some justify the use of analgetics during administration. This can cause more harm observed in children (Yelnik et al. 2009). Botulin toxin, being the most promising pharmaceutical compound for functional recovery (walking, dressing, gait etc), has to be questioned for the the justification of cost effectiveness.

Many proposed treatments inclusive of any type of electrical stimulation have a low level of evidence (mostly around 4) with no or a few hours carryover, except transcutaneous electrical nerve stimulation (TENS) and direct spinal cord stimulation (Krause et al. 2008, Midha & Schmitt 1998, Mills & Dossa 2016, van der Salm & Veltink 2005). Total of three studies evaluate application of TENS in spasticity in SCI (Mills & Dossa 2016). Chung & Cheng (2010) reported a significant reduction in spasticity score for full ROM ankle dorsiflection after 60 minutes of TENS. If this therapy is applied in subacute phase (within 6 months after the lesion) it seems that the clinical spasticity manifestations can be reduced (Oo 2014). Aydn et al. (2005) disclosed a complementary advantage of combining baclofen and TENS for spasticity reduction in lower limbs. Safety aspects of TENS reprimand the use during pregnancy or neurological disorders such as epilepsy, and to

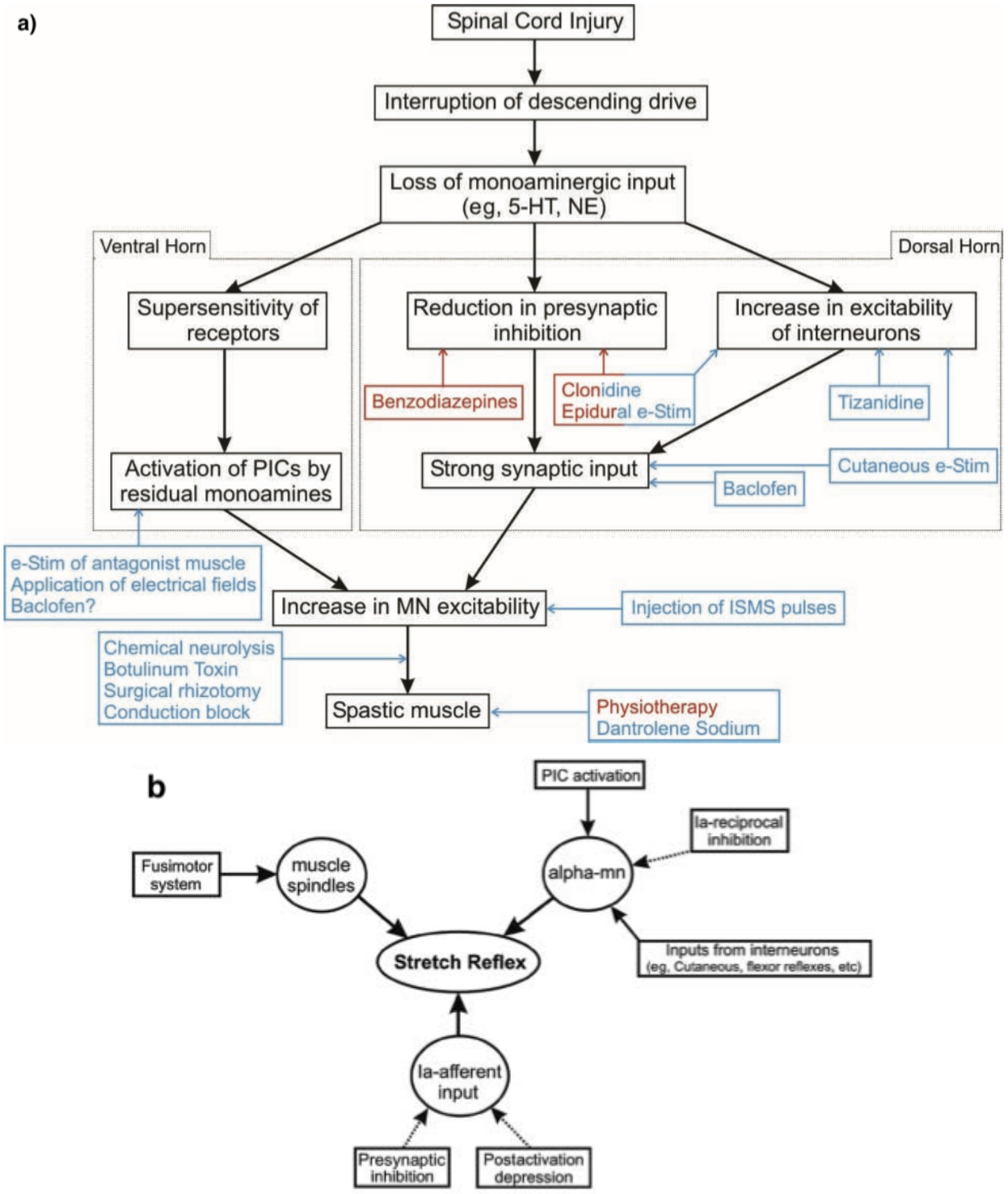


Figure 3.4: a) Block diagram illustrating the flow of events of spasticity treatments following SCI which are summarised in b) as the excitability of the spinal mechanisms contributing to the exaggerated reflexes in spasticity (Elbasiouny et al. 2010).

be avoided when cardiac pacemaker is implanted. TENS electrodes may cause skin irritation or burn for inadequate use (Gracies et al. 1997). Direct spinal cord stimulation have very high cost-effectiveness in spasticity treatment due to its invasiveness and overcarry of the symptomatic relief lasting in average 6 months (Midha & Schmitt 1998). Nonetheless Barolat et al. (1987) reported a significant reduction of the spasticity severity relative to the baseline, persisting up to 2 years post treatment. Spasms intensity reduce over time with subjective rating of spasms and spasticity being 79% at 2 year check up.

Fertility studies imply use of a vibration device applied on the scrotum for 3-5 minutes or until ejaculation. During the fertility studies in men with spasticity in SCI, a coincidental reduction in spasticity is observed above and below level of injury (Hsieh et al. 2012). Biering-Sørensen et al. (2005) reported a spasticity relieve in lower limbs measured by MAS during a fertility study. Additionally participants reported a decrease in spasms occurrence. Study by Alaca et al. (2005) showed a statistically significant reduction in spasticity lasting 6 hours after the penile stimulation. Even though there is reported lessening of spasms frequency and amplitude further along the timeline, the results did not reach statistical significance. A more comprehensive unblinded case-crossover study evaluated possible mechanisms underlying penile stimulation (Læssøe et al. 2004). It is shown that afferent nerve stimulation from penile vibrations is transmitted via the pudendal nerve (combination of afferent neurones from the external genitals in both sexes and motor neurones for pelvic muscles) to the sacral spinal cord (S2-4) and from there to the T10-L2 segments. The efferent innervation of the ejaculatory organs is through motor-pudendal neurones. The study shown significant reduction in involuntary activation of leg muscles as well as muscle tone evaluated with MAS. The study questioned the implication of sexual satisfaction due to ejaculation or clitoris stimulation and found no significant difference in spasticity reduction in participants with versus without reaching the peak of sexual pleasure. Rather, the justification is that the vibration induced neural activity in lumbar spinal cord which may be involved in spasticity pathophysiology. Pudendal neurones could potentially influence the changes in polysynaptic reciprocal inhibition of the primary afferents $\rightarrow$ motoneuron circuits in spinal reflex arch, thereby reducing the spasticity.

The most prevalent spasticity therapy given by therapist or carer is a passive stretch of a single or multiple joints (Hsieh et al. 2012). Sköld (2000) used two motorised tables performing movements within range of motions for knee and hip of a leg. The total number of movement per one

session lasting 30 minuter was between 600 and 900. The acute decrease in spasticity was noted with repetitive passive movements lasting 4 days after the end of 6 weeks of therapy. By evaluating electrical stimulation evoked waves (M and F waves) as a mean of spasticity quantification, Rösche et al. (1997) reported an anti-spastic effect of a passive motorized exercise in paraplegia. Kakebeeke et al. (2005) adopted this approach for 30 minutes passive cycling in motor complete SCI. Interestingly there was no significant change in spasticity reduction, only self-reported estimation of spasticity reduction. Not to be overlooked, this could be the physiological effect of an unblinded study and self-imposed expectation for improvement. Another subjective spasticity self-assessed reduction was reported by Kiser et al. (2016) for an intensive 13 weeks long exercise on motorizes bicycle. It is noted that all of these studies assess the passive stretch of spasticity in lower limbs.

At this point there is a need to question clinically used spasticity assessment MAS, which introduce a passive stretch during the assessment. Is this acceptable considering the spasticity benefits from the action itself? This is more questionable when several people needs to assess MAS in short period of time.

Combination of active, passive and functional therapies are achieved during hippotherapy or horse riding. Lechner et al. (2003) showed an immediate reduction in lower limb spasticity after horse riding (more significant than simulated horse ridings on an improvised mechanical devices such as Bobath roll). These effects are accompanied with a positive short term mental well-being (Lechner et al. 2007). He reported, quoting "Moreover, the warmth of the horseback, the dangling of the lower legs following the movement of the pelvis, and the physiotherapists controlling of subjects sitting position, may have an effect on muscle tone". These conditions may have acted as proprioceptive afferent stimulation causing reciprocal inhibition of a spinal reflexes.

Table 3.4: Level of evidence of effectiveness for various spasticity treatment approaches used in clinical practice (Hsieh et al. 2012).

Approach	Type of approach	Treatment	Mechanism of action	Level of Evidence
Non-Pharmacological Interventions	Passive Movement or Stretching	Passive Muscle Stretching	Excitation of fibro-elastic properties of the muscle accompanied by activation of the corticospinal neural circuits	4
		Neurodevelopmental Therapy (active and passive movements)		1
		Hippotherapy (active and passive movements during horse riding)		2
		Prolonged Standing		4
	Active Movement (Including FES-assisted Movement)	Functional Electrical Stimulation	Activation of spinal reflexes	2
		Volitional movements (reinforcement of residual volitional movements)		No evidence
		Hydrotherapy (exercise in water)		2
	Direct Muscle Electrical Stimulation		Selectively stimulating lower threshold motor neurons to evoke muscle contraction and corticospinal neuroplasticity	2
	Various Forms of Afferent Stimulation	Transcutaneous Electrical Nerve Stimulation	Alternation of motoneurones' excitability through (tonic) sensorymotor reflex arches	1
		Therapeutic Massage (vibrations, various massagers)		4
		Cryotherapy (application of cold stimulus)		4
		Helium-neon Laser Stimulation		2
		Rectal Electrical Stimulation (for fertility purposes)	In addition to the previous mechanism, it seems that relaxation caused by genital stimulation in sexual sense (ejaculation, clitoris stimulation) contributes greatly to the reduction in spasticity	4
		Penile Vibration (for fertility purposes)		1
	Direct Spinal Cord Stimulation	Stimulation via implanted epidural stimulation electrodes	Direct stimulation of motoneurones in spinal cord causing alteration in synaptic activations and firing thresholds	4
Neuro-Surgical Interventions				2
Pharmacological Treatment	Baclofen (derivative of gamma aminobutyric acid (GABA))	Oral Baclofen	Enhancement of the inhibition of the stretch reflex due to increased presynaptic inhibition	1
		Intrathecal Baclofen (injection via programmable pumps)		4
	Medications Other Than Baclofen	Tizanidine	Reduction in brainstem motor activation by targeting presynaptic receptors	1
		Clonidine		1
		4-Aminopyridine	Blocking Potassium (K^+) channels to overcome conduction deficit associated with neural demyelination	1
		Cyproheptadine (first generation antihistamine drug)	Serotonin receptors inhibition, antihistamine effects, local anesthetic benefits	1
		Gabapentin (anticonvulsant drug for epilepsy treatment)	Blocking sodium (Na^+) channels and enhancing GABA function	1
		Orphenadrine Citrate	Blocking neurotransmitters in neuromusclular junctions in both CNS and PNS	1
		Other Potential Anti-Spasmodics	various	Little
	Cannabinoids	Tetra-hydrocannabinol (THC) (psychoactive drug)	Paucity in understanding the underlying mechanisms	2
	Focal Neurolysisn	Botulinum Toxin	Preventing neurotransmitter release into the neuromusclular junction thus causing flaccid paralysis	4
		Phenol	Direct damage to the α-motoneurone fibres sometimes accompanied with afferent nerves damage	4

3.4.1 Spasticity recovery challenges

If all of the presented methods are compared to the ones used for motor function rehabilitation in SCI, the repetition of them is noticeable. This is because many of these paradigms have similar underlying effects on the CNS which gives a great advantage in coupling the most beneficial rehabilitation techniques for achieving multiple outcomes. No treatment option will be equally (not) successful in spasticity repercussions management, regardless to the spasticity sources. Among clinical practice it is agreed to utilize physio- and occupational- rehabilitation approaches first, then to progress to oral and/or injectable pharmacological substances and lastly surgical options.

Physical therapy approaches are criticized for their effectiveness to diminish spasticity because the management concepts concerns volitional ability to perform activities of daily living, which can actually be a spasticity trigger (Adams & Hicks 2005). Medications can potentially have serious side effects. Baclofen's effectiveness is roughly 3.5 hours and the excretion from the body much longer by passing through the liver and renal (urinary) system. Most of the medication side effects include sedation, fatigue, cognitive disfunction, liver abnormalities and other adverse events. More importantly, when there is a need to reduce a dose or stop with medications, some have shown serious withdrawal syndromes including increase in spasticity, fever, seizures, altered mental state and rarely death (Saulino & Jacobs 2006). The use of botulin toxin is questioned because of it's efficacy on spasticity but also reduction residual volitional movements. Not to mention that it has a word *toxin* in its name, and for a good reason: its 8 types can cause disease or death in humans due to the toxicity.

It seems that every spasticity treatment approach isolate a single issue and tries to reduce its repercussions, mainly abnormal increased muscle tone. However the cost calculation for efficacy in comparison to adverse events or even increase in other symptoms needs to be revisited and disputed. And one may argue that this is a direct consequence of lack of understanding of spasticity origins and mechanisms. As previously stated, the spasticity measures are not addressing spasticity genesis and clinical understanding is not efficient enough to capture the moment of spasticity initiation. So this vicious circle of no accurate assessment $\rightarrow$ no comprehensive understanding $\rightarrow$ no sufficient clinical management therapy $\rightarrow$ no comprehensive understanding is repeating and echoing through the literature.

3.5 Chapter summary

The spinal cord injury causes imparements in communication and processing conduit between the brain and the rest of the body. If the conveyance is interrupted by the injury, sensory and motor control over the body is becoming more or less challenging, depending on the type and the location of the injury. Strategies of the spinal cord injury rehabilitation focuses on the recovery of the affected bodily functions, mobility and activities of daily living. However, spasticity is often accompanying a volitional recovery. Spasticity is caused by the imbalance between nervous system and the musculoskeletal structures and is manifested in abnormally increased muscle tone and connected joint stiffness. As spasticity affects one or several parts of the body, it has been proven difficult to agree on the most appropriate quantification methods. Consequently, the origins and mechanisms of action remain inconclusive, which is one of the main obstacles towards recuperation. Despite many non-pharmacological interventions and pharmacological treatment are investigated for their effectiveness against spasticity, the levels of evidence remain low to draw a consensus on the most promising approaches. This is mainly because either they have severe side effects, or the potency is shot-lasted. Nonetheless, the search for the prominent approaches against spasticity continues by exploring non invasive, affordable and easy-to-use methods, such as vibratory stimulation further explored in the next chapters.

CHAPTER 4

Vibrations for spasticity rehabilitation

Introduction and justification for the use of vibrations in rehabilitation is presented in this chapter. Concomitant to the summary of the impact vibration therapy have on able bodied people and people with impairments, underlying mechanisms of action are elucidated.

4.1 Vibrations in rehabilitation

The first research demonstrating the use of vibrations in rehabilitation can be dated to the late 1800 when clinician R. Vigouroux (1878) observed some positive effects mechanical oscillations have on his hysterical patients (Charcot 1892). This work was followed by M. Boudet (1881 and his research on the use of mechanical vibrations for the reduction of pain), J. Mortimer-Granville (1983) and most famously Jean-Martin Charcot (1892) who performed a series of experiments to evaluate the effects of vibrations on skin, joints and disease (Goetz 2009, Saggini et al. 2017). Charcot constructed a chair that can produce *rapid trembling movements* (i.e. vibrations) to contemplate his patients with Parkinson's disease whilst relaxing in the chair for 30 minutes daily. He observed changes in walking, muscle and joint stiffness, improvement in sleep and lessening of agitation in patients' behaviour. Encouraged by these observations he concluded quoting "It is no small gain to be able to relieve the sufferers of paralysis agitans, a disease for which ordinary remedies have, as you know, so little efficacy" (Charcot 1877). His motivation was based on the stories from his patients quoting "I had long been told by patients with paralysis agitans that they derived great relief from prolonged journeys by railroad or carriage... the benefit persisted for some time after the journey" (Charcot 1892).

Since then, the interest in the use of vibrations in various research disciplines raised. Interestingly, the use of vibrations helped Lance (1980) to establish the first spasticity definition by observing afferent nerves behaviour during and after mechanical vibration stimuli. Vibrations are, nowadays, associated with the reduction of pain, hastening of recovery, promoting stability in balance, enhancement of exercise outcomes, improvement in muscle strength, spasticity, gait and the list continues. However, aside from these, some negative connotations are attributed to vibrations such as fatigue, illusionary movements and disturbed proprioception.

Vibration is a mechanical oscillatory motion transpiring about an equilibrium point. Actuators such as those with an eccentric rotating mass, linear resonant actuators, pressurised air controlled by pneumatic systems, oscillating plates, and similar vibro-tactile devices are used to deliver mechanical stimulus to the body. Vibrations used on the body can be grouped into 3 categories, according to: 1) location of application, 2) timing of application and 3) vibration parameters. Based on the location of application, vibrations can be further divided into 3 groups, as illustrated

on Figure 4.1:

- Focal vibration (FV) - stimulus focused only on one body structure, e.g. muscle or tendon or bone.
- Segmental vibration (SV) - vibrations affect several different structures of the body (e.g. several parts or the limb).
- Whole body vibration (WBV) - vibrations are applied on the whole body.

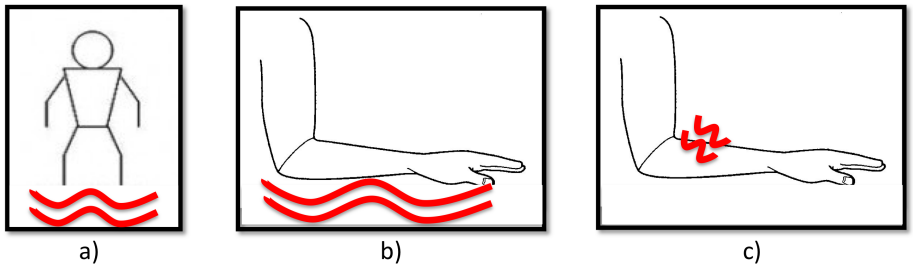


Figure 4.1: a) Whole body b) segmental and c) focal vibratory stimulation.

Timing of the application of vibrations can be before, during or after an action such as muscle contraction, following physiotherapy, relaxation or any other volitional or passive effort. Work on vibration parameterisation is mainly looking at the frequencies and the amplitude of the vibrations. Frequency represents the speed of vibrations in the unit of time (in Hertz [Hz]). Amplitude is the maximal deviation from the equilibrium point (usually in millimetres [mm], sometimes in gravitational acceleration [g] depending on the manufacturer's characterisation). The A_g amplitude in terms of the gravitational acceleration [$g = 9.81m/s^2$] equation correlating these two units is given by 4.1.1:

$$A_g = (2 \cdot \pi \cdot f)^2 \cdot a_{mm} \tag{4.1.1}$$

where f represents vibrations frequency in Hz, a_{mm} amplitude in mm (Kiiski et al. 2008, Liao et al. 2015).

The following sections will discuss justification for the use of vibrations in rehabilitation depending on the place of application with regards to the vibration parameters and timing.

4.2 Segmental vibrations

Vibrations applied to several different structures of the body (e.g. muscles and tendons, parts of the limb or the entire limb) are usually referred to as segmental vibrations (SV). In another words, anything that vibrates more than one segment of the body (i.e. a muscle, bone or a tendon) and less than a whole body, can be referred to as a segmental vibration to the body. Segmental vibrations can be delivered with the employment of several vibration motors on different sites, vibrating, for example, the whole limb using a vibrating plate or a vibration cushion, or simply using (i.e. holding) everyday appliances or machinery such as drilling machines or a blender and a grinder in a kitchen. Segmental vibrations applied to the upper limbs are sometimes called *hand-arm vibrations*.

Concerning the delivery of segmental vibrations by using everyday appliances (e.g. grinders, blenders) or industrial machinery (e.g. grinder, chisel hammer, chainsaw, helicopters, trucks), a few studies investigate their short and long term effects on the body (Armstrong et al. 1987, Griffin 1997, Guignard 1973). Hand-arm vibration syndrome or HAVS is a common neuropatological disorder usually find in workers who handle tools that vibrate (Heaver et al. 2011). The factors contributing to the development of HAVS are: hours of use of machinery, handle design and grip required, vibration parameters and posture. In the early stages of HAVS nerves are affected to a minimum extend, leading to changes in sensation or causing a tingling sensation. This can then be followed by Raynaud's phenomenon (feeling of numbness and cold in fingers) resulting from changes in the blood vessels and causing a white finger. These changes also lead to muscular aches and pains (Rolke et al. 2013). Vibration may increase the risk of chronic tendon and nerve disorders by increasing the force exerted in repetitive manual tasks (Armstrong et al. 1987).

There are suggestions that vibrations of this type are restructuring muscle fibres (found to be regrouping) and nerves (indicated to be denervated and re-innervated), with increased susceptibility to damage, necrosis and fibrosis (Necking et al. 2016). There is weak evidence that segmental vibrations can cause bone and joint changes and slow deterioration (Hagberg 2002). More detrimental SV consequences, such as neuropathy, are those on the large type Ia fibres (Rolke et al. 2013). This is most likely because these fibres are found to be responsible for vibrations' perception and therefore constantly responding to the stimuli, whilst being mechanically perturbed

(Bianconi & Van Der Meulen 1963). Interestingly, the vibratory excitation threshold of the fibres significantly increase during the exposure, reducing the awareness of potentially damaging repercussion of long exposures (Brown et al. 1967). However, the literature does not provide an insight in long-term alterations on the thresholds in HAVS. Complementary, tonic vibration reflex (TVR) could be present throughout the exposure causing continuously increased muscle tone, metabolic and vascular changes and reduced sensory feedback (Necking et al. 2016). The time for recovery could take longer and imposing an exposure to the vibration in the process could systematically degrade muscles.

Regarding vibration parameters, all vibrating heavy machinery have a very high amplitude above 10mm, but the frequencies are in range from 25 to 350Hz. Dong et al. (2001) observed that the effects of vibration above 150Hz remain in the hand and fingers and do not travel proximally through the wrist, elbow and shoulder joints. And, there is an ongoing dispute among researchers investigating HAVS as to which frequencies are the most adverse, with the results favouring those above 100Hz (Reynolds & Angevine 1977). Duration of exposure is also very important. Workers are reportedly exposed minimum of 2 hours per day, during working week and minimum of 3 years. The muscle and neuronal physiological changes are observed in the workers who exceeded 10 000 hours of exposure. Those exposed less than total of 2 000 hours or between 1 and 2 hours a day within 2 years noted changes in sensation which are recovering after a prolonged break from the vibrations (a few days) (Dong et al. 2001, Issurin et al. 1994, Necking et al. 2016).

Nevertheless, this potentially harmful culmination of segmental vibrations on the body is due to the long-term exposure, continuous, hourly and daily use for years on the one and only body part. If timing is reduced and parameters rectified, the scientists noticed some positive effects on able-bodied people. High amplitude low frequency (2.51mm and 50Hz, respectively) SV applied to the hand during exercise draw no changes in hand grip force and EMG amplitude (Garcia-Gutierrez et al. 2014). In contrast, superimposing 28 Hz SV on the hand during continuous flexion and extension of the arm significantly increased an amplitude of EMG recorded from biceps and triceps muscles for the same movement. The primary reason would be the alteration in motor unit recruitment and not a presence of tonic vibration reflex. Hence, if a participant is asked to maintain a desired force level for 20 seconds during the same 30Hz SV, a high degree of fatigue is expressed by EMG analysis (Mischi et al. 2012). Issurin et al. (1994) observed increase in a

maximal output force after exercise accompanied with low amplitude low frequency (0.6-0.8mm and 44Hz, respectively) SV of the forearm and the hand. He remarked that the this could be a direct consequence of vibration induced hyper-activation, synchronisation and discharge of motoneurons, in addition to the motor learning process. Indeed, in research publish prior to this, McDowell et al. (2006) observed a overestimation of grip and push forces during exposure to 40Hz or 125Hz SV of the hand applied for 45 seconds. These effects were not observed for very low frequencies of 12.5Hz or very high frequencies of 250Hz. The force errors were smaller at lower force levels. One justification could be that vibrations altered *a muscle memory of force recall*. Nowak et al. (2004) introduced a concept of a muscle memory as a muscle's mechanisms to perform a similar repetitive grips (recalls) of the familiar object. It seems that muscles tend to remember a fibre activation patterns on the first interaction with an object. Any consequent manipulation will trigger these memories to optimize activation and efficacy. Nowak also remarked that this memory could be altered due to vibrations (further rationalization will be provided in chapter 5). Follow up study revealed that the force recall can depend on the target force (McDowell et al. 2007) but also on the vibration frequency (Mischi et al. 2012). These observations could be exploited in rehabilitation to elicit volitional abilities in SCI.

Segmental vibrations are mainly reported for their use in sports science for enhancing muscle performance and correlated activities such as balance and performance in sports. Also, some efforts are put into rehabilitation. Research suggests that 12 sessions of 30 minute SV stimulation of paretic calf and foot with frequency of 120Hz and amplitude of 0.1mm can improve walking in people with stroke (Paoloni et al. 2010). Work at the Royal National Orthopaedic Hospital in London inspired the investigation of vibrations in rehabilitation reported in this thesis. The occupational therapists use segmental vibrations during their sessions for SCI rehabilitation. They employ circa 15 minutes of 75Hz SV on the relaxed, splinted hands in pronation after which the hands, previously highly spastic, become flaccid. The flaccid hands are then easily engaged in functional mobility exercises. The justification for SV use is a hereditary knowledge passed from previous employees because according to the manufacturer "it works". One question arises: how many spasticity remedies are used in the clinical practice around the world which remain buried in a clinical experience and with limited scientific reasoning due to the clinical $\rightleftarrows$ scientific lack of communication?

4.3 Whole body vibrations

One of the forerunners of the whole body vibration (WBV) devices is the *tre'moussoir or fauteuil de poste* (i.e. vibrator or coach chair that shakes) developed by Abbé de St. Pierre back in the 18th century (Goetz 2009). He dedicated this apparatus to his sedentary patients as a mean of exercise. Even famous writer and philosopher Voltaire wrote to his friend in late 1774 about enjoying relaxation in this chair (Voltair 1744).

At the present time, WBV are usually delivered by the means of vibrating plates, also known as power plates in a common nomenclature (see Figure 4.2). There are two types of platforms:

- Pivotal - provides "seesaw like" vibrations where the sides alternate up and down while the centre remains fixed.
- Lineal - the platform remains horizontal all the time with the entire platform moving up and down by the same amount.

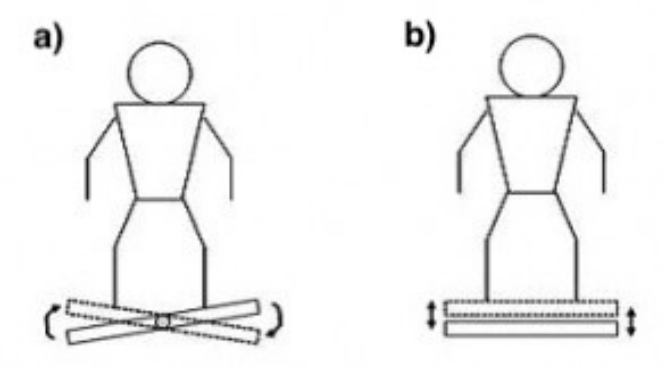


Figure 4.2: a) Pivotal and b) lineal vibrating plates for whole body vibration (*Whole Body Vibration plate types* n.d.).

The use of whole body vibration has increased in the last decade and can be split into 2 categories (Ahlborg et al. 2006*a*):

- WBV therapy - the position of the body should have a zero effect on burning calories so that body is only exposed to the vibrations.
- WBV training - the body is in the exercise pose in combination with vibrations, designed to burn the maximum amount of energy in the shortest time while causing no joint damage.

WBV parameters, consists of a high amplitude and low frequency: amplitudes 3 to 7 mm peak-to-peak and frequencies 10-45Hz.

A simple internet search yields results diverging from plates to purchase, gyms' promotional use offers, to articles questioning effectiveness of the power plates used in the gym (`goo.gl/WHvZBw` accessed on 01.04.2018). Since Issurin et al. (1994) suggested that the use of segmental vibrations with repetitive movements can increase muscle force output, there was an effort to couple exercise with vibrations and capitalize on their benefits. After the first licensing of lineal vibrating plate in 1996 in Germany, many different types became commercially available in the following two years (Ahlborg et al. 2006*a*). Lately in United Kingdom, there is a rising trend to have a WBV plate as a part of a training protocol to, reportedly, improve muscle function or even replace exercise. Nonetheless, there is a scientific background to support these claims. Firstly, a single WBV training with (parameters 0.9mm, 40Hz) including 20 trials of 10 seconds WBV with 10 seconds break, increased growth hormone and testosterone and amplitude of maximal voluntary contraction during which EMG amplitude decreased (Di Giminiani et al. 2014). When compared to the resistance training, a significant increase in strength gain accompanied with increased EMG activity in sedentary women in their twenties with WBV with amplitude in range 2.5mm to 5mm and frequency 35-40Hz (Delecluse et al. 2003). In people older than 65, the optimum frequency of 20 to 30Hz with wide range of amplitudes from 1mm to 8mm may improve strength, power and balance similarly as conventional training (Sitjà-Rabert et al. 2012). It appears that the greatest benefits of WBV are those in lower legs. The transmission of effects of WBV on muscles decays with the distance from the body because many mechanisms are responsible for the transmission including bone and cartilage, synovial fluid, soft tissues, joint kinematics and muscle activation (Pollock et al. 2010). Therefore some authors propose the combination of segmental vibrations on hands with WBV for increase muscle coordination and EMG amplitude in both upper and lower limbs (Garcia-Gutierrez et al. 2014).

The mechanisms of actions of WBV remain a mystery. Research community argues whether (sometime) observed increase of amplitude in EMG can be attributed to the tonic vibration reflex. This is because vibrations travel throughout whole body and it is very difficult to assess the quantity of change, nonetheless its origins. Some researchers undertake simulations of the biomechanical changes in tissue models due to simple harmonic motions (Ahlborg et al. 2006*a*, Judex et al.

2003). Ahlborg et al. (2006*a*) concluded that many factors including those mentioned on macro level (muscles, joints, tissues) and those on micro level (filaments, cells, proteins) are included in the complex response to WBV.

Unlike SV, WBV are lush with examples of its application in rehabilitation, especially for spasticity reduction. WBV used in both children and adults with cerebral palsy reduce spasticity, increase muscle strength and gross motor function with no adverse events (Ahlborg et al. 2006*b*, Honour 2014, Krause et al. 2017). Vibration parameters (always high amplitude and low frequency) are adjusted to the participants' subjective sensation of comfort. These studies recommended commitment to 1 minute WBV once a day for at least 8 weeks (Calabrò et al. 2017).

Conflicting claims are being made on WBV use as a tool to diminish spasticity in stroke. Brogårdh et al. (2012) observed no change in spasticity after 6 weeks of WBV training inclusive of 2 sessions per week, each comprised of 12 stimuli lasting 40-60 seconds. The authors remarked that the training perhaps wasn't long enough or that the proposed training has a little effect on stroke. Additionally, participant included in this study had mild to moderate spasticity in their lower limbs. To reprimand, Pang et al. (2013) used WBV for maximum of 15 minutes 3 days per week for 8 weeks to reduce spasticity in knee and improve muscle strength in people with chronic stroke. Modified Ashworth Scale (MAS) score (clinical measure of spasticity, introduced in previous chapter) decreased, active and passive range of motion of ankle and walking speed and cadence increased after a single 10 minutes WBV session (4mm at 12Hz) (Chan et al. 2012) or 5 minutes (4-8mm at 30Hz) (Miyara et al. 2014). Tihanyi et al. (2010) and Liao et al. (2015) observed an increase in EMG and muscle activity in the paretic leg following WBV. These increases are correlated to a very low frequencies (up to 20Hz) of WBV and strongly dependant upon the state of the neurological and/or muscular impairment.

Among the most notable work in the area of WBV anti-spastic effects for people with SCI is the one from Ness & Field-Fote (2009) enrolling 17 volunteers with SCI for 3 days a week intervention, for the duration of 4 weeks. Total of 12 intervention sessions included four 45 seconds WBV stimulation with 1 minute seated rest. WBV stimulation was set to 2-4mm in amplitude and 50Hz frequency. The Pendulum test (see section 3.3.1) of the quadriceps muscles in lower limbs was used as spasticity outcome measure immediately after the session, 15 minutes after the session and 6-8 days after the last, 12th session. Pronounced spasticity reduction was observed 15 minutes

after each session with a carryover effects persisting a minimum of 8 days post study. Within the recruited population, there was 47% of people using a variety of different anti-spastic agents and yet there was no difference in the amount of spasticity reduction between individuals using and not using them. The main conclusion derived from this study is that WBV can be used in addition to training (such as squatting) to reduce spasticity in people with SCI. Unfortunately, animal models of SCI do not support the hypothesis that WBV can improve muscle function (Schwarz et al. 2015, Streijger et al. 2015, Wirth et al. 2013). However in both studies the examination was made in acute phase of SCI, latest 12 weeks post injury, which may justify observed minimal or no level of change. In contrast, among hopeful ramifications are those observed in chronic SCI phase. Improvements in lower limbs peripheral blood flow and speculation that the increase in oxygenation consumption was due to the increase leg activity after WBV was reported by Yarar-Fisher et al. (2014). These results were observed for every out of 3 sessions of WBV continuous stimulation lasting 3-6 minutes and 2mm in amplitude for each of 20, 30 or 40Hz frequencies and with at least one week between sessions. Herrero et al. (2010) asserted these with a study where peak blood velocity in the femoral artery was increased for the WBV at 20 and 30 Hz frequencies but not 10Hz. EMG activity was increased for each frequency in observed lower leg muscles whose blood was supplied by the femoral artery. Amplitude of the stimulation was 5mm and deliverance in three bouts each 60 seconds in duration followed by 60 second of rest.

Due to such variability of used parameters and inconsistency in reported results, a few papers discuss the concept of *optimal WBV condition*. Hadi et al. (2012) surveyed subjective descriptions from able bodied and people with SCI after use of different types of WBV plates for several different parameter (amplitude and frequency) combinations. Alizadeh-Meghrazi et al. (2012, 2014) addresses the same issue and reported in paper from 2014 that quote "WBV can elicit EMG activity among subjects with chronic SCI, if appropriate vibration parameters are employed". According to these studies, optimal WBV conditions for evoking EMG activity in lower limb muscles are frequency of 45Hz, amplitude of 1.2mm, passive standing with a knee at 140° angle for the duration of 2 minutes. But for all mentioned studies, the main limitation was the number of different parameters (2-3 different amplitudes and frequencies), which are not covering the full spectrum reported in the literature, and to be investigated without altering application times.

There are several criticisms for the use of WBV in rehabilitation:

- There is high uncertainty of the rehabilitation outcomes. This might be due to such a tremendous variability in vibration parameters, application times and plate types.
- The posture is seemingly important for WBV. To prevent the head from being vibrated, researchers propose tilting it forward. However, it is unclear weather this speculation is based on the experience or scientific observations?
- How to comfortably position a person with SCI on vibrating plate without exposing a wheelchair to vibrations and possible damage? Standing frames are one explored option, but a person inside a frame on a vibrating plate have to be constantly monitored for comfort and safety.

To conclude, mechanisms of WBV induced anti-spastic effects mechanisms are complementary to those for focal vibrations which will be deciphered in the next section (Blackburn et al. 2014*a*, Sayenko et al. 2010, Tihanyi et al. 2010). And, aside from the popularism of WBV, there is no firm scientific claim to assure WBV choice over focal vibrations in rehabilitation of spasticity and motor recovery in SCI.

4.4 Focal vibrations

Focal, localised, muscle or tendon or penile, vibro-tactile or mechanical stimulation, or any combination of these words can be referred to as a focal vibration FV, applied onto one tissue type situated in a specific body segment, with examples such as focal vibrations of muscles, tendons or bones in limbs. Focal vibrations found their use for altering muscle output power and fatigue, eliciting illusionary movements, degrading proprioception, evoking ejaculation in men with SCI, modulate spasticity severity, be used as a haptic feedback in gait, balance and proprioception, etc. Substantial number of examples can be found in literature, and some of them will be discussed in this section.

Focal vibrations can be delivered to the targeted tissue with any vibrating device whose size is suitable to cover only the targeted surface. Vibration motors appropriate for use should have surface from a few mm^2 to a few cm^2 (e.g. the first dorsal interosseous muscle $60mm^2$; the forearm flexor muscles $16cm^2$). Depending on the type of the device used, vibrations can propagate in one

or more of the three directions (graphical example is presented in figure 4.3 for focally vibrating forearm muscles when the elbow is in neutral position):

- longitudinal (tangential) vibration direction - movements in coronal plane and the device movements are perpendicular to the surface of the tissue
- transverse (radial) vibration direction - movements in transverse plane and the device is moving across long tissue axis
- feed (axial) vibration direction - movements in sagittal plane and the device moving parallel the long tissue axis

Some devices are able to produce vibration propagation is various directions, for example yawing (i.e. oscillate about vertical axis) in the plane parallel to the surface on the tissue.

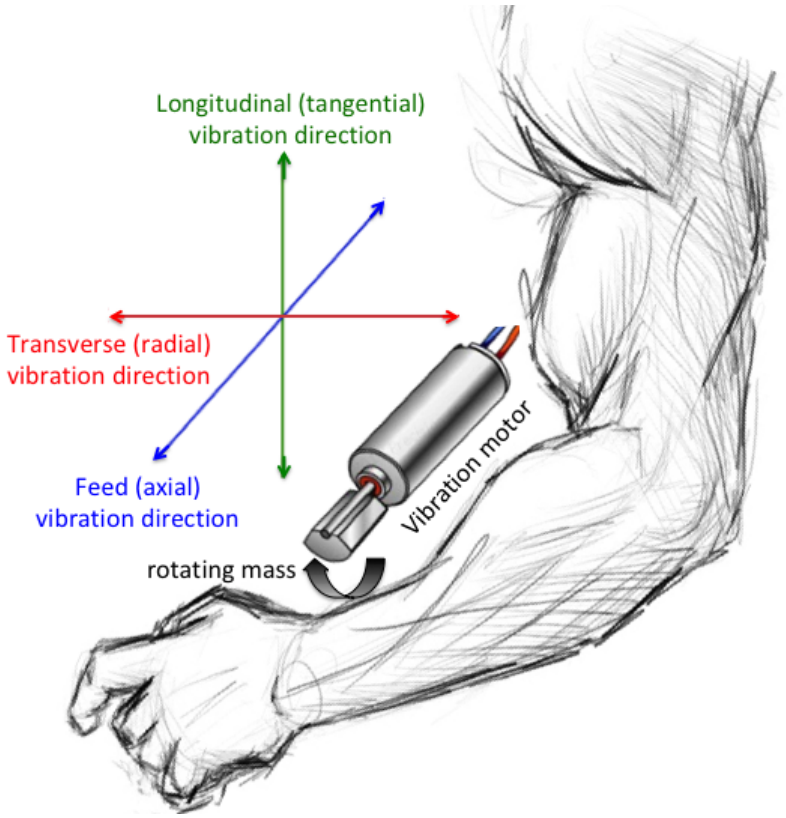


Figure 4.3: Focal vibration propagation directions when applied on the forearm (*Arm sketch* 2001, *Vibration motor* 2015).

4.4.1 Focal vibrations and muscles of able bodied people

Bianconi & Van Der Meulen (1963) studied the muscle-tendon structures and their responsiveness to stretch or focal tendon vibration stimuli. They found that primary I afferents (as a fast conducting afferent fibres firing at frequencies over 70Hz) to be active during both stretch and vibrations, whereas secondary type II afferent fibres remain unresponsive. These apply if the tendon is stationary during vibration stimulation and the vibrations have a high frequency above 30Hz. Under these conditions, excitation thresholds of both muscle spindles' and consequently type I fibres' are lower than without vibration present. The increased discharge of I afferents induces a reflex spinal reaction mediated by α motoneurons that induces a tonic contraction in the muscles connected to the vibrated tendon and this contraction is called *tonic vibration reflex* or short TVR (Eklund & Hagbarth 1966, Hagbarth & Eklund 1966*b*). Hagbarth and Eklund in 1966 are the first observes of TVR in human participants. The mechanism is as follows: focal vibration of an unmovable and relaxed tendon with amplitudes ranging between 0.5 to 3.3mm and frequencies 20-200Hz, activate firing of connected muscle's primary endings, i.e. muscle spindles; agile primary Ia fibres induce a spinal reflex and activation of the agonist muscle and relaxation in the antagonist muscles, both of which were previously at rest. Agonist muscle is continuously stretched with the increase in tonus but the subjective feeling is not unpleasant (Hagbarth & Eklund 1966*a*). In contrast Brown et al. (1967) postulated that if volitional contraction is introduced during focal tendon vibration, muscle spindles became less sensitive and Golgi Tendon Organs (GTO) more responsive to vibration stimuli. This could be the direct consequence of muscle anatomy and the location of muscle spindles and GTOs. The secondary endings (GTOs) lie within extrafusal muscle fibres near the junction between a tendon and the muscle while primary endings (spindles) surround intrafusal muscle fibres and are close to the motoneuron innervation points. Brown et al. (1967) concluded that due to visco-elasticity of the intrafusal fibres they became more susceptible to the foreign mechanical stimuli and reflex responses via motoneurons; whereas during contraction GTO respond to both vibration stimuli and voluntary contraction. Park & Martin (1993) further refined TVR parameters and consequences claiming that it rises with the increase of FV frequency up to 100-150Hz and then decrease. This could be due to increase in the depolarisation and the number of responding motoneurons. TVR seems irrespective of FV amplitude.

Focal vibration applied to a tendon of a blindfolded person can induce illusionary movements of the stationary joint in the direction that the muscle attach to the tendon would stretch (e.g. vibrations applied to the dorsal side of the wrist can induce a sensation of the hand flexing even though the it is motionless) (Kito et al. 2006, Ribot-Ciscar et al. 1998). It is presumed that this effect is not limited to TVR but also long-loop cortical circuits and their responses to muscle spindles excitation. Muscle that is responding to this excitation is the antagonist muscle (with the increase in EMG activity) to the direction of illusionary movements (e.g. dorsal side wrist vibration would excite extensor muscles as antagonist muscles and not flexor muscles as agonist muscles) (Capaday & Cooke 1983). For the multidirectional illusionary movements, multiple tendon vibration with the same parameters recruit muscles in the same biomechanical order as volitional movement would (Calvin-Figuiere et al. 2000). This suggests that perceptual and motor processing may have similar organisational distributions within motoneuron pools. Besides, there is a great correlation between the velocity of illusionary movements and EMG muscle activation: faster the movement seem, greater the amplitude of EMG. One can postulate that this correlation can have cortical origins where the sensory stimulation is answered by the motor cortical areas, or even more plausible supraspinal control of the spinal reflexes (Calvin-Figuiere et al. 1999, Ribot-Ciscar et al. 1996). Forner-Cordero et al. (2008) investigated these claims and observed an increase in motor map volume and motor output areas of the transcranial magnetic stimulation TMS following focal tendon vibration indicating cortical and/or corticospinal reorganisation.

If focal tendon vibration is imposed to a volitional limb movement, proprioceptive awareness is reversibly degraded (Bock et al. 2007). One component of this effect is the rise in GTO sensitivity caused by simultaneous tendon vibration of the contracting muscle (Roll et al. 1989). Provided that the participant is asked to control the limb to accurately match the limb position, there is an under- or overshoot of the targeted position, depending on the movement pattern required. Targeted movement velocity was lower if the vibrated tendon's muscle is required to be lengthening (Sittig et al. 1985) thus undershoot of the position. If vibrations are applied to the tendons of the ago-antagonist pair, the direction and the velocity of the illusionary movements are highly depend on the difference of vibration frequency and amplitude. More pronounced illusionary movement with higher velocity and matching target undershooting will occur for the muscle with lower frequency (e.g. if all tendons of the wrist are vibrated simultaneously but dorsal side with higher

frequency, the movement will again be perceived as flexion because flexion tendons and muscles receive low frequency vibrations) (Gilhodes et al. 1986). In contrast, no illusionary movement will be perceived if ago-antagonistic muscle or tendon pairs are vibrated with same frequency (Kasai et al. 1992).

Calvin-Figuiere et al. (1999) combined vibration of the two antagonistic muscle groups at the same frequency and observed neither kinesthetic illusion nor motor activity. In addition, vibrating the two antagonistic muscle groups at different frequencies induced both a kinesthetic illusion and a motor response in the muscle vibrated at lower frequency. On the spinal lever, if vibrations increased Ia afferent inflow, the usual biomechanical response would be to reduce excitability of the motoneurons. However this was not observed for simultaneous multiple muscle vibrations where motor unit firing increased (Ribot-Ciscar et al. 1996). There is a possibility that the involuntary contractions may be a result of a rebound excitation from the motoneuron pools. The rebound is only present if the lengthening muscle is suffering an mechanical perturbation (Inglish & Frank 1990, Inglish et al. 1991). If so, could this be a safety mechanisms that the muscle is using to prevent damaging of its fibres? This is partly explored in chapter 5 of this thesis .

Four main observations when focal vibrations are applied on a single muscle are outlined in literature as (Murillo et al. 2011):

- facilitation of muscle contraction for functional activity
- improvement of motor control in functional activities
- restoration of sensorimotor organisation in movement disorders
- reduction in spasticity

It seems that focal muscle vibration can recuperate the muscle and magnify performance. Focal vibratory stimulation of the quadriceps muscle with parameters 100Hz and 0.3-0.5mm in total of 9 ten minute sessions during 3 consecutive days increased vertical jump and leg power for at least 90 days after treatment (Filippi et al. 2009). Aprile et al. (2016) added that refinement of the upper limb motor performance after focal vibration can persist up to 10 days but only for frequency of 200Hz and not 100Hz. Vibrations were applied on deltoid, biceps and pectoralis muscles for 30 minutes on three consecutive days. Jackson & Turner (2003) investigated how ipsilateral leg

behaves when 30 minutes of vibrations are applied to the rectus muscle on the contralateral leg. For the amplitude of 1.5-2mm two frequencies are investigated 30 Hz and 120Hz. They observed reduction in both legs peaking 30min post treatment, with 30Hz expressing bigger force depletion.

Timing of the FV might be important for triggering desired muscle output. It is already mentioned that 30 minutes of focal vibration of the relaxed larger muscles can degrade muscle performance (Jackson & Turner 2003). In contrast, after FV (80Hz 1mm) applied over wrist flexors for 5 minutes during which muscles were relaxed, instigated a surge in hand grip force and grip control. This study also outlined no changes in grip forces after FV applied during muscle contraction (Santos & Aruin 2008). Even if participant is repeating a movement during FV with as much as 20-30 seconds of rest in between, a maximal voluntary contraction (MVC) will likely be reduced in both intermittent and sustained MVC (Bongiovanni et al. 1990). It seems that for the increase in muscle performance, it is advised to apply FV while the muscle is relaxing and that vibrations shouldn't be vibrated for a long period of time (e.g. 15 min for larger muscles such as forearm flexor and extensor muscles) (Smith & Brouwer 2005).

One might argue that, similar to WBV, there is again a misunderstanding about FV post effects with regards to different parameters but it is just an illusion. One of the loudest literature messages regarding FV is that a high frequency low amplitude focal vibrations elicit a *busy line* in afferent type Ia pathways because of hyperexcitability of muscle spindles and leading to changes in motor responses. With the advancement in electrophysiological devices and following physiological knowledge, researchers try to scrutinize this statement until full understanding of the underlying mechanisms.

The busy line phenomenon was hypothesised as early as 1960s (Lance et al. 1968). Vibrations might be inducing the busy line of Ia afferents during which these afferents are mostly excited by the vibration and almost not susceptible to the changes in stretch. There are several theories about why is motor response altered and where exactly are origins of the change. To begin with, Perez et al. (2003) observed that the reciprocal inhibition (i.e. relaxation of the antagonist muscle to accommodate contraction of agonist) of a non vibrated antagonist muscle is directly dependent on the pattern of sensory stimulation. Patterned stimulation enhanced reciprocal inhibition regardless to the accompanying cortical stimulation. Reciprocal Ia inhibition mediated via the spinal interneurones is dynamically modulated during volitional movements, leading to alteration in ac-

tivation pattern of both muscles in ago-antagonistic muscle pairs. During vibrations of contracted muscles, it is likely for the antagonist muscle to relax more to allow agonist to sustain contraction. This is not what is observed, especially during tendon vibration. The presence of EMG activity in antagonist muscle coupled with kinaestetic illusionary movement foist a theory that proprioceptive afferents (most likely type II afferents excited by Golgi tendon organs) are evoking sensory projection in sensorimotor cortex. Sensorimotor cortex could be responding to this stimulation by demanding a motor response from the spinal circuits. In the spinal circuits there is insufficient synaptic demand from the reflexory afferents to support this demand, so motoneurons are not efficiently excited to produce a contraction but merely an illusion of a movement. Furthermore, as previously mentioned over- and under- estimation of a position during tendon vibrations could be due to dual mechanisms of performing a contraction as demanded from the agonist muscle and conflicted response of supplying antagonist muscle with a (illusionary) motor response instead of reciprocal inhibition.

H-reflex is a reflexory reaction following electrical stimulation of the Ia fibres. Therefore this method is widely used in FV assessment research. It is observed that vibration may induces a post vibration depression (PVD) in able-bodied people. Abbruzzese et al. (2001) theorised that this depression might be a result of a reduction of the transmitter release from Ia presynaptic terminals in the spinal synapses. Presynaptic inhibition could be interpreted by the spine as a lack of sensory input leading to the overestimation in motor response. This effect is more pronounced if vibrations are applied over the muscle belly than over the tendon (Lee et al. 2014). When addressing vibration parameters, high frequencies are considered those above 50 Hz, and low amplitudes are those lower than 1 mm. Nonetheless it seems that amplitude of 0.1mm for a range of higher frequencies (40, 80 and 120Hz) have a minimum impact on H reflex reduction while the highest is for 80Hz and 0.3mm for the gastrocnemius muscle (Seo et al. 2016).

Transcranial magnetic (TMS) and transcranial electric (TES) stimulations were used to examine motor evoked potentials (MEP) and differentiate between cortical and spinal involvement following muscle FV (80Hz 0.5mm) by Kossev et al. (1999). They reported augmentation of MEPs for TMS and not TES. This observation is discussed in support of a wide cortical involvement in muscle FV. However it is not clear whether this is a chain reaction leading to the cortical action or is limited to a perception. In a follow up study Kossev et al. (2001) suggested that this type of stimulation is more

likely to elicit a spinal reflexory reaction rather than a cortical one. Still, this does not exclude a presence of cortical (co-)activation. Marconi et al. (2008) used different approach of short-interval intracortical inhibition (mediated by $GABA_A$-ergic circuits) and facilitation (mediated by $GABA_B$-ergic circuits) for the both muscles in ago-antagonist pairs observed for muscle FV with contraction and muscle FV with relaxation. By comparing results, they indicated that FV during voluntary contraction indeed induces a cortical excitability in motor cortex even after 2 weeks post-stimulation. The study also assured previous assumption about cortical demand for the motor response prompting illusionary movements: the results suggested the increased MEPs in the vibrated agonist muscle and reduced motor responses in the agonist muscle. Frequency of 160Hz and above will doubtfully induce any changes in MEPs following muscle FV as it seems to involve different dynamic effects (Siggelkow et al. 1999).

To summarise, low amplitude high frequency FV of the muscles can have a beneficial improvement of muscle performance. Vibration lowers firing thresholds of muscle spindles which impose a busy line effect on Ia afferent pathways, irrespective to any accompanying stretch. This type of stimulation is evoking a presynaptic inhibition by means of neurotransmitter reduction in synapses of spinal interneurons that is casing an increase in motoneuron activation. The consequential entrain of events such as post-activation depression and cortical involvement are dependent on the FV parameters and timing. For enhancing motor power duration of the FV needs to be limited to a few minutes, no more than 15 and dependent on the muscle size. Furthermore it is recommended to apply FV while the muscle remains in a relaxed state.

4.4.2 Focal vibrations and hypertonic, spastic muscles

Table 4.1 at the end of this chapter summarises reported research that is assessing the employment of focal vibratory stimulation as a nonpharmaceutical spasticity remedy. The major benefit of focal vibration is hidden in a word *focal* ergo localisation of vibratory stimulation to one selected structure of the body. In research this is important to understand primary reaction channels and even correlates with such a complicated disorder as spasticity.

It seems that focal muscle vibration can equally reduce spasticity in many neurological sequelae such as cerebral palsy and multiple sclerosis, and stroke and spinal cord injury. Etoom & Marchetti (2015) observed a decrease in MAS score in spasticity due to SCI that persisted one month after

the last, the tenth session of FV applied on the triceps muscle. And this decrease is irrespective of the type of the injury (Murillo et al. 2011). A larger number of papers confirm the stroke spasticity diminish by FV measured by MAS (Calabrò et al. 2017, Celletti et al. 2017, Costantino et al. 2016, Harini et al. 2013, Nardone & Schieppati 2005, Noma et al. 2009, 2012, Oh et al. 2017). Nonetheless MAS is a single outcome measure only in the work of Etoom & Marchetti (2015), the other papers correlate MAS score with other more objective assessments of the limb functionality. Those associated with impairment due to stroke are summarised in outcome measure column in table 4.1 in parallel to the changes evoked by FV in latter column. The enhancement is noted immediately after a single FV stimulus and lasts 5 minutes (Liepert & Binder 2010). Tavernese et al. (2013) analysed movement kinematics and observed improvements in velocity, smoothness and duration which might be a principal correlate of functional recovery. Tavernese speculated that this improvement can be linked to FV, not just spasticity reduction. In addition, Costantino et al. (2016) claim that FV of 300Hz after 12 session can boost muscle strength of hemiplegic post-stroke participants.

The only study that did not observe any change in MAS score of upper limb spasticity in participants with SCI following FV is by by Backus et al. (2014). Authors contend that MAS is not sensitive enough to capture changes in muscle tone in SCI and that more objective measure is needed.

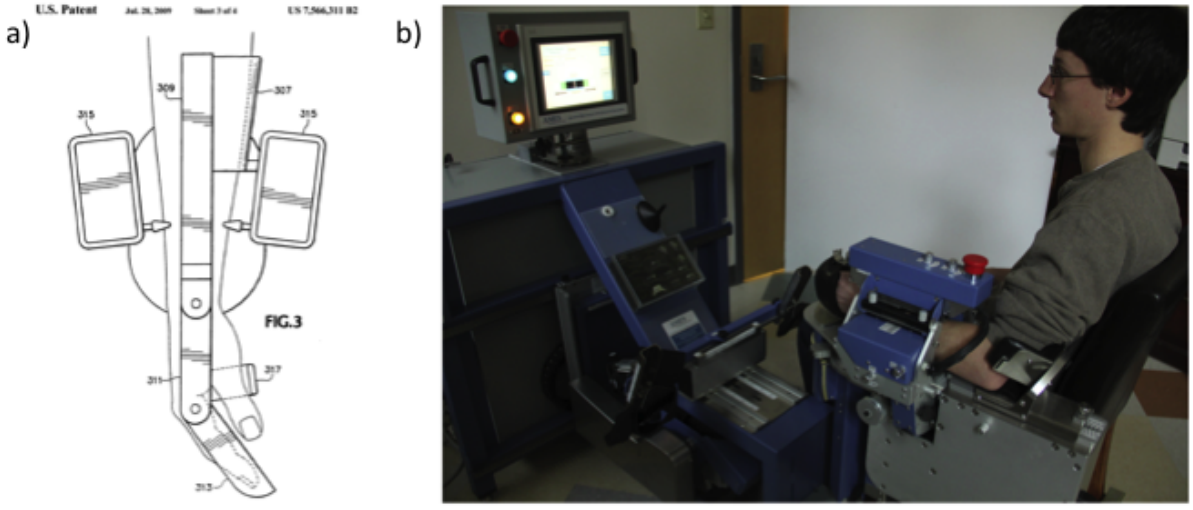


Figure 4.4: a) Diagram of hand's position in AMES device (Cordo 2009) b) User of the AMES device (Backus et al. 2014).

A few studies are found to gauge limb motor function post FV using a robotic device (Backus et al. 2014, Calabrò et al. 2017, Casale et al. 2014, Cordo et al. 2008, 2013*b*). One is for SCI and four are for stroke. Three use the same device (Backus et al. 2014, Cordo et al. 2008, 2013*b*) created by Cordo, while two others are using commercially available devices: Armeo spring, Ocoma (Casale et al. 2014) and Armeo-Power by Hocoma (Calabrò et al. 2017). Cordo et al. (2008) presented AMES (U.S. Patent No. 7,566,311) which is short for Assisted Movement with Enhanced Sensation, that synthesise (1) vibration device for wrist tendons with (2) robotic assisted manipulandum for thumb and fingers which can (3) record EMG from forearm muscles and (4) torque during task execution and (5) provide biofeedback to the user, as seen in figure 4.4. Focal vibration can be delivered by a small arrow-like probe for amplitudes in range of 0.5 to 4mm with 2mm being preferable; frequencies available are ranging between 30-70Hz with preferred around 60-70Hz. Vibrations can be delivered in a longitudinal or a transverse direction. A servo motor is used to deliver movements of the fingers and the wrist via a pivotal mechanisms. Movements that AMES can perform are controlled velocity displacement of the wrist and fingers to flexion or extension while the hand is in midsuppination position. Load cells senses forces applied to different parts of the mechanism and translate data into the torque. The device can record torque and EMG during active movement of fingers and thumb or assistance from the user during imposed movement and provide biofeedback to the user. Cordo et al. (2008) justifies the use of AMES device in stroke participants with the emphasis to its safety features. Cordo et al. (2013*b*) reports benefits of FV during hand opening and closing and an improvement in strength and active range of motion. It is argued that the addition of FV was to mitigate hyperexcitability of the reflexes and strengthen corticospinal pathways, with the focus on motor and proprioceptive signals from the brain. Backus et al. (2014) brought the device to the users with chronic incomplete tetraplegia. They recruited 15 arms from 10 volunteers and observed enhancement of strength and active motions but not in MAS. In all these three AMES studies FV was applied on the wrist tendons of the antagonist muscles during movement to stimulate proprioceptive channels. Vibration parameters were set at 2mm and 60Hz for the duration of 30 minutes. The duration of studies was different between 9 and 13 weeks long, and sessions repeated 2-3 times a week.

Casale et al. (2014) applied FV to the triceps brachii muscle during 5 consecutive days for each of 2 weeks. FV (2mm at 100Hz) was applied during one continuous stimulation lasting 30 minutes us-

ing a pneumatic vibrator powered by compressed air [VIBRA, @Circle]. In addition to vibrator stimulation, participants received traditional physiotherapy. Armeo-spring was used only to measure upper limb function by analysing kinematics of a reaching movement towards a visual target against gravity (figure 4.5). Kinematic analysis included percentage of task completed in a given time, time to fully complete a task and the deviation from the shortest trajectory. Armeo-spring was employed at the beginning of the first and sixth session and 48 hours after 10th session. The authors reported significant improvements in MAS and upper limb functionality as a repercussion of associated FV and physiotherapy. It is unclear why robotic device was not used to engage in controlled movement repetition therapy, and why the choice of these three measurement timings was chosen.

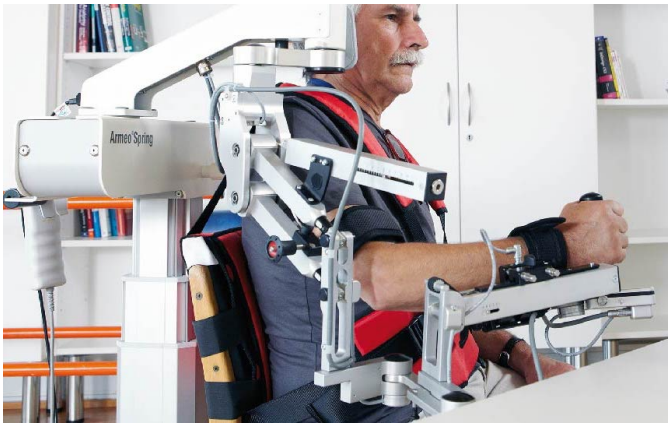


Figure 4.5: Armeo-spring (*Armeo-Spring* 2011).

Calabrò et al. (2017) presented the idea of coupling muscle FV with rehabilitation robotics to reduce upper limb spasticity and improve its functionality in stroke. Commercially available Armeo-Power by Hocoma was a device of choice for robotic, task-oriented, rehabilitation tasks. It is an upper limb exoskeleton providing anti-gravity weight support from the shoulder including the hand. By providing an intelligent assistance when needed to any or any combination of the shoulder, the elbow, the wrist and the grasping movements in a large 3D space, it facilitates controlled, repetitive and task oriented training. It can provide augmented performance feedback of the task execution. It records an objective measures of performance based on sensor and motor data including movement ranges and forces. In this study participants performed a customised group of exercises lasting 1 hour. FV was delivered by Vibra Plus device (EUROTRONIK STUDIOERRE srl), a pneumatic vibrator powered by a compressed air and apply on the muscle by a probe approximately $2cm^2$ in surface. FV amplitude was 0.3 ± 0.1 mm and frequency 80Hz simultaneously applied to triceps brachilis, supraspinatus, and deltoid muscles during task execution (1 hour). The diagram of the entire system is presented in figure 4.6.

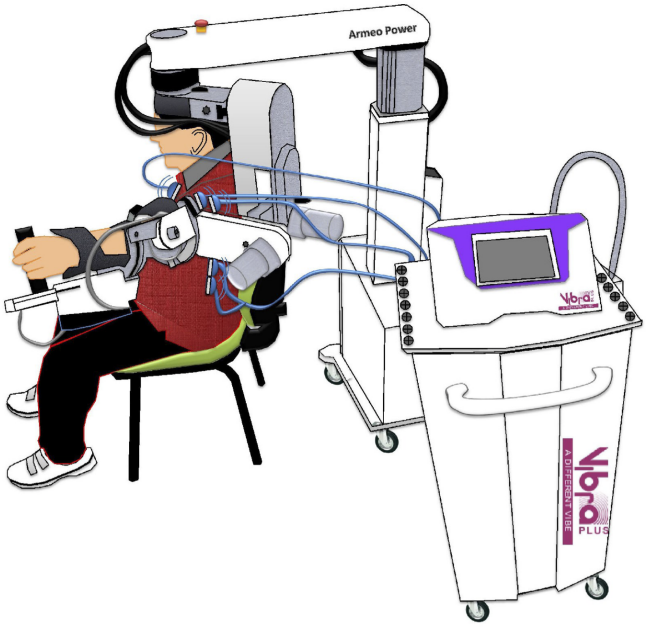


Figure 4.6: Combining rehabilitation robotics with muscle focal vibration for upper limb spasticity and functionality advance (Calabrò et al. 2017).

The trial lasted eight consecutive weeks with 5 days of training each week, bringing total of 40 sessions each lasting 1 hour. Out of all outcome measures, MAS and kinematic movement profiles will be commented here, those remaining in the latter section. It is not clear whether the measures were taken at the end of each session or at the end of the last 40th session, therefore it will be considered to be at the end of the trial as the results provide just one value for the measurements. Nonetheless, authors use FV to provide a rationale for observed spasticity reduction of at least 1 point at MAS scale at the end of trial. Sadly the gradient of MAS change was not provided for in-between sessions therefore the carryover effects remain unknown. Despite the fact that Armeo-Power is able to record kinematic data for each session, this is again not considered in the results section of the report. The increase in force, passive range of motion, and reduction in arm weight support are observed parameters accounting for overall improvement in upper limb performance. This enhancement in performance is elucidated by the use of rehabilitation robotics and intense movement therapy concomitantly with FV. As compared to exercise without FV, the hypothesis was made that FV plays a crucial role in buildout of motor performance rehabilitation, regardless to spasticity. The physiological mechanisms are discussed below.

Mechanisms of action

Because of its ability to selectively stimulate Ia afferent pathway, unpuzzling FV physiological mechanisms includes understanding changes in H-reflexe, T-reflex, M and F waves, EMG and evoked potentials. Most of the studies from table 4.1 for SCI investigates these.

Assessing TVR in able body participants is believed to be a measure of Ia polysynaptic reflex

transmission. A small amplitude of a tonic vibration reflex (TVR) is sometimes observed during FV in SCI, as compared to able-bodied participants. Ashby et al. (1974) reported absence of TVR even after spasticity develops is acute stage of SCI. The two occurrences happened in incomplete SCI. In contrast Dimitrijevic et al. (1977) observed different but always present TVR (for tendon vibration parameters 0.5-1mm and 60-120Hz) in different SCI lesion types (section 3.1). Ribot-Ciscar et al. (2003) argued that roughly half of the study's participant with chronic cervical SCI had TVR because they had less or no impairment between from higher brain centres to the spine. The absence of TVR might also be contributed to the absence of the stretch reflex due to the reinnervation. However, having in mind that it is muscle spindles (and never GTO (Cody et al. 1987)) that drive afferent pathways due to FV stimuli in the first place, perhaps TVR is not limited to just spinal and supraspinal mechanisms, but muscle's responsiveness to the stimulus. Nonetheless, exploration of TVR seems unreliable in SCI and associated spasticity.

H-reflex can be used as a measure of spinal reflex excitation and under different condition, a variety of aspects can be observed. By observing a change of H reflex amplitude with and without vibration Ashby et al. (1974) quantified the degree of presynaptic inhibition of the Ia monosynaptic reflex. They observed a lessening of effectiveness in Ia monosynaptic inhibition and no reflex abilities of the polysynaptic pathways in established spasticity. It seems that loss of supraspinal control of the interneurones could play important role in spasticity and vibration-induced spasticity reduction. Taylor et al. (1984) noticed that FV of the Achilles tendon suppressed the amplitude of the H reflex in SCI much less than in able bodied participants. Therefore Ia presynaptic inhibition induced by FV in able bodied people seems altered due to SCI and spasticity. In acute SCI, FV can entirely abolish H-reflex and in chronic SCI the reflex in less suppressed (Calancie et al. 1993). This leads to several observations about pathways behaviour and spasticity origins in SCI:

- in acute SCI presynaptic inhibition is exaggerated leading to the absence of the reflexes
- in chronic SCI presynaptic inhibition seems almost non existent and contributing to the hypereflexia and spasticity hypertonicity

It could be that the mechanisms underlying this dramatical shift in reflex control, probably from the higher corticospinal centres, leads to the development of spasticity. By enhancing presynaptic inhibition, FV could pave the way towards its diminishing. Butler et al. (2006) disagreed with

this postulation claiming that there is no change in H-reflex following a 2 seconds FV of the Achilles tendon. In addition, the evoked EMG was reduced after the FV. Disregarding more than insufficient duration (1 second) of vibratory stimuli, authors assume that FV in spasticity could cause postsynaptic depression and consequential reduction in muscle tone. And not only that, Hilgevoord et al. (1996) reported FV induced changes in H-reflex thresholds and associated them to the augmentation of motoneuron post-activation depression. This is where a method such as TMS can come in handy because it is able to directly excite motoneurons. Immediately after FV of the flexor carpi radialis tendon in participants with tetraplegia, there was no changes in corticomotor excitability whereas after 30 min of rest it was significantly increased (Gomes-Osman & Field-Fote 2014). Pondering about changes in corticomotor excitability are mainly mediated in supraspinal sites by GABA-eric mechanisms (Kaelin-Lang et al. 2004), could this apply to the FV as well?

Perez et al. (2004) investigated the occurrence of the reciprocal inhibition observed in able bodied participant when FV is applied. They observed both long latency and short latency effects and postulated that FV perhaps does not only alters the presynaptic inhibition of the sensory afferents but also interneurone and post-activation motoneuron behaviours. Polysynaptic reflex could be more affected by the vibratory stimulus creating a chain reaction within corsticospinal tract and resulting in reduction in excitability of motoneuron and, consequentially hypertonicity.

It seems that FV in SCI might create an intricate labyrinth of signals and changes in CNS communication. Underlying mechanisms seem similar for WBV, SV and FV induced reduction in spasticity due to SCI is illustrated in Figure 4.7 (Blackburn et al. 2014*a*, Sayenko et al. 2010):

- increase in Ia firing thresholds
- surge in presynaptic inhibition of Ia afferents in the spine
- primary afferent depolarisation
- postsynaptic depression of motoneuron
- reduction in post-activation depression

The elements in this chain reaction are mutually dependent but also reliant on the spinal interneurone synaptic GABAeric transmission. The control over this transmission have both

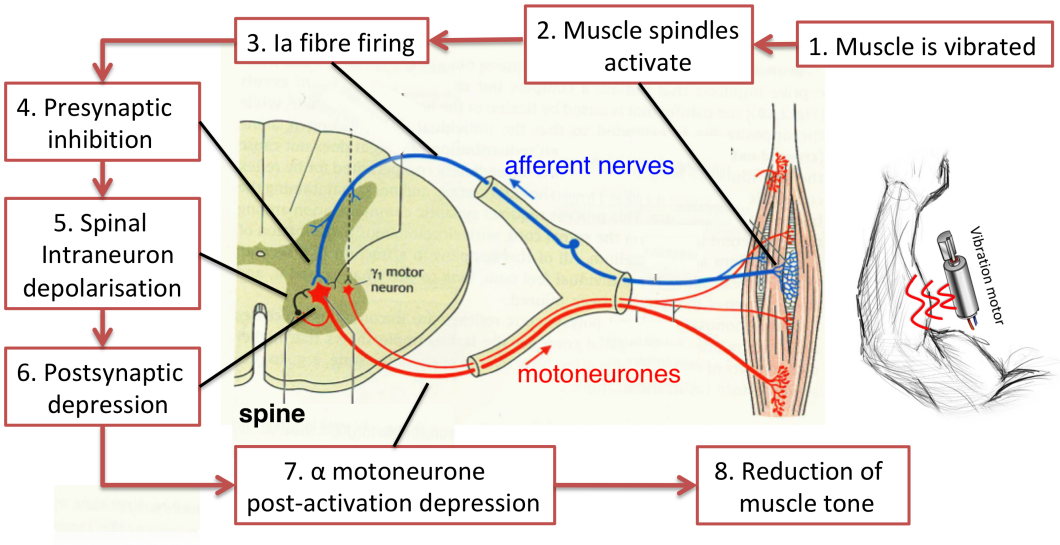


Figure 4.7: Diagram of physiological mechanisms underlying vibratory stimulation to reduce muscle tone in spasticity.

supraspinal and cortical origins so it seems that the entire CNS is differently involved in spasticity and vibration induced spasticity reduction. However, WBV distribution across body gradually decrease further from the site of application and it is not limited to one structure. This could perhaps explain why the spasticity reduction is not as reliable as for FV. Vibration effects on the heart as a muscle is largely unknown. Vibration effects on major organs and organ systems are largely unknown. Who is to say that there are no other unnoticed links contributing or preventing spasticity recovery. Segmental vibration applied on the limb outdo this issue but the disperse of vibration across the limb is still present. Proprioceptive channels could be triggered due to the difference in vibration parameters reaching proximal muscles and tendons. Not to argue that this is necessarily a bad thing, but the rationalisation for the use of a more comprehensive method (FV) over a more complex (SV) with a similar if not the same effects is more than clear.

Taken one step further, a bold question is raised here: can spasticity due to SCI be reduced with similar effectiveness but much less detriment with appropriate FV rehabilitation protocol as compared to widely used pharmaceutical agent Baclofen?

Unfortunately, spasticity is also repercussion following, among others CNS sequelae, a stroke. Faist, Mazevet, Dietz & Brain (1994) compared spasticity ramification due to FV in participants with spasticity due to hemiplegia (in stroke) and paraplegia (in SCI). The results suggested that in hemiplegia presynaptic inhibition remains unchanged and the main anti-spastic facilitator is

post-activation depression of motoneurons following a repetitive synaptic transmission. This is also observed for spasticity due to multiple sclerosis. This is why anti-spastic abilities of FV are mainly investigated by the analysis of F wave, H/M ratios and TMS studies. To summarise, F wave is suppressed following FV in stroke (Noma et al. 2009). This suppression is correlated to α motoneuron decrease in activation. Similar to SCI, TMS studies in stroke following FV increase corticomotor excitation, but also there is a high degree of correlation between level of spasticity and intracortical inhibition (Marconi et al. 2011). Therefore it seems that spasticity as well as FV anti-spastic capabilities, are different to SCI. Nonetheless FV have equally potent effects on spasticity decrease and muscle functionality increase (table 4.1).

Table 4.1: Table outlining literature that is using focal vibration for reduction of hypertonicity in muscles and related stiffness in joint

Reference (Author, year)	Diagnosis	N of participants	Use of robotic devices	FV position	FV intervention (amp/freq and duration)	Outcome measures	Results + follow up	Discussion points
Hagbarth et al 1966	Spinal cyst	1	no	Session 1: Biceps brachii Session 2: triceps brachii	0.05mm/160Hz	EMG, - angular motions, - active and passive muscular tensions	- exaggerated reflexes and reduced voluntary power - flexion of elbow increased by 20deg - vibration of the antagonist completely abolished ability to keep the forearm raised	- Participant 1 fatigued rapidly but the voluntary power is restored as soon as vibration is applied to the biceps tendon. Vibration of the triceps tendon causes a temporary complete paralysis of biceps. - Vibration applied to the tendons of participant 2 extensor muscles had no appreciable effect while the subject remained relaxed, but vibration combined with a voluntary effort to lift the hand resulted in a maximal dorsal flexion of the wrist. A post-vibratory attempt to lift the hand was more successful than the similar attempt prior to the vibration.
	Subfrontal glioma	1		Tendons of wrist extensors of the forearm			- brisk reflexes with no volitional movements - unable to move hand during vibrations	
Ashby et al 1974	SCI	10	no	1cm above Achilles tendon	3mm/60Hz 3 stimuli, each between 2 and 3 sec long	- tonic vibration reflex (TVR), - M wave - H reflex	- phasic spike in reflex that can be associated with TVR - suppression of H-reflex (42.2%) - increase in H/M ratio	- Presynaptic inhibition is greater than normal, transmission in the Ia monosynaptic pathway is reduced, and in the Ia polysynaptic pathway virtually abolished. - In established spasticity, presynaptic inhibition is impaired, transmission in the Ia monosynaptic pathway is increased, but transmission in the Ia polysynaptic pathway never recovers.
Taylor et al 1984	SCI	104	no	Achilles tendon	1.5mm/60Hz 2 stimuli of 20sec repeated every 90sec	- H reflex amplitude	- depression of H reflex amplitude	- The ratio of the maximum H reflex during vibration to the maximum control H reflex was greater in the spastic group than in the normal indicating that vibration was less effective in suppressing the Hreflex in the spastic patients. - This ration increased with the duration of the lesion for all patients, but was unrelated to the level of the lesion or to whether the lesion was complete or incomplete. - The H reflex depression occurred sometime after the onset of vibration and may outlast the vibration by several hundred msec. So it is unlikely to be due to occlusion in the afferent nerve fibres (the "busyline" effect). - Vibration also suppresses the facilitation of single motors unit by group 1 volleys without changing the motor units firing rate (and, by implication, its excitability). If the H reflex is accepted as being largely mediated by a monosynaptic pathway, the locus of the suppressive effect of vibration is "premotoneuronal" (for example, due to presynaptic inhibition, transmitter depletion of failure of invasion of some afferent terminals). Either the mechanisms that normally block the H reflex are less effective in spasticity or vibration produces a greater background facilitation of motoneurons in spasticity.
Calancie et al 1993	SCI	3	no	Achilles tendon	1.1mm/110Hz 3 stimuli for each of 9 increments in range [0.1 10]sec	- EMG, -H reflex, - M wave, - T reflex	- reduction of M wave in chronic SCI - reduction in H reflex and T reflex - reduction in TVR in acute SCI - H/M ration high in chronic SCI: clinical signs of spasticity	- Spinal cord injury disrupts the supraspinal influence over segmental interneurons mediating presynaptic inhibition, and the hyporeflexia associated with 'spinal shock' is due in part to a substantial increase in the efficacy of presynaptic inhibition. - Over time the level of presynaptic inhibition of ankle extensor Ia input in SCI subjects declines to levels less than those of control subjects, contributing to the enhancement of spinal reflexes consistent with the clinical state of 'spasticity' seen in chronic SCI.
Ribot-Ciscar et al 2003	SCI	8	no	triceps or biceps brachii tendons near the elbow	not specified/80Hz First part: 1stimulus of 9 sec during relaxation Second part: 1 stimulus 1 stimulus of 9sec starting 3sec before voluntary contraction	- MVC - TVR - muscle voluntary activation force prediction (FP)	- MVC improved - TVR was not observed in half of the participants with chronic cervical SCI - FP was observed only with participants who had some voluntary contraction over muscle	- Where there is upper motoneuron injury, vibration may enhance force by a number of mechanisms (e.g., enhanced muscle spindle afferent activity resulting in supraspinal and/or spinal excitatory reflex activation of motoneurons). Subjects with lower motoneuron damage may have denervated portions of muscle, but reinnervation is expected to occur from neighboring axons. If reinnervation from intact axons fails, the muscle fibers that remain denervated will not be activated either by volition, reflexly by vibration, or by electrical stimulation of the radial nerve. - The data show that triceps brachii tendon vibration is a way to activate the triceps brachii muscle at rest in some SCI subjects who retain partial voluntary control of this muscle. Vibration induced contractions may be less uncomfortable than electrically induced contractions. Use of a miniaturized vibrator might help these individuals with SCI improve their muscle function but this issue also needs quantitative evaluation in relation to the motor and sensory function that is preserved after the injury. Vibration-induced muscle contractions may be more effective in people who have an incomplete SCI without lower motoneuron involvement, so that the absence of stretch reflexes that occurs with muscle reinnervation is not a consideration.

Table continues from previous page

Reference (Author, year)	Diagnosis	N of partic ipants	Use of robotic devices	FV position	FV intervention (amp/freq and duration)	Outcome measures	Results + follow up	Discussion points
Perez et al 2004	iSCI	14	no	Tibialis anterior tendon	not specified/60Hz Total of 3min of approx 10,000 stimuli (10 pulses at 60Hz every 1.5sec, pulse width 1ms)	- H reflex Ia afferent inhibition - presynaptic inhibition - total reciprocal inhibition -	- H reflex decrease indicating increase in Ia afferent inhibition - no change in presynaptic inhibition - increase in total reciprocal inhibition	- Vibration is proposed as a treatment for improvement of reciprocal inhibition of muscle activity - Vibration (as a form of sensory input repetitive muscle stretch) is a potent stimulus to Ia afferents necessary to change synaptic transmission, especially in those spinal circuits responsible for motor control
Butler et al 2006	SCI	8	no	Achilles tendon	not specified/80Hz 2sec	- EMGtvr, - M wave amplitude (Mmax), -H reflex amplitude (Hmax)	- Depression of EMGtvr - Delay in H resonse - No reduction in Hmax - No change in Mmax	- Reductions in electromyographic activity are unlikely to be mediated by changes at the Ia synapse or motoneuron because vibration did not alter the magnitude of the soleus H reflex. - The electromyographic reductions may involve long-lasting neuromodulatory effects on spinal inhibitory interneurons or synapses involved in the flexor reflex pathway
Murillo et al 2011	SCI	19	no	Rectus femoris	not specified/50Hz 1 stimulus of 10min	T wave, - H/M ratio, - Modified Asworst Scale (MAS), - range of motion (ROM), - duration and frequency of clonus	- T wave amplitude and H/M ratio decreased during stimulation -reduction in MAS and clonus - increase in joint angles and ROM	- Prolonged vibration on proximal lower extremity muscles decreased limb spasticity in patients with spinal cord injury, regardless of whether the lesion is complete or incomplete
Gomes-Osman et al 2014	SCI	20	no	distal tendon of the flexor carpi radialis	not specified/80Hz First 10min of functional task practice training.	- Nine-hole Peg Test (NHPT), - pinch force, - visuomotor tracking, - motor threshold, - cortical excitability,	- no change in posttest effects on the NHPT performance, visuomotor tracking, early modulation in corticomor excitability - posttest improvement in pinch force - increase for cortical excitability observed 30min posttest	- Vibration application time ranging from 3 minutes to 15 minutes (continuously) can be associated with short-term persistence of improvement in functional tasks that can influence the nervous system.
Backus et al 2014	SCI	10	Yes AMES	metacarpophalangeal flexor tendons during hand opening and extensor tendons during hand closing	2mm/60Hz total of 25 session over 9-13 weeks, each one stimulus of 10 minutes	- strength and active motion tests on the AMES device; - International Standards for the Neurological Classification of SCI (ISNCSCI) motor and sensory examinations: - Modified Ashworth Scale (MAS); - grasp and release test (GRT); - Van Lieshout Test (VLT); - Capabilities of Upper Extremity questionnaire (CUE)	- strength and active motion improvements in metacarpophalangeal and wrist movements - increase in GRT scores - no change in ISNCSCI, VLT, CUE no change in MAS	- Treatment with a device that combines repeated movements with targeted vibration to the antagonist muscle led to some improvements in impairments and upper limb function in this population of people with chronic, incomplete tetraplegia as a result of traumatic SCI - No change in MAS could be due to this test's insensitivity to a change in muscle tone of people with SCI.
Etoom et al 2015	SCI	1	no	triceps brachii	2mm/100Hz total of 10 session (3/4 sessions pw, 3 weeks) each 10 stimuli of 30sec with 1min break	- Modified Ashworth Scale (MAS)	- MAS reduction of elbow and wrist started after 5th session, and persisted after one month follow up	- Focal muscle vibration may reduce the spastic muscle tone to the antagonist muscle when applied at agonist muscle
Hilgevoord et al 1996	SCI and spastic paraparesis	33	no	Achilles tendon	not specified/100 Hz 1 stimulus of 1min	- H/M ratio, -H reflex inhibition, - H reflex threshold	- no change H/M ratio - H reflex amplitude inhibition 50% - H reflex threshold decrease	- The average H-reflex threshold decrease suggests a decrease of the motoneuron activation thresholds. A lower reflex threshold in spasticity, may contribute to the observed reduction of vibratory H reflex amplitude inhibition.
Cody et al 1987	MS,	12	no	tendon of flexor carpi 5 cm above the wrist crease	0.25-0.5mm/123Hz or 140Hz 64 or 128 stimuli each lasting 0.25sec with 0.1 or 0.5sec break	- EMG	- an exaggerated short-latency reflex response - no observable long-latency reflex responses	- Excitation of primary endings of muscle spindles, supporting the view that group Ia afferent-mediated reflex action is enhanced in spasticity - No indication of Golgi tendon organ and group II afferent involvement in-mediating reflex to vibration stimuli
	SCI,	3						
	ALS,	3						
	Stroke,	3						
	Cerebral tumour,	1						
	Pontine tumour	1						
Faist et al 1994	stroke	18	no	Soleus	not specified/not specified 20 stimuli each 1ms or 0.5ms	- M wave amplitude (Mmax), - Hmax/Mmax ratio - Ia fascilitation	- consistent increase in mean Mmax values and Ia fascilitation for SCI participants (no change for stroke population) - Hmax/Mmax ratio no difference	- The increased Ia facilitation seen in paraplegic can be ascribed to a decrease in presynaptic inhibition of heteronymous Ia afferents mediating the conditioning volley. It is therefore likely that primary afferent depolarization of homonymous Ia terminals and post-activation depression is also decreased in spastic paraplegic patients. - The most striking finding of the present investigation was the absence of significant difference of Ia facilitation between normal subjects and hemiplegics. - There was no correlation between decreased presynaptic inhibition of Ia terminals and the degree of spasticity measured by Ashworth's scale.
	SCI	17						

Table continues from previous page

Reference (Author, year)	Diagnosis	N of partic ipants	Use of robotic devices	FV position	FV intervention (amp/freq and duration)	Outcome measures	Results + follow up	Discussion points
Nardone et al 2005	stroke	11	no	Achilles tendon on both legs	0.05mm/90Hz 3 sessions (vib applied during assessment) each 1 stimuli of 4min followed by 2min break	- Modified Ashworth Scale (MAS), - resistance to passive movement, - short- (SLR) and - a medium-latency (MLR) EMG response	- SLR increased 110% in both legs - MLR increased 165% on the spastic and 120% on unaffected leg - linear dependency of reduction in MAS and increase in MLR	- Possibility that the increased background EMG in the affected leg of patients might be in part connected with the vibration-induced discharge from the Golgi tendon organ which, though very weak, could induce in the patients a motoneuronal facilitation through an abnormal disynaptic Ib pathway. - The vibration induced hyperexcitability of Ia afferents elicit firing onto group II interneuronal pathway would give rise to diminution of the descending drive because of an abnormal control of the group-II reflex pathway. - Results give evidence that the reflex component of hypertonia depends in particular on the hyperexcitability of the group-II spinal pathway, as disclosed by vibration, rather than group-Ia pathway.
Cordo et al 2008	stroke	20	Yes AMES	lengthening wrist tendons (either flexors or extensor depending on the movement)	2-3mm/60Hz total of 6 months, every other day 1 stimulus of 30 minutes	- self-evaluation at participant's home: - strength test of maximal torque produced - active range of motion - Stroke Impact Scale (SIS)	- improvement of average strength - increase in active range of motion - no change in hand SIS	- AMES is a new treatment approach for stroke rehabilitation and is based on the hypothesis that strengthening sensory-to-motor connectivity within the central nervous system, possibly through a Hebbian-type learning, is an effective means of restoring motor function. - The goal of AMES methodology is to activate—both simultaneously and repetitively—antagonistically related motor-output neurons and sensory-receiving neurons in the sensorimotor cortices to strengthen the connections between these brain areas.
Noma 2009	stroke	14	no	abdominal side of all fingers, the palm, the flexor tendon of the wrist and all of the flexor muscles of the upper limb	1.0mm/91Hz 1 stimulus of 5min	Modified Ashworth Scale (MAS), - F wave amplitude, - F/M ratio, - Active range of motion (AROM), - speed of object manipulation, - finger tapping	- decrease in MAS - decrease in F wave amplitude and F/M ratio, lasting at least 30min oststimulation - increase in AROM, finger tapping and speed of object manipulation	- The direct application of vibratory stimuli is an effective non-pharmacological anti-spastic treatment that could facilitate stroke rehabilitation. - The results provide good evidence of potential short-term benefits of anti-spastic vibratory therapy in post-stroke patients in terms of decreased muscle tonus and improved motor function
Liepert et al 2010	stroke	10	no	tendo-muscular passage of the extensor carpi radialis	Not specified/60Hz 1 stimulus of 5min	- Blocks and box test (BBT), - cortical silent period	- 20% decrease in time to complete BBT test - prolongation of cortical silent period	- Beneficial effects on dexterity lasting at least 15min poststimulus by enhancing inhibitory neuronal circuits targeting the antagonistic muscles
Marconi et al 2011	stroke	30	no	flexor carpi radialis (FCR) and biceps brachii (BB)	0.2-0.5mm/100Hz 3 consecutive days each had 3 times a day of 1 stimuli of 10min	- resting motor threshold (RMT), - map area, - map volume, - short-interval intracortical inhibition (SICI), - intracortical facilitation (ICF)	- reduction in RMT and an increase in motor map areas and map volume. - SICI increased in the flexors and decreased in the extensor - reduction in spasticity and increase in motor function - all observable effects lasting at least 2weeks postsession	- Muscle vibration administered in addition to conventional physiotherapy can reduce certain abnormalities of corticospinal excitability and intracortical inhibitory systems in poststroke chronic patients. This therapy may be used as a nonpharmacological intervention in the neurorehabilitation of mild to moderate hemiparesis. - A significant correlation was found between the degree of spasticity and the amount of intracortical inhibition.
Caliandro et al 2012	stroke	49	no	first session: pectoralis minor and the biceps brachii second session: flexor carpi	0.1-0.25mm/100Hz 3 consecutive days each 3 stimuli of 10 min separated by 1min break	- Functional Ability Scale of the Wolf Motor Function Test (WMFT FAS), - Modified Ashworth Scale (MAS), - visual analog scale (VAS)	trifold increase in average WMFT FAS -no change in MAS and VAS	- Improvement in upper limb functional abilities due to vibration - Possible explanation of absence in MAS change is that the stable contractures of tendons and the reduced joint range of motion determine strong functional limitations in the chronic patients, and consequently this clinical picture prevents a significant improvement of the passive mobilization and of pain when patients are to undergo rehabilitation.
Noma et al 2102	stroke	36	no	abdominal side of all fingers, the palm, the flexor tendon of the wris and all of the flexor muscles of the upper limb	1.0mm/91Hz 1 stimulus of 5min	- Modified Ashworth Scale (MAS), -F/M ratio, -F wave persistence	- reductions in F-wave amplitude, F/M ratio and F-wave persistence - improvements in the MAS scores for elbow and wrist flexor muscles lasting at least 30min poststimulation	- We postulate it is unlikely that presynaptic inhibition was the primary origin of the vibration induces spasticity suppression. - The alteration of motor cortex excitability could thus potentially be involved in the anti-spastic effect of vibrations. - Efficacy of vibrations and stretching cannot be attributed only to the effects of stretching.
Cordo et al 2013	stroke	43	Yes AMES	tendons of flexors digitorum profundus and pollicis longus, extensor digitorum communis, extensor pollicis longus.	2-3mm/60Hz total of 30 session during 10-12 weeks, each session during assisted movements for the duration of 30 minutes	- Fugl-Meyer Assessment of the Upper Extremity (FMA-UE), - box and blocks test (BBT), - Stroke Impairment Scale (SIS) - finger extension	- increase of scores in FMA-UE, BBT - reduction in SIS - from no to significant finger extension	- Assisted movement and muscle vibration, combined with either EMG or torque biofeedback, appears to reduce upper limb impairment, improve volitional activation of the hand muscles, and restore a modicum of hand function in some persons with severe hand impairment due to chronic stroke. - The combination of assisted movement and antagonist muscle vibration was intended to strengthen motor connections between the brain and spinal cord and, thereby, to increase strength by repetitively and synchronously pairing functionally related motor and proprioceptive activity in the brain. Somatosensory stimulation was intended to support such Hebbian-style plasticity.
Harini et al 2013	stroke	30	no	Biceps brachii	not specified/60Hz Total of 24 sessions (6sessions pw, 4 weeks) each 1 stimulus of 10min	- Modified Ashworth scale (MAS), - Passive elbow extension range of motion (PROMe).	- reduction of MAS and improvement in PROMe at the end of trial	- Vibratory stimulation along with conventional physiotherapy was found much effective in reducing biceps brachii spasticity

Table continues from previous page

Reference (Author, year)	Diagnosis	N of partic ipants	Use of robotic devices	FV position	FV intervention (amp/freq and duration)	Outcome measures	Results + follow up	Discussion points
Tavernese et al 2013	stroke	44	no	biceps brachii and flexor carpi ulnaris	0.01mm/120Hz total of 10 sessions (5 sessions pw, 2 weeks) each 30 min stimulation of 6sec stimulus with 1sec break	- normalized jerk (NJ) (i.e. index of smoothness of movement) - mean linear velocity; - movement duration; - movement length; - hand-target distance (HTD) at the end of movement; - mean angular velocity at the shoulder ; - angle at the elbow at the end of movement - angle of arm flexion at end of movement - angle of arm abduction at the end of movement	- decrease in NJ - increase in mean linear and angular velocities - decrease in movement duration - decrease of HTD at the end - increase in angular velocity -no changes in movement length, angle at the elbow at the end of movement, angle of arm flexion at end of movement, angle of arm abduction at the end of movement - all effects lasting at least 2weeks poststimulation	- Since the patients were asked to perform a reaching movement as fast and accurate as possible, and because it has been demonstrated that stroke patients are able to respond to changes in pacing demands during the execution of the reaching movement, it is considered that the increase in arm and shoulder velocities are a real rise of the performance. This is particularly interesting because FV was applied to arm and forearm but not to shoulder muscles. - It is speculated that the effect of FV is more likely to be linked to an overall action on motor execution, more than to a focal activity of vibration.
Casale et al 2014	stroke	30	Yes, Armeo@spring, Ocoma	triceps brachii	2mm/100Hz total of 10 sessions (5 consecutive days pw, 2 weeks) each 1 stimulation of 30 minutes	- Modified Ashworth Scale (MAS), - upper limb motor function (ULMF)	- MAS of flexor agonist, biceps brachii decreased and ULMF increased - effects lasting at least at least 48h post-stimulation	- Antagonist muscle vibration, as a non-pharmacological treatment, can help physiotherapy to reduce extensors spasticity and improve functions in the rehabilitation of the upper limb spasticity
Paolini et al 2014	stroke	22	no	biceps brachii and flexor capri ulnaris	0.01mm/120Hz total of 10 sessions (5 sessions pw, 2 weeks) each 30 min stimulation of 6sec stimulus with 1sec break	- muscle EMG onset time, - co-contraction index (CCI), - modulation ratio (MR), - percentage of activation in relation to the maximal voluntary contraction (%MVC)	- reduction (closer to zero) in muscle EMG onset time - reduction in CCI - increase in MR - decrease in %MVC only for biceps brachii	- The findings demonstrate that focal vibration modulates muscular activity during the execution of reaching movement. In particular, the target muscle, which is responsible for the majority of the changes, generally requires less force and induces a lower degree of co-contraction with the others arm muscles following vibration therapy.
Constantino et al 2016	stroke	32	no	triceps brachii, the extensor carpi radialis longus brevis muscles	not specified/300Hz Total of 12 sessions (3 sessions pw, 4 weeks) 1 stimulus of 30 minutes	- Hand Grip Strength Test (HGST), - Modified Ashworth Scale (MAS), - QuickDASH score, - Fugl-Meyer Assessment (FMA-UL), - Verbal Numerical Rating Scale of pain (VNRS)	- Increase in muscle power in HGST - decrease in MAS score - variation of changes in activities of daily lining assessed with QuickDASH score - enhancement of FMA-UL - decrease in pain in VNRS	- Significant improvement in muscle strength and decrease muscle tonus, disability and pain in upper limb of hemiplegic post-stroke patients due to focal vibration
Calabro et al 2017	stroke	20	Yes Armeo-Power, Hocoma	triceps brachialis, supraspinatus, and deltoid	0.2-0.4mm/80Hz total of 40 sessions, five times a week for eight consecutive weeks each 1 stimulus of 1 hour during exercises	- Modified Ashworth Scale (MAS) SICI - Hmax/Mmax ratio, FMA-UE², - Functional Independence Measure (FIM), - Hamilton Rating Scale for depression and anxiety (HRS-D/A), - Kinematic properties of upper limb, - resting motor threshold, - motor evoked potential (MEP) - EMG	- MAS, SICI, Hmax/Mmax ration reduction - FIM and FMA-UE increase - HRS-D/A decrease - greater kinematic amelioration - MEP increase - No change EMG	- Altogether, the data suggest that the improvement in spasticity (namely, MAS reduction) induced by the association between motor training and MV may depend on a modulation of motor cortex and spinal excitability, i.e., an increase of the inhibitory output from motor cortex to spinal level. The stronger effect of the combined approach on spasticity and upper limb functions may depend on a sort of associative plasticity between the two coupled trainings, which could have reshaped corticospinal plasticity with a consequent reduction of segmental excitability at the spinal level and an entrainment of recovery processes at the cortical level.
Celletti et al 2017	stroke	18	no	Pectoralis minor and biceps brachi	0.1-0.25mm/100Hz 3 consecutive days each 3 stimuli of 10 min separated by 1min break	- Functional Ability Scale of the Wolf Motor Function Test (WMFT FAS), - Modified Ashworht Scale (MAS), - visual analog scale (VAS) - Motricity Index (MI)	- increase in WMFT FAS scores and MI - MAS reduced lasting 1 week post-stimulation	- Multidisciplinary approach by combining neurophysiologically-based rehabilitative technique and vibration therapy may improve functional recovery via a suspected rebalancing of cortical inhibitory and excitatory system
Oh et al 2017	stroke	6	no	calf muscles	0.3mm/80Hz 1 stimulus of 5min	Modified Ashworth Scale (MAS), - Range of motion (ROM), - 10m walking time	-decrease in MAS - increase in ROM - decrease of 10m walking time	- Focal vibration on the gastrocnemius have antispastic effects on clinical, functional, electro-physiological, and kinematic change by inhibit the segmental reflex pathway in chronic stroke patients, especially when it combined with knee extensor spasticity.

Table continues from previous page

Reference (Author, year)	Diagnosis	N of partic ipants	Use of robotic devices	FV position	FV intervention (amp/freq and duration)	Outcome measures	Results + follow up	Discussion points
Celletti et al 2011	Cerebral Palsy	8	no	Achilles tendon on both legs	0,01-0.25mm/100Hz 3 consecutive days each 3 stimuli of 10 min separated by 1 min break	- Modified Ashworth Scale (MAS). - Passive range of motion (PROM)	- MAS decreased and ROM increased and both persisted after 12 weeks post-stimulation	- Focal vibrations (based on a low-amplitude, high-frequency, long-lasting and repeated vibratory treatment, and focused on single and selected muscles) may be a safe, low cost and useful approach to reduce spasticity in children with diplegic spastic Cerebral Palsy
Paolini et al 2013	MS	43	no	Rectus femoris and gastrocnemius medial and lateral	0.01mm/120Hz total of 10 sessions (3 sessions pw, 4 weeks) each 30 min stimulation of 6sec stimulus with 1sec break	- Modified Ashworth Scale (MAS). - Fatigue Severity Scale (FSS)	- MAS decrease - FSS decrease	- The results demonstrate that focal muscle vibration and botulinum toxin, either alone or in combination, decreased muscle tone or reduced fatigue symptoms at both the one-month and three-month follow-up. - In this study, however, the addiction of focal muscle vibration to botulinum toxin caused further advantages, mostly in terms of prolongation of the effect on muscle tone over time.

4.5 Chapter summary

Vibratory stimulation is affordable and easy-to-use neurorehabilitation tool. For example, segmental vibrations applied to the hand appear to influence power of the grip. SV applied before the contraction can boost grip force, whilst imposed to the ongoing grip, reduce it. Whole body vibrations are nowadays widely used in gyms, claiming to enhance exercise achievement. Focal tendon vibrations are useful tool to degrade proprioceptive feedback during the stimulation and to induce illusionary kiaesteatic movements of a stationary joint.

Literature review conducted for this chapter suggests that vibrations can be effective for spasticity reduction. There are two main research directions: one investigating WBV and the other using FV against spasticity. However, WBV devices are costly and can be inappropriate for a wheelchair users, where FV devices are smaller and low-priced. Therefore apparently similar mechanisms of actions against spasticity puts forward focal vibratory stimulation as an obvious choice for the use in rehabilitations. Chapters 5 and 6 are assessing FV impact on a healthy muscle. Pilot clinical trial conducted during this PhD presented in chapter 8, estimate rationale for use of focal muscle vibration in spasticity rehabilitation.

CHAPTER 5

Assessment of the effects of focal vibrations on the healthy muscle of able-bodied participants

Current literature does not provide a clear conduct for where and when focal vibrations should be applied to attain improvements in muscle output. This chapter investigates possible locations (muscle or tendon) and timing (before or during contraction) parameters for application and enhancements of the muscle output force

5.1 Introduction

Focal vibrations can be applied to the muscle or tendon to evoke a variety of effects on muscle performance, as listed in chapter 4. However the choice of location is unclear when it comes to the improvements in force output. McDowell et al. (2007, 2006) reported increase in hand's grip force while the entire hand was exposed to the segmental vibrations. Conversely, Jackson & Turner (2003) observed a reduction in muscle's maximal force following 30 minutes of continuous focal vibration over a relaxed muscle. This discrepancy in results is a direct consequence of a difference in protocols: duration, timing, and position of vibrations. Furthermore, when considering muscle focal vibration, the choice of application before or during contraction will equally influence outcome measures (Santos & Aruin 2008).

A reduction in spasticity is observed when stimulus with "low amplitude high frequency" is applied over the tendon or a muscle. The frequency mostly noted in research for this purpose is in range 50-80Hz mostly because the type Ia afferents seems unresponsive to lower frequency, especially around the most fatiguing one of 30Hz (Hagbarth & Eklund 1968, Mischi et al. 2012). The mechanisms of action are laid in the previous chapter. One of the main advantages for spasticity rehabilitation is the vibration induced presynaptic inhibition as a consequence of hyper-excitability of Ia afferents to this range of frequencies. However, this can explain a reduction in muscle tone and not necessarily an increase in muscle output force.

Nowak et al. (2004) suggested that the muscle uses a very interesting local ability to memorize fibre firing arrangement and other muscle contraction parameters during the first manipulation of the object. This is then considered and reproduced for all following handlings of the same object. This process is referred to as *muscle memory of force recall*. However, it seems that vibrations can alter this process. The suggested process could be of high importance for use in muscle performance rehabilitation, especially in SCI.

This chapter investigates repressions FV have on a muscle's force output when stimulation is applied in a relaxed and in a contracted state. Furthermore vibration frequency in use is reported to be the most fatiguing for the muscle so that the least favourable outcomes can be captured. Additionally EMG was recorded to capture potential changes in overall muscle's activation patterns. The motivation behind this experiment is to determine the most favourable outcomes, based on

the FV timing and application site, to be used for the design of a spasticity rehabilitation clinical trial protocol.

5.2 Method

5.2.1 Participants

To determine appropriate sample size (i.e. population size), an informal experiment was set up to estimate the difference between forces pre and post vibration and calculate effect size. The experimental protocol was the same as presented in latter section of this chapter and the necessity to perform it was mirrored in the lack of appropriate support from the literature. This information was used only to calculate sample size. According to the Rosner (2010) for the desired power of 0.8, probability of making type I error (e.g. false positive) 0.05 and observed changes from the informal experiment, sample size of minimum 21 participant was found suitable.

The study was performed with the approval of the Computer Science Ethics Committee Middlesex University (approved on 3/02/2015, no reference number provided). Twenty-three volunteers were recruited (15 males and 8 females, age ranging between 19-46) based on the inclusion criteria:

- over the age of 18
- no previous history of musculoskeletal disorders of upper limbs
- normal grip strength
- normal range of motion

Participants were informed that this study involved the application of vibrations onto the hand using a small coin vibrating motor. All participants gave informed consent prior to the experimental procedure to the engaging into the study as required by the Helsinki declaration (1964).

5.2.2 Experimental setup

The participants were asked to rest the hand on a tabletop (i.e. place the hand in mid-supination position), laterally in respect to the force gauge sensor, which was positioned above the distal

phalange of the index finger as shown on Figure 5.1. Two surface EMG electrodes were positioned on the proximal and distal ends of the first dorsal interosseous muscle. The participants were asked to abduct the index finger by pushing against the force gauge at specified times during the study in order to achieve the muscle contraction. When not performing muscle contraction, the participants were invited to rest the hand and the finger.

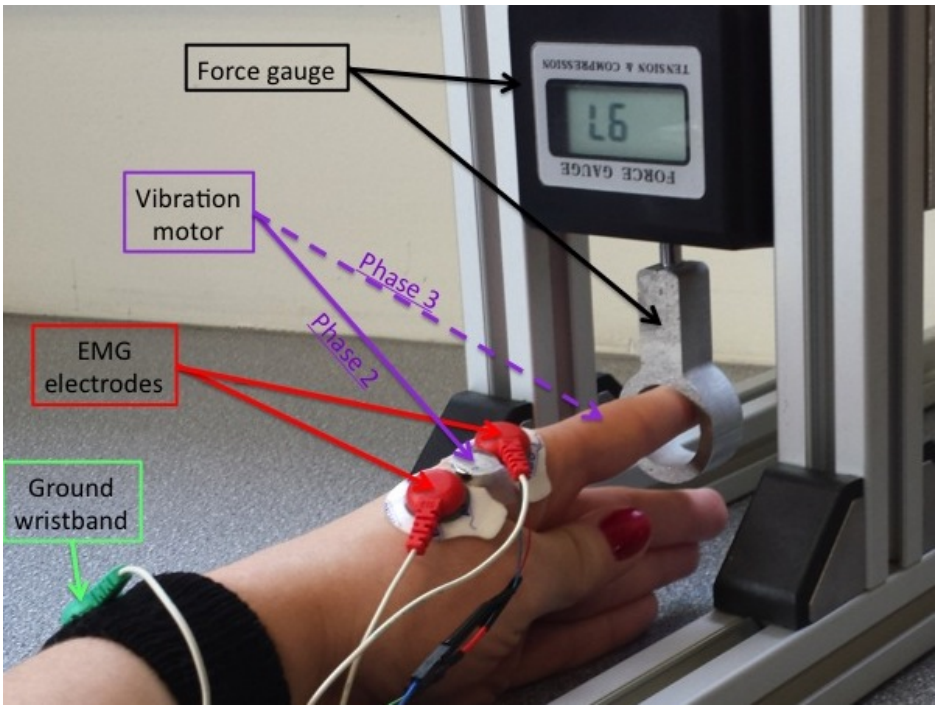


Figure 5.1: Experimental setup. Index finger pushing against the force gauge sensor with EMG electrodes positioned on the first interosseous muscle, marked wth red colour. Purple colour marks two positions of the motor depending on the experimental phase: the muscle belly or the bone.

A force gauge (Extech Instruments Corporation, USA) was used to record the force output. The surface EMG electrodes (H124SG ArboTM) were used to record muscle activity during the experiments. Both force and EMG signals were acquired using TMSi porti7 amplifier (TMSi, Netherlands) as this equipment has the ability to record several signal types simultaneously with a sampling frequency of 2048Hz. A small coin-shaped vibration motor (type 312-101 Pico Vibe^{TM}) was chosen for the application of the focal vibratory stimulation because of its dimension (diameter 11mm) and capacity to be powered by an affordable and easy to use devices such as an Arduino microcontroller. Therefore the motor was connected to an Arduino and controlled from a computer. The frequency of the vibrations generated by the motor was 30Hz and the amplitude 0.3mm.

Having in mind that the most useful frequency for the spasticity rehabilitation is in range 50-75Hz, this study explored the most beneficial effects produced by the most disadvantageous frequency of 30Hz, known for fatiguing the muscle (Mischi et al. 2012). All equipment used in this study was tested for reliability and calibrated according to the manufacturer's manual. Before each experiment, the equipment was checked for accuracy and recalibrated if needed. A repeatability test consisted of a detection of a force and an EMG produced by a lead researcher several times before each experiment.

The participants were seated comfortably at a table, facing the force gauge apparatus and a computer screen. The computer screen displayed the instructions indicating when to start the muscle contractions or resting periods and a simple biofeedback graphic (i.e. a line that moved up and down) indicating the level of force applied by the finger to the force sensor. The participants were asked to maintain the specific bar level during each muscle contraction within three phases.

Table 5.1: Protocol steps in order of application, depending on the condition and phase. Phase MVC was always performed at the beginning of the experiment. Participants were randomized into one of two groups: performing phase MB followed by phase B or executing phase B followed by phase MB.

Step	**Action**	**Condition**	**Phase**
1	Maximal voluntary contraction, 3 repetitions		Phase 1: MVC
2	Resting / maintaining 80% contraction, 3 repetitions	Condition "no": no vibrations applied	Phase 2: MB
3	Maximal voluntary contraction, 1 repetition		
4	Resting / maintaining 80% contraction, 3 repetitions	Condition "bef": vibrations during relaxation	
5	Maximal voluntary contraction, 1 repetition		
6	Resting / maintaining 80% contraction, 3 repetitions	Condition "dur": vibrations during contraction	
7	Maximal voluntary contraction, 1 repetition		
8	Resting / maintaining 80% contraction, 3 repetitions	Condition "no": no vibrations applied	Phase 3: B
9	Maximal voluntary contraction, 1 repetition		
10	Resting / maintaining 80% contraction, 3 repetitions	Condition "bef": vibrations during relaxation	
11	Maximal voluntary contraction, 1 repetition		
12	Resting / maintaining 80% contraction, 3 repetitions	Condition "dur": vibrations during contraction	
13	Maximal voluntary contraction, 1 repetition		

In between each of the phases there was a 5 min break to rest the hand and allow the muscle to recover from the performed contractions.

The protocol for this study is presented in a table 5.1. In phase 1:MVC, the muscles maximum voluntary contraction was recorded and this measurement was used for calculating force levels (80%±5% of maximal voluntary contraction) that participants were maintaining during phases MB and phases B. Participants were asked to perform a maximal muscle contraction three times (i.e. by pushing against the force gauge) as represented on Figure 5.2.

Phase MB and B involved the application of vibrations in three different conditions (see Figure 5.3): condition "no": no vibrations are applied; condition "bef": vibrations applied before muscle contraction; condition "dur": vibrations applied during muscle contraction.

- **Phase MVC (total time 4 min)** : The participants were instructed to perform maximal muscle contraction for 3 sec, three times. Between each contraction there was a resting period of 60s.

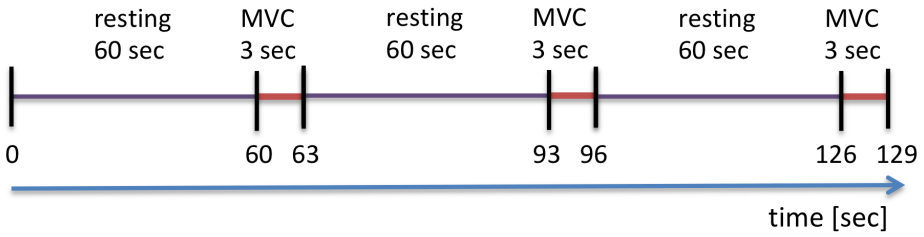


Figure 5.2: Phase MVC timeline.

- **Phase MB (total time 15 min)** : The vibration motor was positioned on the belly of the muscle (therefore letter M for muscle), between two EMG electrodes.

- **Phase B (total time 15 min)** : The vibration motor was positioned on the second phalange of the index finger (therefore letter B for bone).

The experimental protocol for phase MB was the same as for the phase B with the difference in the position of the vibration motor.

- Condition "no" (MBno/Bno) - no vibration (baseline)

  The participants were asked to relax the muscle for 60 sec. Immediately afterwards the participants contracted the muscle while maintaining graphical bar level representing 80%±5%

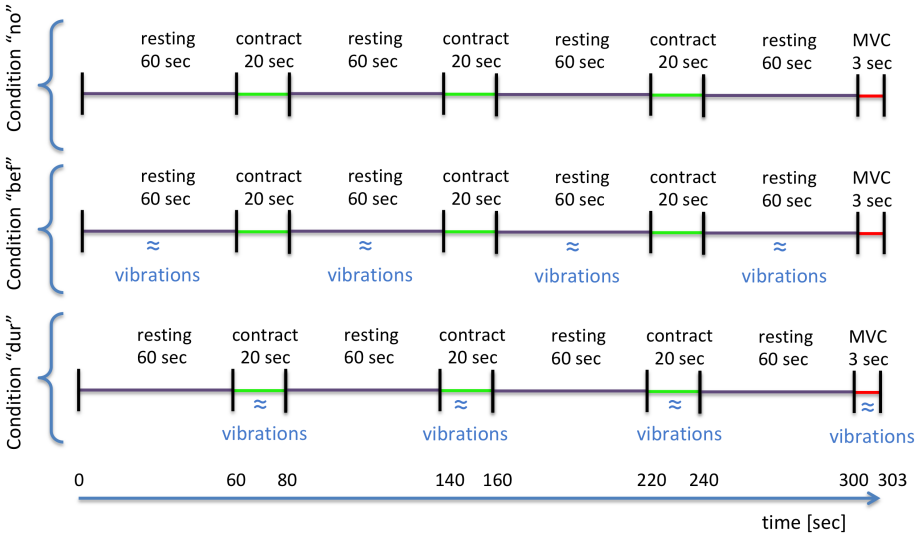


Figure 5.3: Phases MB and B timelines. Conditions depending on the timing of the vibrations are highlighted on the left hand side

of maximal voluntary contraction for 20s. The calculation was made based on the maximal voluntary contraction measurements obtained in phase 1: MVC. This cycle was repeated three times continuously. For the last cycle the participants were asked again to relax for 60s and then perform maximal voluntary contraction for 3s.

- Condition "bef" (MBbef/Mbef) - vibrations before contraction

The participants were asked to relax for 60s while vibrations were applied during this period. Immediately afterwards the participants contracted the muscle while maintaining graphical bar level representing 80%±5% of maximal voluntary contraction for 20s. The calculation was made based on the maximal voluntary contraction measurements obtained in phase 1: MVC. This cycle was repeated three times continuously.

For the last cycle the participants were asked to again relax while vibrations are applied for 60 sec and then perform maximal voluntary contraction for 3 sec.

- Condition "dur" (MBdur/Bdur) - vibration during contraction

The participants were asked to relax the muscle for 60 sec, followed by the muscle contraction during which vibrations were applied while maintaining the graphical bar level rat 80%±5%

of maximal voluntary contraction for 20s. The calculation was made based on the maximal voluntary contraction measurements obtained in phase 1: MVC. This cycle was repeated three times continuously.

For the last cycle the participant was asked to again relax for 60 sec and then perform maximal voluntary contraction for 3 sec while vibrations were applied on the muscle.

Phase 1 was always performed at the beginning of the experiment. Participants were randomized into one of two groups, performing phase MB followed by phase B or vice versa to see if the order of muscle contractions had an effect on possible muscle fatigue.

5.2.3 Data analysis

Data analysis was conducted with MATLAB® using well-established functions and signal processing toolboxes. The EMG processing protocol was based on the toolbox for nonlinear and non-stationary signals developed by Andrade (2005). The statistical analysis was carried out using the statistical package IBM SPSS® for MATLAB. The data analysis strategy consisted of a time-domain and a joint time-frequency analysis stage. The flow chart in Figure 5.4 illustrates data analysis steps.

Time and frequency domain analysis

At the beginning of the analysis, the signal bias was removed and the Empirical Mode Decomposition (EMD) method was used to filter the data (Huang et al. 1998). EMD is based on a better method to preserve useful data than traditional FIR/IIR filtering. This method adaptively decomposes datasets into several oscillation modes called Intrinsic Mode Functions (IMF) based on the analysis of the energy of the instinct time scales. A power spectrum analysis was conducted on the individual IMFs and the IMFs showing the lowest power at known noisy frequency bands (e.g. around 50Hz) was selected for further analysis. The root-mean square (RMS) of the EMG amplitude was calculated from 0.5 seconds equally spaced epochs of the full dataset. A 10th order moving average filter was applied to smooth the EMG RMS signal. For each contraction the mean of EMG RMS data series was calculated with the standard deviation. The mean RMS data samples provide a measure based on the amplitude of EMG signal so it can be used in the statistical

analysis.

The joint time-frequency analysis used the Hilbert Spectrum to estimate and compare the instantaneous attributes of the EMG signal across the subject populations (Huang et al. 1998). The IMFs generated with the EMD method are further used to generate a time-frequency-energy plot (the Hilbert spectrum) representing the IMFs frequency and energy variation over time. The Instantaneous Mean Frequency (IMNF) was estimated from the Hilbert spectrum and used in further statistical analysis. Because muscle fatigue is often associated with the mean frequency of the total spectrum showing a decrease over time, the regression coefficient of the IMNF slope towards lower frequencies can be used as a simple fatigue index. Often muscles start showing signs of fatigue when the IMNF decrement over the time is over 5% of the initial signal (De Luca 1997).

Statistical analysis

Normality of the data was determined using Shapiro Wilk test. As the test indicated that the data was normally distributed ($p>0.05$), parametric tests were performed, followed by a paired sample t-test and a one way ANOVA analysis.

The paired sample t-test was used to calculate the statistical difference between the same timing within different phases. The one way repeated measures analysis of variance (ANOVA) test was conducted to estimate the difference between vibration timing conditions within one phase. In order to establish any correlation patterns between the different measures, phases and timing conditions, the Pearson's correlation coefficients were calculated. The effect of the randomisation of the two phases on the study results was determined with one-way ANOVA for independent groups.

To minimize the type I (rejecting a true null hypothesis) and type II error (failing to reject a false null hypothesis), the confidence level was set to 0.05 when the sample size calculation was made. As the sample size is calculated to be 21 for this confidence level, the inclusion of 23 participants completed the study which allowed the dataset to exhibit a >95% statistical power as per post hoc power calculation thus is further decreasing the probability of type II error.

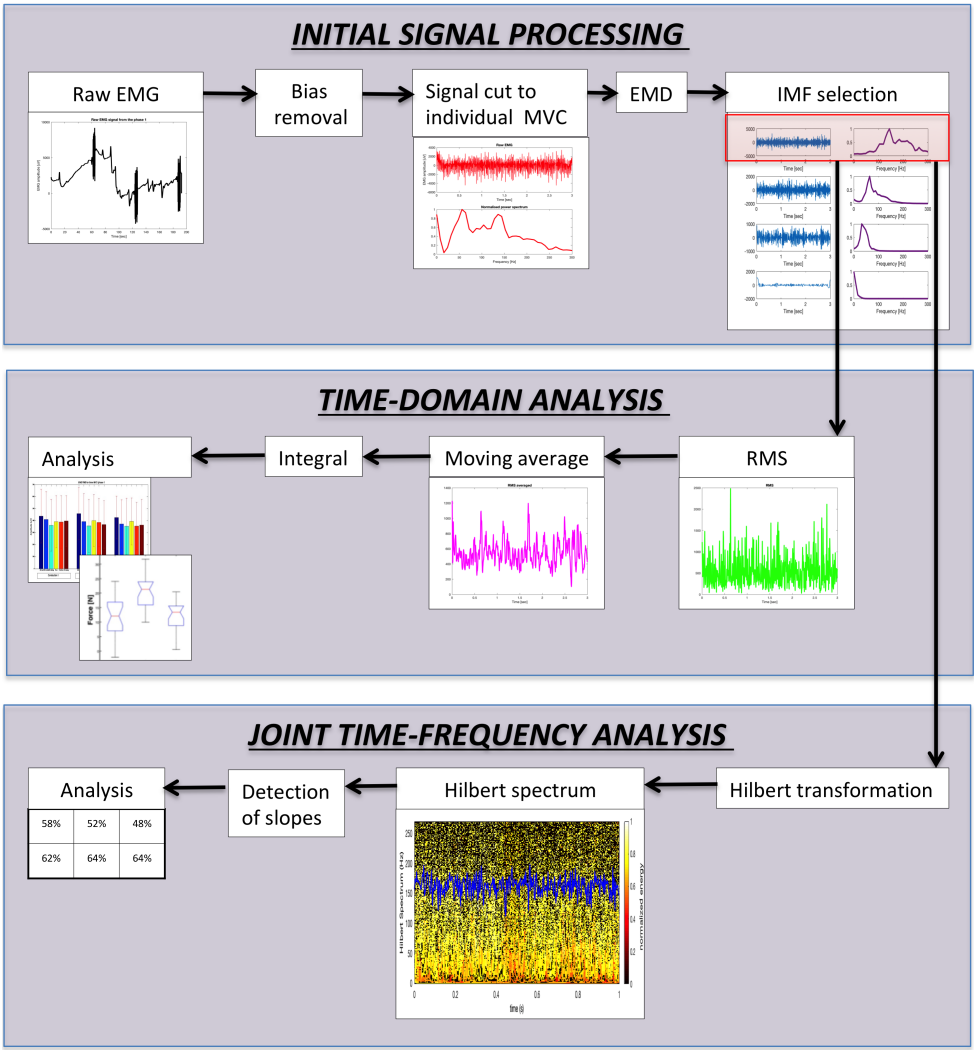


Figure 5.4: Data analysis flow chart. After the initial analysis is conducted and IMNFs are generated, the one with the least power at known noise frequencies is selected for the further time-domain processing and Joint time-frequency analyses.

5.3 Results

The results section is divided into two subsections: the analysis of the phase MB and phase B during which the user was asked to maintain constant force level, and the analysis of MVC from all phases.

Table 5.2: Percentage of detectable IMNF slopes higher than 5% toward lower frequencies for all conditions that could indicate muscle fatigue

muscle belly			**bone**		
no vibration	vibration before	vibration during	no vibration	vibration before	vibration during
58%	52%	48%	62%	64%	64%

5.3.1 Constant force level

One-way ANOVA showed no statistically significant difference within analysed variables for the randomisation of the vibration application position, i.e. the EMG RMS, force or IMNF between the groups where vibrations were applied first on the muscle belly and the group where vibrations were applied on the bone first.

Statistical analysis showed no difference in EMG RMS and IMNF when vibrations are applied to the muscle belly versus applied on the bone, however the difference is observed in the exerted force. The results from the repeated measures ANOVA of the EMG RMS and of the IMNF showed no significant difference between test conditions (no vibrations, vibrations before or vibrations during) when calculated for every phase (vibrations on the muscle belly, vibrations on the bone) and every contraction from the experiment where the participants were asked to maintain a constant force level (every $p>0.05$). The mean and standard deviation were calculated for each phase and vibration timing. Figure 5.5 shows the EMG RMS levels for the three MVCs conducted during phase 1:MVC. Consistent lower EMG RMS levels can be observed when vibrations are applied on the muscle belly during muscle contraction. When vibrations are applied on the bone there is no recognizable EMG RMS pattern.

Regression coefficients were calculated for every EMG IMNF. The frequency slopes at the beginning and at the end of every contraction were calculated based on the regression coefficients. The percentages of detectable slopes higher that 5% towards the lower frequencies for every condition and phase are presented in Table 5.2. If the slope IMNF values at the beginning and the end of contraction show a decrement higher than 5% this could indicate a muscle fatigue (De Luca 1997).

Table 5.2 suggests that the muscle is less fatiguing if vibrations are applied on the muscle belly than on the bone, based on the 15% less detectable prospect fatigues. When vibrations are applied to the bone it seems that the muscle is fatiguing regardless to when vibrations are applied (i.e.

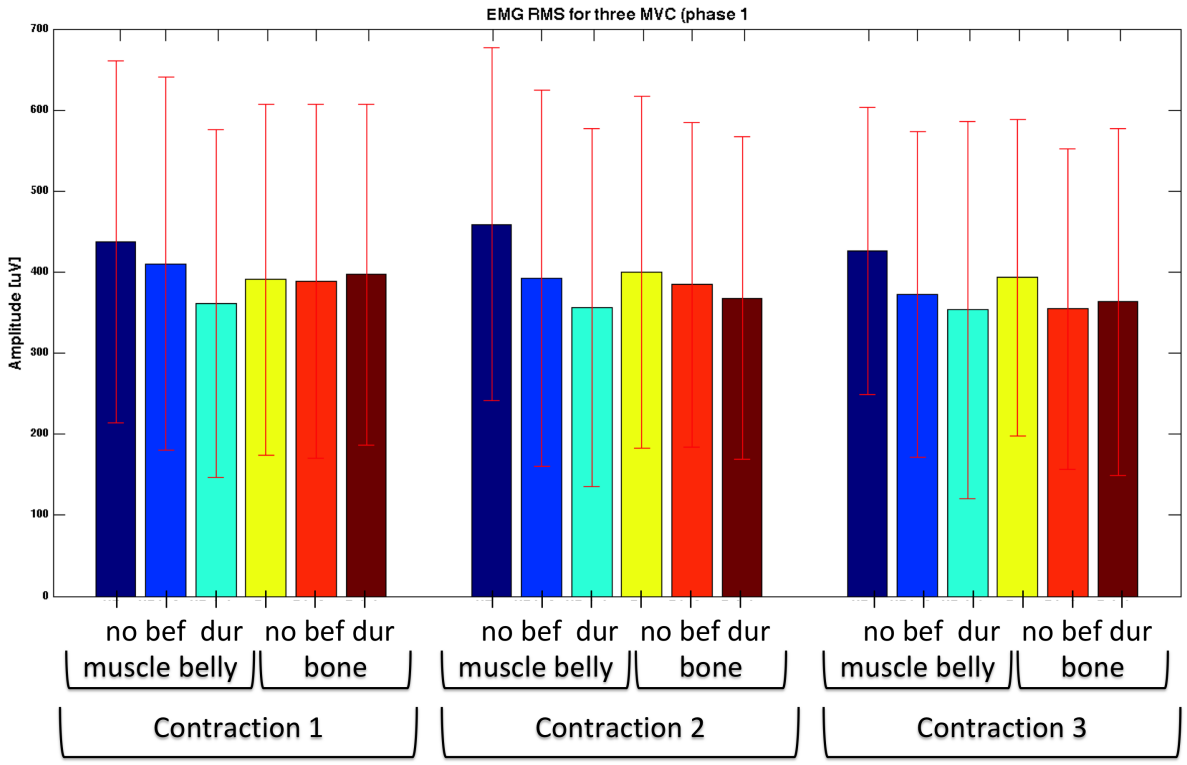


Figure 5.5: EMG RMS values for three contractions obtained while maintaining a specific force level. MB no: no vibrations applied on the muscle belly; MB before: vibrations on the muscle belly before; MB during: vibrations on the muscle belly during contractions; B no: bone no vibrations; B before: vibrations on the bone before contraction; B during: vibrations on the bone during contraction

before or during the contraction, as over 60% possible fatigues are detected).

5.3.2 Maximal Voluntary Contraction

Descriptive statistical analysis of the EMG RMS, force and EMG IMNF of the MVCs at the end of every recording session is presented in Table 5.3 and in Figure 5.6. It can be observed that the mean EMG RMS values for muscle belly decay from no vibrations (mean 610.39uV) to vibrations before (mean 489.70uV), with vibrations during being the lowest with a mean 413.93uV. However when vibrations are applied on the bone, the mean EMG RMS increases by approximately 35% (Figure 5.6 upper). The mean force is the highest when vibrations are applied on the muscle belly before muscle contraction. The values of the mean force for vibrations applied on the bone show a decaying trend (Figure 5.6 lower).

Table 5.3: Descriptive statistical analysis of RMS, force and IMNF values of the MVC for different phases and vibration conditions

	Descriptive analysis			
	Phase	**Vibration Timing**	**Mean**	**St dev**
RMS	muscle belly	no	610.39	50.51
		before	489.70	47.83
		during	413.93	45.73
	bone	no	436.68	42.15
		before	537.69	44.01
		during	590.20	47.89
FORCE	muscle belly	no	11.86	1.47
		before	20.82	1.35
		during	12.09	1.16
	bone	no	14.18	1.14
		before	11.35	1.11
		during	9.99	0.91
IMNF	muscle belly	no	105.00	2.84
		before	108.46	2.73
		during	111.02	2.95
	bone	no	108.86	2.61
		before	107.68	2.83
		during	106.09	3.03

The EMG IMNF values increase when vibrations are applied on the muscle belly and decay when applied on the bone with respect to the vibration conditions.

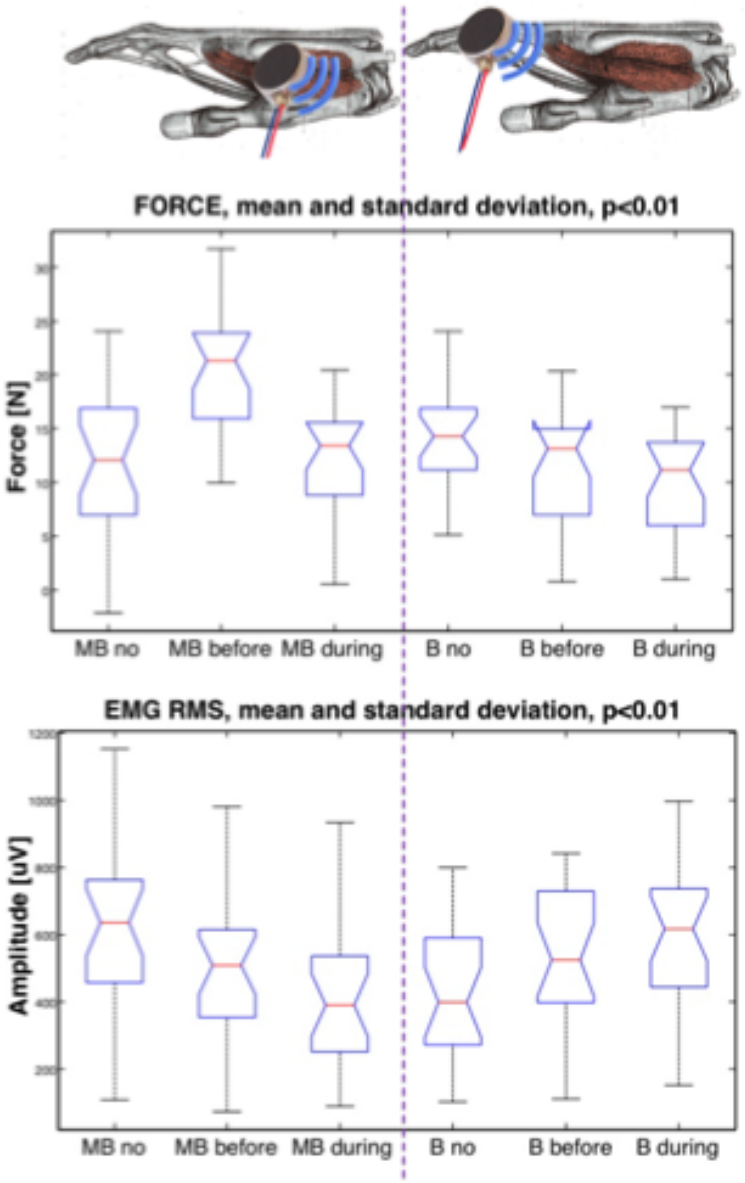


Figure 5.6: Error bars for (Up) force and (Down) EMG RMS variables. For both plots the mean value is presented with red line, blue bar being standard deviation and black lines are the extrema in the data. MB no stands for: no vibrations applied on the muscle belly; MB before: vibrations on the muscle belly before; MB during: vibrations on the muscle belly during contractions; B no: bone no vibrations; B before: vibrations on the bone before contraction; B during: vibrations on the bone during contraction

Repeated measures ANOVA of the EMG RMS of the MVC at the end of every recording session showed significant difference between timings within every phase. The p values are presented in Table 5.4. Repeated measures ANOVA of the force output corresponding to the MVC showed significant differences when vibrations were applied to the muscle belly before the contraction with respect to the other two timing conditions ($p<0.01$). Repeated measures ANOVA for mean IMNF showed significant difference only when there were no vibrations to the muscle belly in respect to the vibrations on the muscle belly before contraction ($p<0.05$).

Table 5.4: Results of the repeated measures ANOVA calculated for the different conditions within each phase. The results are shown for RMS, force output and IMNF. Column sig represents significance i.e. statistical p value and in grey are marked $p>0.05$ that proved the null hypothesis

	Repeated measures		
	Phase	**Timing pairs***	**Sig**
RMS	muscle belly	no - bef	0.000
		bef - dur	0.000
		dur - no	0.000
	bone	no - bef	0.001
		bef - dur	0.000
		dur - no	0.000
FORCE	muscle belly	no - bef	0.000
		bef - dur	0.000
		dur - no	1.000
	bone	no - bef	0.002
		bef - dur	0.204
		dur - no	0.000
IMNF	muscle belly	no - bef	0.035
		bef - dur	0.792
		dur - no	0.130
	bone	no - bef	1.000
		bef - dur	0.880
		dur - no	0.700

* Pairs represent variable and factor set

The paired t-test was used for the comparison of the same timing conditions in different phases (see Table 5.5). A statistically significant difference is noticed in RMS values when there were no vibrations on the muscle belly or on the bone. A statistically significant difference is also noticed in RMS values when vibrations were applied during the contraction on the bone ($p<0.01$).

Table 5.5: Paired-sample t-test. Last column Sig. (2-tailed) represents significance levels of the null hypothesis. In grey is marked where the null hypothesis is not rejected

Variable	Pair*	t	Sig
RMS	MBno - Bno	4.73	0.000
	MBbef - Bbef	-1.60	0.124
	MBdur - Bdur	-4.92	0.000
FORCE	MBno - Bno	-1.87	0.075
	MBbef - Bbef	9.49	0.000
	MBdur - Bdur	2.86	0.009
IMNF	MBno - Bno	-2.06	0.050
	MBbef - Bbef	0.36	0.720
	MBdur - Bdur	1.66	0.111

* Pairs represent variable and factor set

Force output was significantly different when vibrations were applied both before and during the contraction on the muscle belly in comparison to the vibrations applied to the bone ($p<0.01$, $p<0.01$, respectively). The IMNF values have only showed different results for no vibration sessions before any vibrations were applied on the muscle belly and on the bone.

In order to evaluate the correlation between different variables, phases and timings, the Pearsons coefficients were calculated and showed in appendix A-1. Low correlation can be observed for force with both RMS ($Pa<0.4$) and IMNF ($Pa<0.4$) values while RMS and IMNF shows high correlation with one another ($Pa>0.5$).

5.4 Discussion

The main finding emerging from this study is that short-term vibrations when applied to the muscle belly prior to the muscle contraction induced an increase in output force but a reduced electromyography (EMG) room mean square (RMS) while performing maximum voluntary contraction (MVC). Our study results indicate that the vibrations employed prior to muscle contraction increase the subsequent force produced. One could say the observed force overshoot is a consequence of the experimental protocol, i.e. because the contractions without vibration were executed before the one with vibrations suggesting that the muscle was using a muscle learning. Indeed, Häkkinen et al. (1998) observed muscles tendency to optimize the activation of the muscle fibres during

exercise by memorizing the force output. Nowak et al. (2004) named this observation a *muscle memory of force recall*. If muscle force recall is expressed as a consequence of our protocol, then there would be no force overestimation and the muscle would simply optimise all contractions when repeating the previously learned action (Nowak et al. 2004). However if the assumption is made that the force increases as an overestimation of the muscle recall due vibratory intervention (McDowell et al. 2006), it could be that the muscle unit reorganized the individual muscle fibres in order to achieve a MVC. This claim is further supported by observed decrease in the EMG RMS. Regardless, the benefits of the increased muscle power following a focal vibration of the relaxed muscle can be used in gym exercise regimes. For healthy muscles, the benefits are muscular reorganisation and optimisation to produce more force. For rehabilitation paradigms, focal vibrations have a potential to enhance residual motor control.

Our correlation analysis was inconclusive for force output vs. EMG RMS, which is supported by the literature (Disselhorst-Klug et al. 2009). Vibrations applied during the contraction did not elicit any statistically significant change in the force output of the MVC in comparison to muscle contraction without vibrations. Santos & Aruin (2008) observed the similar trends for segmental vibrations of the hand, i.e. increase in the hand's grip if vibrations are applied before the grip and no changes of vibrations are applied during the grip. If so, there is a stronger case for the use of FV instead of SV for force output enhancement, to avoid possible adverse consequences of prolonged segmental vibrations (observed in sections 4.2 of chapter 4).

The second finding of this study is that short-term vibrations applied on the bone induced an increase in the EMG RMS in the MVC. The literature suggests that vibrations applied directly to the bone tissue can be an effective and safe strategy to improve bone and bone marrow mass (Ozcivici et al. 2010), muscle strength (Judex et al. 2003), and possibly independence of children with motor disabilities (Reyes et al. 2011). Also, it induces an increase (about 35%) in the EMG RMS in comparison to the EMG RMS without vibrations, which is observed in our study and by Mischi & Cardinale (2009). This finding imply an elevation of a muscle activity with vibrations, being another possible benefit for rehabilitation strategies. The observed boost of the muscle activity could be an effect of the tonic vibration reflex (TVR).Lebedev & Polyakov (1991, 1992) reported a distinctive peak in EMG power spectrum at the vibration frequency during contraction with imposed vibrations. He attributed this peak as a consequence of the TVR, a spinal reflex to

external vibratory stimuli. Thus, the increase in EMG RMS during contraction with muscle belly vibration with could potentially be a consequence of TVR. Participants didn't verbally reported any discomfort nor unusual behaviour during the course of the application of vibration.

The results of our study showed a decrease of 4N in force output when vibrations were applied to the bone in comparison to no vibrations but a significant increase in EMG RMS of approximately 30%. This finding suggests that the muscle is getting more activated and recruiting more muscle fibres to perform a given task thus increasing exercise capacity of the muscle. Another explanation could be a contribution of TVR which is mostly observed during contracted muscle's tendon vibration (Eklund & Hagbarth 1966). However, it is reported that TVR can be observed for the duration of the reflex and not afterwards. No EMG signal was observed when vibrations were applied during the relaxed state, minimising the possibility of the TVR.

Previous research seems to suggest that a reduction in muscle fatigue can be achieved when vibrations are used (Park & Martin 1993). Our study failed to demonstrate statistically significant correlations in vibrations and muscle fatigue. The changes in EMG IMNFs showed no detectable patterns for the part of our experiment where the participants were asked to maintain the force level for 20 seconds. Further analysis of the Hilbert's power spectrum and regression coefficients of the IMNFs for the vibrations applied to the muscle belly (see Table 5.2) showed lower detectable muscle fatigue percentages when vibrations were applied to muscle belly. Slightly higher fatigue prospect percentages can be observed for the vibrations applied on the bone. Here we derive a theory that the reduction of percentage of muscle fatigue could be affiliated to the appropriate exposure to the vibrations, meaning careful choice of location and timing in respect to the contraction. Considering our results, focal vibratory stimulus delivered to the muscle belly is possibly mitigating muscle's fatiguing. However, the protocol used in this study could also have had an impact on this muscle response and muscle fatigue. The MVC was recorded approximately 15 min after several previous muscle contractions; hence it could be that the muscle fatigued. Some participants did express the feeling of tiredness by the end of every phase. This assumption can be remitted by the fact that the increased force of MVC was observed after three previous contractions.

Claus et al. (1988) instigated the causes associated with the boosted muscle activation during contraction by the $\alpha-\gamma$ motoneuron co-activation as a response to muscle spindle activation due to vibration and contraction happening at the same time. In the relaxed state of the muscle, spindles

(more than any other muscle receptors) are susceptible to the vibratory stimulation of the tendon, causing an activation of the type Ia fibres (Brown et al. 1967). Furthermore, due to the pattern of the vibratory stimulation, it causes a presynaptic inhibition in the spinal monosynaptic reflexes, activating α motoneuron (Dindar & Verrier 1975). But when a contraction is superimposed, it would seem that the spinal refractory circuits can not solely react to these requests. Chapter 3 argues that the illusionary movements and degradation of the proprioceptive channels can be attributed to the supraspinal and cortical control of the reflexes. So it might be plausible that the observations of our study are dependent on similar control mechanisms. Contrary to the previous belief that "only spinal involvement in facilitation of the muscle focal vibration" Kossev et al. (1999) showed different responses to TMS and ES stimulus after vibrations thus suggesting both cerebral and spinal facilitation of the vibrations. Besides, vibrational stimuli can modulate excitability in motor and sensory cortical circuits (Rosenkranz & Rothwell 2004). In summary it seems that vibrations induce an activation of afferent Ia spindles causing spinal reflex, and brain activation, with the reflex response from the CNS. If vibrations are applied on the bone, we hypotesise that the Golgi tendon organ might activate Ib and II fibres and inhibitory γ motoneuron reflex to the contracting muscle. Conversely vibrations applied to the muscle belly might activate Ia afferents and presynaptic inhibition, accompanied by the exaggerated α motoneuron response.

5.4.1 Hypotheses revisited

Hypotheses tested by this chapter are the central and the first one defined in chapter 1:

Central Hypothesis: Focal muscle vibration can enhance muscle's performance and associated joint function.
Statistically significant ($p<0.001$) increase in force output when vibrations are applied focally on a muscle belly classifies this hypothesis as proven.

Hypothesis 1: Focal muscle vibration applied to the relaxed muscle belly is a beneficial tool for muscle strength enhancement.
Analysis of the force and muscle's activation under several conditions and the accompanying discussion in previous section suggested this hypothesis is strongly supported.

5.5 Chapter summary

The research presented in this chapter imply that short-term focal vibrations could be used to enhance muscle performance. When FV are applied to the relaxed muscle, the increase in muscle's force is observed. FV of the connected tendon/bone imposed to a contraction has potential to increase muscle fibre activation. Any of these observed reactions could be used in rehabilitation strategies. The frequency of vibratory stimulations is chosen to be the least favourable and fatiguing 30Hz as compared to the most favourable one 75Hz for spasticity rehabilitation. Nonetheless, the observations from this chapter guided the selection of vibration schedule, presented in section 7.3 of a chapter 7 and within clinical trial protocol in detailed in chapter 8.

Analysis of the muscle fatigue phenomena under different vibratory conditions presented in this chapter, does not support a presence of discomfort or adverse prospects. The increase in force output is attributed to the vibratory induced changes in spinal reflex firing thresholds and muscle's fibres reorganisation. However, literature allege that similar mechanisms are happening when vibration are coupled with a contraction and the muscle activation is increased. Here is a discrepancy in the literature consensuses that needs to be further explored, possibly with analysis of brain responses presented in the next chapter.

CHAPTER 6

Assessment of brain response during muscle focal vibration of able-bodied participants

Chapter 6 explore cortical involvement in facilitation and modulation of muscle focal vibration in able bodied participants. The two studies addressed in this chapter are reflected on the results from the chapter 5, to guide a direction for the utilization of muscle focal vibrations in rehabilitation of muscle related impairments

6.1 Introduction

Chapter 5 introduced advantageous effects which focal vibrations can have on the targeted muscle's performance. Among others, increase of muscle activation in addition to decrease of produced force or, contradictory increase of produced force in addition to decrease in muscle activation seems to be induced under certain conditions. These two examples present inconsistent results after vibratory stimulation. Interestingly, the literature consent that the same underlying physiological mechanisms are facilitating these responses: reorganisation of the spinal reflex apparatus and alteration in neuronal firing thresholds (Blackburn et al. 2014*b*, Sayenko et al. 2010). To further the knowledge of the cortical involvement in vibratory stimulation neuromodulation, this chapter explores certain cortical signals under the conditions reported in chapter 5.

Physiological characteristics of the electroenchephalogram (EEG) are explained in Chapter 2 section 2.6. Very little is known about EEG signals related to vibrations. The main reason is the sensitivity of EEG equipment to the noise. But with the advancement in technology and hardware/software filters, nowadays it is not to be considered problematic. It is important to keep vibration devices on a safe distance not to contaminate EEG signals. The advantage of using equipment such as g.TEC system and online signal visualisation is that the distance can be evaluated and signal quickly scanned for obvious contamination.

Tempel & Perlmutter (1992) investigated the changes in cerebral blood flow by means of positron emission tomography or PET scanning due to vibro-tactile stimulation. Participant's finger pads were stimulated with vibratory stimulation with parameters of 130Hz and 2mm applied to the finger pads during relaxation. The results indicated an increase of the cerebral blood flow in the contralateral primary sensory motor area and supplementary motor areas. This elevation could be an indicator of a change in neural activity. Münte et al. (1996) varied a brief focal vibratory stimulus lasting 1-2 seconds between left and right forearm's extensor muscles. EEG recording 120ms after the stimuli have ended showed a drop in voltage observed over a large primary sensory-motor cortex.

This chapter is investigating EEG signals recorded in two steps: the first step investigated the features extracted from the initial study for this PhD explained in the chapter 5. The aim of the initial pilot study was to layout principal cortical features associated with the vibratory stimulation.

The observations from this single case study was used to optimize the experimental setup for the controlled crossover EEG study detailed in second part of the chapter 6. Observations from these two studies confirmed the need to further study cortical signals and include these measurements as a part of the system in chapter 7 for the clinical trial with people with SCI and spasticity. Moreover, the findings from these two studies are considered as a part of discussion in the chapter 8 when analysing and comparing results obtained from volunteers with spinal cord injury.

6.2 Pilot single case EEG study

6.2.1 Method

Participants

A single participant was recruited for this study, a left-handed healthy male volunteer. The experiments were performed with approval of the local Ethics Committee (no reference number provided). The participant gave informed consent to the experimental procedure as required by the Helsinki declaration (1964).

Experimental setup

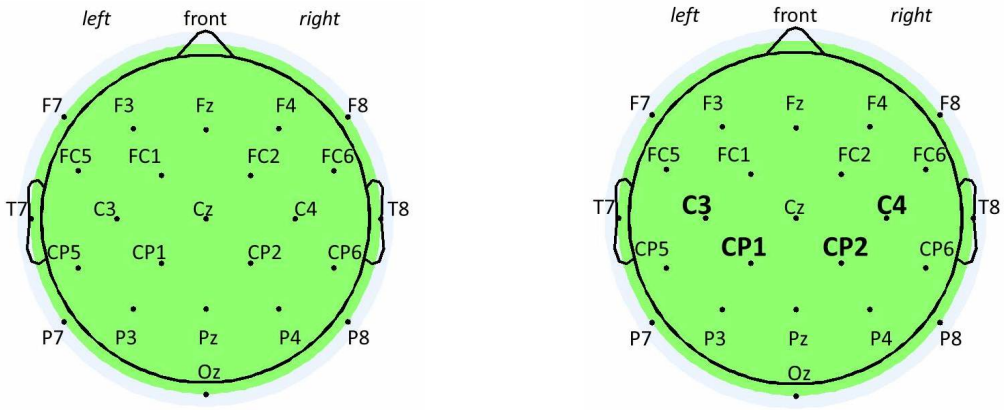
The experimental setup, table 6.1, is adapted from the study presented in the section 5.2.2. The participant was asked to rest the hand on a table, in a mid-supination position. To achieve muscle contraction the participant was instructed to abduct the index finger by pushing against a force transducer (see Figure 5.1). The vibrations are applied in two conditions over the muscle belly of the first interosseous muscle: before the contraction (i.e. during the relaxation period) or during the muscle contraction. Experimental protocol comprised of three repetitions of relaxation period lasting 60 seconds followed by 20 seconds of muscle contraction (see Figure 5.3). During the contraction phase the participant was asked to maintain the specified force limits, which represented 80%±5% of maximal voluntary contraction force recorded during phase MVC as a baseline measure.

Focal vibrations were applied using a small vibration motor (12mm Pico VibeTM) with the frequency generated by the motor modulated to 30Hz.

Table 6.1: Protocol steps in order of application, depending on the condition and phase.

Step	Action	Condition	Phase
1	Maximal voluntary contraction, 3 repetitions		Baseline MVC
2	Resting / maintaining 80% contraction, 3 repetitions	Condition "no": no vibrations applied	Muscle Belly (MB) phase
3	Maximal voluntary contraction, 1 repetition		
4	Resting / maintaining 80% contraction, 3 repetitions	Condition "bef": vibrations during relaxation	
5	Maximal voluntary contraction, 1 repetition		
6	Resting / maintaining 80% contraction, 3 repetitions	Condition "dur": vibrations during contraction	
7	Maximal voluntary contraction, 1 repetition		

EEG was recorded using TMSi water based electrodes with spatial representation as on Figure 5.1, connected to a porti7 amplifier (TMSi, Netherlands). The advantage of this system over others is the use of water instead of a gel as a mediator between the skin on the head and the electrodes. Water mitigates the need for hair washing and/or drying to remove excess gel. According to the manufacturer's manual, this system does not need calibration, however before each experiment a simple test was performed to assess presence of cortical signals. The test consisted of detection of



(a) EEG electrode placement (10-20 system).

(b) Bolded electrodes C3, C4, CP1 and CP2 are of interest within the analysis

Figure 6.1: Graphical representation of electrodes placement

changes in signal envelope after volitional blinking and jaw clutching.

Data analysis

The data analysis was conducted with MATLAB®. The analysis was performed both on the whole signal from every electrode and on different epochs of the signals. Each whole signal was time stamped and cut to individual epochs corresponding the experimental phase i.e. relaxation or contraction.

The raw signals were band pass filtered between 5 and 35Hz using two-way least-squares FIR filtering to extrapolate the most useful EEG waves related to movement performance (as described in chapter 2, section 2.6.2). Time frequency domain was represented using a spectrogram function, which calculates time-frequency dependency based on short time Fourier transformation. Power spectral density was calculated using the Welch method on both whole signal and on cut subsignals.

After the Welch power spectrum was calculated for subsignals, and the initial data analysis performed, the maximum value of mu band was extracted for the frequency in range of 8 to 12Hz. The maximum(s) were represented with a topographic heatmap function corresponding the electrode placement on a head.

Considering this study is a pilot single case study, no statistical analysis has been conducted.

6.2.2 Results

The spectrogram of the full experiment timeline, of the CP2 electrode corresponding to the sensory cortex, is presented in Figure 6.2. An increase in mu frequency band (8-12Hz) spectral power is noted in red colour during relaxation with vibrations.

The power spectral density using the Welch method in mu band of the CP2 electrode is presented in Figure 6.3. Correlating to the previous result, the increase in the Welch power when comparing relaxation with vibration versus contraction is presented.

On the single topographic head heatmaps, all electrodes are represented corresponding to their spatial placement (see Figure 6.1a) over the head (every topograph in Figure 6.4). Each electrode is presented with corresponding maximal Welch power spectral density of the mu wave. Six topographs are lined vertically based on the time of phase execution during the experiment (i.e.

vibration condition) in Figure 6.4 and horizontally corresponding three phase repetitions. Considering the side bar, increase in mu band power is presented in dark red and decrease in yellow and green colours.

Comparative topographic representations corresponding to vibrations applied during relaxation are represented on the two top plots, and during contraction on the two bottom plots of the Figure 6.5. If comparing the right two contraction heatmaps, the pattern corresponding to the movement event related desynchrinisation (ERD) is observed on the top heatmap over the area of the electrodes Cz, C4 and CP2, for the contraction without the vibrations. The analysis of the contraction with vibrations did not show similar trends on the bottom heatmap.

Spectral analysis of the relaxation-contraction last (i.e. third) repetition from electrodes C3, C4, CP1 and CP2 is represented on Figure 6.6. On the same subplot the corresponding Welch power spectral densities of the mu waves are presented in blue lines. White circles mark observed elevations of activation in beta band (marked in dark red colour) corresponding to movement (i.e. contraction).

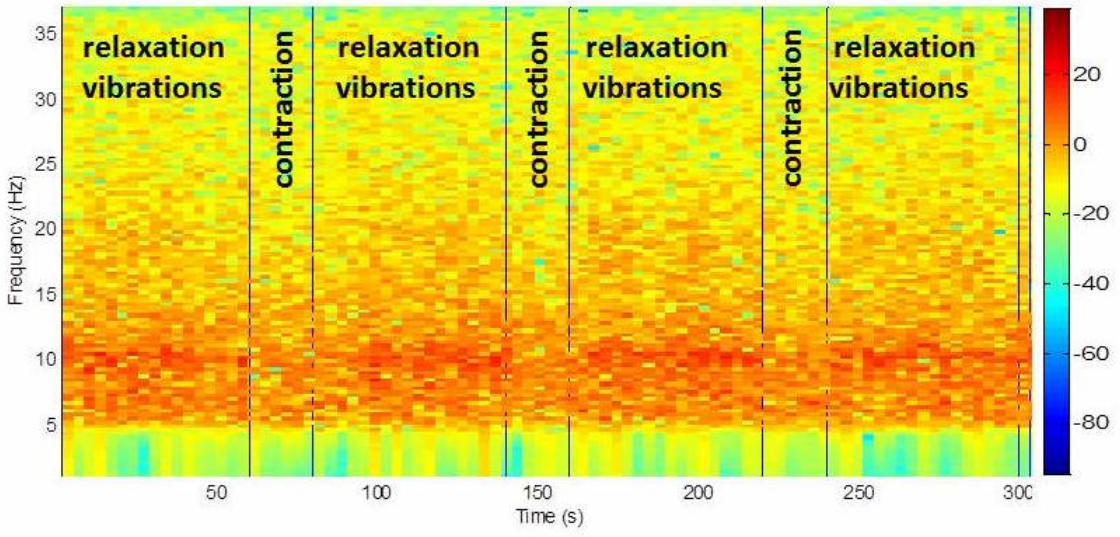


Figure 6.2: Spectrogram of the CP2 electrode. Vertical lines separate the different phases during the experimental protocol: three repetitions of relaxation followed by contraction.

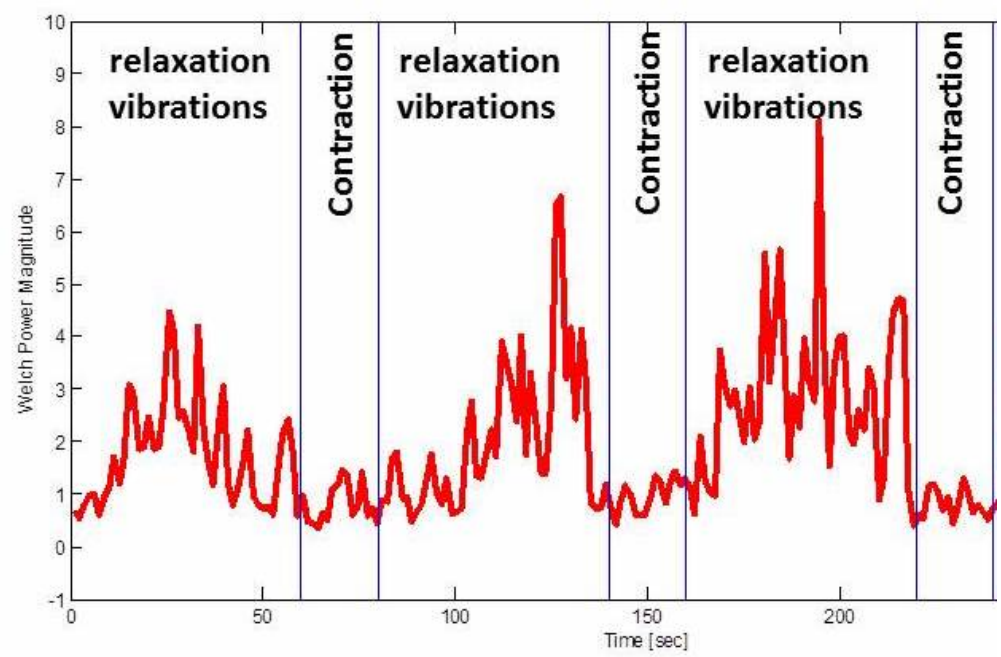


Figure 6.3: Welch power spectral density of electrode CP2. Vertical lines separate the different phases during experimental protocol: three repetitions of relaxation followed by contraction.

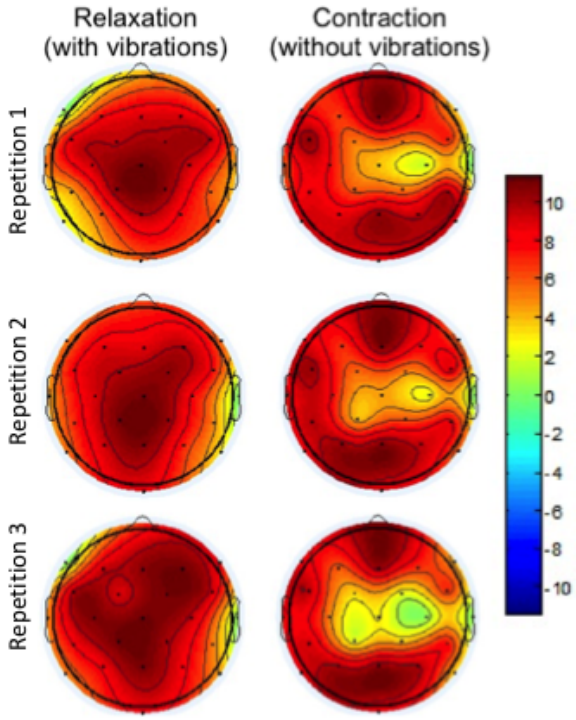


Figure 6.4: Topographic head heatmaps corresponding physical placements of all of the electrodes. The results are presented for each consecutive trial during the study: relaxation and contraction.

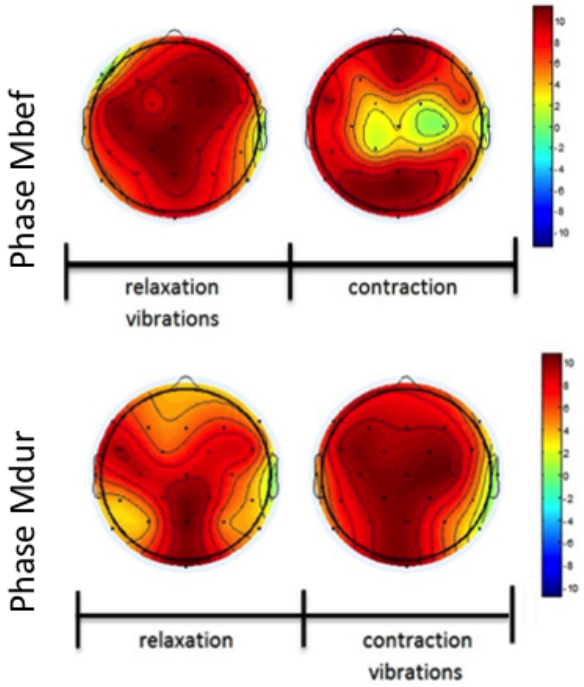


Figure 6.5: Magnitude of mu waves in head topographic heat maps corresponding two vibration conditions: vibrations applied (top) during relaxation and (bottom) during contraction.

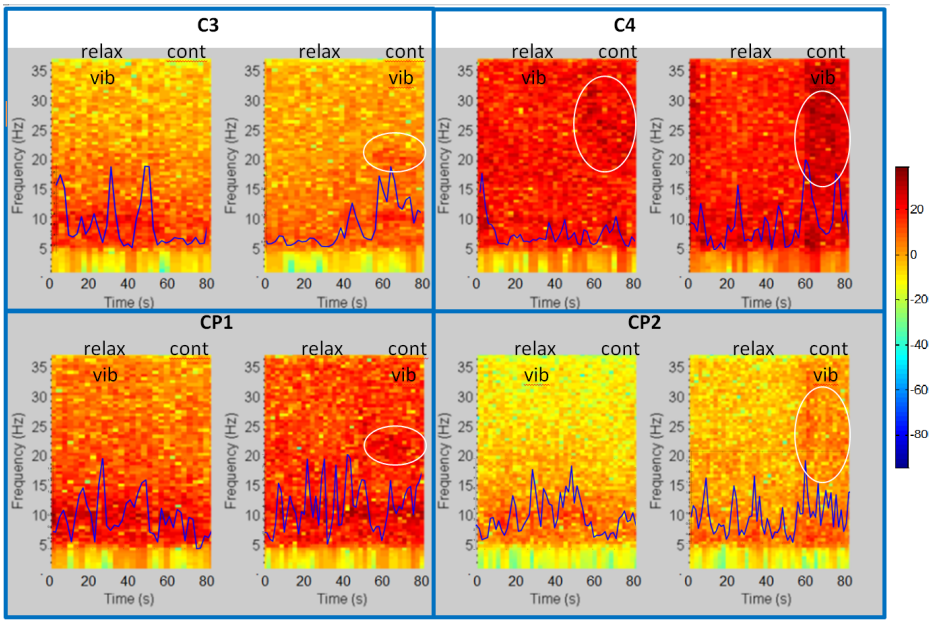


Figure 6.6: Spectral analysis of one relaxation-contraction repetition for electrodes C3, C4, CP1 and CP2. The corresponding Welch power spectral density of mu waves is represented by the trace line in blue. White circles mark activation in beta band corresponding to movement (contraction).

6.2.3 Discussion

Visual inspection of the spectrogram shown on Figure 6.2, seems to indicate an increase in mu power (approximately 20%) when vibrations are applied during relaxation period. This might relate to the coactivation of the sensorimotor cortex during the relaxation period due to the focal muscle vibration. It seems the brain also perceives the vibratory stimulus and perhaps vibration perception is not limited to muscle's sensory system and the spine (Mima et al. 2000).

Due to spectrogram limitations and low resolution, further data analysis was conducted. Welchs power spectral density shown in Figure 6.3 represents the mu power envelope for the duration of one experimental phase, taken from the electrode CP2. The increase in the mu power can be observed during the relaxation period with imposed vibrations. The drop in the mu power during contraction might be mu desynchronization ERD corresponding to the movement execution. In line with the Figure 6.3, the results of the rest of the electrodes follow the similar pattern, one of them having the highest magnitude of mu power over the last (i.e. third) relaxation period. This high amplitude over the last relaxation period could suggest that vibrations enhance muscle memory recall in conjunction with motor learning, as we previously argued in chapter 5 (Jevtic et al. 2015, McDowell et al. 2007). Focal vibration preconditioning in this context would tap into muscle memory in order to optimize upcoming contraction in parallel with repetition-based learning. The repetition would thus facilitate the cortex to predetermine and assist with the optimisation and execution of the subsequent contraction of the vibrated muscle. In another words, one could argue towards the possibility of vibration-evoked neuroplasticity (Lynskey et al. 2008).

Figure 6.4 shows an increase in mu waves over the sensory cortex during the phase of relaxation coupled with vibrations. This corresponds to the nature of the mu waves during relaxation (Chambers & Jonathan 2007). Conversely, as the mu waves can also be associated with the muscle activation, consistency with the decreased peak values over the CP1, Cz and CP2 electrodes suggest the feasibility of detecting mu waves as a response to the focal muscle vibrations. Conversely, desynchronization of the mu waves can be observed during the contraction phase over the central sensorimotor cortex that correlates to movement execution. Interestingly both of the effects are pronounced during the last, third relaxation and contraction phases. Following on the previous assumption of muscle memory recall and vibratory-neuroplasticity, it is important to reflect that

the stimulation and the contraction parameters and requirements are not changing during the timeline of the study. Since it is the third consecutive repetition of same tasks, could the muscles memorize the optimum activation without muscle stabilization?

Vibration induced neuroplasticity and cerebral-muscular shared control reserves a deeper discussion. During the first relaxation phase, it is assumed that the brain perceives a foreign focal vibratory stimulus and responds with the intention to stabilize the muscle. The stabilization could potentially be achieved with the increased muscle stretch and increase in thresholds of muscle spindles and Golgi tendon organs type I and II afferent pathways (Kasai et al. 1992). A consequent increase in a lever of the stretched muscle, urges for the brain responses toward a decreasing a number of active muscle units to perform the task. These presumptions can be further supported by Figure 5.6 where the increase in force is noticeably accompanied with a decrease in the amplitude of the EMG signal (Jevtic et al. 2015). With each vibration repetition, the brain is sharing more and more control over the upcoming contraction with the lower level centres, as the muscle memorizes the activation pattern. The localised neuroplasticity facilitates control of the last completion over the upcoming contraction, and the evidence could potentially be the mu decreased peak values over the entire sensorimotor cortex.

The dependency of the mu waves in relation to the movement can be observed in the first row of the Figure 6.5 topographic maps. The four heat maps represent results from the third experimental repetition as these effects are then most pronounced. Here we note an increase of the mu waves when vibrations are applied during the contraction (Figure 6.5 bottom-right plot). The brain in this case seems to be involved in facilitating vibratory stimulus in order to stabilise the muscle response, i.e. by recruiting less muscle fibres during contraction (Thickbroom et al. 2003), which could explain the reduced muscle activation observed in our previous study (Jevtic et al. 2015).

Further analysis of the time-frequency spectrograms shown on Figure 6.6 reveals an surge in the beta activity over the entire beta range (15-35 Hz) on the contralateral side (marked with white circles on the electrode C4), the desynchronisation ERD of the mu waves, i.e. movement onset is noticed after every 60 seconds. Nonetheless, the unexpected rise in the mu waves when vibrations are applied during contraction is observed over the contralateral side (right sub-plots of electrode C4 and CP2 plots). Perhaps this relates to the co-activation of the movement execution in conjunction with the vibration stimulation (muscle stabilisation). This claim is further supported

with the appearance of lower beta waves in the ipsilateral side around 20Hz (white circles on the right sub-plots of electrode C3 and CP1). Based on the previous assumption that the entire sensory cortex is active due to the focal vibrations, the ipsilateral side of the motor cortex seems to be gearing up to respond to the contralateral activation (Thickbroom et al. 2003). And the response might just be a tonic vibration reflex generated via spinal circuits.

6.3 Crossover EEG study

6.3.1 Method

Participants

The results from the pilot study were used to calculate appropriate sample size for the crossover experiment. The power analysis indicate that the sample size of minimum of 10 is suitable for the desired power of 0.8, probability of making type I error (e.g. false positive) 0.05 and observed changes from the pilot study Rosner (2010). The data set exhibited a >95% statistical power after a post-hoc power calculation of the completed 13 datasets (recorded from 13 recruited participants).

Thirteen able bodied volunteers participated in the experiment (9 males and 4 female aged 18-54) based on the following inclusion criteria:

- individuals above the age of 18
- able-bodied individuals
- normal grip strength and range of motion
- no previous history of neural or musculoskeletal disorders affecting the upper limbs

The experiment was performed with approval of Middlesex University Research Ethics Committee (reference number 0764). All the participants gave informed consent to the experimental procedure as required by the Helsinki declaration (1964).

Experimental setup

The experimental setup was adapted from the study introduced in previous section (6.2) of this Chapter and presented in Figure 6.7a). The participants were asked to rest both hands on a table, in a mid-supination position. To achieve muscle contraction the participant was instructed to abduct the index finger (for either the dominant or non-dominant hand) by pushing against a force transducer. The vibrations were applied over the muscle belly of the first interosseous muscle during the relaxation period (i.e. before the contraction). Participants were instructed to

1. keep their eyes closed for the duration of the experiment

2. to relax entire body when focal muscle vibration was ongoing

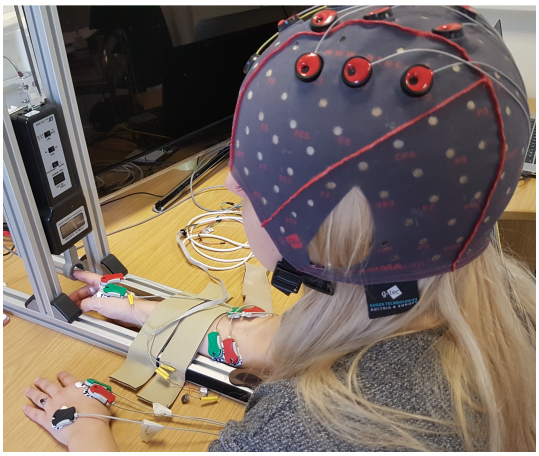
3. to exert maximal voluntary contraction (MVC) against the force gauge with index finger as soon as the vibrations stop.

The experiment began with focal muscle vibration lasting 30s followed by 4s of MVC. Each participant engaged in 10 continuous repetitions of this protocol. Both the dominant and non dominant hands were considered in the experiment in 6 different conditions, as presented in Table 6.2.

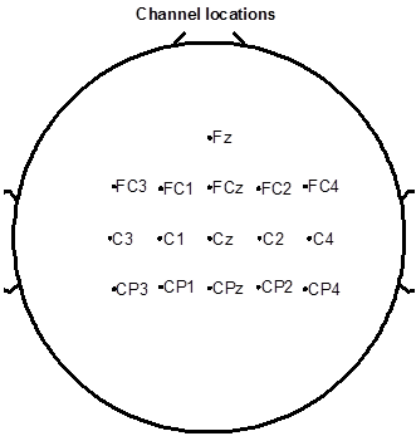
Focal vibrations were applied using a small vibration motor (type 312-001, Precision MicroDrivers^{TM}) with the frequency generated by the motor modulated to 75Hz and amplitude 0.3mm. This motor was chosen partly because of its small dimensions and partly for its frequency characteristic. In this experiment, it was decided to adapt the protocol to the preferred frequency for use in rehabilitation i.e. 75Hz (see chapter 4) and anticipate the similar outcomes as in previous section. EEG was recorded using the g.Tec active electrode system (g.GAMMA), with electrodes positioned according to Figure 6.7b, at a sampling frequency of 512 Hz. As TMSi water based electrodes used in previous experiments are observed to be highly receptive of the environmental electrical noise under certain conditions, advisors on the project suggested the use of a common EEG and BCI equipment which is g.Tech. The EEG recording system was provided by the manufacturer and it does not need calibration. Before each experiment a simple test was performed to assess presence of cortical signals, which consisted of a detection of changes in signal envelope after volitional blinking and jaw clutching.

Table 6.2: Conditions of vibrations and contraction execution

	Conditions	
Code	**Vibrations**	**Maximal Voluntary Contraction (MVC)**
xD	Not applied	Dominant hand
xN	Not applied	Non dominant hand
NN	Non dominant hand	Non dominant hand
ND	Non dominant hand	Dominant hand
DD	Dominant hand	Dominant hand
DN	Dominant hand	Non dominant hand



(a) Experimental set up.



(b) Electrodes placement.

Figure 6.7: Experimental set up with graphical representation of electrodes placement.

Data Analysis

The signal processing and analyse were conducted in MATLAB® using well established functions and toolboxes. In addition, functions from EEGLab were adapted according to our specific needs (Delorme & Makeig 2004). A notch filter was used to cut 50Hz from the raw EEG signals to filter common electrical artefact from the main's supply. Afterwards, the signals were band-pass filtered between 1 and 40Hz using two-way least-square FIR filtering to extrapolate useful EEG signals. To minimize interference between electrodes due to the proximity, the adapted surface Laplacian spatial filter was applied using the CSD toolbox (Kayser & Tenke 2006). The EEG data was cut into epochs, marked by the borders of vibration onset and offset. The power spectral density PSD of each epoch was calculated using the Welch method for the period from 0 to 500ms in respect to the vibrations onset, and 500ms-1s the same timings for the end of vibrations. Additionally, each epoch was filtered between 8-12 Hz to extract mu activity for further analysis, as indicated by the previous pilot analysis in section 6.2.

The statistical analysis was carried out using the statistical package IBM SPSS®. After Shapiro-Wilk test suggested that the data was normally distributed ($p>0.05$), parametric test was performed. Repeated measure ANOVA was used to determine statistical significance of the difference in mu power between experimental conditions.

To minimize the type I (rejecting a true null hypothesis) and type II error (failing to reject a false null hypothesis), the confidence level is set to 0.05 when the sample size calculation was made.

As the sample size is calculated to be 10 for this confidence level, the inclusion of 13 participants is further decreasing the probability of type II error as per post-hoc analysis suggesting the data set statistical power to be >95%.

6.3.2 Results

Repeated measures ANOVA showed no significant difference ($p>0.05$) in mu power between conditions where the vibrations are applied on one hand and the MVC exerted by the same hand versus the other (conditions DD versus DN and condition NN versus ND from Table 6.2). Therefore the analysis of the results is focused on the contractions executed by the dominant hand with vibrations not applied vs. applied on the dominant hand (DD) vs. applied on the non-dominant hand (ND). Analysis of the spectrograms across the subject population for the relaxation with vibrations suggests consistency with an increase in mu activity lasting a few seconds from the beginning of the stimulation. This trend then subsides in the middle of relaxation period and reappears near the end of the stimulation.

Figure 6.8 illustrates the observed phenomena for a typical subject. Power of a mu band is represented in different colour bars for three different conditions as summarized in Table 6.2: (dominant right hand is contracting) vibrations are not applied (blue), applied to the same hand (green) and applied to non-dominant hand (red). The statistically significant elevation ($p<0.01$) in mu band power is noticeable over the sensorimotor cortex when vibrations are applied, but seems dependent on the side of application. If the vibrations are applied to the dominant hand, the mu band power increases over the contralateral side of the brain (i.e. electrode CP1). The same pattern applies to the vibrated non-dominant hand. In addition, a statistically significant rise in mu band power is observed over the electrodes C2 ($p<0.01$) and C1 ($p<0.05$). According to the Penfield's homunculus (introduced in chapter 2 on Figure 2.2), the hands are represented in the brain around the area of electrodes C1, C2, CP2 and CP2, exactly where the statistically significant changes were observed. Hence, the analysis of these electrodes is further considered.

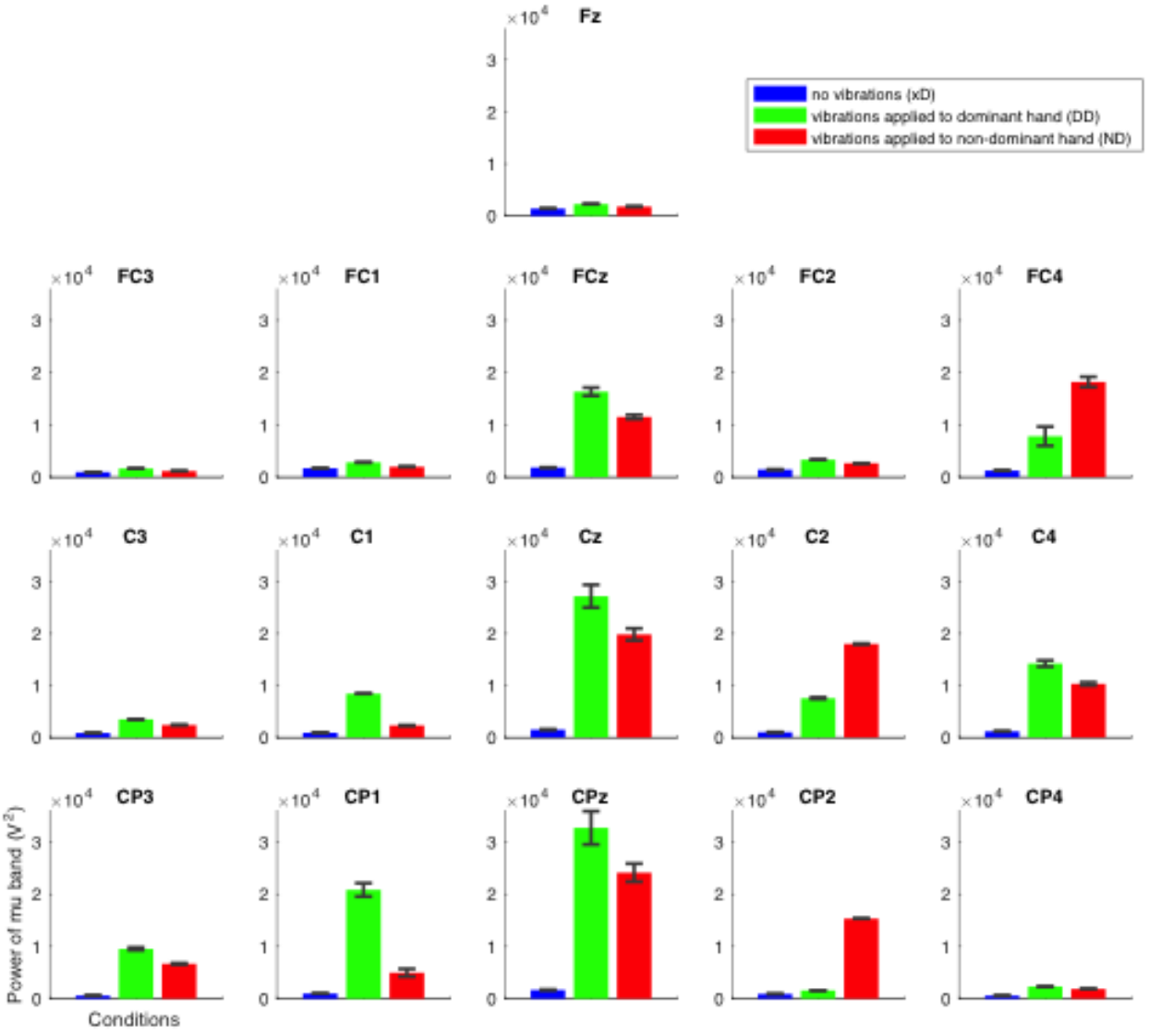


Figure 6.8: Graphical representation of mu band (8-12Hz) power (bars) with a standard deviation (lines) for a representative case. Channels are positioned according to the montage (position on the head). When vibrations are applied, an increase in mu power is noticeable over the contralateral side of the somatosensory cortex (c.f. CP1 versus CP2)..

6.3.3 Discussion

The results from this study support the findings from the pilot single case EEG study.

Comparison of the differences between ipsilateral and contralateral sides are in disagreement with those observed by Jackson & Turner (2003). Our results demonstrate the dependency on the side of the vibratory stimulation application but no transfer of these effects onto the contralateral side

of the body. Similar to Tempel & Perlmutter (1992), it seems that the post-vibratory enhancement in power is limited to the targeted muscle and does not devolve in the non vibrated side.

Pilot EEG results showed the increase of mu activity over the sensorimotor cortex during the relaxation period during which a focal muscle vibration is applied. The results from this study endorse these findings with a distinct amplification of the mu activity over sensorimotor cortex (see Figure 6.8, electrodes CP1 and CP2). Having in mind the nature of mu waves Chambers & Jonathan (2007) suggest that the presence of this waves indicate the body is relaxed with no intention to move. It can be argued that the contribution observed in our study is due to the experimental set up, i.e. participants had their eyes closed. Seeing that the gain in mu power is also observed across C1 and C2 electrodes over the sensorimotor cortex, the assumption of no intention to move during the focal vibration stimulation stands strong. Perhaps, there is no cortical involvement in the response to the focal vibrations. While recent evidence points towards the use of focal vibration to precondition the muscle to increase its force, there is still the question as to which mechanism is responsible for this effect (Aprile et al. 2016, Fitts 1954).

Kossev et al. (1999) observed an increase in corticospinal excitability a few seconds after the muscle vibration onset for transcranial magnetic stimulation TMS but not for transcranial electrical stimulation TES which leads to the assumption that there may be a degree of cortical involvement. Smith (2004) showed that 15 minutes after the onset of muscle vibrations cortical excitability is unchanged in comparison to the onset of vibrations. We hypotesise that there is a cortical involvement in the perception of the onset of vibrations followed by the transfer of the response control to the spinal reflexes or even muscles. If so, then the activation of type Ia sensory afferents due to FV, and consequently lowering of the presynaptic thresholds, could be managed merely by the spine and the supraspinal circuits. One assumption is that the reason behind this is to optimize cortical attention to continuous stimulation. Complementary second assumption being made here is that the muscle, the spine and the brain have a differential roles and effects in the excitability to muscle vibration stimulation. This means that the brain, the spine and the vibrated muscle's behaviour varies outside of standard conditions and responses, and that these reactions to FV are dependent on the vibration stimulation time and parameters (Rosenkranz & Rothwell 2004).

6.4 Hypothesis revisited

Hypothesis considered by this chapter is further investigation of the central and the first one from chapter 1:

Central Hypothesis: Focal muscle vibration can enhance muscle's performance and associated joint function.
Even though the research presented in this thesis does not directly evaluate muscle's performance, the correlation of the underlying mechanisms (cortical responses when vibratory stimulation was applied and when it is not) is the main contribution point. It is noted that the brain has very little involvement in the focal vibratory stimulation, therefore the modulation being conducted by the spinal cord or muscle locally. The results therefore are indicative of a positive outcome and hence suggesting that the hypothesis is supported.

Hypothesis 1: Focal muscle vibration applied to the relaxed muscle belly is a beneficial tool for muscle strength enhancement.
According to the results and discussion arising from the two studies reported in this chapter, mainly considering cortical behaviour as encouraging, the hypothesis is strongly supported.

6.5 Chapter summary

The pilot single case EEG study reported sensorimotor cortex involvement in vibratory modulation. The results agreed that the brain seems to perceive vibratory stimulation during the relax muscle stimulation. As chapter 5 revealed that the force produced by the muscle during a subsequent contraction is boosted by the vibrations, there is no evidence of cortical modulation of the force increase. We theorise that cerebral vibration facilitation is reflected with the increase of the muscle spindle and Golgi tendon organ stretch thresholds, allowing the muscle to stretch and potentially execute greater force with less activated fibres. The results also indicate that preconditioning the muscle with focal muscle vibration elicit differential behavioural effects on CNS and local actuators. Nonetheless timing of vibration stimulation appear to have an important role in this effect where the brain suggests to share the control over the stimuli modulation as the time

of stimulation progresses or it repeats. All these implications to indicate a form of neuroplasticity as a result of repetitive vibration stimulation and cerebral learning process.

The findings emerging from the previous chapters, further assured with this one, support the rationale for the use of focal vibrations to enhance motor control with positive, beneficial and no-adverse side-effects in healthy population with considerations for the use in SCI repercussions rehabilitation. The prospect of this rehabilitation proposition is explored in chapter 8. Moreover, the embrace of cortical recording is explained in chapter 7 with rationale and results discussion in chapter 8.

CHAPTER 7

VIBROfocus system design

Favourable effects of FV are presented in chapters 4, 5 and 6. However, the limitations of the current state-of-art are the lack of an objective assessment of spasticity and movement performance. This chapter introduces the design and integration of a standalone apparatus to measure several aspects of spasticity related repercussions and movement impairments

7.1 Introduction

Marconi et al. (2011) stated that vibration therapy accompanied with physiotherapy has a high potential to decrease spasticity in stroke. Physiotherapy includes exercise of movements by repetition by tapping into neuroplastic channels. Calabrò et al. (2017) observed a change in spasticity, minimum of 1 point in the Modified Ashworth Scale, after the engagement of participants with stroke in combined vibration and robotic-aided rehabilitation.

The need for affordable, easy to use robotic technologies in clinical and home environments is increasing. Commercially available robots such as Armeo family by Hocoma can cost several thousands of pounds and can be expensive even for hospitals. This chapter presents the design of a simple one-degree of freedom robotic-assistive device coupling repetitive movement exercise of the wrist joint with outcome measurement. It is designed for the spasticity evaluation in participants with spinal cord injury.

Previous chapters 4,5 and 6 explored electrophysiological consequences following focal vibratory stimulation on a healthy muscle. The findings guided the selection of FV application site, timing and frequency. Accordingly, the set of measurement tools to be included in the clinical trial is chosen from both direct and indirect measures and taking into consideration the most beneficial repercussions on a healthy muscle. However, as spasticity might be altering the muscle's mechanisms and responses to joint mobilisation, clinical input and considerations are incorporated for comfort and safety.

7.2 Design requirements

A spastic arm tends to curl up in an all-arm flexion as the spasticity level increases, while volitional movements are almost unmanageable. Often the joint extension of the spastic arm demands the use of external forces (e.g. splints or therapist's help) that needs to be applied carefully, precisely and causing minimal pain (Elbasiouny et al. 2010). The design of a device for spastic arm/hand rehabilitation needs to take into consideration the ease of positioning the curled arm/hand in the device which was one of the main aspects to be incorporated into design as advised by the clinical advisors.

Consultation with clinical colleagues at the Royal National Orthopaedic Hospital at Stanmore, London, United Kingdom, indicated the need for a rehabilitation system that would lower the stiffness in the wrist joint. In clinical practice, the initial treatment targets muscle and joint stiffness reduction either by means of medication, physiotherapy or other techniques, followed by the mobilisation of the limb and application of FES to stimulate muscles (e.g. grip retraining). A robot-aided spasticity system should therefore also consider more inclusive rehabilitation of any residual volitional movements (Loureiro et al. 2014). The robotic-aided system (hereafter referred to as the *apparatus*) presented in this chapter is designed to fulfil as many of the clinical needs as possible given the engineering limitations.

The fingers of the hand affected with spasticity, when in curled position, have to be carefully opened and comfortably positioned against a flat support splint or a plate. In addition to supporting the flexion of the hand and fingers, the extension should be limited with the supplementary support. The final design is revisited by the clinical partner to ensure proper positioning according to their experience. The apparatus needs to lock the hand in the mid-supination position to achieve a firm position and prevent slipping of the hand or the wrist. Only in this position is a participant able to control the wrist. Moreover, the elbow and the shoulder should complement the wrist's position within the apparatus. Considering that the maximal wrist range of motion (ROM) is approximately 155° (75° for flexion and 80° for extension), the apparatus should be equipped with software stops to limit maximum rotation to 155°. In addition, two hardware stops are to be added to ensure that the device's rotation does not excite a maximum of 160° (Hamill & Knutzen 2006). The radius of the wrist's rotation is the maximal length from the wrist's centre of rotation to the end of the longest finger, limited to r_w=210mm.

Spasticity affects the ability to volitionally control the muscles generating, as it were, "locked movements" (Ibuki & Bernhardt 2007). Depending on the severity of the spasticity, the ability to move could be higher, lower or none. The clinical guidance urged for the system should allow the user a few options if able, unable or somewhat able to use the apparatus.

To ensure safety and comfort, robotic systems need to be easily attached and detached from the user, by experienced therapist but also by anyone as needed. It is important for the user to be able to see the hand in a system, to balance the ergonomics of the movement and enhance the user's comfort. Hence, the apparatus should support the hand for comfortable, easy and quick

positioning and removal, similar to many equipment used in daily clinical practice. An emergency stop button should always be at hand for immediate system shut down.

Table 7.1 summarise the design requirements and solutions:

Table 7.1: Summary of design requirements and solutions

Design Consideration	**Requirements**	**Solutions**
hand positioning	splinting fingers and palm	two flat contact plates to support hand on both sides
range of motion	160°	hardware and software stops
motor	backdrivable	EC90 brushless
	continuous stall torque 0.5Nm	
	angular velocity 5000rpm	
apparatus	emergency stop button	attached
	arm rest	capstan and elbow rest
	movement abilities	active, passive and active-assisted

7.3 Focal muscle vibration considerations

Focal muscle vibration should be applied on the flexor and extensor muscles of the forearm with vibrations being "high frequency 50-100Hz, low amplitude 0.2-2mm" (Sadeghi & Sawatzky 2014). The research presented in chapter 5 stipulates the stimulation of a relaxed muscle belly for the most advantageous outcomes. The entire device needs to be encapsulated so that the surface touching the user's skin can be appropriately sterilised. This surface should not excite more than 11 cm in the direction of the muscle fibres and more than 8 cm across the muscle fibres to avoid vibrations being directly applied to the neighbouring bones, tendons or other structures. Both vibration devices are required to be secured in such a way to stabilise possible slipping against skin and minimise the oscillations in other axes other then towards the muscle. The choice of stimulating both flexor and extensor muscles as opposed to only one (as per chapters 4 and 5) was agreed with the clinical partners to maximise potential effectiveness on all joint's movements.

Previous use of the vibro-motors manufactured by Precision MicroDrives^{TM} showed reliability,

repeatability and ease-of-use as suggested by the work from chapters 5 and 6. However, due to the size of the muscles to be stimulated by the motors in clinical trial, the search yuilded type 334-401 as the most appropriate. It can produce vibrations with a frequency of 75Hz and amplitude 0.4mm (which equals 7g). This amplitude is higher in comparison to the one used in chapter 6 due to the difference in size of the targeted muscles. The motor's specifications fit the "high frequency, low amplitude" requirements when driven with voltage 11V and current 1.5A as advised by the work summarised in chapter 4 regarding spasticity rehabilitation. The case of the motor is printed on a 3D printer Ultimaker2+ (Ultimaker B. V.) around which a velcro strap can be wrapped. Two motors are connected via one velcro strap to be safely and firmly positioned on the desired body locations (two muscle bellies). Application of vibrations as a part of a clinical pilot study is presented in figure 7.1.

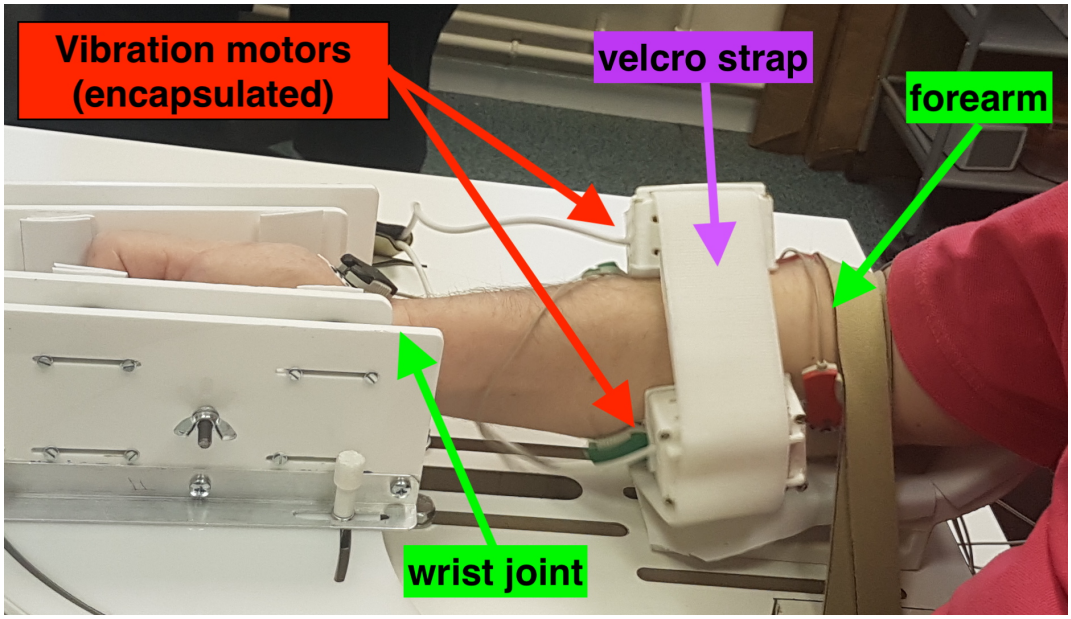


Figure 7.1: Encapsulated vibration motors delivering focal vibrations to the wrist flexor and extensor muscles located in the proximal anterior and posterior parts of the forearm.

7.4 Mechanical and kinematical design

The wrist robotic-aided device comprises of several static and dynamic elements shown on Figure 7.3 and takes into account the design considerations presented in the previous section.

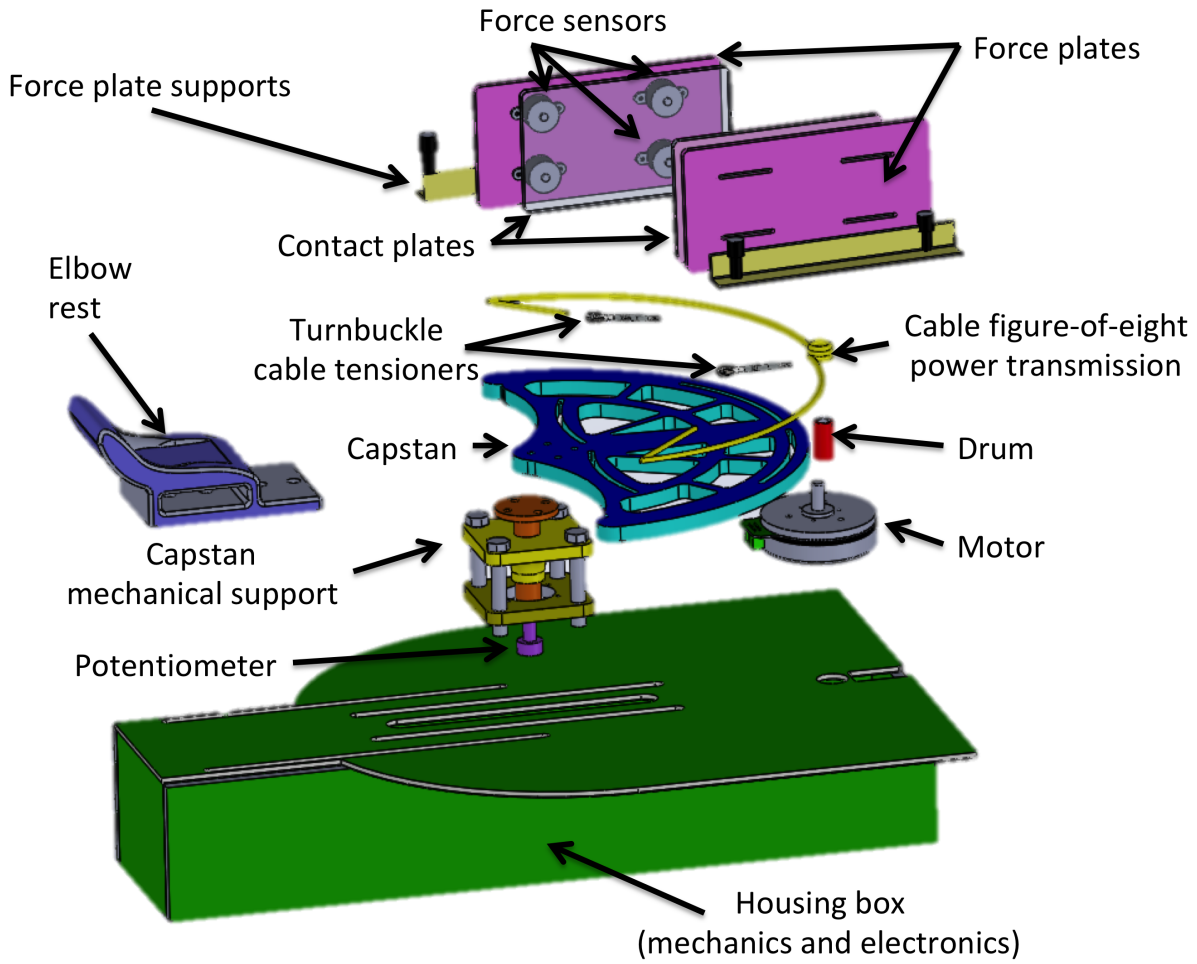


Figure 7.2: Simplified CAD drawing of the robotic-aided system. The hand rests between two force measuring plates both equipped with 4 force sensors. The plates and the hand rest on the capstan that is being driven by the cable attached to the motor. The transmission of the capstan rotation is transferred to a potentiometer to measure position.

The elbow is comfortably positioned in a rest splint that can be adjusted to the length of the forearm. The elbow is strapped in the splint to avoid the forearm flexion. The hand is comfortably fixed between two plates in mid-supination position so the wrist is free to produce flexion and extension .

The hand, fixed between the two contact plates, lies on the semi-circular hand-rest called *the*

capstan, and is free to rotate. The rotation is achieved by a motor positioned tangential to the capstan. The capstan is driven by a cable wrapped around the drum mounted on the motor shaft in a figure-of-eight pattern. This is the primary component for the power transmission, which is widely used in a capstan-driven haptic devices (Baser & Ilhan Konukseven 2010). The capstan has physical limits at both ends, matching the wrist range of motion, to ensure the users safety as described in the above section.

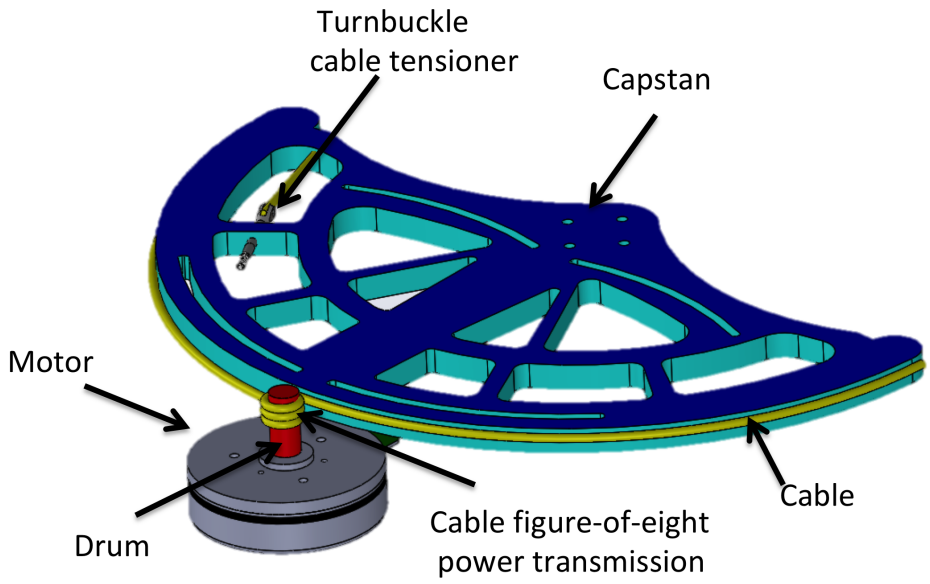


Figure 7.3: Simplified CAD drawing of the power transmission. The motor shaft is extended to the capstan via the drum. In a figure-of-eight pattern a cable is wrapped around the drum and extended to the ends of the capstan. Two turnbuckle cable tensioners, one on each end of the cable can adjust the tension in the cable.

In order to select a suitable motor, the speed and torque specifications of the motor were estimated in the following way. By simple observation and measurement, the angle between full flexion and full extension of the wrist, $\alpha_{lock2lock}$, was 160° and the maximum speed over this range of motion, $t_{lock2lock}$, was about 1s. So, the angular velocity in rotations per minute rpm, ω_{rpm} is:

$$\alpha_{lock2lock} = 160°;$$

$$t_{lock2lock} = 1s; \Leftrightarrow f_{lock2lock} = 1Hz \Leftrightarrow \text{ travelling } 160° \text{ 60 times in one minute}$$

$$\alpha_{lock2lock} : 60 = 360° : x \tag{7.4.1}$$

$$x = \frac{360 \cdot 60}{160} = 135 \text{ times in one minute}$$

$$\omega_w \approx 135rpm,$$

This value is for the rotation of the capstan. The diameter of the drum driven by the motor shaft is 5.5mm and the diameter of the capstan is 210mm, so the transmission equation t and the corresponding specification for the motor's angular velocity ω_m are:

$$t = \frac{r_w}{r_m} = \frac{210}{5.5} = 38.18$$

$$\omega_m = \omega_w \cdot t = 135 \cdot 38.18 \approx 5000rpm \tag{7.4.2}$$

Assuming very high stall torque from the spasticity $\tau_w \approx 20$Nm, the corresponding demand for the motor torque is:

$$\tau_m = \frac{\tau_w}{t} = \frac{20}{38.18} \approx 0.5Nm \tag{7.4.3}$$

The motor chosen for the task was a Maxon Motor EC90 brushless 90 Watt with Hall Effect sensors (Maxon Motor AG). For more details please see Appendix C-1. It combines a high continuous stall torque with high velocity capabilities. The motor is back-drivable to allow for the user's volitional movements, satisfying maximal wrist kinematics profiles observed in able-bodied people (Jessop & Pain 2016).

The motor is accompanied by a quadrature encoder (ENC MILE 1024lmp 2K, maxon motors) measuring the motor's angular displacement with a binary resolution of 1024 impulses per turn. The encoder is used to control the position of the capstan. The motor is directly controlled via a closed-loop servo controller (ESCON 50/5, maxon motors) and indirectly via LabView (National Instruments). In order to ensure communication between the motor and the transducers, a myRIO-1900 (National Instruments) is used. The myRIO is an portable reconfigurable Input/Output (RIO) device that can be used to provide (analog and digital) output or acquire (analog and digital) input signals from different sources. The connection scheme is presented on Figure 7.4.

The capstan's centre of rotation is aligned with the wrist's and connected via a shaft to a

potentiometer that measures rotation and is used to monitor the capstan's absolute position. The encoder attached to the motor can measure relative position produced by the output drum. The encoder's counts and potentiometer's voltage are mapped to correspond to the capstan's movements in degrees via the following equations:

$$angle[\text{degrees}] = \frac{potentiometer[\text{Volts}]}{0.1105} = \frac{encoder[\text{counts}]}{416.67} \tag{7.4.4}$$

The movement of the hand exerts a force on the plates that is measured by a total of 8 force sensors (FC22 Compression Load Cell, TE connectivity). Sensors are grouped in 4 for the palmar and 4 for the dorsal side of the hand. All sensors are embedded between the contact plate and the support plate and mounted in such a way that two sensors measure the force exerted by the fingers and two by the palm. Not all sensors have to be used; software switches provide the ability to select the most appropriate sensors to be used within the control paradigms. However, at least one sensor on the palmar and one on the dorsal side have to be selected. Before each session, the preloads (constant forces present when the hand is secured within the contact plates) from the selected sensors are measured and subtracted to null the force readings.

According to the force sensor data sheet in Appendix C-2, the conversion relationship between the volts read from the sensor and the force is linear. Due to the preload when the hand is positioned in the apparatus, the linearisation need to be adjusted to take the preload into consideration. The range of 0 to 5 Volts is linearised to the range of 0 to 5 grams of force. Once the data is transformed to grams, the calculation for Newtons is 7.4.5:

$$\begin{aligned} force[\text{grams}] &= k \cdot force[\text{Volts}] + n \\ force[\text{Newtons}] &= force[\text{grams}] \cdot \frac{1000}{9.81} \end{aligned} \tag{7.4.5}$$

where k is a slope and n is an intercept of the fitted line between the two ranges (i.e. between the two units).

All the components except the elbow rest, capstan with the motor output drum, and the plates are positioned inside a wooden box. The content of the box comprises of the motor with the encoder, motor controller, myRIO, potentiometer and connecting cables. Power supplies are positioned on a safe distance from the user and in such a position to minimise possibility of cable

entanglement.

7.4.1 Control strategies

The ESCON motor controller implements PID closed-loop velocity control. PID is an acronym for "proportional, integral, derivative" which are parameters that can be adjusted to provide optimum control of the system that follows the set-point value (Araki 2009):

- proportional (P) element − proportional to the error of the controlled system at the instant t i.e. the current error
- integral (I) element − proportional to the integral of the error up to the instant t i.e. accumulation of the past error
- derivative (D) element − proportional to the derivative of the error at the instant t i.e. prediction of the future error.

There are a few methods for optimisation of these parameters. The motor used in VIBROfocus can be PID auto-tuned within the ESCON controller. Auto-tuning takes into consideration the entire system attached to the motor to ensure the most suitable parameter output with the optimisation of the entire system, not just the motor. The PI parameters used for the VIBROfocus within the closed loop speed control are: P=3183, I=17.6ms, D=not used. Also within the ESCON controller there is an option to set up the ramping up of the velocity (to avoid sudden increases of the velocity from and to stop position), therefore the parameters are: velocity ramp acceleration=350 rpm/s, velocity ramp deceleration=2000rpm/s.

All of the fore-mentioned values are for the inner controller loop within the ESCON controller. However, to specify the system's behaviour to the purpose of the system, the velocity set-point and velocity control duration need to be assessed and sent to the ESCON. These values corresponds to the outer loop of the control system presented in Figure 7.4. Two controllers are implemented within the outer loop and used when selected: position controller and friction compensation controller (Amirabdollahian et al. 2002, Loureiro & Harwin 2007).

The position controller is selected when capstan needs to move the hand to the specific location (e.g. passive or active-assisted movements of the hand). The current capstan's position $x_{current}$

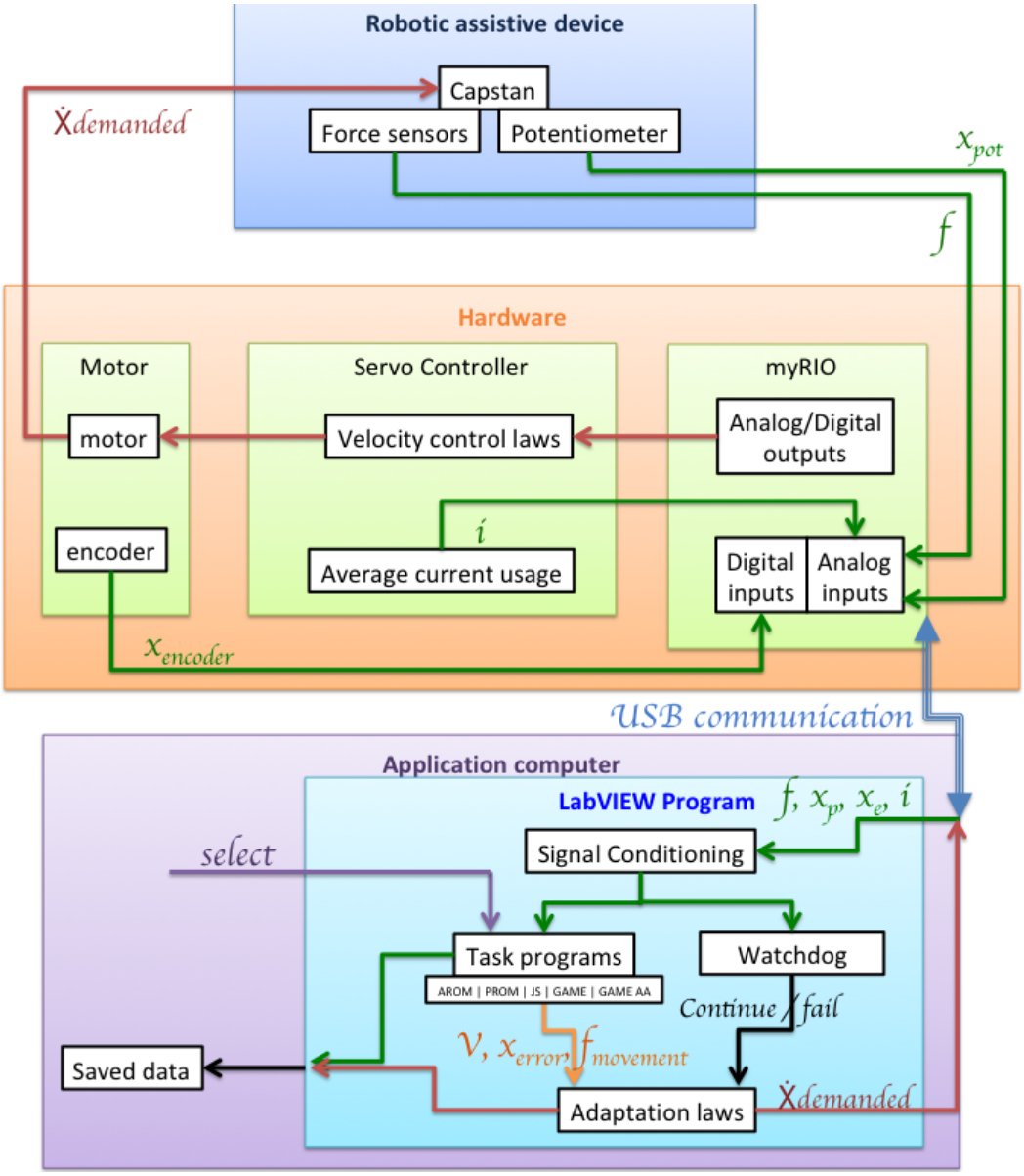


Figure 7.4: System controll flow diagram

when subtracted from the needed position x_{needed} generates a position error x_{error}. This error is used as a multiplier for the velocity demand $\dot{x}_{demanded}$ and does not consider the forces from the hand. Hence, this controller is used for the joint stiffness measurements or passively playing the game. Also it is used to complete the movement in active-assisted game mode if user is unable to do so.

The friction compensation controller is used when the user is asked to volitionally move the hand to the specific location (e.g. active or active-assisted movements). The friction controller is active

for a short period of time to overcome the initial friction due to the weight of the mobile parts of the apparatus. Force $f_{movement}$ in the direction of the movement is measured and as soon as it passes a threshold, the controller sends a velocity demand $\dot{x}_{demanded}$ proportional to the force. The software monitors forces $f_{movement}$ and velocity $\dot{x}_{actual}$ achieved and it stops the controller when velocity exceeds and the force falls below a set thresholds th_{force}. $th_{velocity}$. The assumption is that this controller should only activate to assist with the movement initiation and the rest of the movement should be completed by the user pushing against a contact plate in the direction of the movement. Therefore this controller is used whilst measuring active range of motion or actively playing the game. Also it is used to perform a volitional movement during actively-assisted game playing.

Software limit stops are programmed using the position controller. If the capstan position passes a certain value (usually the user's range of motion), a counter-directional position of a few degrees is demanded to move the capstan back to the operational range. To ensure comfort when the limit is reached, the user has a sensation of a light bump on a spring that is pushing the hand back inside the range of motion.

Taking the advantage of the inner loop's PID controller and velocity ramping, the position and force controller was given a velocity set-point V as a gain to the controller specific value. This set-point velocity gain allows for the controller to be further adjusted for the uses within different tasks. The control strategy scheme for the demanded velocity $\dot{x}_{demanded}$ is given by:

$$\dot{x}_{demanded} = \begin{cases} V \cdot x_{error} & \text{if } x_{actual} \geq ROM, \text{ where } x_{error} = x_{current} - 1^{\circ} \\ V \cdot x_{error} & \text{if } select = position\ controller, \text{ where } x_{error} = x_{current} - x_{demanded} \\ V \cdot f_{movement} & \text{if } select = force\ compensation\ controller, \\ & \text{and } f_{movement} \geq th_{force}, \text{ and } \dot{x}_{current} \leq th_{velocity} \end{cases}$$

Device software safety

Besides the mechanical stops limiting the total range of motion of the capstan, the apparatus also benefits from additional safety features. These features are programmed to constantly monitor logged variables such as position and forces independently from the main control loops. All

task programs have a real-time software stop button which immediately terminates the program execution. Also, the current program will immediately stop if the watchdog detects any untypical behaviour of the system based on the monitored values.

Forces are monitored and compared to a safety threshold of 100N as advised by National Health Executive Risk Assessment (*Push and pull risk assessment* 2016). The position from the encoder and potentiometer are compared and if the difference is greater than 3^o the system reports slipping. Any sudden jump in velocity or acceleration will be sanctioned and either by the watchdog or software limit stops. myRIO together with LabVIEW programs have a built-in ability to monitor the USB communication between myRIO and targets, in this project between the computer, myRIO and the ESCON controller. The state of the communication is also sent to the watchdog for monitoring.

Flowchart of the watchdog is presented on the Figure 7.5

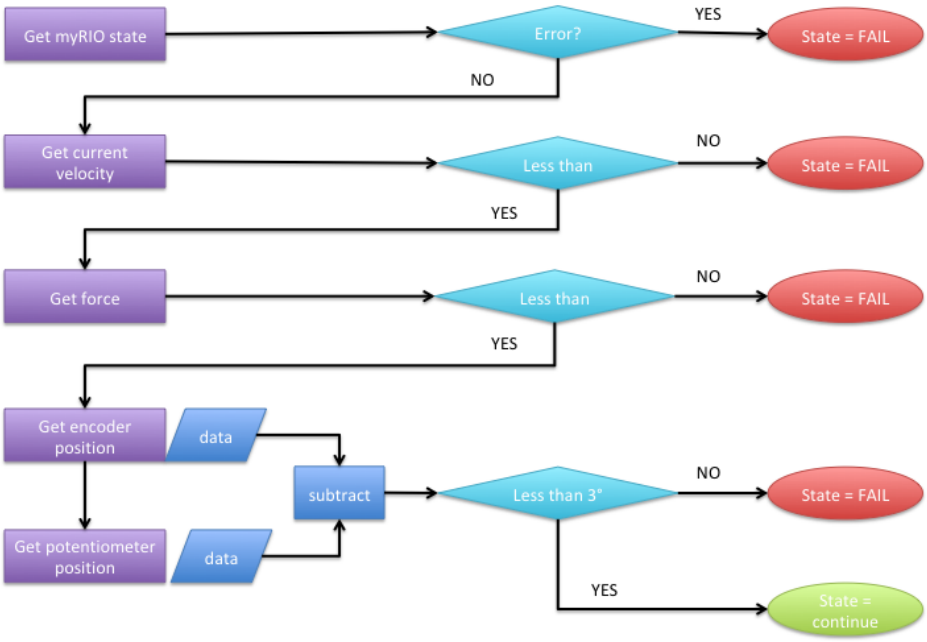


Figure 7.5: Watchdog flowchart

7.5 Experimental tests

A range of tests were performed to evaluate system's response to different conditions within control strategies. These tests can optimise velocity demands and gain usage within different

software programs, system use and device safety.

7.5.1 Step response

Step response was carried out to estimate behaviour of the system when an instantaneous change in the reference input is introduces using a position controller. The three gains are chosen to be tested G={3, 5, 10} as a representatives of the different velocity profiles. Various angles are to cover small {10^o, 35^o} medium {80^o} and large {100^o, 140^o} angular jumps from position to position. Recorded step responses are presented on figure 7.6.

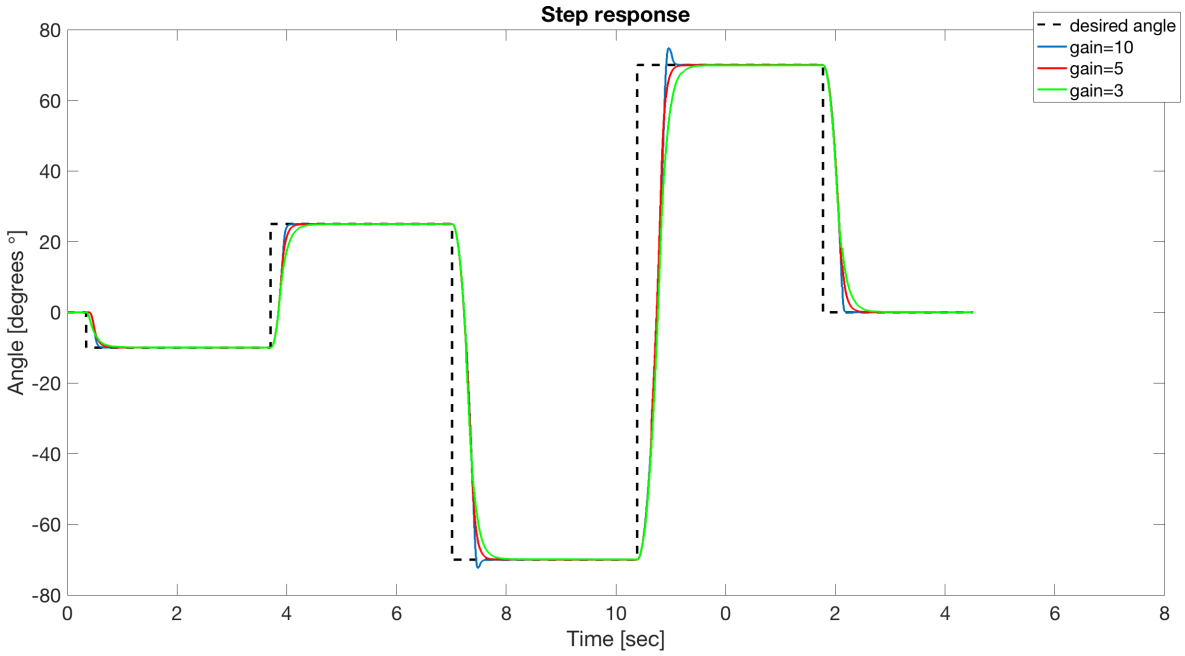


Figure 7.6: Step responses to various input angles and three gains

The G=10 presented a small overshoot of [1^o 5^o] when introduced with the high angular requirements however having the quickest reaching of the desired position. The smallest gain G=3 had the slowest response.

7.5.2 Dynamic response

A sine waves with 70^o amplitude and various frequencies in range [0.001 0.01]Hz were introduced to the system. The system is to follow the change using the position controller. Dynamic response

depending on the change in amplitude and time delay from the system response is presented on figure 7.7.

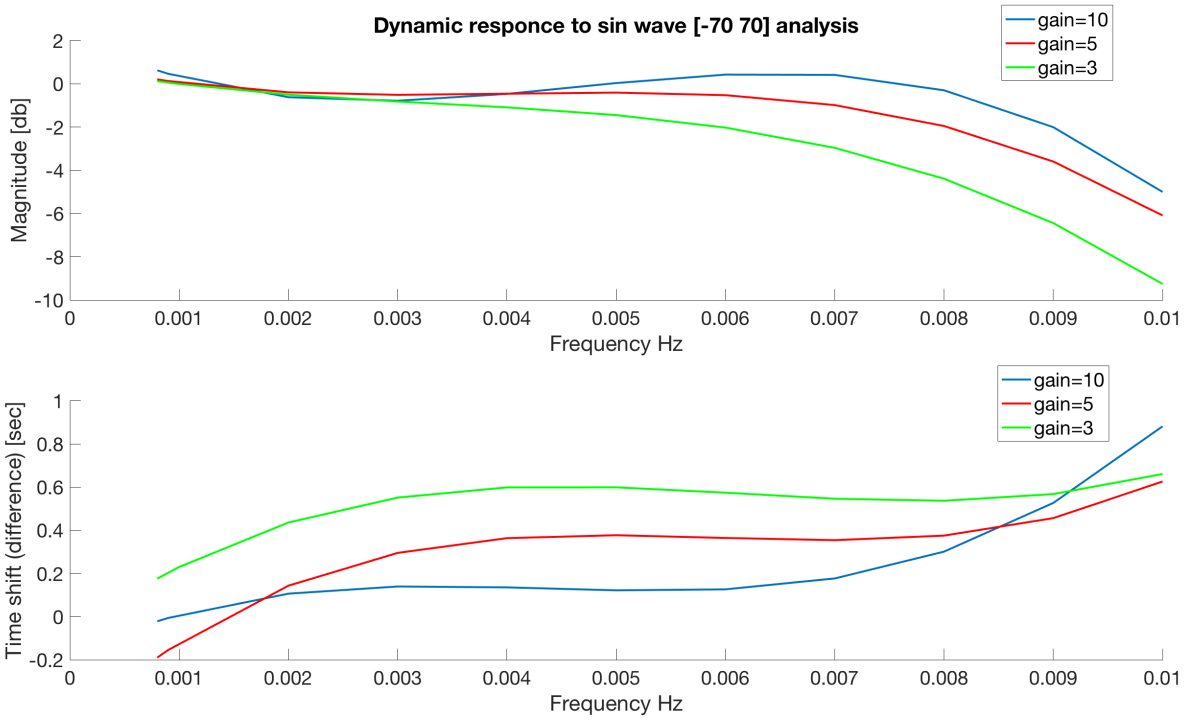


Figure 7.7: Dynamic responses to sinusoidal wave for three gains

The decay in magnitude of the system's response is to be expected: the lowest being for the highest gain G=10; followed by the G=5 and the highest reduction in amplitude being G=3. Interestingly, the high gain G=10 has a small delay for the low frequencies, altering this behaviour for frequencies f>0.008Hz. For high frequencies this gain is increasing in delay up to 1sec. The other two gains have reciprocal and expected time shifts.

7.5.3 Force response

In order to test force controller responsiveness to different changes in the system, a manual test was performed. The hand is positioned in the apparatus and performed a several different scenarios: quick changes, slow changes, starting movement, transitioning movement and lock-to-lock travelling. The score of responsiveness is calculated based on the anticipated activation of friction controller (i.e. controller should only assist with the movement initiation and stay off for the rest of the tests). Calculated score is 100% for friction controller responsiveness. Figure 7.8

illustrates the response for G=5 (the same behaviour is observed for all other gains) and movement initiation (for the first 7 sec) and the transition during continuous movement (rest of the signal).

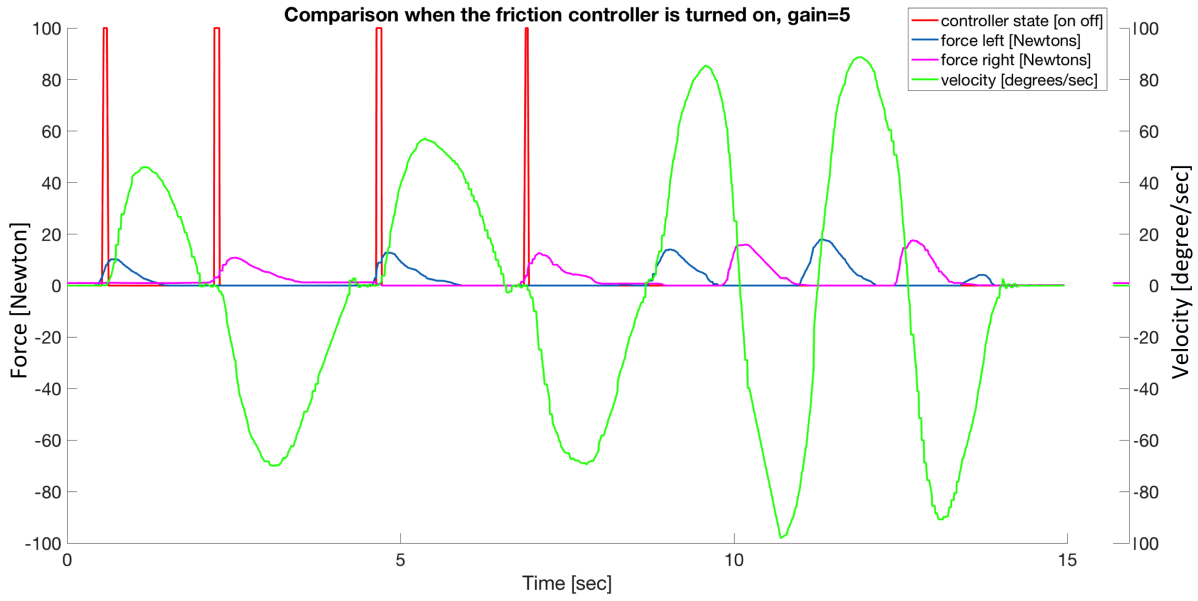


Figure 7.8: Velocity responses (in green) of the friction controller (active state in red) to various force inputs (colour blue for left and magenta for right force plate) presented for one gain as behaviour of the system is the same for any gain.

7.6 System integration

The VIBROfocus system integrates several elements: a vibrations generator, a robotic-aided wrist manipulandum, electrophysiological and physiological measurements and a repetitive movement therapy (designed as a game) as presented on Figure 7.9).

The participant is seated comfortably in a chair facing a computer screen and the robotic manipulandum. Except during the assessment of the level of spasticity by means of the Modified Ashworth Scale, the hand is positioned in the robotic manipulandum in mid-supination position. The vibrations are applied to the flexors and extensor muscles of the forearm while the hand is positioned in the system. The active and passive range of motion and stiffness of the wrist can be measured and used to adapt the movement ranges to suit movement requirements of the game. The equipment was tested for reliability and calibrated according to the manufacturer's manual. Before each experiment, the equipment should be checked for accuracy and recalibrated by need.

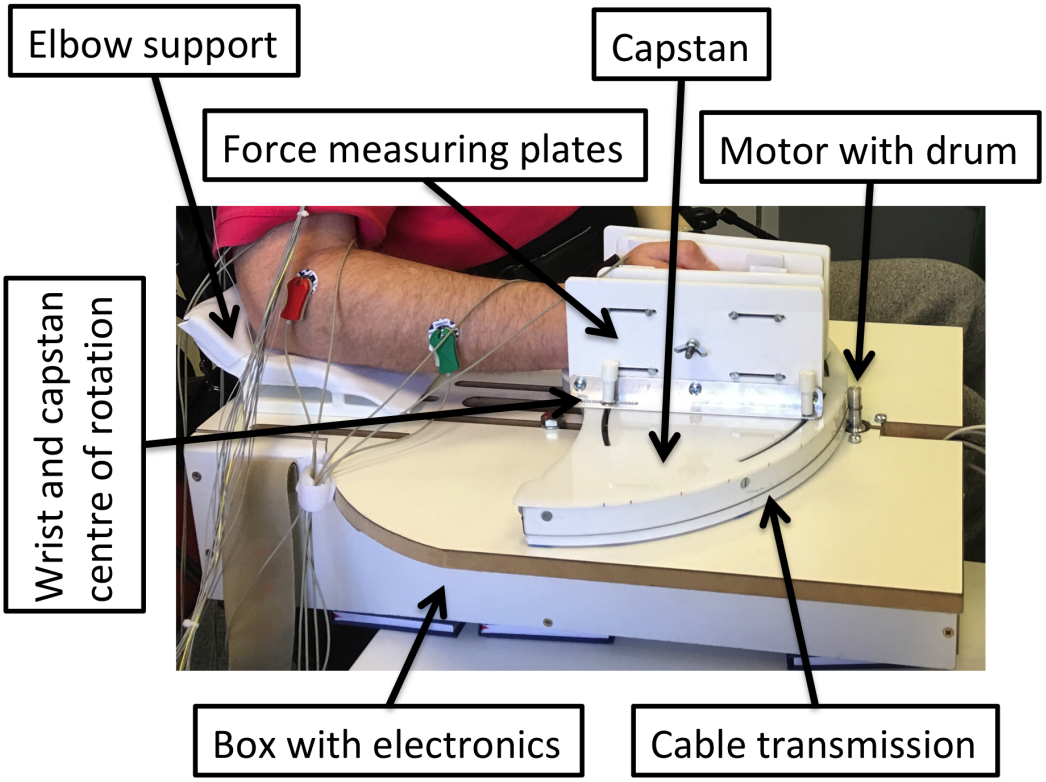


Figure 7.9: The VIBROfocus apparatus in use

EMG and EEG equipment can be tested for the presence of muscle's electrical activity, blinking or jaw clutching artefacts. Force sensors are expected to be tensioned due to the presence of spasticity but that is treated as a preload and can calibrated to zero before each measurement and for each user.

The software can manage the collection and the control of the data between the wrist device and the game. Forces f and potentiometer x_{pot} values from the capstan, counts $x_{encoder}$ from the motor encoder and and motor current i usage from the motor servo controller are acquired by myRIO and sent to the computer via USB connection. In the LabVIEW environment the data is processed and sent to selected program. Independently, these values are delivered to the watchdog. Selected program task and watchdog variables (such as force or position error, or continue/fail from watchdog) are considered and adapted to a velocity demand $\dot{x}_demanded$ sent to ESCON via myRIO. ESCON moves the motor's shaft and consequently the hand with the demanded velocity.

The timeline of the VIBROfocus clinical trial protocol is presented in following chapter. The tasks available for the trial are presented in the further sections of this chapter.

7.6.1 Physiological measurements

Active range of motion (AROM) is a measure of the farthest positions during volitional flexion and extension of the wrist. The user is instructed to move the wrist to "the furthest left and then furthest right position" while pushing against the support plate on the capstan. Friction compensation controller ensures user's ease and control of the movement. Measured values in degrees are noted.

Passive range of motion (PROM) is a measure of the farthest comfortable positions during wrist flexion and extension by an external means (e.g. robot or another person). The user's hand is moved to "the furthest left and then furthest right position within the limits of comfort" by the operator of the apparatus. The measured values in degrees are noted.

Joint stiffness (JS) is a measure of a stiffness inside a joint. It is calculated by observing a forces on the contact pates during passive movements of the wrist within passive range of motion. By determining the maximal force during these movements (which is most likely to be at the edges of the PROM) and including them in the equation 7.6.1, the statical stiffness is calculated:

$$k_m = \frac{M}{\Theta} = \frac{F_{max} \cdot 0.01}{\Theta} \left[\frac{N \cdot m}{deg} \right] \tag{7.6.1}$$

where $M{=}F{\cdot}d$ is a torque, F maximal force, d distance from the centre of rotation and Θ is an angle of the corresponding force.

7.6.2 The Pong game

The Pong game is selected to be integrated within the VIBROfocus system because of its simplicity of playing, programming and data analysis. The user needs to move *a paddle* in one of the two direction which can be mapped to the flexion and extension of the wrist. The Pong game is adapted from ©Complete Test 2002, in which original form the two players' movements are following the x position of the ball, while the randomisation of the y position of the ball (the slope) is calculated during the ball hit by a player.

Several adaptations of the game are developed. Firstly, *the player* is the user of the apparatus while *the opponent* is an automatic player that always scores. The score is the number of the ball hits. Length of the playing field (i.e. game's $x-axis$) is scaled to accommodate player's ROM. At

all times the player is aware where the paddle needs to be positioned in order to "hit the ball" by the marker/indicator positioned below the paddle. The marker is recalculated every time the ball hits the player's paddle to provide enough time for movement planning and execution. Because the game is programmed within a loop, the loop's execution time can be used to manipulate ball's speed and therefore the game's difficulty level. However, the optimum difficulty level is set for all user's unless requested otherwise.

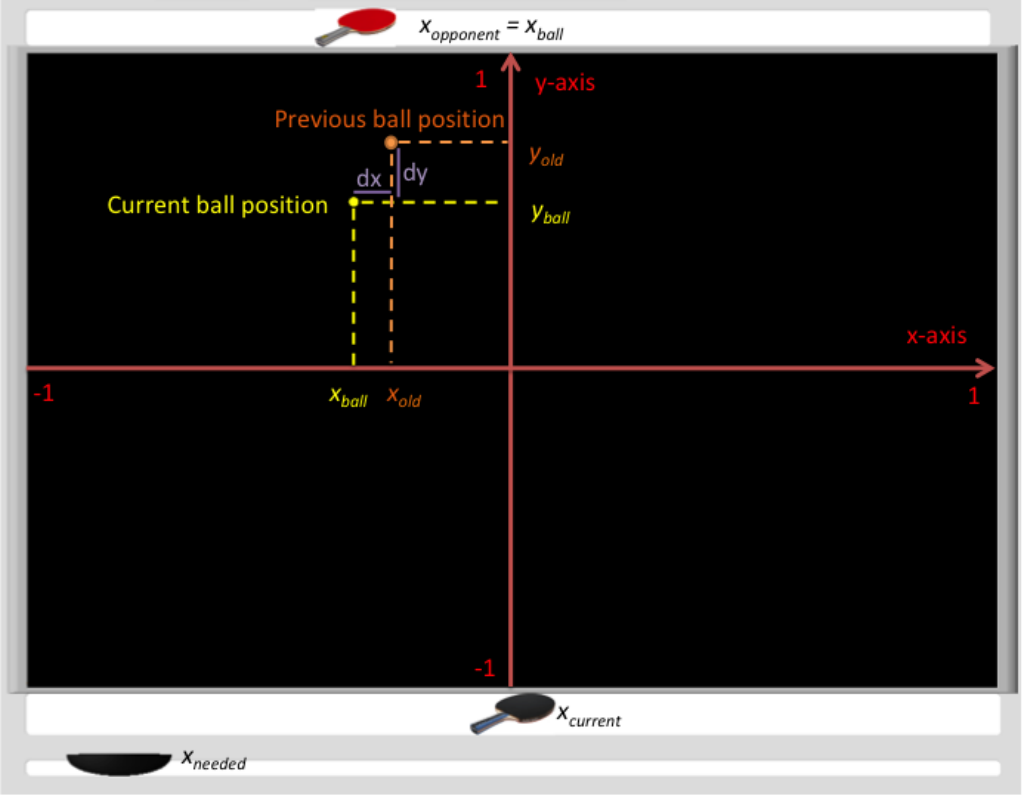


Figure 7.10: The Pong game variable presented in the graphical environment within game's coordinate system

For the purposes of the game calculations, it uses its own coordinate system in which all the values are mapped in range of $[-11]$ for both the $x - axis$ and the $y - axis$. The variables used are as follows:

- $x_{current}$ - current position of the player's paddle
- x_{needed} - position that the player needs to reach in order to score
- x_{ball} - current x position of the ball

- y_{ball} - current y position of the ball
- x_{old} - previous x position of the ball
- y_{old} - previous y position of the ball
- dx - a step ball is making in x direction from the previous to the current position within each loop iteration, i.e. the run
- dy - a step ball is making in y direction from the previous to the current position within each loop iteration, i.e. the rise
- $x_{direction}$ - the number indicating the direction of the ball in $x - axis$
- $y_{direction}$ - he number indicating the direction of the ball in $y - axis$

$$x/y_{direction} = \begin{cases} 1 & \text{if the ball is moving from the lower to the higher numbers on the axis,} \\ -1 & \text{if the ball is moving from higher to lower numbers on the axis} \end{cases}$$

During the game, when the ball is in the playing field, the next ball position is calculated based on the previous ball position and the rise and the run. (equation 7.6.2).

$$\begin{aligned} x_{ball} &= x_{old} + x_{direction} \cdot dx_{old} \\ y_{ball} &= y_{old} + y_{direction} \cdot dy_{old} \end{aligned} \tag{7.6.2}$$

When the ball hits either the paddle (score) or the bottom (not score) of the playing field (in both which cases $y_{ball} = -1$ and the $y_{direction}$ changes the sign because the ball is bouncing back into playing field) the calculations are made for the rise and the run (equations 7.6.3)

$$\begin{aligned} dx &= (x_{paddle} - x_{ball}) \cdot (-0.5) \cdot x_{direction} \cdot dx_{old} \\ dx &= \text{limit } (-0.02, dx, 0) \text{ or } (0, dx, 0.02) \text{ to avoid steep ball angles} \\ dy &= \text{limit } (0, dy_{old} + 0.002, 0.05) \end{aligned} \tag{7.6.3}$$

The second equation that is calculated when the ball bounces back from the bottom is a prediction of the following x-position where the ball will hit the bottom of the playing field. (equation

7.6.4). The prediction is a marker position where the player should position the paddle in order to score. Because at the moment of calculation the ball is at the bottom, the total y-distance is $1-(-1)=2$, and therefore the multiplier. Considering the dimension of the playing field $[-11]$, the expression $1-y_{ball}=$ gives the distance of the ball in y-axes. If this distance is divided with the rise (which is how much the ball is moving in y-axis) the number obtained is the number of steps, or loops in which the ball will reach the top of the playing field. This number of loops when then multiplied with the run (which is how much the ball is moving in $x-axis$) and the direction of the movement gives the distance of the prediction in $x-axis$. This distance is then added to the current position to obtain the absolute prediction.

$$x_{needed}=x_{current}+2\cdot\frac{1-y_{ball}}{dy}\cdot dx\cdot x_{direction} \tag{7.6.4}$$

However these calculations are based on the "triangular bouncing movement" calculations where the ball will travel under a certain angle to the top of the playing field and bounce back under the same angle. It doesn't consider the left and right boundaries of the playing field which, if reached, will cause another bounce. To rectify the numbers to fit the limits $[-11]$, the calculations are corrected based on the following cases which provides a prediction (i.e. x needed position) in numbers suitable for the playing field:

$$x_{neededcorrected}=\begin{cases}4+x_{needed} & \text{if } x_{needed}<-3\\ -2-x_{needed} & \text{if } -3\leq x_{needed}<-1\\ x_{needed} & \text{if } -1\leq x_{needed}\geq 1\\ 2-x_{needed} & \text{if } 1<x_{needed}\geq 3\\ 4+x_{needed} & \text{if } x_{needed}>3\end{cases}$$

Bearing in mind that the game will be played by users with limited or no volitional ROMs, the game can be played in one of the three modes:

- active - the user can play the game volitionally and with no external assistance
- passive - the user have no volitional abilities, therefore the movements are in fully controlled by the apparatus

- active assisted - the user have volitional control of some movements however needs assistance with others

Game playing modes

Active Pong game is programmed using friction compensation controller. The user can actively move the hand to hit the ball by pushing agains the contact plates, by matching the controlled paddle to the marker in the game.

Passive Pong game is programmed using position controller. The needed position for the controller is the one of the marker while the current is the one of the player's paddle. The time of the execution (and therefore the success of the hit) is dependent on the velocity set-point V where high constant reduces the time of execution but can cause user's discomfort due to the high velocity demand. That is why in some cases the score is not guaranteed in this mode. But this is acceptable to mimic the reality of actual volitional hit-or-miss scenario.

Active assisted Pong game is based on *lead-lag paradigm* which couples both controllers (Chemuturi & Amirabdollahian 2012). The player is given an opportunity to volitionally initiate the movement using friction compensation controller. The progress of the movement execution is inspected when the ball is hit by the opponent (i.e. when it bounces back from the top of the playing field). At this moment the player's current paddle position and the movement velocity is used to calculate *the lead* or *the lag* against the needed movement to reach the marker (Chemuturi 2014). If the player is lagging, in which case it has not passed roughly half way to the marker or the velocity is too small, the position controller takes over and completes the movement. If the user is leading, in which case is to successfully hit the ball, the friction controller continues to be in operation. The lead-lag calculations are reflecting on the distance between the player's current $x_{current}$ and needed position x_{needed} and the distance of the ball x_{ball} from the needed position, equation 7.6.5:

$$ll = |x_{ball} - x_{needed}| - |x_{current} - x_{needed}|$$

if $ll > 0$ the player's paddle is leading and will most likely reach the scoring position (7.6.5)

if $ll < 0$ the player's paddle is lagging and needs assistance to reach the scoring position

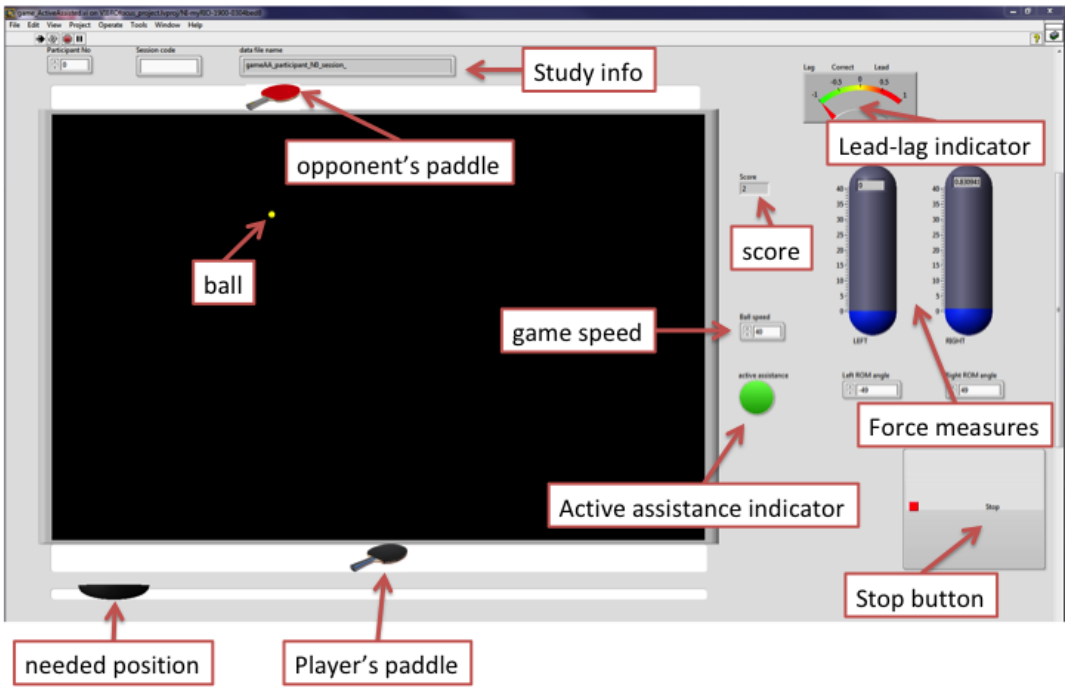


Figure 7.11: The Pong game active assistive mode

Game speed is dependent on the time needed to complete one programming loop, i.e. to change ball's position from the current to the next one. Dependency of loop times and game speed is given by:

- Game loop time = 20ms ⇒ game speed = 500 steps/sec
- Game loop time = 40ms ⇒ game speed = 250 steps/sec
- Game loop time = 60ms ⇒ game speed = 167 steps/sec

7.7 Chapter summary

This chapter focuses on the design and integration of the VIBROfocus apparatus, based on literature suggestions, clinical consultations and findings emerging from chapters 5 and 6. The system is able to measure certain aspects of the wrist joint movement kinematics. Additionally it can be used for repetitive movement exercise of the wrist with or without movement assistance.

Safety aspects of the system are considered as the targeted users are people with spasticity.

The positioning of the wrist joint, the hand and the forearm into the apparatus is simple and comfortable for the user. All actions derived by the apparatus are compared against safety limits and can be terminated on the given mark. The design and development combined measurement abilities and assistance to the movement. The apparatus can measure active and passive ranges of motion, joint stiffness under different velocities, and volitional movement kinematics. To engage the user into repetitive movement exercise, the game of PONG is integrated into the system. Depending on the level of motor control, movements can be actively assisted, fully passive or active (i.e. completely volitionally performed).

CHAPTER 8

Assessment of the effects of focal vibration on spasticity: pilot clinical trial

Chapters 5 and 6 identified positive effects FV can have on the healthy muscle and muscle performance. This chapter assesses the effects of muscle FV coupled with robotic mediated therapy have on hypertonic muscle, correlated joint stiffness and motor performance in people with SCI.

8.1 Introduction

Spasticity is, quote, "a motor disorder, characterised by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex as one component of the upper motor neurone UMN syndrome" (Lance 1980) and is one of the repercussions of a spinal cord injury. It leaves the skeletal muscles unable to control and locked in state of a high muscle tone as discussed in chapter 3 because of the signal imbalance between nervous system and muscles. Therapeutic approaches include combination of one or more pharmacological or non-pharmacological techniques, with a cost of adverse consequences.

Vibratory stimulation is one of the promising treatments for spasticity, with the least side effects (Hsieh et al. 2012). As discussed in chapter 4, out of all vibration types, focal vibration seems most appropriate choice against spasticity. Given that vibrations have similar vibration modulation mechanisms (Blackburn et al. 2014*a*, Sayenko et al. 2010) regardless of the type, the low-cost and ease-of-use puts focal vibration at the top of the list as a preferred candidate. Furthermore, unlike for focal vibrations, the literature provides inconsistent effectiveness of whole body vibrations and segmental vibrations against spasticity (Brogårdh et al. 2012, Pang et al. 2013).

The salient point to arise from chapters 5 and 6 is that focal vibration applied to the relaxed muscle have the potential to enhance muscle power by altering the spinal reflex mechanisms and reorganising muscle's activation patterns. This could be of importance in spinal cord injury rehabilitation to increase motor abilities of the residual movements. Moreover, for those people with SCI also affected by spasticity, FV might provide a double advantage against these two disorders. Calabrò et al. (2017) applied to tendon and Casale et al. (2014) to several arm and shoulder muscles during robotic-aided exercise for people with stroke and observed effectiveness in decreasing spasticity. On the other hand, Backus et al. (2014) followed a similar approach for people with spinal cord injury with focal tendon vibration and reported little or no change in spasticity.

The clinical trial for this thesis is evaluating the effects of focal muscle vibration on spasticity using an apparatus designed and developed to measure different aspects of spasticity and movement kinematics as well as assisting with the wrist joint movements. Focal vibrations are to be applied whilst targeted muscles are relaxing as suggested in chapter 5 and 6. The apparatus descried in chapter 7 is used to measure volitional abilities, range of motion, joint stiffness and movement

exercise performance. Additionally electrophysiological measurements from the brain and targeted muscles are recorded and analysed.

8.2 Clinical study design

The clinical pilot study presented in this chapter is classified as an unblinded, case study, where each case (participant) serves as his/her own control. This type of methodology is used to investigate the transient effects resulting from exposure to the focal muscle vibration on the acute outcomes of spasticity in motor incomplete SCI population, using VIBROfocus system described in Chapter 7. The study was reviewed by NHS Health Research Authority - Bromley Research Ethics Committee (IRAS number 217559) who raised no objection on ethical grounds and allowed the project to proceed. The ethical documentations can be found in appendix B.

Due to time constrains, 2 participants took part in this study. However, the future work is considering recruitment and completion of at least 5 volunteers.

8.3 Method

8.3.1 Participants

Participants were recruited from London Spinal Cord Injury Centre at the Royal National Orthopaedic Hospital (RNOH) NHS Trust, Stanmore. Five people were assessed for eligibility based on the inclusion and exclusion criteria below. A participant information sheet (appendix B-8) was provided and detailed explanation given prior to signing a consent form (appendix B-9). Inclusion and exclusion criteria are as follows:

- Inclusion Criteria
  - Over the age of 18
  - Normal eye sight (able to look at and read from a computer screen)
  - Spinal Cord Injured level C1-6, AIS A-D
  - Clinically diagnosed abnormal rigidity of the wrist (spasticity) at least Modified Ashworth Scale 1+

- Exclusion Criteria
  - Under the age of 18
  - Participants that do not adequately understand verbal explanations or written information given in English (or are not accompanied by an interpreter), and adults lacking capacity to consent. In case of doubt on the participants ability to consent, the investigator will seek advice from their GP/ rehabilitation consultant before proceeding.
  - Pregnancy
  - Other medical reasons that participants are unsuitable to take part e.g. blindness, unstable psychiatric illness

8.3.2 Experimental setup

Each participant took part in total of 6 intervention sessions dispersed in 3 sessions during each of 2 consecutive weeks. All sessions were performed in Aspire Centre for Rehabilitation Engineering and Assistive Technologies (Aspire CREATe) located at RNOH. The decision for a training exposure of 6 sessions over a two-week period is based on the experience with spasticity rehabilitation treatment and the minimum time needed to record expected changes (Etoom & Marchetti 2015). Results reported in the literature are showing that such exposure to robot therapy is often necessary to observe significant cortical reorganisation with the damaged brain and improved kinematic features (e.g. limb synergies and task oriented movements) (Aprile et al. 2016).

At the beginning of the first session, an initial measurements were recorded: initial Modified Ashworth Scale (MAS) Score followed by Spasticity and Pain Assessment: initial questionnaire (appendix B-10). Each of the 6 interventional sessions protocol consisted of the steps presented in table 8.1. These sessions begun and ended with Spasticity and Pain Assessment: session beginning (appendix B-11) and Spasticity and Pain Assessment: session end questionnaire (appendix B-12).

Participants came using their personal wheelchairs and were positioned in parallel to the table with VIBROfocus apparatus as illustrated on Figure 8.1. The two questionnaires and Modified Ashworth Scales were performed at the beginning and end of each session with participant's hand

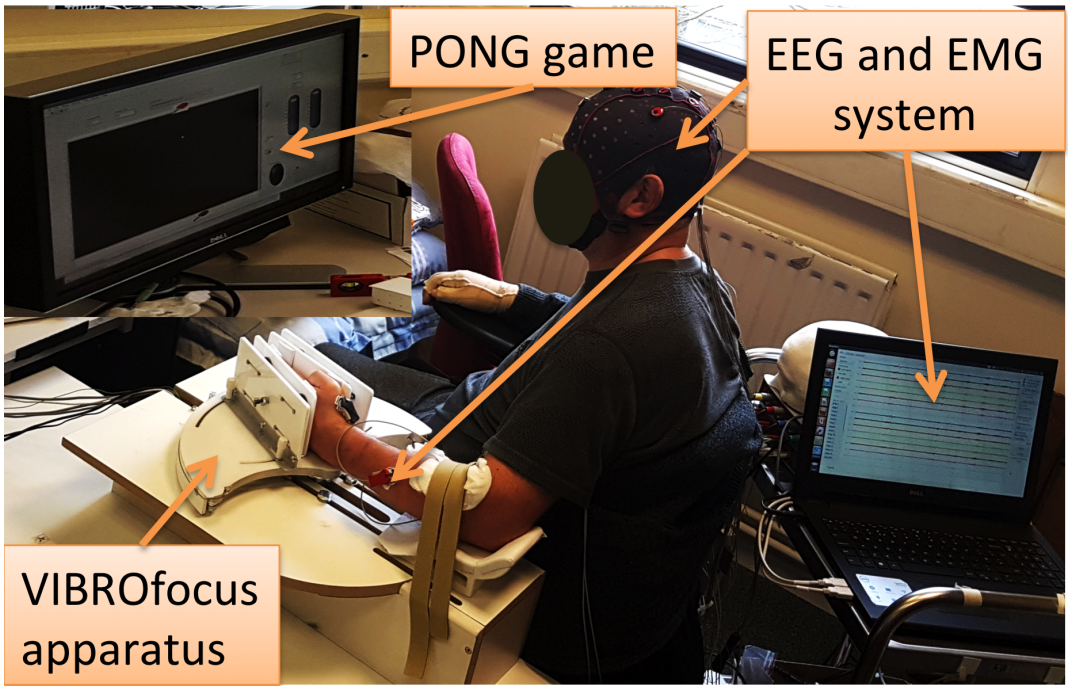


Figure 8.1: Experimental setup. The user has the hand and the forearm positioned in the apparatus whilst playing the PONG game. EEG and EMG recordings are also highlighted

outside of the apparatus. Electrophysiological EEG and EMG signals were measured for the duration of the session 1, 4 and 6. MAS was only measured at the beginning and at the end of each session to minimise perturbation and repositioning of forearm/hand into the device and potentially induce a stretch or trigger spasticity. However, as can be noted in table 8.1, AROM, PROM, and JS (steps 11-13) were measured after the applied vibration stimulation. Table height and the apparatus were adjusted to comfortably embed the elbow and the wrist joints, the forearm and the hand. Setting up sensors consisted of measuring force preload due to the hand's spasticity and/or embrace from the support plates (see section 7.4), reseting all measurement values and consideration of any other sensors by need. Firstly, measurement of AROM was performed to capture volitional abilities a participant might have. This is followed by PROM measured by a team member manually and slowly moving the capstan within able-bodied full range of motion. Participants were advised to inform if it got uncomfortable during the measurement. Limits to the range were recorded at the moment when the assessor started to felt an increase in resistance to the movement. The justification for this type of measurement, aside from its similarity to performing a MAS, is to establish joint's limits to be set for the upcoming joint stiffness mea-

surement. Joint stiffness was measured three times for three different velocities 8°/sec, 44°/sec and 80°/sec (Nardone & Schieppati 2005). The lowest and the fastest velocities are chosen as the most comfortable velocities with minimum acceleration time and maximum constant velocity time during movements. This is to avoid potential jerks and assess joint's behaviour during slow and fast movements. Velocity of 44°/sec is selected as a midrange velocity. The joint stiffness measure was always performed in the same order, starting with the 8°/sec and finishing with 80°/sec because fast movements are known spasticity triggers (see section 3.3). Participants were advised to inform the experimenter if anytime during JS measurement any discomfort, stiffening, spasms or other uncomfortable event occurred. These measures, AROM, PROM and JS are measurements performed at the each session beginning (i.e. before vibration), end (i.e. after the game) and after vibration stimulation.

Table 8.1: Protocol

1 2	Complete Spasticity and Pain Assessment: session beginning questionnaire Determine level of wrist spasticity using Modified Ashworth Scale
3	Set up the wrist in the apparatus
4	Set up the sensors and prepare for the measurements
5	Measure Active Range of Motion (AROM)
6	Measure Passive Range of Motion (PROM)
7	Measure Joint Stiffness (JS) 3 velocities
8	Set up the vibration motors
9	Apply focal vibro-tactile stimulation
10	Remove vibration motors
11	Measure Active Range of Motion (AROM)
12	Measure Passive Range of Motion (PROM)
13	Measure Joint Stiffness (JS) 3 velocities
14	Play a PONG game (in one of the three modes depending on participants abilities: active (user controlled), passive (RAD controlled) or active assisted (shared control))
15	Measure Active Range of Motion (AROM)
16	Measure Passive Range of Motion (PROM)
17	Measure Joint Stiffness (JS) 3 velocities
18	Take off the sensors
19	Remove arm from the apparatus
20	Determine level of wrist spasticity using Modified Ashworth Scale
21	Complete Spasticity and Pain Assessment: session end questionnaire

Focal vibrations were applied on the anterior and the posterior aspect of the forearm, approx-

imately 5-7cm from the elbow to cover muscle bellies for the majority of the wrist extensor and flexor muscles (see section 2.5.1). Stimulation lasted 15 minutes at 75Hz frequency and 0.4mm amplitude. The game was set to be played for the minimum of 15 minutes to capture anticipated neuroplastic changes. However, during the first session was noticed that participants might not have enough strength to play for that long. Therefore an amendment to the protocol was made and the game was played until participant would report tiredness, fatigue, or play time would exceed 20 minutes. Nonetheless, participants were encouraged to play the game as long as playing would imply enjoying and not any discomfort.

8.3.3 Outcome measures and data analysis

Outcome measures

Outcome measures for this study were:

- Primary outcome measure
  - Modified Ashworth Scale - clinical measure used to quantify spasticity level
- Secondary outcome measures
  - Joint Passive Range of Motion (PROM) - limits to passively move wrist into flexion and extension with no effort from the user.
  - Joint Active Range of Motion (AROM) - limits of user's ability to volitional move wrist into flexion and extension.
  - Joint Stiffness (JS) - quantified by evaluating the joint force resistance against joint movements performed by the apparatus within PROM during constant velocities.
  - Kinematic data of the game - limb movement profiles captured by the apparatus and movement sensors:
    * Reaction time (Tr) - time passed from the target's change of position to the observed reaction from the user
    * Movement efficacy (Me) - percentage of time used in respect to the time available to reach the target

    * Movement accuracy (Ma) - distance from the target at the movement of scoring
    * Total number of movement (Mn) performed during the game
  - Movement performance (IP) - index estimating movement based on the time and accuracy of the task execution.
  - Assistance level - measurements of the movement assistance needed during task execution:
    * Average lead or lag in the time before active assistance takeover (LL) - estimation of the movement against optimum movement to score. Optimum movement to score is calculated as movement with minimum jerks within maximal allowed time in order to successfully reach the target and score.
    * Mean distance at the moment of active assistance takeover (D) - distance user achieved during the available time for volitional movement.
    * Number of movements performed volitionally and number of movements performed with the assistance to complete.
  - Normalized jerk (NJ) - unit-free measure of motor fine movement based on the jerk.
  - Spasticity and Pain Assessment questionnaire - used to measure participants' subjective perception of the spasticity levels and associated pain and any changes. The questionnaire in its form was designed to allow a participant to numerically assess the levels of spasms and pain but also to report any and all changes in state. This is noted in the corresponding additional notes sections.
  - Electrophysiological measures - electroencephalography (EEG) and electromyography (EMG).

Data analysis

Programs controlling task execution, measuring and recording the data were written and executed in LabView environment (National Instruments). Recorded data were processes in MATLAB (The MathWorks, Inc.). PROM and AROM were programmed to capture both motion leading to the maximal angles of ROMs and maximal values in angles. The information was simply obtained

by reading a measurement file. Joint stiffness and game kinematic parameters needed further processing and game's kinematic data.

Force is extracted in Newtons and joint stiffness calculated according to equations presented in section 7.6.1. All other variables listed previously are calculated according to their definition. Smooth movements are assessed based on jerks, mathematically referred as the change of acceleration, which is a third derivative of the position (first equation in 8.3.1) (Flash & Hogan 1985, Hogan 1984). Because spasticity can have different severities, there is a need for a unit free normalised measure of movement smoothness, dependent on all assessment variables such as time, duration and level of difficulty. Normalized jerk was calculated based on the equation proposed by Teulings et al. (1997) and used in research evaluating movement performance (Aprile et al. 2016, Tavernese et al. 2013). Normalized jerk is a unit-free measure of movement smoothness or, in another words, estimate of the presence of the fast twitch like-movements. The calculation is based on the analysis of the absolute jerk, which is a third derivative of the position, estimating changes in acceleration. Equation used in this thesis is considering the jerk and the time and the distance performed during the movement. Normalized jerk is calculated using the equation 8.3.1

$$j(t) = \dddot{\Theta}(t) = \frac{\mathrm{d}^3}{\mathrm{d}t^3}(\Theta)$$
$$NJ = \sqrt{\frac{1}{2} \cdot \frac{t_{movement}^5}{\Theta_{movement}^2} \cdot \int_{t_{beginning}}^{t_{end}} \mathrm{j(t)\,dt}} \tag{8.3.1}$$

where $j(t)$ is absolute jerk calculated as a third derivative of the position Θ in time, NJ - normalized jerk, $t_{movement}$ - total time needed to perform the movement and travel $\Theta_{movement}$ distance, between times $t_{beginning}$ and t_{end} representing movement beginning and end, respectively.

Movement performance was based on the Fitt's Law (Fitts 1954, Tran 2013). Firstly the index of difficulty was calculated to estimate how difficult is for the user to perform the movement. Fitt's law stated that the difficulty of movement performance is dependant on the distance from the target and the size of the target. Shannon's formulation was used instead to regard information transmission in the human-computer interaction (Mackenzie 1992). The first adaptation of the Fitt's law for this study was to disregard target size and substitute it with the paddle size. This adaptation is considered because the task success (hitting the ball with the paddle) is directly

reliant on the distance of the paddle from the target. The Fitt's law proposes calculation of the index of performance as a function of the index of difficulty against movement execution time. In modern adaptation of the Fitt's law researchers use linear regression to calculate average movement time to deem choice of an input device and adjust to the purpose. Calculations for this study rely on the original equation due to large number of movement and movement differences. The complete set of equations is given by 8.3.2

$$\begin{aligned} ID &= \log_2(\frac{D}{W} + 1) \\ IP &= \frac{ID}{t_{movement}} \end{aligned} \tag{8.3.2}$$

where ID is the index of difficulty, D-distance from the target calculated immediately after the target had changed, W-width of the paddle, IP is the index of movement performance and $t_{movement}$ is the movement execution time. Movement execution time is detected by analysing velocity of the movement. Velocity is calculated as a first derivative of the displacement. After the peak velocity for each individual targets was found, the threshold was established at 10% to dismiss movement adjustments for the ball hit. These movements were detected in the last few movements attempts to position the middle of the paddle to the ball and did not contribute to the main movement performed between target change. All times from the list of outcome measures calculations for the active game playing were based on: the beginning and the end of the movement and the beginning and the end of target time. For the active assistance game and for the outcome measures associated to this mode, the additional time is the time when the assistance took over to complete the movement. It is the time before that action, i.e. the time given to the user to volitionally complete the movement.

EMG signals were filtered using Empirical Mode Decomposition described in chapter 5, section 5.2.3. EEG signals processing included Laplacian and band pass filtering, following steps from chapter 6, section 6.3.1.

Statistical analysis

The statistical analysis was carried out using the statistical package IBM SPSS®. Shapiro-Wilk test was used to determine normality distribution of the data for each variable. For the normally distributed data ($p>0.05$) parametric test were used. Scores of the Modified Ashworth Scale and

joint stiffness values were not normally distributed ($p<0.05$). The Wilcoxon signed-rank test was used to estimate the statistical significance for the change in MAS score at the beginning and at the end of each session. Friedman test was performed on the joint stiffness values to estimate statistical significance of the changes for each session and for each measurement in one session. Repeated measure Analysis of variance ANOVA was used to calculate statistical significance between sessions for all other variables. Correlation between MAS and JS at the session beginning and at the session end was estimated by calculating Pearson correlation coefficient.

8.4 Results

Two participants were recruited with the demographics characteristic presented in the table 8.2. The results will be presented for each case independently. The participation Gantt charts are available in appendix B-13.

Table 8.2: Demographical characteristics of the two participants

Participant ID	Gender	Age	Time since injury in months	Cause of Injury	Level of Injury	Type of injury (ASIA)	Use of assistive devices	Spasticity side (arms)	Time post injury when spasticity started	Spasticity triggers	Spasticity medications	Spasticity treatment	Pain side (arms)	Pain medications
1	male	50	14	trauma	C2-T2	C	- Motorized wheelchair; - Standing frame; - Stretch splints; - Lycra garments; - Lumbar support; - Gypsum suits;	both	3 months post injury *- as volitional control of upper limbs movements begun to recover, spasticity started to manifest*	- Stress is the main one; - Driving in a car; - Cold; - (Un)dressing;	-Baclofen; - Dantrolene; - Clonazepam *subjective assessment of effectiveness 5/10*	- Physiotherapy; - Occupational therapy; - Botulin Toxin injections *at home:* - Whole body vibration , - Segmental vibration; - Splints; - Garments; - Functional electrical stimulation	both	- Fentanyl patch; - Ibuprofen; - Paracetamol; - Gabapentin - Liquid morphine (as needed) *subjective assessment of effectiveness 4/10*
2	male	56	8	trauma	C3-C4	C	- Motorized wheelchair; - Splints; - Lycra stretch garments; - Standing frame;	both	5 weeks post injury *- as volitional control of upper limbs movements begun to recover, spasticity started to manifest*	- (un)dressing; - Closing fingers; - Driving in a car; - Unexpected noise	- Baclofen; *subjective assessment of effectiveness 7/10*	- Occupational therapy; *at home* - Whole body vibration - Functional electrical stimulation - Garments;	both	- Gabapentin *subjective assessment of effectiveness 7/10*

8.4.1 Case one

Mr R suffered a traumatic SCI as a consequence of falling off a horse, which resulted in a motor incomplete injury at C2 and complete at T2. The injury happened 14 months prior to taking part in the study. During hospitalisation 3 months post injury, therapy focused on the recovery of the volitional movements. As the volitional control of the upper limbs was restoring, spasticity started

to manifest itself. Since then upper limb recovery was compromised by the spasticity. Spasticity severity of both upper limbs can be categorised as moderate to severe.

Mr R was taking three different spasticity medicaments (maximum doses of Baclofen, Dantrolene and Clonazepam) accompanied by occasional botulin toxin injections and outpatient therapy at the hospital and at home. This therapy includes whole body vibrations, segmental vibration of the upper limbs, use of variety of splints and mobilization devices. Subjective estimation of the medication effectiveness on the spasticity was 5/10 with the remark about the severity of his spasticity quoting "I don't even want to imagine what would happen without medications". The spasticity triggers include dressing and undressing, driving in a car and cold from the environment. However, the main and most devastating spasticity trigger is stress. Mr R expressed that even thinking about an uncomfortable situation can trigger stiffness in the whole body.

Mr R's activities of the daily living were affected by the spasticity. Among others, it is limiting his ability to drive his wheelchair most of the time. Spasticity is especially difficult during the night when he is unable to sleep. During the night, temperature of the room has a direct impact to spasms; cold room can perpetuate spasms in the body while warm room prevents sleep. Mr R selected his dominant right hand to participate in the study.

Qualitative analysis

The summary of the questionnaires [appendix B10, B-11, B-12] related to the assessment of spasm and pain occurrence at the beginning and at the end of the session is presented in Figure 8.2. Mr R reported the decrease in pain in at least one point at the end of each session. However the pain had a recurrence at the beginning of the following session. Mr R reported the pain in the right hand had a feeling like a "cold clamp". Spasms were not reported during the sessions. However the occurrence was noted outside of the sessions, being more prominent during the night. The only manifestation of mild spasms during the intervention was reported in muscle biceps brachii during joint stiffness measurements in sessions 5 and 6 (first plot on the right in figure 8.2).

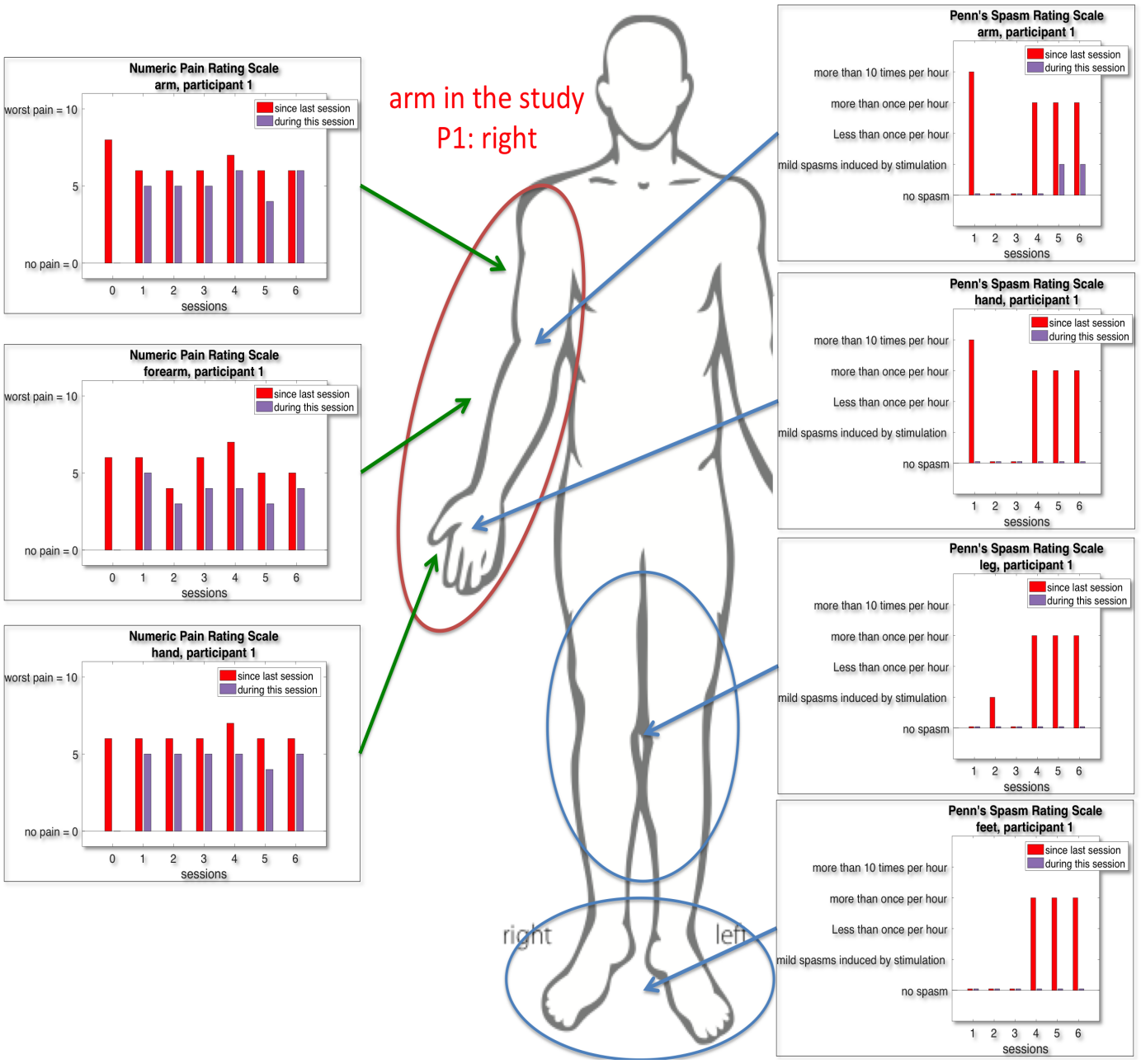


Figure 8.2: Summary of the questionnaires of the subjective assessment of the spasms (plots on the right hand side in respect to the reader) and pain (plot on the left hand side in respect to the reader) depending on the assessment location. Session 0 is included as an initial baseline assessment. Spasms were reported during sessions 5 and 6, and were often in-between sessions (red bars). With regards to the pain, the interventions during the sessions seems to reduce the pain, evident when comparing red to the purple bars.

Subjective assessment of the improvement in spasticity measured by questionnaires was noted at the end of every session (left plot in figure 8.3). In the first three sessions, Mr R had a recurrence

of spasticity triggered by stress or sleeping. However, in the last three sessions it would seem that the spasticity had a carryover and was lessen by the treatment. With regards to the scores on the Patient's Global Impression of Change Scale (right-up plot in figure 8.3), it appears that the usual triggers were still present, hence the low score for the symptoms (blue bar) and emotions (yellow bar). Rating of the degree of change since the beginning of participation in the study was always marked as much better (right-down plot in figure 8.3).

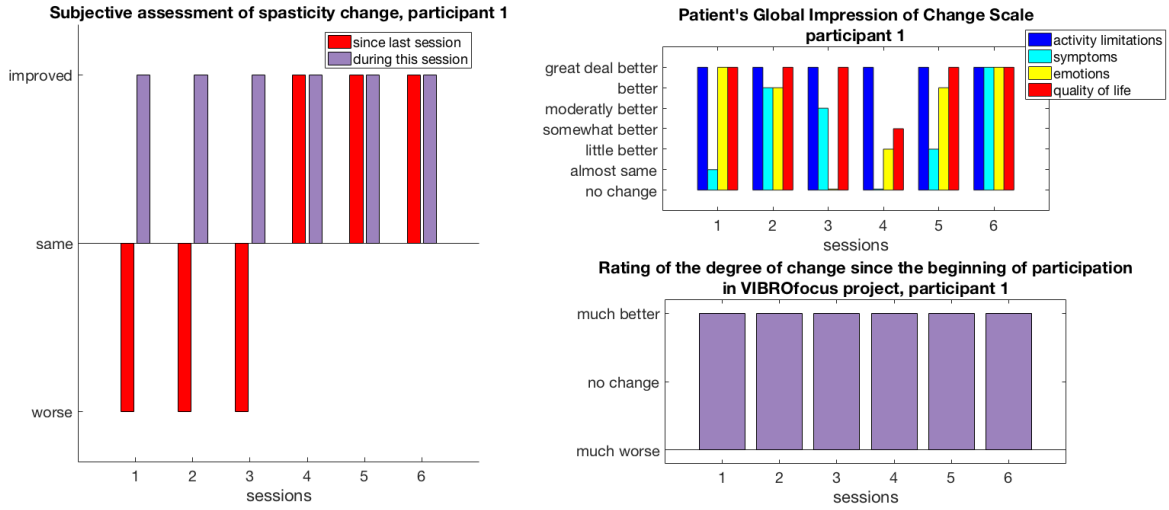


Figure 8.3: Summary of the questionnaires of the subjective assessment of the spasticity on the left, Patient's impression of change on right up and rating of the change since the beginning of participation on right down. Mr G reported subjective improvements in many aspects.

Additional notes from the questionnaires revealed that after the first session Mr R was able to drive his motorized wheelchair by himself, even with spasticity triggers, such as stress, were present. This ability lasted, on average, until the end of the session day. After session 5, Mr R noticed that the entire upper limb ipsilateral in the study felt more relaxed and less uncomfortable. The spasms were reduced during the night and Mr R was able to sleep comfortably.

At the end of the the session 2 the capacity to volitionally move the little finger returned after 5-6 months. However minimal at the beginning of the session 3, the potential to move the little finger increased as the study progressed. Followed by the little finger, the other fingers were able to move after sessions 3 to 6 but with carryover effects highly dependent on the spasticity triggers after the session. The volitional control of the wrist movements outside of the apparatus improved after the session 3 and persisted at least until the end of the session 6. Mr R was able to pronate

and supinate the wrist, extend and flex volitionally the wrist, as well as fingers to a certain extent.

As per the protocol, Mr R was asked to review and sign a two questionnaires at the end of each session. In the first two sessions, Mr R was hardly able to sign the first letter of his name. Session 3 yielded a signature of the three letter name, easily readable. At the end of sessions 5 and 6, he signed all questionnaires with a full name and surname with a minimum of 12 letters. This was a first time after the injury he was able to do so. He even observed a change in the way he was holding a pen, claiming that the grip had improved and eased the writing effort.

Among detrimental observations at the beginning of each session were the following:

- driving to attend the session 2 triggered spasticity and sensation of cold clamp in upper limbs.
- dressing and driving prior to the session 4 yielded cramps and spasms and brought back the uncomfortable sensation in the upper limbs.
- there was a strong pain present in the shoulder of the ipsilateral upper limb during session 5 and 6

Spasticity assessment

Modified Ashworth Scale was measured at the beginning (before muscle focal vibration) and at the end (after game) of each session. The results are presented in figure 8.4. Statistically significant decrease in MAS score can be observed when comparing scores at session beginning versus session end, in both flexion and extension ($p<0.05$, last two rows in table 8.4). The gradual decrease in MAS at the beginning of each session and compared between sessions can be observed for the extension but not for flexion, as seen on figure 8.4.

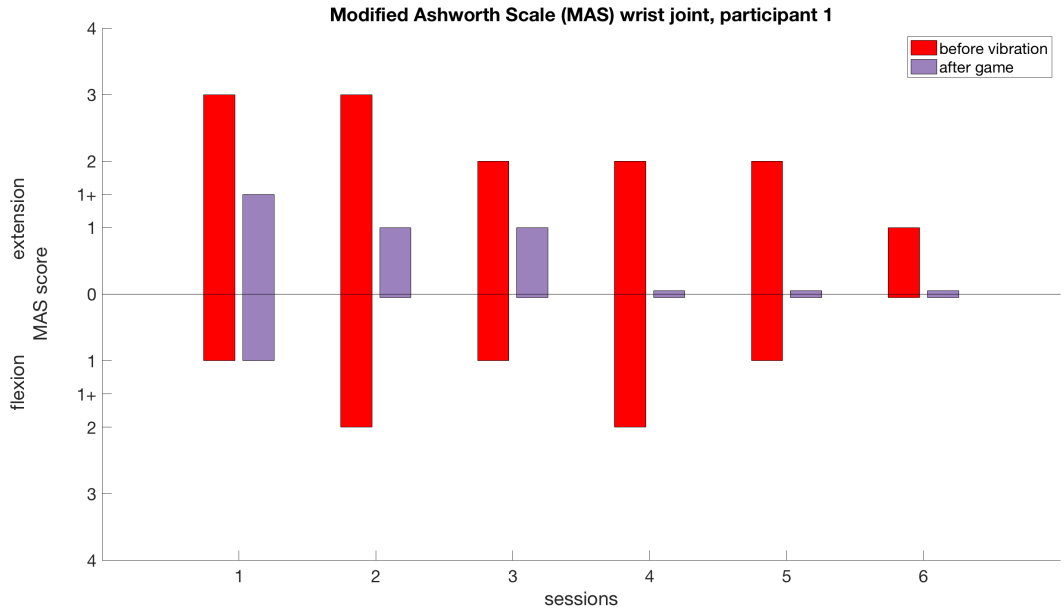


Figure 8.4: Modified Ashworth Scale measured at two occasions during each sessions: red - before focal vibration, purple - after game.

A full passive range of motion (PROM > 110 degrees) was observed during each measurement for every session. Mr R had some active (volitional) movements in flexion, but the extension seems difficult to perform. Numerical values of the achieved flexion and extension are presented in table 8.3. AROM values in extension with a minus sign in front represent achieved extension in flexion range of movement (taking neutral or position = zero degrees in mid-supination). This means that, Mr R had a neutral wrist position approximately in half flexion and was able to move the wrist in respect to that position. After the game in session 1, 2 and 5 Mr R was able to move wrist into extension as calculated from the neutral mid-supination position. Active range of motion, presented in figure 8.5 seems to improve after every muscle focal vibration stimulation during each

Table 8.3: Numerical values of mean and standard deviation for AROM and MAS for each measurement during each session.

sessions	*time*	*Measured variables for the wrist joint*				
		AROM flexion	**AROM extension**	**AROM**	**MAS flexion**	**MAS extension**
1	**bef vib**	15.95	-14.77	1.18	2	3
	aft vib	15.64	0.27	15.91		
	aft game	17.67	7.84	25.51	1	1
2	**bef vib**	20.26	-2.06	18.20	2	3
	aft vib	25.63	-1.19	24.44		
	aft game	29.92	1.90	31.82	0	1
3	**bef vib**	24.38	-15.43	8.95	1	2
	aft vib	26.12	-8.35	17.70		
	aft game	27.90	-1.24	26.66	0	1
4	**bef vib**	20.29	-14.41	5.88	2	2
	aft vib	25.84	-12.25	13.59		
	aft game	28.33	-10.54	17.79	0	0
5	**bef vib**	35.49	-21.30	14.19	1	2
	aft vib	36.45	-1.73	34.72		
	aft game	37.82	3.97	41.79	0	0
6	**bef vib**	19.72	-12.74	6.98	0	1
	aft vib	20.28	-9.76	10.52		
	aft game	21.65	-2.31	19.34	0	0

Table 8.4: Results of the repeated measure ANOVA of AROM and MAS for the changes during each session

Variables	*Comparison pair*	*Sig. (p-value)*
AROM	**before vib – after vib**	0.031
	before vib – after game	0.001
	after vib – after game	0.04
MAS flexion	**before vib – after game**	0.038
MAS extension	**before vib – after game**	0.023

Comparison pair represents variable and factor set.

session. With the statistical significance present between each measurement during each session ($p<0.05$) it seems that both muscle focal vibration and robot-assisted exercise contribute to the improvement in the volitional ability to flex and extend the wrist joint between 30-60%.

The wrist joint stiffness is presented in a bar plot for extension (up) and flexion (down) in figure 8.6 for three velocities in columns. Extension joint stiffness seems more pronounced than flexion. In extension, FV was able to reduce JS for every session. In flexion and faster movements during JS (44deg/sec and 88deg/sec) measurement in session 2 it can be observed that the joint stiffness slightly increased after the vibratory stimulation. Nonetheless it was reduced after game play. Numerical values for the mean joint stiffness for each measurement followed by the standard deviation is presented in table 8.5. Table summarising statistical analysis for the JS is in appendix A-2.

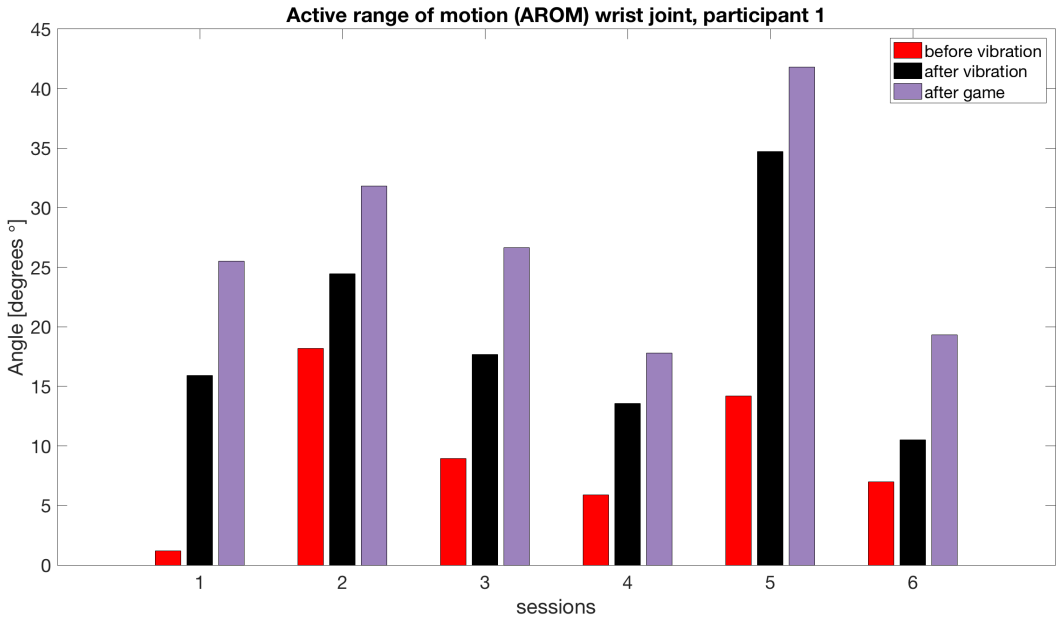


Figure 8.5: Full active range of motion (AROM) measured at three occasion during each session: red - before focal vibration, black - after focal vibration, purple - after game.

Table 8.5: Numerical values of mean and standard deviation for wrist JS for each measurement during each session.

sessions	*time*	Wrist joint stiffness											
		flexion						extension					
	velocities	8 deg/sec mean	8 deg/sec std	44deg/sec mean	44deg/sec std	88deg/sec mean	88deg/sec std	8 deg/sec mean	8 deg/sec std	44deg/sec mean	44deg/sec std	88deg/sec mean	88deg/sec std
1	bef vib	-0.0236	0.0020	-0.0212	0.0020	-0.0219	0.0020	0.0330	0.0026	0.0395	0.0021	0.03935	0.0009
	aft vib	-0.0177	0.0006	-0.0163	0.0006	-0.0149	0.0006	0.0148	0.0012	0.0315	0.0009	0.02862	0.0024
	aft game	-0.0171	0.0020	-0.0147	0.0020	-0.0154	0.0020	0.0074	0.0032	0.0168	0.0038	0.01661	0.0007
2	bef vib	-0.0269	0.0022	-0.0210	0.0022	-0.0219	0.0022	0.0409	0.0058	0.0342	0.0008	0.03440	0.0046
	aft vib	-0.0266	0.0038	-0.0249	0.0038	-0.0255	0.0038	0.0176	0.0035	0.0180	0.0022	0.02303	0.0037
	aft game	-0.0172	0.0009	-0.0161	0.0009	-0.0173	0.0009	0.0148	0.0031	0.0165	0.0033	0.02064	0.0056
3	bef vib	-0.0314	0.0026	-0.0253	0.0026	-0.0296	0.0026	0.0295	0.0052	0.0365	0.0047	0.03484	0.0050
	aft vib	-0.0215	0.0026	-0.0217	0.0026	-0.0208	0.0026	0.0254	0.0011	0.0299	0.0013	0.02555	0.0016
	aft game	-0.0194	0.0007	-0.0204	0.0007	-0.0201	0.0007	0.0179	0.0039	0.0239	0.0029	0.01798	0.0020
4	bef vib	-0.0333	0.0029	-0.0277	0.0029	-0.0271	0.0029	0.0539	0.0157	0.0430	0.0004	0.03870	0.0016
	aft vib	-0.0176	0.0004	-0.0156	0.0004	-0.0155	0.0004	0.0126	0.0044	0.0222	0.0013	0.01687	0.0007
	aft game	-0.0154	0.0034	-0.0084	0.0034	-0.0008	0.0034	0.0070	0.0018	0.0120	0.0055	0.00664	0.0008
5	bef vib	-0.0251	0.0013	-0.0273	0.0013	-0.0266	0.0013	0.0359	0.0185	0.0460	0.0100	0.05012	0.0088
	aft vib	-0.0253	0.0026	-0.0262	0.0026	-0.0250	0.0026	0.0080	0.0038	0.0192	0.0061	0.02019	0.0026
	aft game	-0.0076	0.0025	-0.0078	0.0025	-0.0087	0.0025	0.0001	0.0009	0.0002	0.0007	0.00735	0.0008
6	bef vib	-0.0232	0.0001	-0.0238	0.0001	-0.0229	0.0001	0.0232	0.0009	0.0393	0.0093	0.03625	0.0020
	aft vib	-0.0160	0.0034	-0.0108	0.0034	-0.0149	0.0034	0.0180	0.0029	0.0188	0.0031	0.02313	0.0046
	aft game	-0.0104	0.0021	-0.0070	0.0021	-0.0050	0.0021	0.0074	0.0014	0.0071	0.0038	0.00877	0.0031

Joint stiffness at the beginning (before vibration) and end (after game) for each session was correlated with MAS scores of the corresponding measurement. The Pearson's correlation coefficients are presented in table 8.6. Strong correlation (Pa> 0.7) can be observed for the MAS and JS in extension after the game.

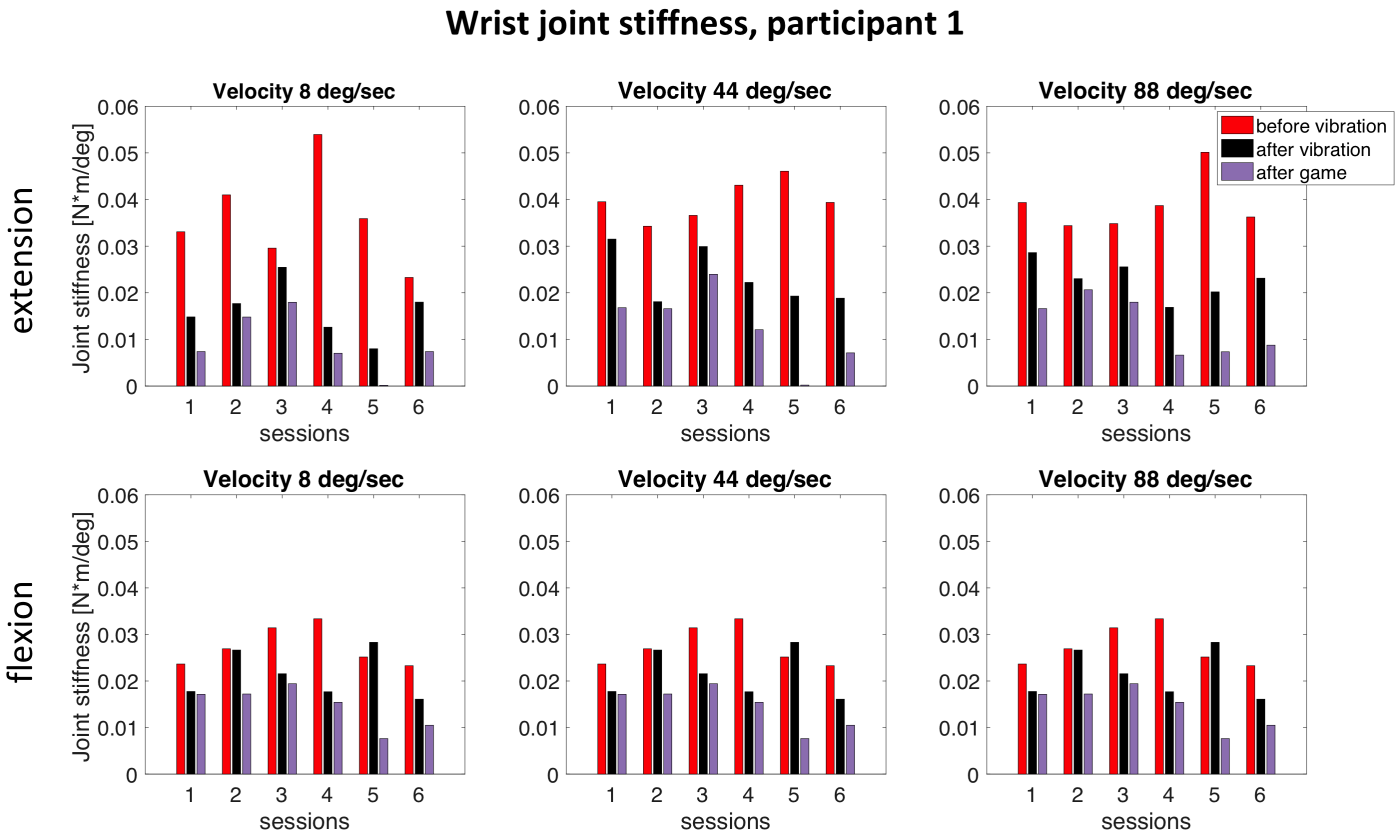


Figure 8.6: Wrist joint stiffness (JS) measured at three occasion during each session: red - before focal vibration, black - after focal vibration, purple - after game. Upper plots are for extension and lower for flexion for each of the three velocities mapped into columns.

Table 8.6: Pearson's correlation coefficient for MAS and JS measured at the session beginning (before focal vibration) and at the end of session (after game).

Variable				MAS			
				flexion		extension	
		velocity	*time*	bef vib	after game	bef vib	after game
Wrist Joint stiffness	flexion	8 deg/sec	bef vib	0.353			
			after game		0.280		
		44 deg/sec	bef vib	0.220			
			after game		0.209		
		88 deg/sec	bef vib	0.157			
			after game		0.271		
	extension	8 deg/sec	bef vib			0.369	
			after game				0.736
		44 deg/sec	bef vib			0.344	
			after game				0.832*
		88 deg/sec	bef vib			0.059	
			after game				0.971**

Result's column and row pair corresponds to factors set used for the calculation

Game parameters assessment

Mr R played the game in active assisted mode in sessions 1 to 3. Afterwards was decided to engage Mr R into playing a game in active-assistance mode followed by passive mode to allow the user to relax and reduce stress and stress related consequences (sessions 4 to 6). Passive game playing was not included into analysis as Mr R was instructed to relax and allow the device to move the wrist in stead. Numerical values of the analysed variables, mean and standard deviation, are laid in table 8.7. Statistical analysis parameters are showed in following table 8.8, calculated for the changes between sessions.

Other game parameters such as range of motion and game speed did not change. Game speed was kept at low and range of motion at 15 degrees in flexion and 5 in extension (where zero position is mid-suppination).

Table 8.7: Numerical values of mean and standard deviation for game parameters during each session.

Variables			*sessions*					
			1	**2**	**3**	**4**	**5**	**6**
Index of performance	**extension**	**mean**	1.3406	0	4.5569	0	2.8435	0.8753
		std	0.2178	0	0.4441	0	0.6769	0.0743
	flexion	**mean**	0.8831	1.5632	3.4322	3.2482	4.8011	2.0996
		std	0.0942	0.3776	0.4863	0.5849	0.8421	0.4887
Distance from the target at AA takeover	**extension**	**mean**	8.9876	12.4091	-0.8498	-0.6759	-6.2977	2.509
		std	5.9453	7.0106	5.5276	6.7035	4.2783	4.9578
	flexion	**mean**	0.6788	0.2573	-8.8605	-6.3736	-23.2549	-5.6385
		std	2.6367	9.6585	7.541	6.4811	5.8293	5.4697
Lead lag estimation	**extension**	**mean**	-0.5405	-0.9839	-0.9769	-0.9315	-0.1083	-0.7249
		std	0.5614	0.0436	0.0696	0.1664	0.0537	0.4858
	flexion	**mean**	-0.9605	-0.416	-0.5969	-0.5863	-0.1415	-0.416
		std	0.0718	0.5095	0.4831	0.5022	0.0538	0.4153
Normalized jerk	**extension**	**mean**	0.1703	0	0.0479	0	0.76493	0.1517
		std	0.1677	0	0.1465	0	0.18174	0.2221
	flexion	**mean**	0.1925	0.4114	0.0392	0.1925	0.4734	0.2032
		std	0.0944	0.2137	0.0847	0.1675	0.2385	0.2582

The total number of movements dispersed in those fully active (dark blue for extension and light blue flexion) and those assisted (orange - extension, yellow - flexion) per session are presented in upper bars in the figure 8.7. Mr R exerted highest amount of movements for game playing during session 3 and session 6. Most prominent volitional movement is that in flexion while volitional movements in extension were not achieved during sessions 2 and 4. Bottom pie charts represent percentage of each movement type (active, assisted, flexion, extension). It would seem that while percentage of volitional movement in extension increases, percentage in flexion decreases.

Index of performance is calculated only for fully volitional (active) movements. IP seems to be increasing for the flexion in sessions 1 to 5 ($p<0.05$) and then drops in session 6 (comparison

Table 8.8: Results of the repeated measure ANOVA of game parameters for the changes between each session.

Comparison pairs (sessions)	*Variables*							
	Index of performance		**Distance at AA**		**Lead lag**		**Normalized jerk**	
	extension	**flexion**	**extension**	**flexion**	**extension**	**flexion**	**extension**	**flexion**
1-2	0.000	0.000	1.000	1.000	0.004	0.016	0.595	0.035
1-3	0.000	0.000	0.001	0.006	0.009	0.232	1.000	0.027
1-4	0.000	0.000	0.001	0.000	0.028	1.000	0.595	1.000
1-5	0.000	0.000	0.000	0.000	0.333	0.000	0.000	0.000
1-6	0.000	0.000	0.004	0.009	0.565	0.011	1.000	1.000
2-3	0.000	0.000	0.016	0.153	1.000	1.000	0.671	0.000
2-4	.	0.000	0.004	0.198	1.000	1.000	.	0.004
2-5	0.000	0.000	0.000	0.000	0.000	1.000	0.000	1.000
2-6	0.000	0.266	0.098	1.000	0.161	1.000	0.214	0.290
3-4	0.000	0.158	1.000	1.000	1.000	1.000	0.671	0.090
3-5	0.001	0.000	0.015	0.003	0.000	0.003	0.000	0.000
3-6	0.000	0.000	1.000	0.675	0.214	1.000	1.000	0.537
4-5	0.000	0.000	0.068	0.000	0.000	0.022	0.000	0.000
4-6	0.000	0.000	1.000	0.272	0.354	1.000	0.214	1.000
5-6	0.000	0.000	0.000	0.000	0.000	0.057	0.000	0.039

Comparison pair represents variable and factor set.

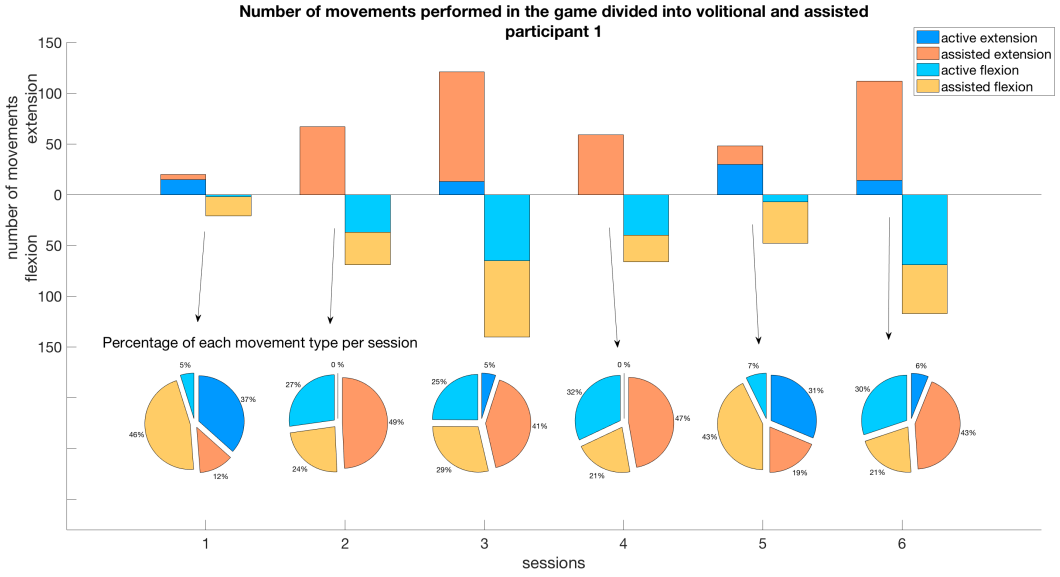


Figure 8.7: (Up) Bar representation of the number of movements performed in fully active (volitional) and active-assisted mode in the game. (Down) Pie charts of the percentages in contribution for the active flexion (dark blue), active flexion (dark orange) and assisted extension (light blue) assisted flexion (yellow) movements.

between session 2 and 6 is not significant $p>0.05$). In extension, IP seems at highest for the session 3.

Active movements were smooth in average except for the session 5 ($p<0.05$ as compared to other sessions) in extension and sessions 2 and 5 in flexion (both $p<0.05$ as compared to other sessions)

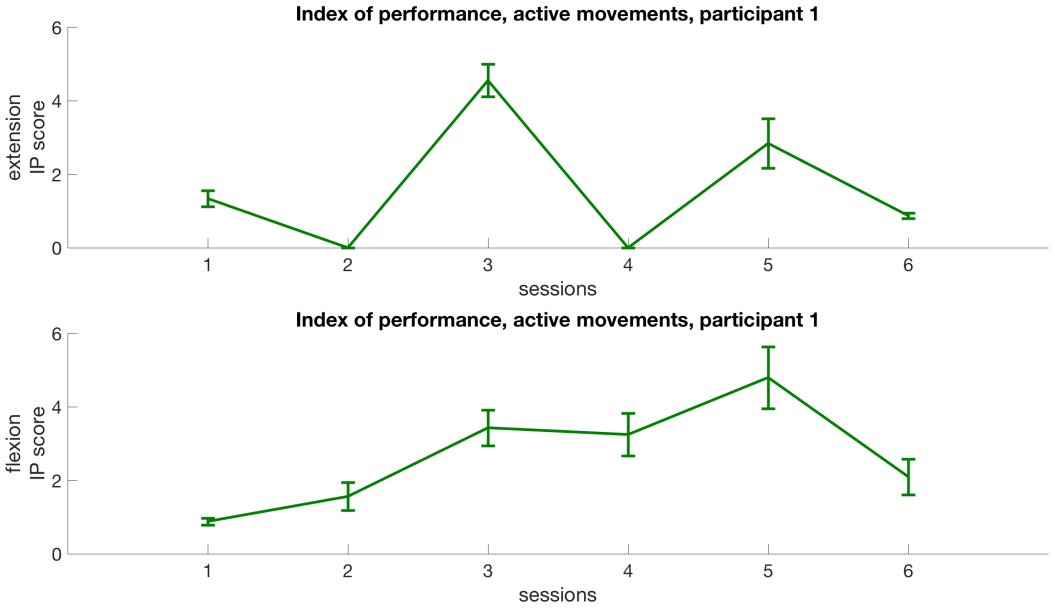


Figure 8.8: Index of performance based on Fitt's law

as seen in table 8.7.

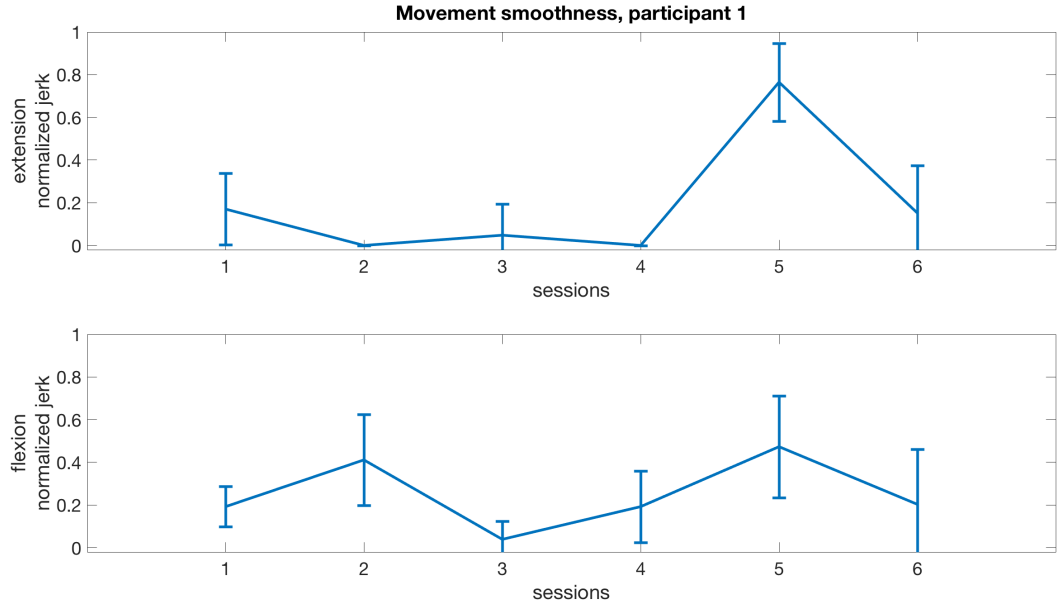


Figure 8.9: Assessment of movement smoothness based on normalized jerk.

Average lead lag was calculated for the assisted movements and the time before active assistance took over (i.e. time given to the user to attempt to achieve active movement). Mr R seems to be lagging in both extension and flexion. However, the presence of occasional leading can not be excluded due to high standard deviation in flexion. Interestingly the results indicate that during

session 5 the lagging was minimal.

Mean distance from the target at the moment of active assistance take over (Figure 8.10) offers additional information about movement behaviour during the time preceding it. It would seem that in both flexion and extension (more in flexion) the standard deviation reveals the presence of the overshooting the target. The overshoot is more pronounced in flexion for the session 5.

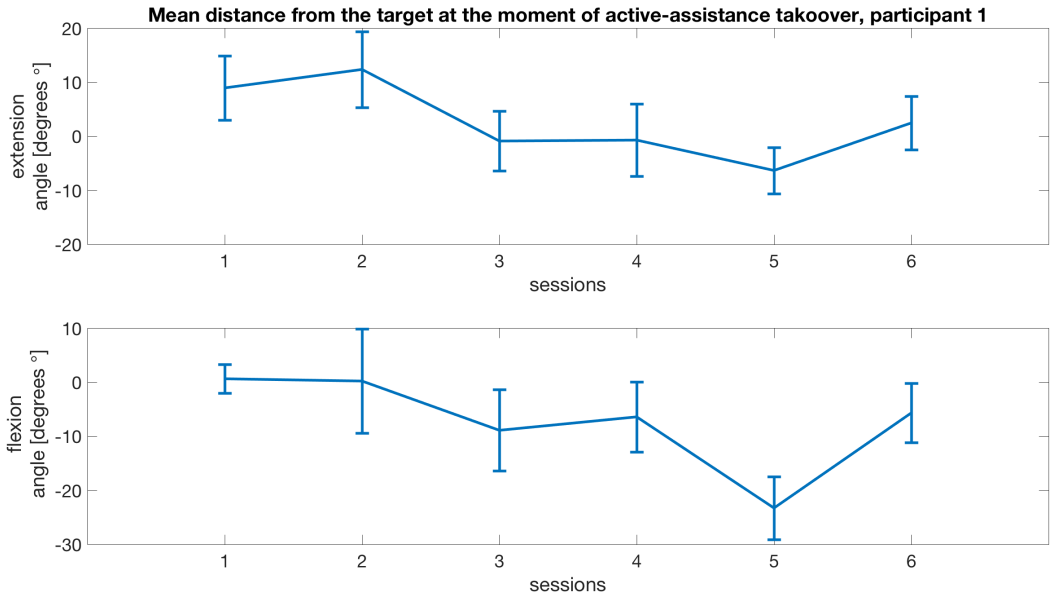


Figure 8.10: Mean distance at the movement of active-assistance takeover.

8.4.2 Case two

Mr G was a male who suffered a traumatic SCI during a bicycle traffic accident. His injury is motor incomplete at C3 and C4. The injury occurred 8 months before participation in the study. After the injury, Mr G had a small amount of residual movements in upper and lower limbs. Intensive physical therapy in the first few weeks post injury started to enhance volitional movements. However, 5 weeks post injury spasticity started to manifest and prevented further progress with volitional control. Spasticity severity of the both upper limbs can be categorised as mild to moderate.

Only Baclofen in maximum dose is used to pharmaceutically treat spasticity. Therapeutic management at home includes the use of whole body vibration. Spasticity is triggered by unexpected noises, dressing and undressing, driving in a car and volitional movements into flexion. Mr G is having a chronic problem with left hip and this includes spasticity triggering. The hip is one of the main issues preventing recovery of the lower limbs function and upper limb control.

Mr G is unable to functionally use hands as any attempt of volitional movement might trigger stiffening of the hand. Furthermore standing in a frame and residual gait reinforcement can be interrupted by the rise in spasticity. When presented with the choice Mr G wished to improve symptoms of his left hand as the level of volitional control is more prominent and he was already using it in his activities of daily living.

Qualitative analysis

The summary of the questionnaires at the beginning [appendix B-11] and at the end of the session [appendix B-12] is presented in figure 8.11. Mr G have had a high recurrence of spasms in upper and lower limbs triggered by dressing, undressing and travelling by car (plots on the left side in figure 8.11). In contrast, no spasms were reported during sessions. Mr G had a moderate pain in the left arm, forearm and hand during initial assessment, which seems to have decreased and diminished in session 4, 5 and 6 (plots on the right side in figure 8.11).

Spasms were reported during sessions 5 and 6, and were often in-between sessions (red bars). With regards to the pain, the interventions during the sessions seems to reduce the pain, evident when comparing red to the purple bars.

Mr G observed no changes in spasticity between sessions, as carryover effects persisted until next session (left plot in figure 8.12). Except the session 6, the participation in the study improved the spastic symptoms. For the session 6 Mr G was enthusiastic that there was no changes as his subjective feeling in the hand and arm was quote "flaccid" at the beginning of the session, meaning there was no subjective tension in the muscles as a consequence of the abnormal increased muscle tone. No changes in emotion (yellow bar of the upper right plot in figure 8.12) was stated. During session 3 Mr G remarked that symptoms did not change as the usual triggers were still affecting the spasticity level. From session 4 it seems that this was no longer the case as Mr G noticed that, when at home, volitional movements and standing in the frame no longer triggered spasticity. This is reflected in Rating of the degree of change since the beginning of participation in the study, with the highest scores observed for the sessions 4 to 6 (bottom right plot in figure 8.12).

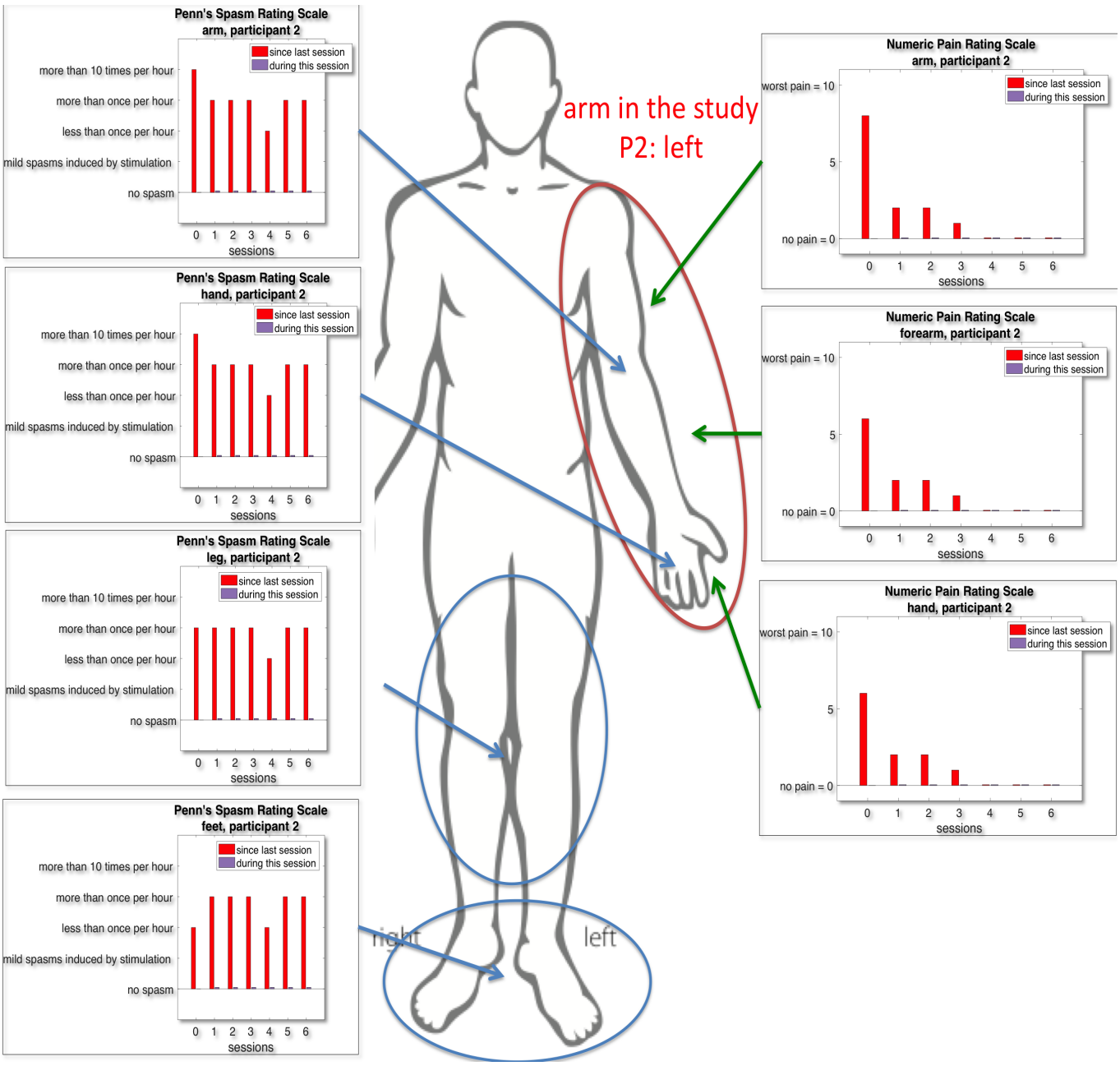


Figure 8.11: Summary of the questionnaires of the subjective assessment of the spasms (plots on the left) and pain (plot on the right) depending on the assessment location. Session 0 is included as an initial baseline assessment. Despite spasms occurrence was reported to be high in-between sessions, non was reported during sessions. The pain was high at the beginning of the participation in the trial, and it seems to be fully diminished after third session.

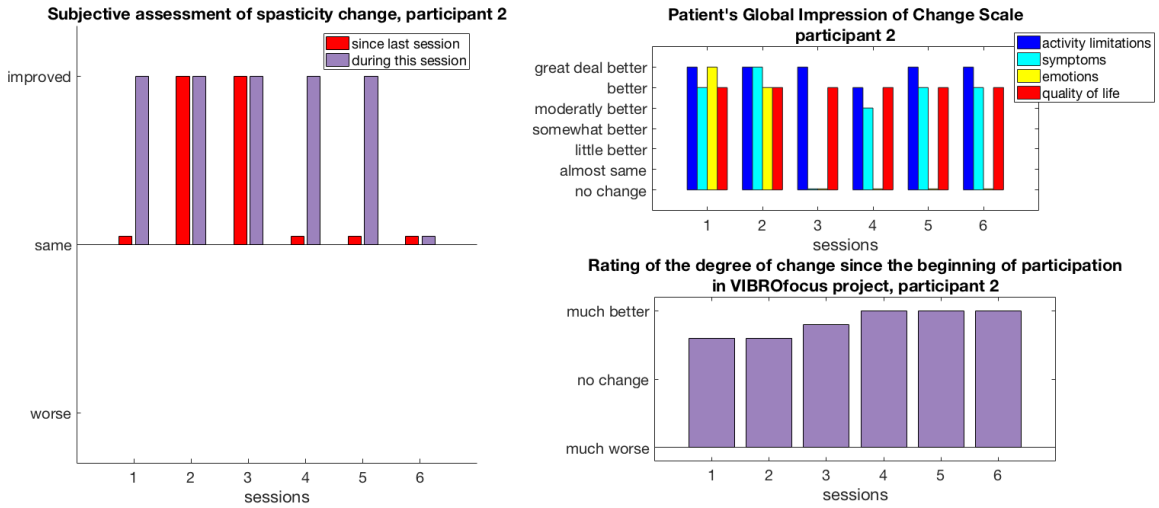


Figure 8.12: Summary of the questionnaires of the subjective assessment of the spasticity on the left, Patient's impression of change on right up and rating of the change since the beginning of participation on right down. Mr G reported subjective improvements in many aspects.

After the session 1 Mr G was able to fully independently grab and hold a glass of water and drink from it. Later that day Mr G had an occurrence of spasticity triggered by his daily routine to stand in a standing frame. This revoked achieved effects and volitional control. Despite that, in additional notes at the beginning of session 2 he reported that the ipsilateral hand felt more relaxed and looser. After session 2, the volitional abilities of the hand carried over at least until the end of session 6. Persisting after session 3 and at least after session 6, the spasticity trigger correlated to the volitional flexion of the fingers (e.g. closing a fist or manipulating a glass) appears to be diminished as Mr G did not observe any manifestation of this.

Keeping to his daily exercises, Mr G had no repetition of spasticity triggered by standing in the frame until the day after session 5. Because game parameters have changed, making the game harder, Mr G expressed a feeling of a fatigue after session 5 and less after session 6. He assumed that this fatigue could have been the reason behind onset of a mild spasticity symptoms. However, the hand returned to the quote "good state" at the beginning of session 6. At the end of session 6 Mr G autonomously opened the hand and grabbed a glass from a tray, drunk some water and released the glass.

Spasticity assessment

Numerical values for MAS and AROM are reported in table 8.9. Results of statistical analysis to yield a difference between measurements during each session are presented in table 8.10.

According to the MAS scores in figure 8.13, session one is the only one where the score did not change at the end of the session. Sessions 2 and 3 had some resistance in extension while sessions 4, 5 and 6 had no spasticity observed while assessing MAS. However, MAS scores at the beginning of each session did not change much in extension, but was diminished in sessions 2,4 and 5 im extension. The difference in MAS scores compared at the beginning (before muscle focal vibration) and end (after game) for extension did reach statistical significance ($p<0.05$) while for flexion did not ($p>0.05$).

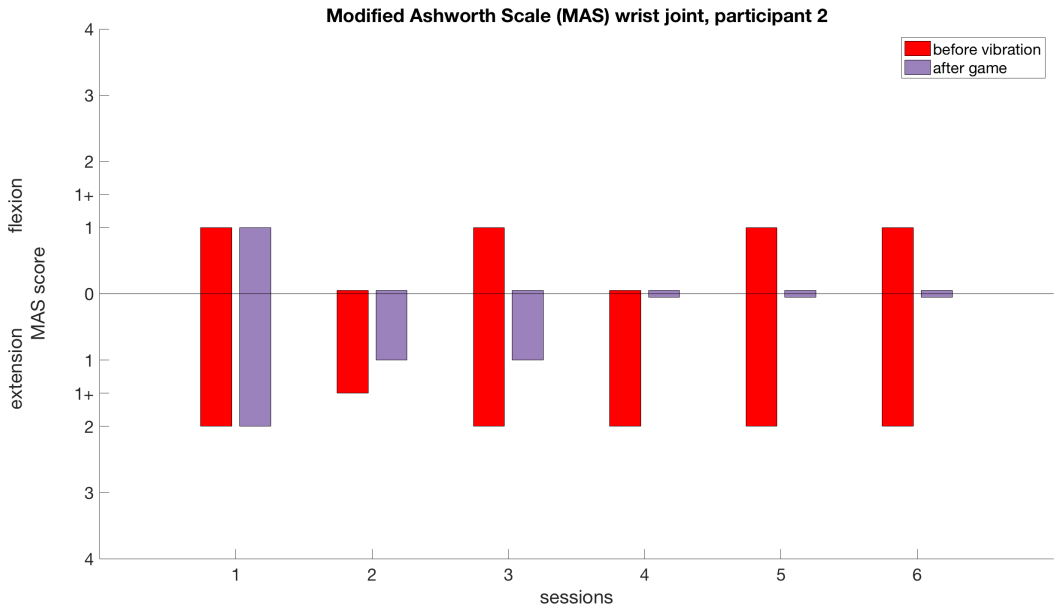


Figure 8.13: Modified Ashworth Scale measured at two occasion during each session: red - before focal vibration, purple - after game.

A full passive range of motion (PROM > 110 degrees) was observed during each measurement for every session. Mr G had the ability to volitionally move the wrist in flexion and extension, as compared to the neutral mid-suppination position. AROM did change statistically significantly after the game ($p<0.05$), but not after vibratory stimulation ($p>0.05$). The change is, however present even though it is a few degrees. Mr G did perform high in the AROM measures during sessions 5 and 6, yet not much of a difference is observed in between session measures.

Table 8.9: Numerical values of mean and standard deviation for AROM and MAS for each measurement during each session.

sessions	*time*	*Measured variables for the wrist joint*				
		AROM flexion	**AROM extension**	**AROM**	**MAS flexion**	**MAS extension**
1	**bef vib**	-12.32	46.02	58.34	1	2
	aft vib	-35.83	62.85	98.68		
	aft game	-64.85	66.10	130.95	1	2
2	**bef vib**	-37.23	57.68	94.91	0	1.5
	Aft vib	-37.21	61.40	98.61		
	aft game	-50.70	65.09	115.79	0	1
3	**bef vib**	-30.50	57.41	87.91	1	2
	aft vib	-31.97	57.67	89.54		
	aft game	-57.93	62.15	120.08	0	1
4	**bef vib**	-34.31	61.00	95.31	0	2
	aft vib	-37.01	66.65	103.66		
	aft game	-54.13	69.77	123.90	0	0
5	**bef vib**	-34.01	62.01	96.02	1	2
	aft vib	-35.37	65.87	101.24		
	aft game	-40.01	65.76	105.77	0	0
6	**bef vib**	-40.19	62.52	102.71	1	2
	aft vib	-43.08	63.26	106.34		
	aft game	-44.97	66.45	111.42	0	0

Table 8.10: Results of the repeated measure ANOVA of AROM and MAS for the changes during each session.

Variables	*Comparison pair*	*Sig. (p-value)*
AROM	**before vib – after vib**	0.258
	before vib – after game	0.001
	after vib – after game	0.029
MAS flexion	**before vib – after game**	0.083
MAS extension	**before vib – after game**	0.039

Comparison pair represents variable and factor set.

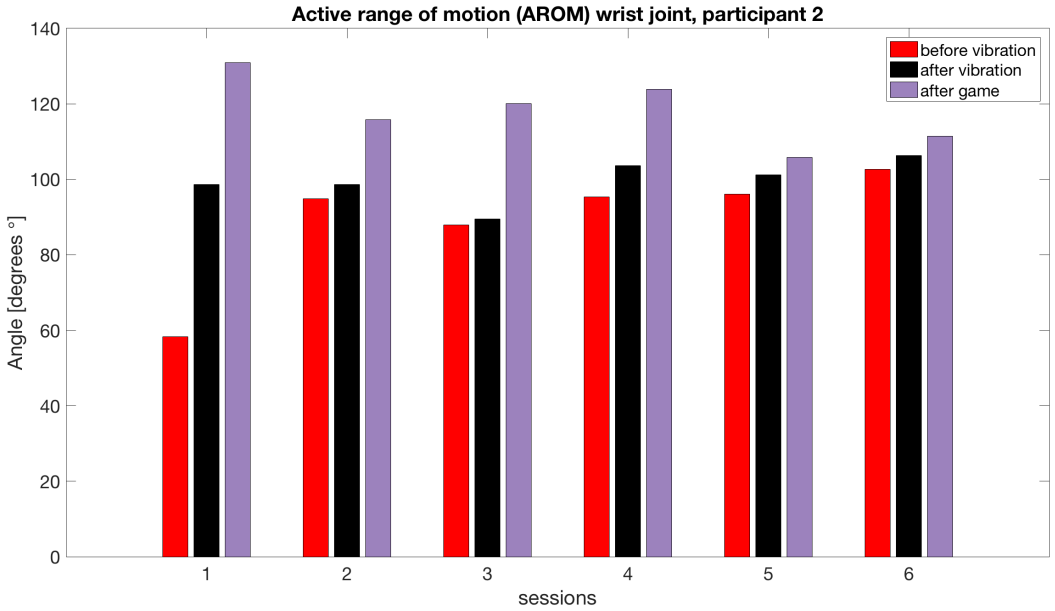


Figure 8.14: Full active range of motion (AROM) measured at three occasion during each session: red - before focal vibration, black - after focal vibration, purple - after game.

Wrist joint stiffness is presented in figure 8.15, upper row for extension, bottom for flexion and columns for different velocities. High joint stiffness before vibrations (in red) was successfully reduced as compared after vibration (colour black) and after game (colour purple) (both $p<0.05$) in extension and flexion ($p< 0.05$). While after the game there was some residual stiffness in extension, for flexion it was almost diminished. Results of statistical analysis for wrist joint stiffness measurements are presented in appendix A-3. Numerical values for all joint stiffness measurements are reported in table 8.11

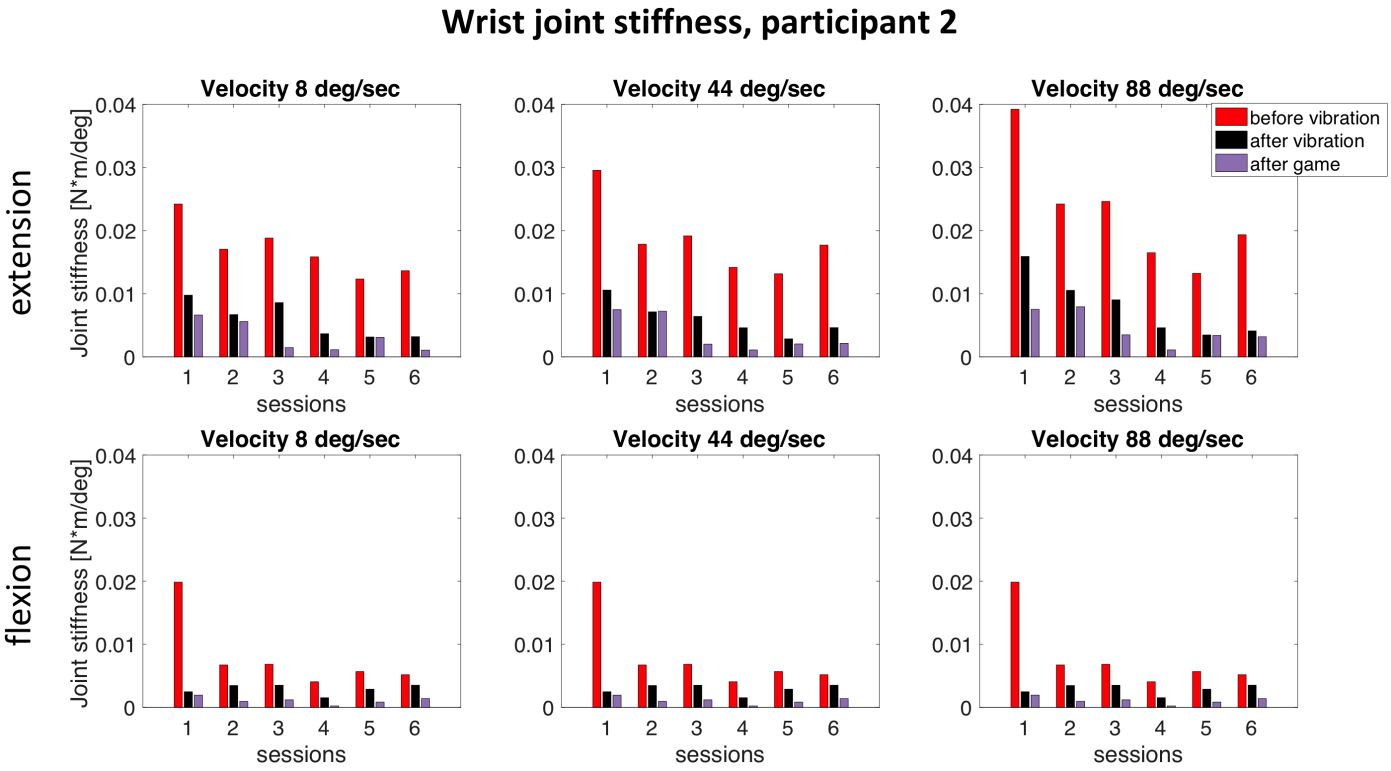


Figure 8.15: Wrist joint stiffness (JS) measured at three occasion during each session: red - before focal vibration, black - after focal vibration, purple - after game. Upper plots are for extension and lower for flexion for each of the three velocities mapped into columns.

Table 8.11: Numerical values of mean and standard deviation for wrist JS for each measurement during each session.

sessions	*time*	**Wrist joint stiffness**											
		flexion						**extension**					
	velocities	8 deg/sec mean	8 deg/sec std	44deg/sec mean	44deg/sec std	88deg/sec mean	88deg/sec std	8 deg/sec mean	8 deg/sec std	44deg/sec mean	44deg/sec std	88deg/sec mean	88deg/sec std
1	**bef vib**	0.0198	0.0014	0.0245	0.0016	0.0262	0.0017	-0.0242	0.0025	-0.0295	0.0054	-0.0392	0.0011
	aft vib	0.0024	0.0001	0.0068	0.0001	0.0070	0.0004	-0.0097	0.0034	-0.0105	0.0007	-0.0158	0.0014
	aft game	0.0019	0.0003	0.0026	0.0001	0.0044	0.0005	-0.0066	0.0017	-0.0074	0.0036	-0.0075	0.0019
2	**bef vib**	0.0067	0.0007	0.0069	0.0006	0.0070	0.0006	-0.0170	0.0017	-0.0178	0.0018	-0.0242	0.0010
	aft vib	0.0034	0.0003	0.0052	0.0004	0.0048	0.0008	-0.0066	0.0045	-0.0071	0.0014	-0.0105	0.0002
	aft game	0.0009	0.0005	0.0011	0.0003	0.0017	0.0001	-0.0055	0.0002	-0.0072	0.0002	-0.0079	0.0016
3	**bef vib**	0.0068	0.0001	0.0090	0.0002	0.0093	0.0008	-0.0188	0.0031	-0.0191	0.0042	-0.0246	0.0002
	aft vib	0.0035	0.0002	0.0046	0.0002	0.0043	0.0002	-0.0085	0.0002	-0.0064	0.0008	-0.0090	0.0009
	aft game	0.0012	0.0007	0.0029	0.0003	0.0021	0.0003	-0.0014	0.0061	-0.0020	0.0007	-0.0034	0.0084
4	**bef vib**	0.0040	0.0001	0.0058	0.0002	0.0057	0.0008	-0.0158	0.0075	-0.0141	0.0118	-0.0164	0.0059
	aft vib	0.0015	0.0004	0.0015	0.0004	0.0014	0.0004	-0.0036	0.0013	-0.0046	0.0003	-0.0046	0.0003
	aft game	0.0002	0.0003	0.0006	0.0003	0.0006	0.0001	-0.0011	0.0001	-0.0010	0.0002	-0.0010	0.0004
5	**bef vib**	0.0056	0.0003	0.0050	0.0010	0.0069	0.0013	-0.0123	0.0032	-0.0131	0.0005	-0.0132	0.0010
	aft vib	0.0028	0.0001	0.0034	0.0006	0.0034	0.0026	-0.0031	0.0010	-0.0028	0.0024	-0.0034	0.0019
	aft game	0.0008	0.0002	0.0005	0.0009	0.0003	0.0025	-0.0030	0.0014	-0.0020	0.0004	-0.0033	0.0009
6	**bef vib**	0.0051	0.0009	0.0057	0.0006	0.0093	0.0001	-0.0136	0.0044	-0.0176	0.0048	-0.0193	0.0027
	aft vib	-0.0160	0.0034	-0.0108	0.0034	-0.0149	0.0034	-0.0031	0.0029	-0.0046	0.0031	-0.0041	0.0046
	aft game	-0.0104	0.0021	-0.0070	0.0021	-0.0050	0.0021	-0.0010	0.0014	-0.0021	0.0038	-0.0031	0.0031

Table 8.12: Pearson's correlation coefficient for MAS and JS measured at the session beginning (before focal vibration) and at the end of session (after game).

Variable				**MAS**			
				flexion		**extension**	
		velocity	*time*	**bef vib**	**after game**	**bef vib**	**after game**
Wrist Joint stiffness	**flexion**	**8 deg/sec**	**bef vib**	0.351			
			after game		0.724		
		44 deg/sec	**bef vib**	0324			
			after game		0.514		
		88 deg/sec	**bef vib**	0.439			
			after game		0.893*		
	extension	**8 deg/sec**	**bef vib**			0.008	
			after game				0.775
		44 deg/sec	**bef vib**			0.063	
			after game				0.811*
		88 deg/sec	**bef vib**			0.073	
			after game				0.791

Result's column and row pair corresponds to factors set used for the calculation

Game parameters assessment

Numerical values for game related variables are reported in 8.13 with statistical analysis in table 8.14. As participation is the study progresses and Mr G reported decrease in the symptoms and augmentation in the wrist and the hand functionality, game parameters are adjusted accordingly. The range of motion was increased after the session 1, and game speed after session 4. The changes in game parameters did affect game variables.

Table 8.13: Numerical values of mean and standard deviation for game parameters during each session.

Variables			sessions					
			1	2	3	4	5	6
Index of performance	extension	mean	1.9398	1.5475	1.6472	1.8670	1.7667	1.7805
		std	0.5290	0.0467	0.0639	0.0691	0.6469	0.0810
	flexion	mean	1.5839	1.6766	1.9073	1.8845	1.5775	1.6136
		std	0.0649	0.0656	0.0583	0.0658	0.0620	0.0577
Reaction time	extension	mean	1.1378	0.6316	0.8705	0.6808	0.6404	0.5680
		std	0.5753	0.4036	0.6450	0.3072	0.3317	0.3550
	flexion	mean	0.9901	0.9382	0.7512	0.7044	0.6250	0.8112
		std	0.5249	1.0779	0.5118	0.3882	0.4726	0.5110
% Time used for movement	extension	mean	67.7147	71.6482	67.4068	65.6053	58.4425	57.8034
		std	2.2262	0.8123	1.7907	1.5709	1.4139	1.9665
	flexion	mean	76.1997	63.5776	68.9564	67.6558	54.0259	52.1819
		std	1.5361	1.5581	1.8084	1.4664	1.5583	1.9613
Normalized jerk	extension	mean	0.0302	0.1090	0.4201	0.0463	0.0406	0.1194
		std	0.0550	0.1606	0.2192	0.1128	0.1546	0.0759
	flexion	mean	0.0936	0.0510	0.3897	0.0544	0.0295	0.1615
		std	0.1626	0.0524	0.2462	0.1416	0.0717	0.1891

Table 8.14: Results of the repeated measure ANOVA of game parameters for the changes between each session.

Comparison pairs (sessions)	*Variables*							
	Index of performance		Reaction time		%time used for movement		Normalized jerk	
	extension	flexion	extension	flexion	extension	flexion	extension	flexion
1-2	0.000	0.000	0.000	1.000	0.000	0.000	0.277	1.000
1-3	0.000	0.000	0.403	0.066	1.000	0.000	0.000	0.000
1-4	0.000	0.000	0.000	0.380	0.000	0.000	0.873	1.000
1-5	0.000	0.000	0.000	0.000	0.000	0.000	0.316	0.021
1-6	0.000	0.000	0.000	1.000	0.000	0.000	0.000	0.061
2-3	0.000	0.000	0.455	0.192	0.000	0.000	0.000	0.000
2-4	0.000	0.000	0.537	0.529	0.000	0.000	1.000	1.000
2-5	0.000	0.000	0.363	0.009	0.000	0.000	1.000	0.097
2-6	0.000	0.000	0.024	1.000	0.000	0.000	0.138	0.000
3-4	0.000	0.000	0.002	1.000	0.000	0.000	0.000	0.000
3-5	0.000	0.000	0.001	0.800	0.000	0.000	0.000	0.000
3-6	0.000	0.000	0.001	1.000	0.000	0.000	0.000	0.000
4-5	0.000	0.000	1.000	0.012	0.000	0.000	1.000	1.000
4-6	0.000	0.000	1.000	1.000	0.000	0.000	0.000	0.000
5-6	1.000	1.000	1.000	0.083	0.167	0.000	0.161	0.000

Comparison pair represents variable and factor set.

Total number of movement, and consequently the time spent playing the game grew for every session, and it almost triples at the session 6. This is presented in bottom plot in figure 8.16.

Index of performance was very high during session 1 in flexion, but low for extension (blue plot in upper an middle plots in figure 8.16). When change in ROM is launched, IP dropped for session 2 but gradually increased for flexion (green plots in figure 8.16). Interestingly, this change in ROM produced an increase in IP for flexion, that kept amplifying until the change in game speed was introduced. The last two sessions, 5 and 6, were affected by coupled changes in game parameters and induced a decrease in IP (pink plots in figure 8.16). Statistical significance was reported for all changes in IP between sessions ($p<0.05$).

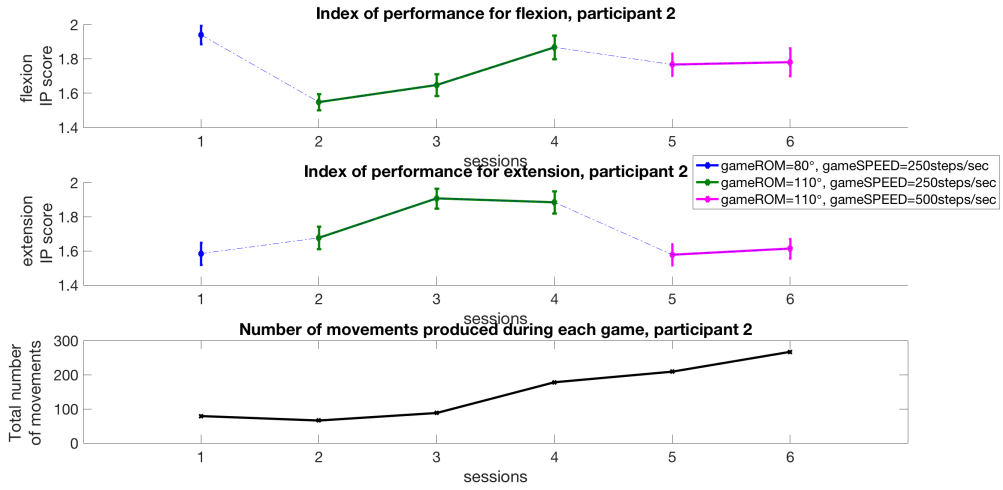


Figure 8.16: (Up and middle) Index of performance based on Fitt's law (Down) Total number of movement performed during game.

There was no observable changes in a very smooth movements performed by Mr G. However, a few jerks were observed in session 3 when Mr G attempted to adjust the paddle to be perfectly aligned with the target. These did yield a statistically significant change for session 3 when compare to others ($p<0.05$).

Movement accuracy in the moment of target hitting for each session is presented in pie charts in figure 8.17. No extension overshoot was observed whereas a few flexion overshoots ere present (yellow slice in 8.17). Some undershoots were present especially during sessions 5 and 6 (light blue and green slices in in 8.17) but most of the time Mr G was able to successfully score and align paddle to the target.

Movement efficacy is presented in red and calculated as a percentage of the time used to complete the movement out of the time available. The percentage is presented in blue line in figure 8.18.

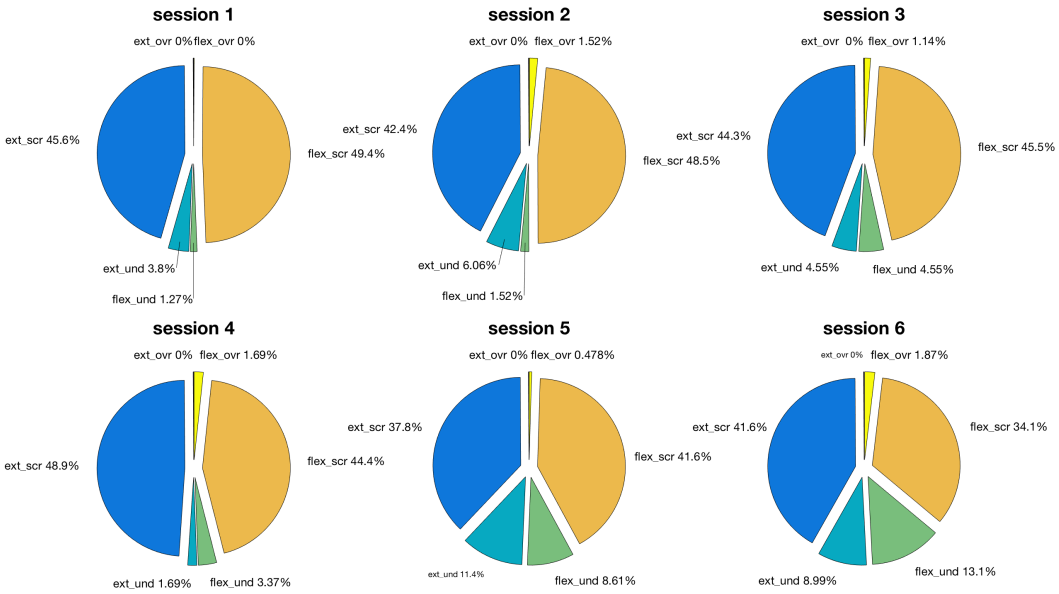


Figure 8.17: Movement accuracy (distance from the target) in the moment of scoring in the game.

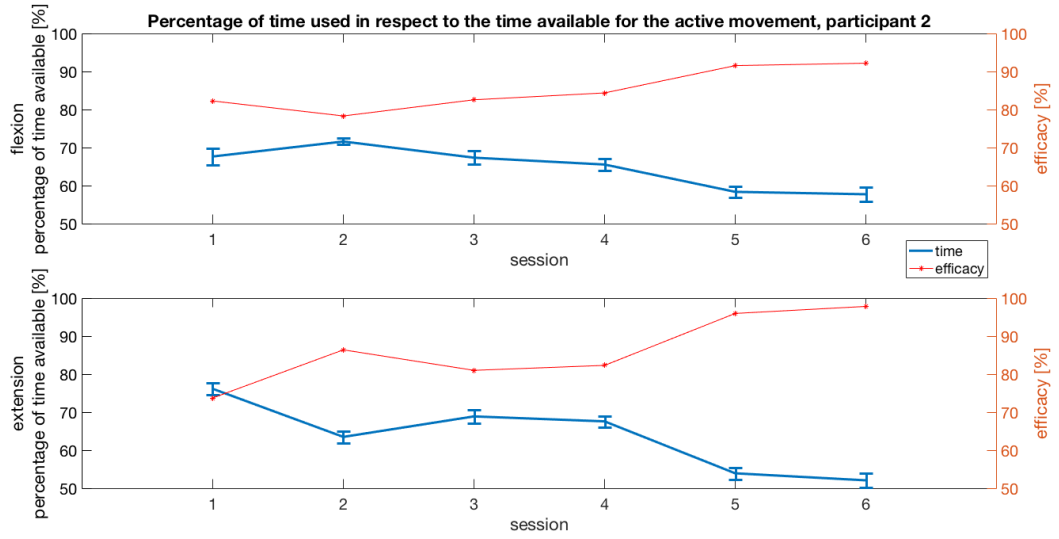


Figure 8.18: Movement efficacy, i.e. time used to complete the movement from the time available.

8.4.3 Electrophysiological measurements: EMG and EEG

The time domain analysis of the EMG reveal an increase in EMG amplitude at the moment of vibratory stimulation onset present in the wrist's flexor and extensor muscles. Illustrative example can be seen in Figure 8.19. Dark blue, light red and orange lines represent normalised EMG amplitudes for Mr R and purple, green and light blue for Mr G's forearm flexors muscles recorded during sessions 1, 4 and 6. The EMG amplitude is normalised for easier visualisation. Vibratory stimulation beginning is marked with dark red vertical line. In this example all EMG amplitudes increase after the vibration beginning.

No observable patterns in EEG signals were found for the analysis of the power of the mu waves. Nonetheless, some data did yield the increase of mu waves observed in chapter 6 following vibratory onset. This can be seen on Figure 8.20 for Mr G session 6. The increase in mu waves is observed for vibration onset (second plot) as compared to session beginning for electrodes Cz and C1, corresponding to the sensorimotor cortex. The mu power on these electrodes decays as soon as vibrations are turned off, determined by the visual inspection of Cz and C1 electrodes on third and fourth plots.

Further examination of the EEG signals in the time domain, 500ms before and 500ms after the vibration onset, showed a distinctive positive wave between 200 and 400ms after the vibration stimulation began. These signals can be observed in plots of electrodes C3, C1, CP3, CP1 and CPz, Figure8.21 representing Mr R's sensorimotor cortex during session 4. On this figure vertical red line indicate vibration onset. Having in mind that Mr R chose his right hand for the intervention, these positive waves correspond to activation of the cortex on the contralateral side in respect to the side of vibratory stimulation application.

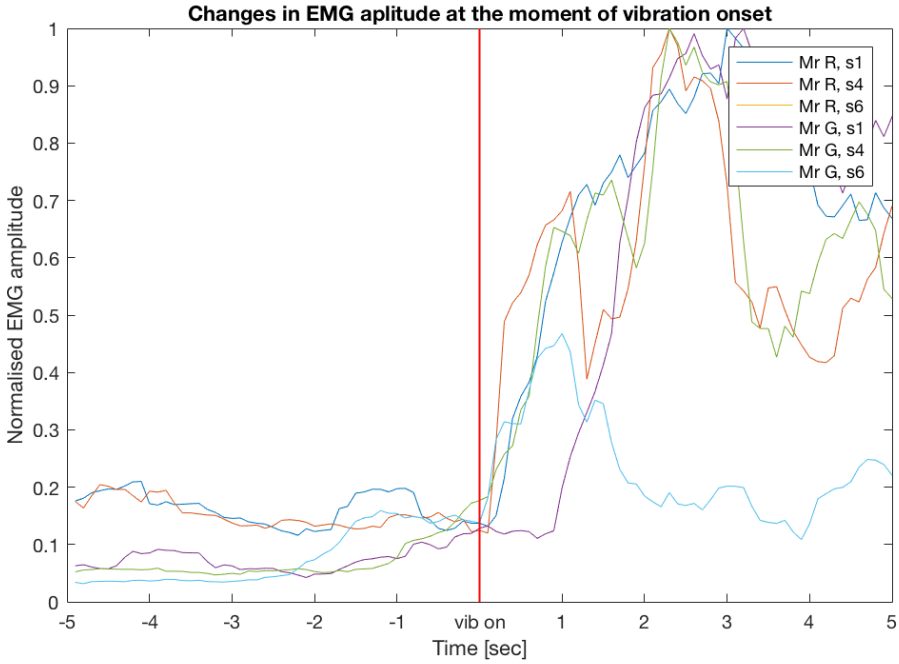


Figure 8.19: Normalised EMG amplitudes of 5 seconds preceding and 5 seconds post-vibratory stimulus onset for both cases. The red line represent the beginning of the vibrations.

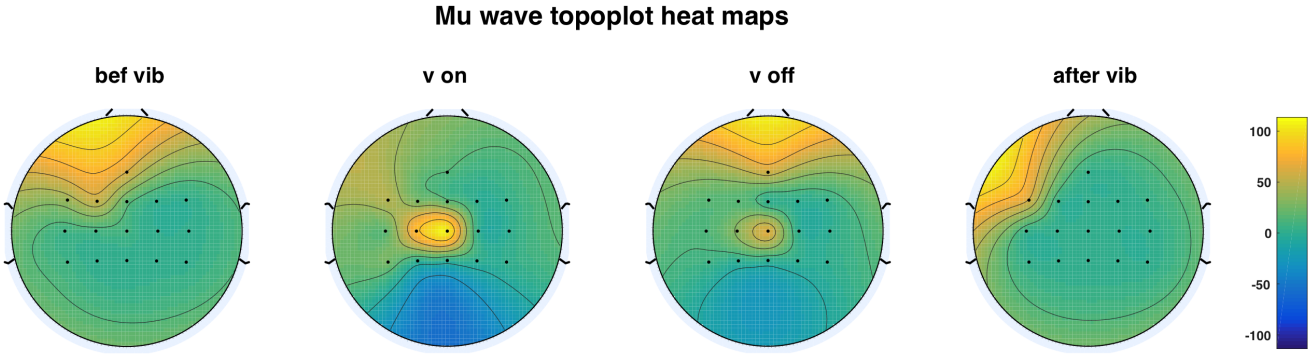


Figure 8.20: Topographic head heat maps corresponding physical placements of the EEG electrodes for participant 1, session 6. Topoplots are presented for session beginning, vibration onset, vibrations offset and session end. The increase in mu waves in noticeable for vibration onset (second plot) and decays as soon as vibrations are turned off (third and fourth plot).

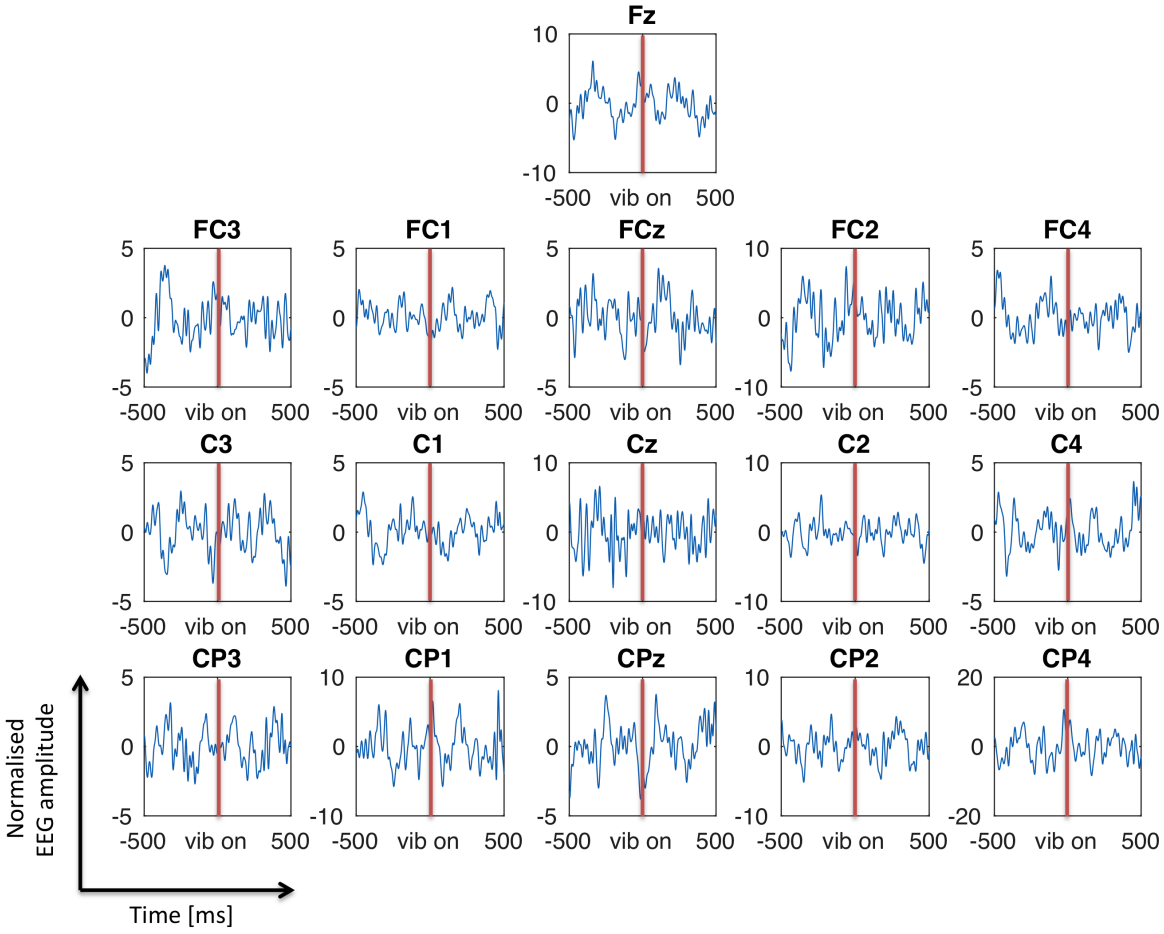


Figure 8.21: Time series for each EEG electrode corresponding its location on the measurement cap. Signals are representing 1 second surrounding vibration onset. The red line represent vibration beginning.

8.5 Discussion

The two cases with SCI are reported in this study with two different severity levels of spasticity present in the upper limbs. The main message that can be drawn is that 15 minutes of high frequency (75Hz) low amplitude (0.4mm) muscle focal vibration (FV) followed by robotic mediated movement therapy (RMT), over 6 sessions, can decrease spasticity and induce functional improvements in volitional movements. Scores on the Modified Ashworth Scale decreased in parallel to the joint stiffness when compared at the beginning and at the end of each session. Amelioration of the kinematic movement parameters measured throughout robot-mediated exercises is observed when compared between sessions. However promising, a larger sample study is needed to further assure these assumptions and correlate outcomes with spasticity severity and other triggering factors.

The two cases were very different in spasticity triggers, severity and residual volitional control as a consequence of the difference in the SCI injury. However, the consistency in spasticity reduction after six sessions, as measured with MAS and JS, was observed. Both cases reported a change in subjective feeling of the hand and the wrist movements: quoting "feeling more relaxed and loose". The carryover effects seem to depend on the usual triggers such as stress and dressing related activities. Nonetheless those correlated with the volitional control might have been minimised by this therapy. Both cases were excited with the functional improvements in the activities of the daily living such as handling a pen and writing and handling a glass.

Calabrò et al. (2017) reported that a similar approach applied to participants with stroke can decrease spasticity and enhance movement kinematics. They applied focal vibrations on the tendons whereas in this study FV was applied on the wrist joint flexor and extensor muscles of the forearm. The difference in location is very encouraging for the entire idea of FV spasticity aiding because the different application sites can induce different beneficial effects (Lee et al. 2014). Studies of the application of the FV to the spastic muscles of people with SCI, report reduction in spasticity measured by MAS (Etoom & Marchetti 2015, Murillo et al. 2011), complementing results of our study. Thus, Murillo et al. (2011) observed a decrease in limb spasticity irrespective to the lesion being motor complete or incomplete after muscle FV. This finding is important to assure that the exclusion criteria for FV doesn't necessarily need to regard the type of injury. In addition, our proposition to use FV coupled with RMT could advance the outcomes in movement therapy even

after spasticity is diminished (Aprile et al. 2016, Colombo et al. 2001, Tefertiller et al. 2011).

In this study MAS is used as a clinical outcome measure and JS as robot-mediated measure of the combined therapy at the beginning and at the end of each session. Unlike Katz et al. (1992), the correlation between the two measures is not consistent: it is high for the measurements at the end of each session but not for the beginning. Thus the decrease in both measures is reported, perhaps the consistency or the level of change is affecting the correlation calculations. MAS is a measure subjective to the assessor with 5 levels while JS is a numerical value objectively measured by a robotic device (Bohannon & Smith 1987). The principles of the two measures are similar:

- MAS - manual velocity dependent evoking of the catch and release in a joint as a consequence of the spasticity and assessment of resistance to the movement
- JS - robotic velocity dependent evoking of the stiffness in a moving joint and assessment of the resistance to the movement

The main difference in methodology is that the JS proposed in this study does not attempt to induce a catch and release. But the question is whether the catch is absolutely necessary for the spasticity assessment. Going back to the spasticity definition by Lance (1980) spasticity is correlated to an increase in stretch and a presence of jerks as a consequence of velocity dependent movement. The catch in the MAS could be introduced by a quick passive displacement of the joint; this catch is induced to allow more accuracy to the assessor of the spasticity (Pandyan et al. 2016). Perell et al. (1996) proposed use of isokinetic measurement of torque during a passive movement of knee joint for the estimation of the change in spasticity. The justification for the use of this method among others (presented in section 3.3.1 of the chapter 3) is that the controlled displacement parameters such as velocity and range of motion can be either standardised or customised to suit the needs and still respecting the spasticity definition and MAS procedure. One might argue that these two measures could be inclusive, but in the absence of the experienced MAS assessor, the JS can be used as more objective measure of stiffness in a wrist affected by hypertonic muscle.

One might argue that JS might not be enough for spasticity evaluation. This is one of the reasons why measurement of active and passive ROMs and movement kinematics is proposed in this study in addition to JS (Backus et al. 2014, Cordo et al. 2008, Harini et al. 2013, Noma et al. 2009, Oh et al. 2017). Interestingly enough, both cases had a full passive range of motion but different

volitional ranges. This is somewhat expected due to the difference in SCI level. Nonetheless, the increase in volitional range of motion at the beginning and at the end of the study is consistent in both cases, and in line with other ROM assessment due to FV stimulation by Murillo et al. (2011). Oh et al. (2017) observed an increase in range of motion in the hemiplegic knee joint following 5 minutes of continuous calf muscle FV. The results suggests the increase in ROM solely as a culmination of FV. In our study, during each session, there is a surge in volitional angular displacement in extension and flexion, and therefore AROM, following both FV and RMT. For Mr R the AROM persistence is highly dependent on the spasticity triggers such as stress level and activities of daily living. For example, the AROM measures during session 3 are lower than previous (sessions 1, 2 and 3 performed in three consecutive days) possibly due to the 3 days difference between sessions 3 and 4. Session 4 evoked a high increase in AROM which is lower again, possibly as a consequence of the reported pain in the ipsilateral shoulder. In contrast, Mr G had a consistent AROM with a few degrees in change. During qualitative assessment, both cases reported the strengthening of volitional abilities related to the wrist and hand movements. So, even though the increase in AROM is observed after FV, it seems reinforced after RMT.

Lucas et al. (2004) and Pedrocchi et al. (2013) published promising results for recovery of volitional abilities of the hand in SCI, after a single session of RMT. Some of the mechanisms are inclusive of neuroplastic changes in the spinal and cortical level (Fouad & Tetzlaff 2012). Neural plasticity in SCI consists of the alterations or sprouting of the new neural connections in order to reinforce and/or recreate control over activities, behaviours and sensory acquisition (Ding et al. 2005). The repetition of the training over a period of time is essential for long term plasticity development. This is the reason why minimum of 6 sessions over 2 weeks is needed to observe the initial movement recovery patterns (Mark et al. 2006). Moreover, this is in line with the time line for the FV spasticity recovery (Casale et al. 2014). To accommodate the difference in residual movements, a game of PONG had three modes of playing: active (fully volitional), active assisted (movement is completed by the apparatus) and passive (movements are fully conducted by the apparatus). Mr R played a game in active-assisted and passive mode and Mr G in active mode.

Our study results (active mode for Mr R; active-assisted mode for Mr G) suggested an increase in index of performance when playing a game of PONG, which entitles a single degree of movement of the wrist joint. Mr G improvement in IP was observed even after the difficulty of the game

increased for movements into flexion. As extension is highly affected by spasticity mechanisms, movement in this direction were more susceptible to the increase in difficulty, resulting in a drop of IP in session 5 and 6. The change in game difficulty also impacted the accuracy in reaching a target. An small increase ($< 10\%$) in undershoot is observed. It appears the total time of playing a game and movement efficacy gradually elevate regardless to the game parameters. Total number of movement performed during the game tripled between sessions 1 and 6. The time used to complete the movement in respect to the time available subsided despite the decrease in time available as game speed risen. Perhaps this is the reason why an undershoot is acknowledged. Nonetheless, abridged results indicate the increase in the volitional wrist movement abilities.

A variability in movement kinematic outcome measures is highly present for the Mr R. Emotional state, stress and anxiety apparently impacted spasticity level, and this was reflected in movement performance in session to session bases. The results of total number of movements performed during the game was highest at the end of sessions 3 and session 6. If compared to the Mr R study participation Gantt chart, sessions 1 to 3 were executed in three consecutive days of week one, and sessions 4 to 6 in the other week. It appears that accumulation in benefits as a consequence of a daily exercise should be acknowledged when dealing with a less prominent volitional movements. This consistency is not apparent in the other variables. Participant was unable to complete any volitional extension without assistance from the apparatus during session 2 and 4. More over, the number of not assisted movements into flexion decline as extension movements intensify. While variability of the index of performance for active extension is observed, for active flexion movements rises for sessions 1 to 5 and then drops during session 6. In contrast, session 5 had a very high IP in spite of this session being affected by the high ipsilateral shoulder pain. During session 5 a statistically significant rise in normalized jerks in extension and flexion is observed. Also this is the session where Mr R had the furthest distance in flexion from the target at the moment of active-assistance take over. Nonetheless, during this session Mr R was able to achieve some movements and rise in lead-lag coefficient. In simple terms, we postulate that during session 5 Mr R used jerk-like-movements to reach the target, but these movements yielded either high performance in active or very low one in assisted game playing. Another possibility is that Mr R did not performed all movements solely relying on the wrist joint movements but co-ativation and support from other upper limb muscles and joints. Even when the apparatus is designed only to yield

one joint movements, with the appropriate lever from other neighbouring joints a co-activation is achievable (Bizzi et al. 1992). Having in mind the severity of spasticity and impairment in volitional movements, we theorise that 6 sessions might not be sufficient to achieve a consistent gradual and longer term boost in wrist joint movement performance.

Tavernese et al. (2013) observed upper limb reaching movements with 8 infrared camera movement tracking system before and after application of FV to biceps brachii and flexor carpi ulnaris in post-stroke participants. Similar to our study, they observed decrease in movement duration and decrease in normalized jerks as a consequence of FV with therapeutic exercise. However, other observed variables such as no changes in movement length, angle at the elbow at the end of movement, angle of arm flexion at end of movement, angle of arm abduction at the end of movement dod not changed after FV and exercise. Tavernese argued that the lack of pattern in outcomes is a ramification of a summarised activation of multiple joints and muscles which were not stimulated or affected by FV. Casale et al. (2014) applied FV to the hemiplegic triceps brachii muscle and reported a decrease in time needed to complete the task and increase in percentage of completed tasks, but no statistical difference for the deviation from the fastest route in 3D space. Casale used a robotic device Armeo-spring to only to measure movement parameters after FV followed by conventional physiotherapy. They justified these effects with vibration induced Ia presynaptic inhibition and spasticity reduction which accommodate better motor control. Celletti et al. (2017) assured that combination of neurophysiologically-based rehabilitation techniques coupled with muscle FV have a high potential to recover hemiplegic impairments by altering spinal and supraspinal control of the movements.

The study conducted with healthy participants presented in chapter 5 indicated the decrease in mean power of EMG signal following vibration of the relaxed muscle. However, the analysis of the onset of vibratory stimulation derived from this pilot clinical trial indicated momentary increase in EMG amplitude. This could be justified with the difference in vibration parameters: the first study set frequency vibrations to 30Hz and this trial to 75Hz. According to the Lebedev & Polyakov (1991) and Ashby et al. (1974) this increase can only be attributed to the tonic vibration reflex. Thus, the justification for the effectiveness of focal vibration against spasticity can be found in the changes in spinal reflex circuitry mechanisms (Blackburn et al. 2014*a*). The question arises: assuming only spinal involvement in the modulation of vibrations, does it mean that the

cortical structures have very little impact? Our EEG analysis theorise a presence of a positive wave 200-400ms post-vibration onset. P200 or P2 is the cortical event related potential associated to the perception of external stimulus applied to the body. Similarly to the findings in chapter 6, the brain seems to be aware of the presence of the vibratory stimulus but the reactions are dependant on the other structures such as spinal intracircuitry and different muscle cells. This yields important hypothesis that the afferent information is reaching the brain despite incomplete spinal lesion. Complex mechanisms seems to be involved in decrease of abnormally increase muscle tone following a vibratory stimulation, however we are arguing that the brain has an important role in it. Backus et al. (2014) concluded that the FV combined with RMT is effective in a population with chronic incomplete tetraplegia. The emphasis is on the word "incomplete" where spinal reflex arc is somewhat present and corticospinal tract remains operational. Knowing that the brainstem's role is to preprocess and send sensorimotor information between cerebral cortex and the spine, it could be of interest to further examine its and other supraspinal roles in spasticity and vibration modulation.

8.5.1 Hypothesis revisited

The central as well as the second and the third sub-hypotheses stated in chapter 1 are evaluated by the findings from this clinical trial:

Central Hypothesis: Focal muscle vibration can enhance muscle's performance and associated joint function.

Joint function mirrored in the stretch of a volitional active range of motion, reduction in stiffness and improvements in kinematic parameters associated to the movements is enhancing after the focal vibrations of a relaxed muscle belly. This evidence is proving the central hypothesis.

Hypothesis 2: Focal vibration applied on a relaxed muscle with abnormally increased tone (spasticity) can reduce related joint stiffness (tightness) and increase range of motion of the connected joint for a short period of time.

Analysis of the active and passive range of motion and engineering biomechanical measure of joint stiffness suggested that strong evidence was found towards this hypothesis but more results are needed.

Hypothesis 3: The combination of focal muscle vibrations with subsequent robotic-assisted movement of the wrist joint can reduce spasticity and enhance functional recovery by improving strength and volitional control of the targeted muscles. Clinical measure of spasticity as well as many engineering ones employed in this chapter support this hypothesis. As the power analysis is inconclusive due to a low sample size, more evidence is required.

8.6 Chapter summary

This chapter presented a single case clinical trial with two participants investigating feasibility of the use of focal muscle vibration combined with robotic-aided therapy in treatment of spasticity due to incomplete spinal cord injury. This approach suggests the use of focal vibration on relaxed spasticity affect muscle for 15min. After this it is advised to engage the joints in movement robotic-aided therapy to tap into motor circuitry to enhance volitional control. This theory is based on several measures used in the clinical trial.

The primary set of assessments analysed the change in clinically acceptable spasticity measure using Modified Ashworth Scale. Both participants had spasticity reduction of several points on the scale, with the complete diminish in measured in last three sessions. Considering that MAS was measured only at the beginning and at the end of each session, reduction in spasticity can not be attributed solely to vibrations.

The second set of measures were conducted using apparatus design for this trial. Analysis of the changes in joint stiffness under different velocities showed a decrease immediately following vibrations, but the reduction was more prominent after the robotic-aided therapy. Similarly the increase in active range of motion was less obvious after the vibrations yet exaggerated after the therapy. This could signify that the combination of the two interventions can prevail over traditional spasticity and motor management.

Assessment of the kinematic movement parameters justify the use of robotic-aided therapy. Index of performance was ramping up during the trial peaking at the session six for the less severe spasticity type in bot flexion and extension. Similar trends were not observed for the severe case, yet control of flexion was showing prominent improvements. Other parameters dependent on the

level of volitional control shower tendency towards the improvement in volitional control for both cases.

Because of the differences in type and location of the spinal lesion, severity of the spasticity symptoms and level of volitional control, the success of the vibratory stimulation combined with robotic-aided therapy can not be generalised. However, it can be said that the results are promising with the suggestion for the increase in intensity and trial duration.

CHAPTER 9

Thesis summary, conclusions and recommendations

Summaries of the promising results yielded by the three studies conducted during this PhD are presented in this chapter and reflected on the hypotheses. The contribution of this thesis to the body of knowledge is discussed. Correlating conclusions and limitations of the studies, this chapter and thesis ends with recommendations for future work

9.1 Summary of the results

This section summarizes the results of the three main studies conducted during this PhD. To complement, application guides are proposed for each study.

9.1.1 Study I - muscle focal vibration and EMG and force

The aim of the first study was to investigate the effects of the timing and location of muscle focal vibration on the force and EMG profiles. Four different conditions are investigated: FV applied to the muscle belly or to the bone (i.e. tendon) and FV employed before muscle contraction or during muscle contraction. The analysis considered maximal force output and EMG activity. The results implied an increase in vibrated muscle force output when focal vibration was applied on the relaxed muscle's belly before the contraction. This protocol seems to elicit muscle memory force recall that is optimising muscle fibres to achieve higher performance. The optimisation is reflected in decrease of the EMG amplitude observed. Focal vibratory stimulus applied on the tendon/bone controlled by the muscle, did not enhance muscle force. In contrast, it seems that FV applied to this location during the contraction might evoke tonic vibration reflex contributing to the surge in EMG amplitude.

Sports science could directly benefit from these results. Application of FV to achieve better muscle performance can be accomplished by a simple, affordable and easy to use vibration device. Depending on the movement to be enhanced, one or more muscles could be vibrated simultaneously with the same parameters (Kossev et al. 2001). To avoid possible adverse consequences of WBV, FV coupled with muscle contractions is proposed as a mean of muscle training paradigm. This could evoke tonic vibration reflex and enhance refractory circuits (Eklund & Hagbarth 1966, Filippi et al. 2009).

Application of the assumptions produced by this study could be used in rehabilitation. One might suppose that the ability to operate a force controlled device can be enhanced by FV. A bolder expectation, somewhat assured by the literature, is that FV might evoke augmentation in movement performance and depletion of the impairment.

9.1.2 Study II - muscle focal vibration and EEG

Following further investigation of the mechanisms behind results from study one, the second study aimed to estimate the level of cortical involvement in the modulation and the facilitation of FV. The study conducted in two parts: part one as a pilot single case study and part two as a crossover trial. EEG analysis of the different cortical waves (mu and beta) was implemented.

When muscle focal vibration was applied onto the relaxed muscle, an increase in mu wave spectral power was observed over sensorimotor cortex. The surge is more prominent after the second and third repetition of the same protocol. Because the increase of mu waves is correlated to the relaxed state of the body, assumption was made that the brain has no intention to move. This would mean that the brain is not facilitating any movement-related action towards the vibrations. After the FV has stopped and the muscle contraction is demanded, the brain seems to return to the usual movement planning and execution pattern. In contrast, when vibrations are imposed to a muscle contraction a spread of mu and beta waves is observed. Increase in the two brain signal types suggests that the brain is trying to suppress volitional movement (beta activation) elicited by the sensory stimulation (mu activation). As the presence of the tonic vibration reflex is assumed during FV + contraction, it would seem reasonable that the lower level of CNS, such as the spine is modulating this sensory-motor arc.

Comparing the two observed behaviours of the brain, we hypotesised that the brain and the spine have a differential behavioural effects in FV modulation that are dependent on the timing of FV application. According to the literature, FV induces the changes in the spinal arc's synaptic behaviours. By lowering presynaptic inhibition, the consequent decrease in motor control is noted. However, this is not what we have observed. In able bodied participants an increase in volitional abilities after FV is observed and that can be accomplished by the cortical takeover of the response.

These observations can find an application in furthering the knowledge of the movement impairment sequelae. By comparing underlying mechanisms of the neural circuits reactions to the FV in different conditions, the observed differences can lead to the better understanding of impairments, diseases and repercussions. Moreover, literature proposes the use of vibrations to diminish spasticity and we advise its use for the enhancement of the motor control. Combining these claims and adequately applying them in rehabilitation, could bring us one step closer in wining the battle

against devastating repercussions of motor related diseases and disorders.

9.1.3 Study III - Clinical trial: muscle focal vibration and spasticity

A pilot clinical trial aimed to investigate the effects focal vibrations combined with robot-mediated therapy have on spasticity and residual volitional movements in people with spinal cord injury. For this purpose, an apparatus was designed and used as an assessment and a therapeutic device during different stages of the study. Additionally, a clinical measure of spasticity used was Modified Ashworth Scale (MAS). The results indicate that hypertonicity of the muscle and correlated joint stiffness can be reduced by applying fifteen minutes of focal vibratory stimulation with high frequency (75Hz) and low amplitude (0.4mm) to the relaxed flexor and extensor muscles of the wrist joint. Repetitive movement therapy accomplished by playing a game induced different levels of improvements.

A variety of measures was obtained and analysed. MAS was compared to the joint stiffness (JS). Even if there was no strong consistent correlation between the two measures, we propose the use of both in an attempt to objectify spasticity assessment. Results from this study indicated a gradual decline in MAS scores and JS numerical values. In people with incomplete SCI and a level of residual volitional movements, an increase in the active range of motion after a FV intervention suggests an improvement of motor control. After spasticity is reduced, we propose engaging a person with incomplete SCI in movement training. Six sessions across two weeks showed an improvement in functional volitional control of the wrist joint and the hand. This is noted by the analysis of both quantitative and qualitative results. The two recruited participants reported improvements in some activities of the daily living such as driving a wheelchair, drinking from a glass and writing. Scrutiny of the game related movement kinematic variables showed a gradual rise in abilities, mainly looking at the time to complete and the performance of the movement, and total time that the participant is able to play a game before fatiguing.

The vibration device and robot mediated therapy apparatus are both developed minding the clinical approaches and current trends in physio- and occupational therapy. Both are made as a test versions to be adjusted and adapted to a simple and affordable clinical and perhaps home spasticity therapy. With this approach we aim to bridge the gab between available and used technologies in clinical and home environments and help with self management of spasticity and

movement imparts.

9.2 Hypotheses revisited

Central Hypothesis: Focal muscle vibration can enhance muscle's performance and associated joint function.

Proven. The three studies explained in chapters 5, 6 and 8 are estimating effects focal vibratory stimulation have on exerted muscle force, cortical signals, volitional control (active range of motion) and joint stiffness and functionality (repetitive movement kinematic parameters). All of these measures are shown to be improving as a consequence of focal vibration applied to the relaxed muscle before contraction. This seems enough evidence, supported by the statistical analysis to declare this hypothesis as proven. However, the sub-hypotheses are revisited individually and more evidence is needed to fully prove them.

Hypothesis 1: Focal muscle vibrations (applied directly to the muscle belly) are a harmless and beneficial aid for enhancing muscle strength.

Strongly supported. The results from this thesis evaluated the force performance after a single session of muscle focal vibration indicates that this type of stimulation can precondition an increase in muscle's output strength. No unfavourable features were observed within the results nor orally reported by participants during the studies. Similar observations were previously reported by Rothmuller & Cafarelli (1995) and Santos & Aruin (2008).

Hypothesis 2: Focal vibrations applied on a muscle with abnormally increased tone reduce the high tone of the vibrated muscle (spasticity) and related stiffness (tightness) of the connected joint for a short period of time.

Strong evidence was found towards it. Analysis of the clinical measurement of increased muscle tone (Modified Ashworth Scale) in addition to the characterisation of the connected joint stiffness, when compared before and after the application of focal muscle vibration to a muscle affected by spasticity, resulted in a consisted decrease of the measures in the extension but less in the flexion joint movement. Moreover, this hypothesis is supported by the literature. A reduction of MAS was reported after a single focal vibratory stimulation of spastic rectus femoris muscle in SCI (Murillo et al. 2011). In addition Etoom & Marchetti (2015) observed a persistence of the MAS

diminishment starting after 5th session of triceps brachii muscle focal vibration.

Hypothesis 3: The combination of focal muscle vibrations with subsequent robotic-assisted movement of the wrist joint enhances functional recovery by improving volitional control of targeted muscles.

Supported, but more experimental data is needed to verify the movement performance endorsement for different severity levels of the spasticity. Different parameters are used to estimate the functional recovery level of the targeted muscles. Active range of motion of the joint controlled by targeted muscles increased after focal vibration and after movement repetition robot mediated therapy. Index of performance, time dedicated to a functional task (i.e. duration of the Pong game playing), accuracy, efficacy, reaction time and level of assistance, seem very dependent on the spasticity level and the subjective to the spasticity triggers. For the mild to moderate spasticity level, the gradual increase in the functional recovery is observed. On the contrary, moderate to severe spasticity level is prone to the unexpected variability of the spasticity levels in the targeted muscles and other muscles in the targeted limb, which is reflected in the discrepancy of the functional recovery results. Additionally, the rise in pain can affect participation in the tasked activities. Nonetheless, the residual volitional movements did ameliorate throughout the course of the clinical trial in both cases.

9.3 Summary of contributions to the body of knowledge

The contributions of this research can be summarized as:

- **The ability to precondition the muscle to enhance the output force with focal vibration applied to the relaxed muscle belly** - the vibration parameters for muscle preconditioning such as position, timing and the state of the muscle are of a vital importance. Furthermore achieving this with focal vibration is much underused in the current literature.

- **Level of the cortical involvement in the modulation of the focal vibrations applied to the resting muscle** - modulation of the focal vibration responses seems to be localised in the lower central nervous system areas as the brain does not seem to create motor responses during the course of focal vibratory stimuli. Current state-of-the-art relies on the analysis of

the evoked motor potentials whereas the signals recorded for this research are solely reliant on the cortical state due to vibrations.

- **Spasticity decrease as a consequence of coupling focal vibration with robot mediated therapy in spinal cord injury** - this novel approach is the first to be investigated in the spinal cord injury. Complementary effectiveness of the combined approach appears to tackle muscle sensory apparatus and, via the spinal reflex and cortical motor arcs, release the grip of the abnormally increased muscle tone.

- **Enhancement of functional recovery of the volitional movements by preconditioning the muscles with focal vibration and afterwards engaging the user in movement robot mediated therapy in spinal cord injury** - probably because of the limited residual control of the volitional movements in the upper limbs, this approach was never explored before. Nonetheless, the movements trapped by spasticity can be recovered by robotic mediated therapy, after spasticity has decreased with focal vibrations. This is of a great interest to the rehabilitation research community, especially since the author's initial publication (section 1.4) on the beneficial ramifications of the muscle focal vibration and the proposition of a coupling therapy, there has been a growing interest in this approach by other groups for applications in stroke (Calabrò et al. 2017).

- **Acknowledgment of the presence of sensory induced potential in sensorimotor cortex in incomplete spinal cord injury** - this could be a consequence of the afferent sensory information traveling through the residual circuits of the spine. This could be of importance in the assessment of the brain's involvement in spasticity rehabilitation but also origins.

9.4 Limitations

The main limitation of the research conducted for this thesis is related to the number and demography of the participants recruited for the studies. A larger sample size, especially for the clinical trial, would provide a greater confidence levels. According to the initial results from the pilot case studies, the sample size calculation taken with a probability threshold of .05, anticipated

effect .80 with an analysis of variance design expecting a change in the mean spasticity level of 2 points (on the Modified Ashworth Scale) with a standard deviation of 2 indicates that a minimum of 16 participants will be needed. Furthermore the demography of the participants is limited to the two divergent spasticity severity levels and injury types. The time constrains, design and development prolongations and exclusion criteria limited the clinical trial recruitment number to two.

The nature of the second study and EEG signals resulted in a low number of available data to analyse. Three datasets were corrupted by external noise possibly due to the movements, blinking and other factors. EEG resolution (number of channels) of the cap used to record the signals seems to be low for a deeper investigation of the crossover effects between small areas of the somatosensory and motor cortex. This could have impacted the assumed cortical motor responses.

The results of the first and second study could be limited by the choice of the vibration parameters. Literature suggests that the responses to the vibration therapy depends on the frequencies, and frequency used in these studies seems to evoke least favourable effects. Furthermore, the effects of low frequencies vibration induced changes in spinal circuits are largely unknown. Therefore the postulation regarding the implication of the spinal circuits could be subject to criticism.

Spasticity was observed to vary across days as a consequence of the spasticity triggers and activities of a daily routines. The lack of the follow up after research is confiding the estimation of the carryover effects and the dependancy on the daily routine. This could be important for tailoring the therapy for every participant individually depending on the spasticity severity and spinal cord injury levels. Furthermore, participants were not deprived of the additional therapies such as oral medicaments, stretching, physical therapy or any other potential spasticity influencer.

9.5 Recommendations and future directions

Analysis of the effects that ranges of frequencies have on the muscle performance in able bodied participant could be the following step towards understanding the origins of the increase in muscle power. Combining different electrophysiological recording techniques like EEG and EMG with the exploration into cotricomuscular coherence could provide an insight into dependency of the cortical and muscular signals.

Testing the premise of the cortical involvement in focal vibration facilitation within a population with motor complete and incomplete spinal cord injury could reveal the level of communication and likely organization within focal vibrations facilitation from the brain, from spine, from muscle, even to spastic response. This may not only lead to a more comprehensive understanding of the spasticity mechanisms but also provide insight into the communications between central and peripheral nervous systems.

A randomized controlled clinical trial, with a larger sample size and a wide range of the population with shared characteristics, is needed to provide a better understanding of the focal vibration therapy for the spasticity management. Inclusion of different electrophysiological measurements such as EMG, EEG, TMS, MRI and similar techniques could provide an advancement in understanding underlying spasticity and spasticity relieve mechanisms. In order to enhance the upper limb abilities, the robotic therapy should incorporate multiple joints of the upper limbs with the emphasis of the hand and fingers for reinforcement of the object manipulation abilities. Proposed clinical trial could benefit from intensification of the therapy: if not increasing the number of the sessions during one week to more than 3, at least doubling the number of participation weeks to minimum of 5 weeks and at least 15 sessions.

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Appendix A: Statistical results

A-1: Table of Pearson correlation coefficient

Pearson correlation coefficient

Variable	Phase	Condition	RMS						FORCE						IMNF					
			muscle belly			bone			muscle belly			bone			muscle belly			bone		
			no	before	during	no	before	during	no	before	during	no	before	during	no	before	during	no	before	during
RMS	muscle belly	no	1	.908**	.846**	.700**	.748**	.731**	-.072	-.293	-.223	-.276	-.205	-.279	.753**	.813**	.637**	.618**	.512*	.523*
		before	.908**	1	.962**	.669**	.790**	.781**	-.072	-.329	-.271	-.284	-.238	-.274	.690**	.797**	.760**	.615**	.536*	.564*
		during	.846**	.962**	1	.579**	.708**	.709**	-.136	-.315	-.282	-.297	-.277	-.274	.622*	.691**	.780**	.588*	.456*	.469*
	bone	no	.700**	.669**	.579**	1	.845**	.806**	-.100	-.134	-.231	-.257	-.143	-.091	.451*	.609*	.509*	.440*	.571**	.581**
		before	.748**	.790**	.708**	.845**	1	.972**	-.014	-.130	-.224	-.289	-.179	-.167	.587**	.736**	.660**	.651**	.691**	.643**
		during	.731**	.781**	.709**	.806**	.972**	1	-.010	-.122	-.182	-.236	-.179	-.117	.636*	.755**	.690**	.608**	.659**	.645**
FORCE	muscle belly	no	-.072	-.072	-.136	-.100	-.014	-.010	1	.715**	.697**	.616**	.481*	.568**	.053	.008	.238	.198	.257	.082
		before	-.293	-.329	-.315	-.134	-.130	-.122	.715**	1	.802**	.757**	.690**	.798**	.341	.230	.271	.398	.361	.289
		during	-.223	-.271	-.282	-.231	-.224	-.182	.697**	.802**	1	.855**	.726**	.783**	.150	.127	.268	.330	.261	.118
	bone	no	-.276	-.284	-.297	-.257	-.289	-.236	.616**	.757**	.855**	1	.800**	.840**	.280	.178	.245	.469*	.427*	.272
		before	-.205	-.238	-.277	-.143	-.179	-.160	.481*	.690**	.726**	.800**	1	.770**	.216	.065	.173	.209	.211	.121
		during	-.279	-.274	-.274	-.091	-.167	-.117	.568**	.798**	.783**	.840**	.770**	1	.244	.162	.200	.361	.285	.195
IMNF	muscle belly	no	.753**	.690**	.622**	.451*	.587**	.636**	.053	.341	.150	.280	.216	.244	1	.899**	.531**	.769**	.678**	.706**
		before	.813**	.797**	.691**	.609**	.736**	.755**	.008	.230	.127	.178	.065	.162	.899**	1	.695**	.739**	.705**	.687**
		during	.637**	.760**	.780**	.509*	.660**	.690**	.238	.271	.268	.245	.173	.200	.531**	.695**	1	.543**	.528**	.510*
	bone	no	.618**	.615**	.588**	.440*	.651**	.608**	.198	.398	.330	.469*	.209	.361	.769**	.739**	.543**	1	.819**	.690**
		before	.512*	.536*	.456*	.571**	.691**	.659**	.257	.361	.261	.427*	.211	.285	.678**	.705**	.528**	.819**	1	.876**
		during	.523*	.564*	.469*	.581**	.643**	.645**	.082	.289	.118	.272	.121	.195	.706**	.687**	.510*	.690**	.876**	1

A-2: Mr R Joint Stiffness one way ANOVA

		JS01e01	JS01e05	JS01e10	JS01f01	JS01f05	JS01f10
1-bv	1-av	0.001	0.867	0.192	0.107	0.766	0.002
	1-ag	0.000	0.000	0.000	0.076	0.053	0.004
	2-bf	1.000	1.000	0.115	0.604	1.000	1.000
	2-av	0.001	0.000	0.000	0.998	0.800	0.667
	2-ag	0.000	0.000	0.000	0.048	0.260	0.205
	3-bf	1.000	1.000	0.912	0.001	0.595	0.001
	3-av	0.652	0.343	0.001	1.000	1.000	1.000
	3-ag	0.010	0.001	0.000	0.579	1.000	0.954
	4-bf	0.000	0.902	1.000	0.001	0.093	0.036
	4-av	0.000	0.001	0.000	0.093	0.295	0.006
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	0.962	0.997	0.685	1.000	0.193	0.188
	5-av	0.000	0.003	0.000	0.252	0.115	0.757
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.147	0.227	0.949	1.000	1.000	1.000
	6-av	0.007	0.000	0.000	0.000	0.010	0.030
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
1-av	1-ag	0.311	0.003	0.001	1.000	0.977	1.000
	2-bf	0.001	0.999	1.000	0.000	0.809	0.013
	2-av	1.000	0.007	0.007	0.004	0.014	0.000
	2-ag	0.311	0.050	0.467	1.000	1.000	0.936
	3-bf	0.006	0.414	0.997	0.000	0.006	0.000
	3-av	0.261	1.000	0.860	0.628	0.501	0.031
	3-ag	1.000	0.200	0.000	1.000	0.985	0.179
	4-bf	0.000	0.040	0.215	0.000	0.000	0.000
	4-av	0.998	0.186	0.000	1.000	1.000	1.000
	4-ag	0.283	0.000	0.000	0.415	0.149	0.000
	5-bf	0.063	0.158	0.000	0.045	0.001	0.000
	5-av	0.400	0.305	0.102	0.000	0.000	0.000
	5-ag	0.005	0.000	0.000	0.003	0.005	0.000
	6-bf	0.829	1.000	0.991	0.330	0.667	0.001
	6-av	1.000	0.023	0.506	0.206	0.724	1.000

	6-ag	0.659	0.000	0.000	0.035	0.000	0.000
1-ag	2-bf	0.000	0.000	0.001	0.000	0.064	0.020
	2-av	0.311	1.000	1.000	0.003	0.000	0.000
	2-ag	1.000	1.000	0.374	1.000	1.000	0.974
	3-bf	0.000	0.000	0.000	0.000	0.000	0.000
	3-av	0.000	0.028	0.111	0.525	0.019	0.049
	3-ag	0.043	0.949	1.000	0.999	0.220	0.251
	4-bf	0.000	0.000	0.000	0.000	0.000	0.000
	4-av	0.963	0.957	1.000	1.000	1.000	1.000
	4-ag	1.000	0.463	0.071	0.513	0.954	0.000
	5-bf	0.000	0.000	0.000	0.031	0.000	0.000
	5-av	1.000	0.872	0.877	0.000	0.000	0.000
	5-ag	0.946	0.001	0.093	0.004	0.239	0.000
	6-bf	0.002	0.050	0.000	0.253	0.036	0.001
	6-av	0.056	1.000	0.340	0.274	1.000	1.000
	6-ag	1.000	0.428	0.857	0.052	0.008	0.000
2-bv	2-av	0.001	0.000	0.013	0.999	0.756	0.293
	2-ag	0.000	0.002	0.632	0.000	0.298	0.537
	3-bf	1.000	0.984	0.981	0.339	0.543	0.000
	3-av	0.652	0.827	0.947	0.099	1.000	1.000
	3-ag	0.010	0.012	0.001	0.003	1.000	0.999
	4-bf	0.000	0.444	0.130	0.329	0.078	0.007
	4-av	0.000	0.011	0.000	0.000	0.336	0.029
	4-ag	0.000	0.000	0.000	0.000	0.001	0.000
	5-bf	0.962	0.824	0.000	0.828	0.165	0.049
	5-av	0.000	0.022	0.172	1.000	0.097	0.372
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.147	0.690	0.961	0.257	1.000	1.000
	6-av	0.007	0.001	0.672	0.000	0.012	0.122
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
2-av	2-ag	0.311	1.000	0.892	0.002	0.001	0.000
	3-bf	0.006	0.000	0.000	0.028	1.000	0.296
	3-av	0.261	0.061	0.516	0.673	0.956	0.151
	3-ag	1.000	0.992	0.999	0.055	0.383	0.025
	4-bf	0.000	0.000	0.000	0.027	0.993	0.978

	4-av	0.998	0.994	0.999	0.003	0.002	0.000
	4-ag	0.283	0.280	0.008	0.000	0.000	0.000
	5-bf	0.063	0.000	0.000	1.000	1.000	1.000
	5-av	0.400	0.967	1.000	0.945	0.997	1.000
	5-ag	0.005	0.000	0.011	0.000	0.000	0.000
	6-bf	0.829	0.105	0.000	0.916	0.877	0.924
	6-av	1.000	1.000	0.867	0.000	0.000	0.000
	6-ag	0.659	0.253	0.327	0.000	0.000	0.000
2-ag	3-bf	0.000	0.000	0.034	0.000	0.001	0.000
	3-av	0.000	0.305	1.000	0.403	0.115	0.761
	3-ag	0.043	1.000	0.240	0.996	0.660	0.992
	4-bf	0.000	0.000	0.000	0.000	0.000	0.000
	4-av	0.963	1.000	0.230	1.000	1.000	0.989
	4-ag	1.000	0.054	0.000	0.641	0.581	0.000
	5-bf	0.000	0.000	0.000	0.019	0.000	0.000
	5-av	1.000	1.000	1.000	0.000	0.000	0.001
	5-ag	0.946	0.000	0.000	0.007	0.047	0.000
	6-bf	0.002	0.442	0.024	0.175	0.193	0.069
	6-av	0.056	1.000	1.000	0.376	0.992	1.000
	6-ag	1.000	0.047	0.003	0.081	0.001	0.000
3-bv	3-av	0.975	0.078	0.148	0.000	0.841	0.000
	3-ag	0.066	0.000	0.000	0.000	0.217	0.000
	4-bf	0.000	0.999	0.930	1.000	1.000	0.995
	4-av	0.000	0.000	0.000	0.000	0.001	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	1.000	1.000	0.019	0.002	1.000	0.815
	5-av	0.000	0.000	0.004	0.715	1.000	0.229
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.530	0.045	1.000	0.000	0.699	0.004
	6-av	0.051	0.000	0.039	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
3-av	3-ag	0.827	0.701	0.061	0.992	1.000	1.000
	4-bf	0.000	0.004	0.001	0.000	0.218	0.003
	4-av	0.016	0.678	0.058	0.584	0.134	0.069
	4-ag	0.000	0.000	0.000	0.001	0.000	0.000

	5-bf	1.000	0.021	0.000	0.992	0.394	0.021
	5-av	0.000	0.834	0.988	0.024	0.260	0.202
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	1.000	1.000	0.113	1.000	1.000	0.989
	6-av	0.768	0.174	1.000	0.000	0.003	0.245
	6-ag	0.001	0.000	0.001	0.000	0.000	0.000
3-ag	4-bf	0.000	0.000	0.000	0.000	0.019	0.000
	4-av	0.767	1.000	1.000	1.000	0.705	0.323
	4-ag	0.037	0.011	0.126	0.060	0.003	0.000
	5-bf	0.400	0.000	0.000	0.347	0.045	0.003
	5-av	0.063	1.000	0.742	0.000	0.024	0.037
	5-ag	0.000	0.000	0.162	0.000	0.000	0.000
	6-bf	0.999	0.837	0.000	0.904	1.000	0.737
	6-av	1.000	1.000	0.214	0.022	0.052	0.705
	6-ag	0.151	0.009	0.948	0.003	0.000	0.000
4-bv	4-av	0.000	0.000	0.000	0.000	0.000	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	0.000	1.000	0.648	0.002	1.000	1.000
	5-av	0.000	0.000	0.000	0.703	1.000	0.952
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.000	0.002	0.961	0.000	0.132	0.118
	6-av	0.000	0.000	0.000	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
4-av	4-ag	0.952	0.012	0.133	0.455	0.535	0.000
	5-bf	0.002	0.000	0.000	0.039	0.000	0.000
	5-av	0.985	1.000	0.728	0.000	0.000	0.000
	5-ag	0.115	0.000	0.170	0.003	0.040	0.000
	6-bf	0.149	0.818	0.000	0.296	0.221	0.001
	6-av	0.825	1.000	0.205	0.233	0.987	1.000
	6-ag	0.999	0.010	0.953	0.041	0.001	0.000
4-ag	5-bf	0.000	0.000	0.000	0.000	0.000	0.000
	5-av	1.000	0.006	0.000	0.000	0.000	0.000
	5-ag	0.959	0.455	1.000	0.774	0.996	0.007
	6-bf	0.002	0.000	0.000	0.000	0.000	0.000
	6-av	0.049	0.108	0.000	1.000	1.000	0.000

	6-ag	1.000	1.000	0.970	0.999	0.377	0.173
5-bv	5-av	0.000	0.000	0.000	0.457	1.000	1.000
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.971	0.011	0.026	1.000	0.260	0.445
	6-av	0.338	0.000	0.000	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
5-av	5-ag	0.897	0.000	0.000	0.000	0.000	0.000
	6-bf	0.003	0.928	0.003	0.075	0.161	0.961
	6-av	0.080	0.999	1.000	0.000	0.000	0.000
	6-ag	1.000	0.005	0.032	0.000	0.000	0.000
5-ag	6-bf	0.000	0.000	0.000	0.000	0.000	0.000
	6-av	0.000	0.000	0.000	0.945	0.632	0.000
	6-ag	0.687	0.491	0.985	1.000	0.990	0.997
6-bf	6-av	0.998	0.272	0.028	0.000	0.006	0.008
	6-ag	0.010	0.000	0.000	0.000	0.000	0.000
6-av	6-ag	0.188	0.096	0.003	1.000	0.044	0.000

		JS02f10	JS02e01	JS02e05	JS02e10	JS02f01	JS02f05	JS02f10
1-bv	1-av	0.002	0.029	0.440	0.169	0.007	0.986	0.139
	1-ag	0.004	0.000	0.000	0.000	0.000	0.116	0.207
	2-bf	1.000	0.420	0.980	0.964	0.519	1.000	1.000
	2-av	0.667	0.104	0.000	0.000	0.722	0.896	0.833
	2-ag	0.205	0.004	0.000	0.000	0.001	0.539	0.567
	3-bf	0.001	1.000	0.972	0.311	0.000	0.001	0.085
	3-av	1.000	0.943	0.158	0.032	0.584	1.000	1.000
	3-ag	0.954	0.145	0.009	0.000	0.039	1.000	1.000
	4-bf	0.036	0.001	1.000	1.000	0.000	0.074	0.287
	4-av	0.006	0.000	0.000	0.000	0.007	0.502	0.105
	4-ag	0.000	0.000	0.000	0.000	0.000	0.003	0.000
	5-bf	0.188	1.000	0.999	0.002	1.000	0.347	0.563
	5-av	0.757	0.000	0.000	0.000	0.187	0.713	0.892
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	1.000	0.667	0.999	0.994	1.000	1.000	1.000
	6-av	0.030	0.108	0.000	0.000	0.002	0.001	0.002
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
1-av	1-ag	1.000	0.640	0.002	0.002	0.993	0.894	1.000
	2-bf	0.013	0.000	0.999	0.979	0.000	0.993	0.338
	2-av	0.000	1.000	0.017	0.040	0.000	0.117	0.001
	2-ag	0.936	1.000	0.001	0.000	1.000	1.000	1.000
	3-bf	0.000	0.012	1.000	1.000	0.000	0.000	0.000
	3-av	0.031	0.726	1.000	1.000	0.808	0.881	0.279
	3-ag	0.179	1.000	0.941	0.023	1.000	1.000	0.679
	4-bf	0.000	0.000	0.084	0.171	0.000	0.001	0.000
	4-av	1.000	0.975	0.275	0.006	1.000	1.000	1.000
	4-ag	0.000	0.738	0.000	0.000	0.991	0.123	0.000
	5-bf	0.000	0.264	0.044	0.000	0.013	0.012	0.000
	5-av	0.000	0.412	0.040	0.042	0.000	0.052	0.001
	5-ag	0.000	0.062	0.000	0.000	0.001	0.000	0.031
	6-bf	0.001	0.963	0.046	0.917	0.095	0.814	0.023
	6-av	1.000	1.000	0.001	0.419	1.000	0.058	0.963
	6-ag	0.000	0.704	0.000	0.000	0.052	0.001	0.001

1-ag	2-bf	0.020	0.000	0.000	0.000	0.000	0.144	0.455
	2-av	0.000	0.305	1.000	0.999	0.000	0.001	0.001
	2-ag	0.974	0.962	1.000	0.967	1.000	1.000	1.000
	3-bf	0.000	0.000	0.000	0.001	0.000	0.000	0.000
	3-av	0.049	0.006	0.012	0.014	0.097	0.041	0.386
	3-ag	0.251	0.230	0.200	1.000	0.824	0.270	0.798
	4-bf	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	4-av	1.000	1.000	0.883	1.000	0.992	1.000	1.000
	4-ag	0.000	1.000	0.998	0.162	1.000	0.988	0.000
	5-bf	0.000	0.001	0.000	0.000	0.000	0.000	0.000
	5-av	0.000	1.000	1.000	0.999	0.000	0.000	0.002
	5-ag	0.000	0.997	0.001	0.121	0.033	0.001	0.019
	6-bf	0.001	0.026	0.000	0.000	0.003	0.029	0.037
	6-av	1.000	0.296	1.000	0.692	1.000	0.930	0.911
	6-ag	0.000	1.000	0.083	0.802	0.645	0.104	0.001
2-bv	2-av	0.293	0.000	0.001	0.001	1.000	0.854	0.542
	2-ag	0.537	0.000	0.000	0.000	0.000	0.607	0.852
	3-bf	0.000	0.645	1.000	0.998	0.131	0.001	0.027
	3-av	1.000	0.008	0.956	0.693	0.002	1.000	1.000
	3-ag	0.999	0.000	0.320	0.000	0.000	1.000	1.000
	4-bf	0.007	0.601	0.598	0.965	0.001	0.059	0.113
	4-av	0.029	0.000	0.023	0.000	0.000	0.569	0.269
	4-ag	0.000	0.000	0.000	0.000	0.000	0.003	0.000
	5-bf	0.049	0.058	0.420	0.000	0.356	0.293	0.279
	5-av	0.372	0.000	0.002	0.001	1.000	0.648	0.630
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	1.000	0.002	0.433	1.000	0.074	1.000	0.998
	6-av	0.122	0.000	0.000	0.014	0.000	0.001	0.007
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2-av	2-ag	0.000	0.998	1.000	0.374	0.000	0.009	0.007
	3-bf	0.296	0.047	0.001	0.017	0.066	0.127	0.986
	3-av	0.151	0.956	0.072	0.202	0.004	0.989	0.617
	3-ag	0.025	1.000	0.594	1.000	0.000	0.667	0.235
	4-bf	0.978	0.000	0.000	0.000	0.000	0.956	1.000
	4-av	0.000	0.788	0.998	1.000	0.000	0.008	0.000

	4-ag	0.000	0.391	0.873	0.010	0.000	0.000	0.000
	5-bf	1.000	0.584	0.000	0.000	0.551	1.000	1.000
	5-av	1.000	0.159	1.000	1.000	1.000	1.000	1.000
	5-ag	0.000	0.016	0.000	0.007	0.000	0.000	0.000
	6-bf	0.924	0.999	0.000	0.000	0.146	0.996	0.997
	6-av	0.000	1.000	1.000	0.999	0.000	0.000	0.000
	6-ag	0.000	0.359	0.014	0.163	0.000	0.000	0.000
2-ag	3-bf	0.000	0.002	0.000	0.000	0.000	0.000	0.000
	3-av	0.761	0.290	0.007	0.000	0.471	0.276	0.795
	3-ag	0.992	0.993	0.126	0.517	0.999	0.808	0.988
	4-bf	0.000	0.000	0.000	0.000	0.000	0.000	0.001
	4-av	0.989	1.000	0.771	0.832	1.000	1.000	1.000
	4-ag	0.000	0.984	1.000	0.974	1.000	0.651	0.000
	5-bf	0.000	0.060	0.000	0.000	0.003	0.001	0.002
	5-av	0.001	0.846	0.997	0.366	0.000	0.003	0.010
	5-ag	0.000	0.269	0.003	0.947	0.003	0.000	0.003
	6-bf	0.069	0.644	0.000	0.000	0.026	0.212	0.162
	6-av	1.000	0.998	1.000	0.033	1.000	0.433	0.550
	6-ag	0.000	0.978	0.135	1.000	0.170	0.012	0.000
3-bv	3-av	0.000	0.806	0.967	1.000	0.000	0.003	0.036
	3-ag	0.000	0.068	0.349	0.009	0.000	0.000	0.006
	4-bf	0.995	0.003	0.562	0.314	0.808	0.964	1.000
	4-av	0.000	0.000	0.026	0.002	0.000	0.000	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	0.815	0.995	0.388	0.000	0.000	0.598	1.000
	5-av	0.229	0.000	0.002	0.018	0.408	0.257	0.969
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.004	0.441	0.400	0.984	0.000	0.005	0.377
	6-av	0.000	0.049	0.000	0.243	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
3-av	3-ag	1.000	0.982	0.999	0.127	0.992	1.000	1.000
	4-bf	0.003	0.000	0.020	0.033	0.000	0.192	0.144
	4-av	0.069	0.043	0.631	0.039	0.822	0.249	0.219
	4-ag	0.000	0.009	0.000	0.000	0.089	0.001	0.000
	5-bf	0.021	1.000	0.010	0.000	0.752	0.630	0.338

	5-av	0.202	0.002	0.153	0.208	0.000	0.927	0.703
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.989	1.000	0.010	0.507	0.993	1.000	0.999
	6-av	0.245	0.960	0.006	0.863	0.550	0.000	0.005
	6-ag	0.000	0.007	0.000	0.000	0.000	0.000	0.000
3-ag	4-bf	0.000	0.000	0.001	0.000	0.000	0.026	0.032
	4-av	0.323	0.694	0.999	1.000	1.000	0.777	0.592
	4-ag	0.000	0.303	0.010	0.019	0.802	0.009	0.000
	5-bf	0.003	0.688	0.000	0.000	0.073	0.158	0.095
	5-av	0.037	0.114	0.808	1.000	0.000	0.433	0.297
	5-ag	0.000	0.011	0.000	0.013	0.000	0.000	0.000
	6-bf	0.737	1.000	0.000	0.000	0.354	1.000	0.938
	6-av	0.705	1.000	0.114	0.994	1.000	0.003	0.030
	6-ag	0.000	0.276	0.000	0.252	0.009	0.000	0.000
4-bv	4-av	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	1.000	0.000	1.000	0.001	0.000	1.000	1.000
	5-av	0.952	0.000	0.000	0.000	0.003	0.995	1.000
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.118	0.000	1.000	0.994	0.000	0.252	0.762
	6-av	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
4-av	4-ag	0.000	1.000	0.179	0.067	0.989	0.688	0.000
	5-bf	0.000	0.006	0.000	0.000	0.014	0.001	0.000
	5-av	0.000	0.999	1.000	1.000	0.000	0.003	0.001
	5-ag	0.000	0.812	0.000	0.048	0.001	0.000	0.043
	6-bf	0.001	0.158	0.000	0.000	0.101	0.190	0.016
	6-av	1.000	0.778	0.744	0.902	1.000	0.468	0.983
	6-ag	0.000	1.000	0.000	0.548	0.049	0.014	0.002
4-ag	5-bf	0.000	0.001	0.000	0.000	0.000	0.000	0.000
	5-av	0.000	1.000	0.682	0.010	0.000	0.000	0.000
	5-ag	0.007	0.989	0.045	1.000	0.036	0.036	0.131
	6-bf	0.000	0.038	0.000	0.000	0.002	0.000	0.000
	6-av	0.000	0.381	1.000	0.000	1.000	1.000	0.000
	6-ag	0.173	1.000	0.688	0.999	0.672	0.863	0.724

5-bv	5-av	1.000	0.000	0.000	0.000	0.109	1.000	1.000
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.445	0.996	1.000	0.000	1.000	0.722	0.952
	6-av	0.000	0.596	0.000	0.000	0.004	0.000	0.000
	6-ag	0.000	0.001	0.000	0.000	0.000	0.000	0.000
5-av	5-ag	0.000	1.000	0.000	0.007	0.000	0.000	0.000
	6-bf	0.961	0.010	0.000	0.000	0.016	0.962	0.999
	6-av	0.000	0.153	0.996	0.999	0.000	0.000	0.000
	6-ag	0.000	1.000	0.006	0.158	0.000	0.000	0.000
5-ag	6-bf	0.000	0.001	0.000	0.000	0.000	0.000	0.000
	6-av	0.000	0.015	0.003	0.000	0.002	0.080	0.688
	6-ag	0.997	0.992	0.984	0.997	0.977	0.889	1.000
6-bf	6-av	0.008	1.000	0.000	0.006	0.036	0.000	0.000
	6-ag	0.000	0.033	0.000	0.000	0.000	0.000	0.000
6-av	6-ag	0.000	0.349	0.149	0.010	0.133	0.966	0.115

A-3: Mr G Joint Stiffness one way ANOVA

		JS02e01	JS02e05	JS02e10	JS02f01	JS02f05	JS02f10
1-bv	1-av	0.029	0.440	0.169	0.007	0.986	0.139
	1-ag	0.000	0.000	0.000	0.000	0.116	0.207
	2-bf	0.420	0.980	0.964	0.519	1.000	1.000
	2-av	0.104	0.000	0.000	0.722	0.896	0.833
	2-ag	0.004	0.000	0.000	0.001	0.539	0.567
	3-bf	1.000	0.972	0.311	0.000	0.001	0.085
	3-av	0.943	0.158	0.032	0.584	1.000	1.000
	3-ag	0.145	0.009	0.000	0.039	1.000	1.000
	4-bf	0.001	1.000	1.000	0.000	0.074	0.287
	4-av	0.000	0.000	0.000	0.007	0.502	0.105
	4-ag	0.000	0.000	0.000	0.000	0.003	0.000
	5-bf	1.000	0.999	0.002	1.000	0.347	0.563
	5-av	0.000	0.000	0.000	0.187	0.713	0.892
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.667	0.999	0.994	1.000	1.000	1.000
	6-av	0.108	0.000	0.000	0.002	0.001	0.002
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
1-av	1-ag	0.640	0.002	0.002	0.993	0.894	1.000
	2-bf	0.000	0.999	0.979	0.000	0.993	0.338
	2-av	1.000	0.017	0.040	0.000	0.117	0.001
	2-ag	1.000	0.001	0.000	1.000	1.000	1.000
	3-bf	0.012	1.000	1.000	0.000	0.000	0.000
	3-av	0.726	1.000	1.000	0.808	0.881	0.279
	3-ag	1.000	0.941	0.023	1.000	1.000	0.679
	4-bf	0.000	0.084	0.171	0.000	0.001	0.000
	4-av	0.975	0.275	0.006	1.000	1.000	1.000
	4-ag	0.738	0.000	0.000	0.991	0.123	0.000
	5-bf	0.264	0.044	0.000	0.013	0.012	0.000
	5-av	0.412	0.040	0.042	0.000	0.052	0.001
	5-ag	0.062	0.000	0.000	0.001	0.000	0.031
	6-bf	0.963	0.046	0.917	0.095	0.814	0.023
	6-av	1.000	0.001	0.419	1.000	0.058	0.963
	6-ag	0.704	0.000	0.000	0.052	0.001	0.001

1-ag	2-bf	0.000	0.000	0.000	0.000	0.144	0.455
	2-av	0.305	1.000	0.999	0.000	0.001	0.001
	2-ag	0.962	1.000	0.967	1.000	1.000	1.000
	3-bf	0.000	0.000	0.001	0.000	0.000	0.000
	3-av	0.006	0.012	0.014	0.097	0.041	0.386
	3-ag	0.230	0.200	1.000	0.824	0.270	0.798
	4-bf	0.000	0.000	0.000	0.000	0.000	0.000
	4-av	1.000	0.883	1.000	0.992	1.000	1.000
	4-ag	1.000	0.998	0.162	1.000	0.988	0.000
	5-bf	0.001	0.000	0.000	0.000	0.000	0.000
	5-av	1.000	1.000	0.999	0.000	0.000	0.002
	5-ag	0.997	0.001	0.121	0.033	0.001	0.019
	6-bf	0.026	0.000	0.000	0.003	0.029	0.037
	6-av	0.296	1.000	0.692	1.000	0.930	0.911
	6-ag	1.000	0.083	0.802	0.645	0.104	0.001
2-bv	2-av	0.000	0.001	0.001	1.000	0.854	0.542
	2-ag	0.000	0.000	0.000	0.000	0.607	0.852
	3-bf	0.645	1.000	0.998	0.131	0.001	0.027
	3-av	0.008	0.956	0.693	0.002	1.000	1.000
	3-ag	0.000	0.320	0.000	0.000	1.000	1.000
	4-bf	0.601	0.598	0.965	0.001	0.059	0.113
	4-av	0.000	0.023	0.000	0.000	0.569	0.269
	4-ag	0.000	0.000	0.000	0.000	0.003	0.000
	5-bf	0.058	0.420	0.000	0.356	0.293	0.279
	5-av	0.000	0.002	0.001	1.000	0.648	0.630
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.002	0.433	1.000	0.074	1.000	0.998
	6-av	0.000	0.000	0.014	0.000	0.001	0.007
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
2-av	2-ag	0.998	1.000	0.374	0.000	0.009	0.007
	3-bf	0.047	0.001	0.017	0.066	0.127	0.986
	3-av	0.956	0.072	0.202	0.004	0.989	0.617
	3-ag	1.000	0.594	1.000	0.000	0.667	0.235
	4-bf	0.000	0.000	0.000	0.000	0.956	1.000
	4-av	0.788	0.998	1.000	0.000	0.008	0.000

	4-ag	0.391	0.873	0.010	0.000	0.000	0.000
	5-bf	0.584	0.000	0.000	0.551	1.000	1.000
	5-av	0.159	1.000	1.000	1.000	1.000	1.000
	5-ag	0.016	0.000	0.007	0.000	0.000	0.000
	6-bf	0.999	0.000	0.000	0.146	0.996	0.997
	6-av	1.000	1.000	0.999	0.000	0.000	0.000
	6-ag	0.359	0.014	0.163	0.000	0.000	0.000
2-ag	3-bf	0.002	0.000	0.000	0.000	0.000	0.000
	3-av	0.290	0.007	0.000	0.471	0.276	0.795
	3-ag	0.993	0.126	0.517	0.999	0.808	0.988
	4-bf	0.000	0.000	0.000	0.000	0.000	0.001
	4-av	1.000	0.771	0.832	1.000	1.000	1.000
	4-ag	0.984	1.000	0.974	1.000	0.651	0.000
	5-bf	0.060	0.000	0.000	0.003	0.001	0.002
	5-av	0.846	0.997	0.366	0.000	0.003	0.010
	5-ag	0.269	0.003	0.947	0.003	0.000	0.003
	6-bf	0.644	0.000	0.000	0.026	0.212	0.162
	6-av	0.998	1.000	0.033	1.000	0.433	0.550
	6-ag	0.978	0.135	1.000	0.170	0.012	0.000
3-bv	3-av	0.806	0.967	1.000	0.000	0.003	0.036
	3-ag	0.068	0.349	0.009	0.000	0.000	0.006
	4-bf	0.003	0.562	0.314	0.808	0.964	1.000
	4-av	0.000	0.026	0.002	0.000	0.000	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	0.995	0.388	0.000	0.000	0.598	1.000
	5-av	0.000	0.002	0.018	0.408	0.257	0.969
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.441	0.400	0.984	0.000	0.005	0.377
	6-av	0.049	0.000	0.243	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
3-av	3-ag	0.982	0.999	0.127	0.992	1.000	1.000
	4-bf	0.000	0.020	0.033	0.000	0.192	0.144
	4-av	0.043	0.631	0.039	0.822	0.249	0.219
	4-ag	0.009	0.000	0.000	0.089	0.001	0.000
	5-bf	1.000	0.010	0.000	0.752	0.630	0.338

	5-av	0.002	0.153	0.208	0.000	0.927	0.703
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	1.000	0.010	0.507	0.993	1.000	0.999
	6-av	0.960	0.006	0.863	0.550	0.000	0.005
	6-ag	0.007	0.000	0.000	0.000	0.000	0.000
3-ag	4-bf	0.000	0.001	0.000	0.000	0.026	0.032
	4-av	0.694	0.999	1.000	1.000	0.777	0.592
	4-ag	0.303	0.010	0.019	0.802	0.009	0.000
	5-bf	0.688	0.000	0.000	0.073	0.158	0.095
	5-av	0.114	0.808	1.000	0.000	0.433	0.297
	5-ag	0.011	0.000	0.013	0.000	0.000	0.000
	6-bf	1.000	0.000	0.000	0.354	1.000	0.938
	6-av	1.000	0.114	0.994	1.000	0.003	0.030
	6-ag	0.276	0.000	0.252	0.009	0.000	0.000
4-bv	4-av	0.000	0.000	0.000	0.000	0.000	0.000
	4-ag	0.000	0.000	0.000	0.000	0.000	0.000
	5-bf	0.000	1.000	0.001	0.000	1.000	1.000
	5-av	0.000	0.000	0.000	0.003	0.995	1.000
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.000	1.000	0.994	0.000	0.252	0.762
	6-av	0.000	0.000	0.000	0.000	0.000	0.000
	6-ag	0.000	0.000	0.000	0.000	0.000	0.000
4-av	4-ag	1.000	0.179	0.067	0.989	0.688	0.000
	5-bf	0.006	0.000	0.000	0.014	0.001	0.000
	5-av	0.999	1.000	1.000	0.000	0.003	0.001
	5-ag	0.812	0.000	0.048	0.001	0.000	0.043
	6-bf	0.158	0.000	0.000	0.101	0.190	0.016
	6-av	0.778	0.744	0.902	1.000	0.468	0.983
	6-ag	1.000	0.000	0.548	0.049	0.014	0.002
4-ag	5-bf	0.001	0.000	0.000	0.000	0.000	0.000
	5-av	1.000	0.682	0.010	0.000	0.000	0.000
	5-ag	0.989	0.045	1.000	0.036	0.036	0.131
	6-bf	0.038	0.000	0.000	0.002	0.000	0.000
	6-av	0.381	1.000	0.000	1.000	1.000	0.000
	6-ag	1.000	0.688	0.999	0.672	0.863	0.724

5-bv	5-av	0.000	0.000	0.000	0.109	1.000	1.000
	5-ag	0.000	0.000	0.000	0.000	0.000	0.000
	6-bf	0.996	1.000	0.000	1.000	0.722	0.952
	6-av	0.596	0.000	0.000	0.004	0.000	0.000
	6-ag	0.001	0.000	0.000	0.000	0.000	0.000
5-av	5-ag	1.000	0.000	0.007	0.000	0.000	0.000
	6-bf	0.010	0.000	0.000	0.016	0.962	0.999
	6-av	0.153	0.996	0.999	0.000	0.000	0.000
	6-ag	1.000	0.006	0.158	0.000	0.000	0.000
5-ag	6-bf	0.001	0.000	0.000	0.000	0.000	0.000
	6-av	0.015	0.003	0.000	0.002	0.080	0.688
	6-ag	0.992	0.984	0.997	0.977	0.889	1.000
6-bf	6-av	1.000	0.000	0.006	0.036	0.000	0.000
	6-ag	0.033	0.000	0.000	0.000	0.000	0.000
6-av	6-ag	0.349	0.149	0.010	0.133	0.966	0.115

Appendix B: Ethical documentation

B-1: Ethical approvals

The two studies conducted for this thesis included healthy able body people with no previous history of neuromuscular diseases or disorders. The ethical approvals was granted by Computer Science Ethics Committee from Middlesex University (Ref No 0764).

The third study included people with spasticity due to the spinal cord injury. Ethical approval was granted from the NHS Health Research Authority - Bromley Research Ethics Committee (REC 17/LO/0853).

B-2: Vibration effect on muscle performance information sheet

Vibration effect on muscle performance

Researchers: Miss Tijana Jevtic, Dr Rui Loureiro, Dr Aleksandar Zivanovic
School of Science and Technology, Middlesex University, The Burroughs, Hendon, London, NW4 4BT

You are being invited to take part in a research study. Before you decide to participate, it is important for you to understand why the research is being done and what it will involve. Please take your time to read the following information carefully, and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part. Participation in this research is entirely voluntary. You do not have to take part if you do not want to. If you do decide to take part, then you may withdraw at any time, and you do not need to give a reason for you leaving the research.

What is the purpose of this research?

The research is being conducted to better understand how vibrations impact muscle performance. We would like to compare the effect vibrations have on muscle performance when applied directly on the muscle to when vibrations are applied on the bone that the muscle is attached to. Also we would like to evaluate its efficiency when applied before and when applied during muscle activation i.e. when the muscle contracts.

What will happen to me if I take part in this research?

If you agree to participate in this research, then you will be invited to perform movements with your index finger while vibrations are applied to the muscle. This experiment will take about 35-40 minutes of your time.

You will be seated at a tabletop facing the force gauge apparatus and a computer. You will be asked to place a hand underneath the force gauge sensor and push against it with your index finger (see Figure 1). During this study you will perform several small experiments divided into three phases and during each you will repeat cycles of relaxing (60 sec) and pushing (20 sec) with your index finger against the sensor. On the computer screen you will see the instructions that will tell you when to relax your finger and when to push against the sensor. On the computer screen you will also see a red line that goes up and down. You will be instructed to maintain that line within specified limits whenever you're pushing.

To record your muscle activity, two surface electromyography (EMG) electrodes will be placed on the back of your hand, on the muscle between your index finger and your thumb. Vibrations will be applied during experimental cycles either when you're relaxing your finger or when you're pushing against the force gauge. The position of the EMG electrodes and the vibration motor are presented in Figure 1.

You will be required to participate in the following three phases:

Phase 1: You will be asked to push with your index finger as hard as you can against the force gauge.

Phase 2: The small vibration motor will be attached in the middle of your muscle, in between the two surface EMG electrodes and you will be asked to push against the force gauge.

Phase 3: The vibration motor will be attached to the middle of your index finger, e.g. middle phalange, and you will be asked to push against the force gauge.

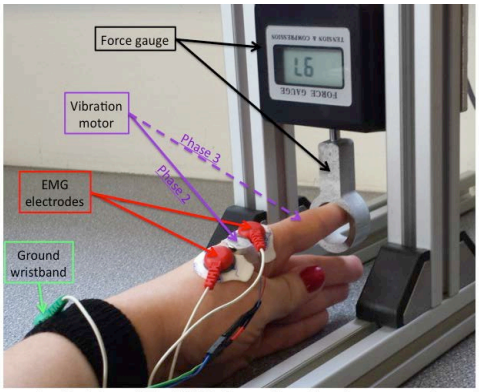


Figure 1 – Position of the EMG electrodes, vibration motor depending on the phase and force gauge in respect to the index finger.

What are the possible disadvantages and risks of taking part?

There are no obvious risks to taking part in this research and very unlikely you will feel any discomfort. All data collected during the experiment will be kept confidential and your identity anonymous.

Consent

You will be given a copy of this information sheet to take away with you and you will be asked to sign a consent form before taking part in the research.

What will happen to the information I provide?

The information and data we collect as part of this evaluation may be used for analysis and subsequent publication. No individuals will be identified in any of the results or reports.

Who has reviewed the study?

All proposals for research using human participants are reviewed by an Ethics Committee before they can proceed. The Middlesex Computing Science Research Ethics Committee has reviewed this proposal.

Thank you for taking the time to read through this form. If you have any further questions about the research, please feel free to contact the research team directly.

B-3: Vibration effect on muscle performance consent form

Middlesex University School of Science and Technology

CONSENT FORM

Participant Identification Number:

Title of Project: Vibration effect on muscle performance

Researchers: Miss Tijana Jevtic, Dr Rui Loureiro, Dr Aleksandar Zivanovic

1. I confirm that I have read and understood the information sheet dated .....……..for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.
3. I agree that this form that bears my signature may be seen by a designated auditor.
4. I agree that my non-identifiable research data may be stored in National Archives and be used anonymously by others for future research. I am assured that the confidentiality of my personal data will be upheld through the removal of any identifiers.
5. I agree to take part in the above study.

_____ _____

Date Signature

A copy of this consent form has been given to you to keep for your records and reference.

B-4: Vibration effect on muscle performance debriefing sheet

DEBRIEFING SHEET

Vibration effect on muscle performance

Researchers: Miss Tijana Jevtic (t.jevtic@mdx.ac.uk), Dr Rui Loureiro, Dr Aleksandar Zivanovic
School of Science and Technology,
Middlesex University,
The Burroughs, Hendon, London, NW4 4BT

Thank you for taking part in this research today.

When the experiment is complete, we will analyse the data using a mixture of research techniques.

Do you have any additional questions for me about the research process or what will happen to this information?

If you have any questions about this research or the findings, then do please get in touch with us using the details at the top of this sheet.

B-5: Cortical and muscle response to focal vibro-tactile stimuli information sheet

MIDDLESEX UNIVERSITY

PARTICIPANT INFORMATION SHEET (PIS)

Participant ID Code:……

1. Study title

Cortical and muscle response to focal vibro-tactile stimuli

2. Invitation paragraph

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

3. What is the purpose of the study?

The research is being conducted to better understand how vibrations impact brain's signals and muscle performance. We would like to compare the difference between signals from the brain and muscles on the arm before, during and after vibrations are applied to the muscle.

4. Why have I been chosen?

It is important that we assess as many participants as possible, and you have indicated that you are interested in taking part in this study. Our aim is to have up to 23 participants in this study.

5. Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you do decide to withdraw from the study then please inform the

researcher as soon as possible, and they will facilitate your withdrawal. If, for any reason, you wish to withdraw your data please contact the researcher within a month of your participation. After this data it may not be possible to withdraw your individual data as the results may have already been published. However, as all data are anonymised, your individual data will not be identifiable in any way. A decision to withdraw at any time, or a decision not to take part, will not affect you in any way.

6. What will I have to do?

If you agree to participate in this research, then you will be invited to perform movements with your index finger after vibrations are applied to the muscle. This experiment will take about one hour of your time.

To record your muscle activity, ten surface electromyography (EMG) electrodes will be placed on the various muscles of your arm. Position of the EMG electrodes and vibration motor are presented on Figure 1.

To record signals from the brain we will use surface electroencephalography (EEG) system. The EEG system non-invasively records the electrical activity of the brain and consists of a cap, rather like a swimming cap, which holds a number of metal electrodes against the user's scalp and these electrodes are connected to a computer, as presented on Figure 2. A conductive gel is applied between the scalp and each EEG electrode. We shall use special gel called g.GAMMAgel (made by g.Tec). The gel can be washed out of your hair with water and we will provide a towel.

A small vibration motor will be positioned on a back of your hand just bellow your index finger as shown on a Figure 1.

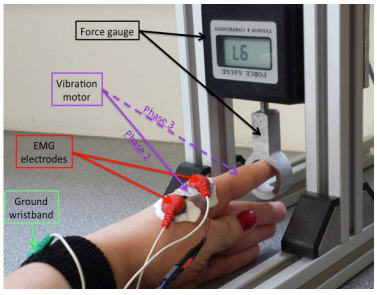


Figure 1 – Position of two EMG electrodes and a vibration motor. The index finger is pushing against the force gauge sensor.

Figure 2 – EEG cap on a head with electrodes on top.

You will be seated at a tabletop facing the force gauge apparatus and a computer. You will be asked to place both hands on a table top. During this study you will perform six small experiments divided into six phases and during each you will repeat

cycles of relaxing (30 sec) and maximally pushing (3 sec) with your index finger against the sensor. The only difference between the phases is which hand will be vibrated and which will push against the sensor.

Please note that in order to ensure quality assurance and equity this project may be selected for audit by a designated member of the committee. This means that the designated member can request to see signed consent forms. However, if this is the case your signed consent form will only be accessed by the designated auditor or member of the audit team.

7. Will I have to provide any bodily samples (i.e. blood/saliva/urine)?

No

8. What are the possible disadvantages and risks of taking part?

There are no obvious risks to taking part in this research and very unlikely you will feel any discomfort. All data collected during the experiment will be kept confidential and your identity anonymous.

Appropriate risk assessments for all procedures have been conducted, and will be followed throughout the duration of the study.

9. What are the possible benefits of taking part?

We cannot promise the study will help you personally but the information we get might help people with spasticity in the future. Your contribution will help us towards establishing a more solid scientific framework for advancing the knowledge of using vibrations in the treatment of spasticity.

9. Will my taking part in this study be kept confidential?

The research team has put a number of procedures in place to protect the confidentiality of participants. You will be allocated a participant code that will always be used to identify any data you provide. Your name or other personal details will not be associated with your data, for example, the consent form that you sign will be kept separate from your data. All paper records will be stored in a locked filing cabinet, accessible only to the research team, and all electronic data will be stored on a password protected computer. All information you provide will be treated in accordance with the UK Data Protection Act.

10. What will happen to the results of the research study?

The results of the research study will be used as part of an postgraduate PhD dissertation. The results may also be presented at conferences or in journal articles. However, the data will only be used by members of the research team and at no point will your personal information or data be revealed

11. Who has reviewed the study?

The study has received full ethical clearance from the Research ethics committee who reviewed the study. The committee is the Computing Research Ethical Committee.

12. Contact for further information

If you require further information, have any questions or would like to withdraw your data then please contact:

Researcher: Mrs Tijana Jevtic Vojinovic[1,2] (t.jevtic@mdx.ac.uk)

Supervisors: Dr Rui Loureiro[1,2], Dr Aleksandar Zivanovic[1], Dr Tom Carlson[2]

[1]*Faculty of Science and Technology, Middlesex University, The Burroughs, Hendon, London, NW4 4BT*

[2]*Aspire CREATE, University College London, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, HA7 4LP*

Thank you for taking part in this study. You should keep this participant information sheet as it contains your participant code, important information and the research teams contact details.

B-6: Cortical and muscle response to focal vibro-tactile stimuli consent form

CONSENT FORM

Title of Project: Cortical and muscle response to focal vibro-tactile stimuli

Name of Researchers: Mrs. Tijana Jevtic Vojinovic, Dr. Rui Loureiro, Dr. Aleksandar Zivanovic, Dr. Tom Carlson

1. I confirm that I have read and understand the information sheet dated .....……..for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason.

3. I agree that this form that bears my name and signature may be seen by a designated auditor.

4. I agree that my non-identifiable research data may be stored in National Archives and be used anonymously by others for future research. I am assured that the confidentiality of my data will be upheld through the removal of any personal identifiers.

5. Optional:
I hereby grant the permission to record and use images during the experiments. I understand that the film footage taken will be stored in the photo library for use in present and future publications and marketing materials. I understand my identity will be hidden. I relinquish any and all rights to said footage and consent to any and all uses of the film, picture and other recordings which may be used in all media and all territories of perpetuity.

   Please select one of the following: YES NO

6. I agree to take part in the above study.

Name of participant	Date	Signature
Researcher	Date	Signature

1 copy for participant; 1 copy for researcher;

B-7: Cortical and muscle response to focal vibro-tactile stimuli debriefing sheet

MIDDLESEX UNIVERSITY

DEBRIEFING SHEET

Study title: Cortical and muscle response to focal vibro-tactile stimuli

Contact for further information:

If you require further information, have any questions or would like to withdraw your data then please contact:

Researcher: Mrs Tijana Jevtic Vojinovic[1,2] (t.jevtic@mdx.ac.uk)

Supervisors: Dr Rui Loureiro[1,2], Dr Aleksandar Zivanovic[1], Dr Tom Carlson[2]

[1]*Faculty of Science and Technology, Middlesex University, The Burroughs, Hendon, London, NW4 4BT*

[2]*Aspire CREATE, University College London, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, HA7 4LP*

Thank you for taking part in this research today. This research can not promise benefits to you personally but the conclusions could help people with spasticity in the future.

When the experiment is complete, we will analyse the data using a mixture of research techniques. The conclusions will help us towards establishing a more solid scientific framework for advancing the knowledge of using vibrations in the treatment of spasticity.

If you have any questions about this research or the findings, research process or what will happen to the process data, then do please get in touch with us using the details at the top of this sheet.

B-8: VIBROfocus clinical trial information sheet

Royal National Orthopaedic Hospital NHS
NHS Trust

Participant Information Sheet for Adults

Version 2.0

19/06/2017

Project Title: A study investigating the effect of focal vibro-tactile stimulation on muscle performance as a possible technique for neurorehabilitation of spastic impaired upper limbs.

Chief Investigator: Dr Rui Loureiro
Principal Investigator: Ms Emma Linley

Sponsor: University College London

We would like to invite you to take part in a research study. Before deciding if you will give permission to take part in this study, you need to understand why the research is being done and what it will involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Only NHS patients will be participating in the study.

Why have I been invited?

You are being asked to take part in this study because you have diagnosed wrist spasticity as a consequence of your spinal cord injury.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to read and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

Why is this study being done?

After hospital discharge a large percentage of people with common neurological disorders (67-78%) are diagnosed with spasticity. If left untreated, spasticity contributes to decreased quality of life affecting mobility and dexterity, ability to carry out hygiene tasks, inability to wear corrective instrumentation for long periods, leading to declining participation in social activities and low self-esteem.

The origins of spasticity are not well understood and it is therefore very difficult to treat. It has been suggested that spasticity arises as a result of the abnormal responses from the spine. When we want to move, signals are sent from our brain to the part of our body we want to move. The brain receives feedback about the movement primarily through our sense of touch and vision, but also from our other senses. However the spine, that keeps the muscles safe from stretching too far, causes the muscles to get over activated, i.e. spastic. What we want to investigate in this research is whether it is possible, through the use of modern technology, to reduce spasticity through a series of combined vibration and robotic controlled tasks.

We would like to evaluate the effects vibrations have on spastic muscles. What is proposed in this research is to employ the vibration stimulation to precondition the muscle for the execution of robotic-assisted tasks. The tasks will provide us the information of any residual movement of the wrist.

What will I have to do?

You will have to commit to attend six sessions in two consecutive weeks and each will last approximately 2 hours.

At the beginning of each session we will measure the level of your spasticity. Your hand will be comfortably positioned in robotic assistive device that will record the levels of resistance from your wrist. Then, you will be asked to take a part in approximately 10-15 minutes of vibration stimulation of your forearm muscles. The vibration stimulations are delivered using small vibro-tactile motors attached to your forearm. In order to detect any changes following the vibrations, we will measure the resistance of your wrist again.

You will be asked to play a simple game for about 30 minutes by moving your hand left or right using the robotic assistive device. If you cannot perform the movement required by the game, the robotic device will provide the necessary assistance to move your wrist. During this time we will record a variety of information such as the movements you perform with the robot, and your muscles and brain electrical activity. The muscles' activity will be measured using surface electromyography (EMG) by using electrodes (i.e. pads) placed on the surface of the skin as your muscles contract or relax. Brain activity is measured with electroencephalography (EEG) using a system of electrodes placed in a cap positioned on your head.

You will be allowed to take up to 10 minutes break at any time during the sessions.

Spasticity and associated pain will be assessed by a clinically validated questionnaire at the beginning of the study, and at the beginning and end of each interventional session.

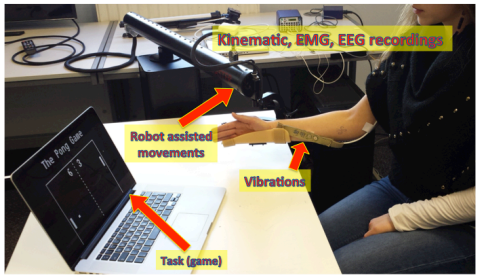


Figure 1: Example of the system you will be using.

What are the possible disadvantages and risks of taking part?

The research team have conducted a risk assessment and the necessary measures are in place to mitigate any equipment operational risks. The vibrations and robotic devices should not present any inconvenience or distress for the user.

In the unlikely event that you feel increased discomfort, you will be advised not continue to participate in the study.

What are the side effects of any treatment received when taking part?

There is a small chance that the treatment might cause you temporary increased discomfort, or itchiness or other distress. Experts will be on hand to assess you, should it be deemed too uncomfortable then you will be withdrawn.

What are the possible benefits of taking part?

We cannot promise the study will help you personally but the information we get might help people with spasticity in the future. Your contribution will help us towards establishing a more solid scientific framework for advancing the knowledge of using the vibrational therapies together with a robotic system in the treatment of spasticity.

What happens when the research study stops?

The results of the study will be published in appropriate scientific publications. The results obtained with this study will help us towards establishing a more solid scientific framework for advancing the knowledge of using the vibration therapy and a robotic system in the treatment of spasticity.

Are there any expenses and payments which I will get?

We will be reimbursing all travel expenses after you have kindly provided us with the travel receipts.

What will happen if I don't want to carry on with the study?

Your right to refuse to participate without giving reasons will be respected. Participation in this study will not affect in any way care that you receives from health care professionals. Furthermore, all participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment, simply by notifying the investigators.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do so via the normal National Health Service complaints mechanisms will still be available to you.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against University College London but you may have to pay your legal costs.

Will my taking part in this study be kept confidential?

All information collected about you during the course of the research will be kept strictly confidential, and any information about you, which leaves the hospital/surgery, will have your name and address removed so that you cannot be recognised.

You will have an option to be filmed during the study or to deny the permission to be filmed. If you agree, you will relinquish any right to the recording. Facial and other identifiable body parts will, whenever possible, not be recorded by the camera. Any identifying features will be removed before

use during video/image post processing. You will have the right to withdraw the consent for the use of the recording at any point before, during or after filming.

Involvement of the General Practitioner/Family doctor (GP)

If you decide to participate in this study, the decision to inform your GP of your participation is completely yours.

What will happen to the results of the research study?

The results of the study will be published in scientific conferences/ journals. All the data presented will be anonymised and you will not be identified in any report/ publication. Upon request a summary of the results will be made available to participants.

Who is organising and funding the research?

This investigation is part of research at UCL Aspire Centre for Rehabilitation Engineering and Assistive Technologies (Aspire CREATe), UCL Institute of Orthopaedics and Musculoskeletal Sciences, University College London and Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, Middlesex, HA7 4LP.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by _____Research Ethics Committee.

Who do I contact for general information about research?

You can contact the R&D office via research@rnoh.nhs.uk or 020 8909 5529

Who do I contact for specific information about this research project?

Principal Investigator: Ms Emma Linley, Clinical Specialist Occupational Therapist
London Spinal Cord Injury Centre, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, 30sex, HA7 4LP, UK.
Phone: 020 8909 5509

Chief Investigator: Dr Rui C.V. Loureiro, Head of Centre, Aspire CREATe
Aspire Centre for Rehabilitation Engineering and Assistive Technology
UCL Institute of Orthopaedics and Musculoskeletal Sciences, Division of Surgery & Interventional Science, University College London, Royal National Orthopaedic Hospital, Brockley Hill, Stanmore, Middlesex, HA7 4LP, UK.
Phone: 0208 385 3049

Who should I approach if unhappy with the study?

Patient Advice and Liaison Service via pals@rnoh.nhs.uk or 020 8909 5439/5717

Chief Investigator: Dr Rui Loureiro
Principal Investigator: Ms Emma Linley

B-9: VIBROfocus clinical trial consent form

Royal National Orthopaedic Hospital NHS
NHS Trust

RNOH Stanmore
Brockley Hill
Stanmore
Middlesex
HA7 4LP

Title of Project: A study investigating the effect of focal vibro-tactile stimulation on muscle performance as a possible technique for neurorehabilitation of spastic impaired upper limbs.

Patient Identification Number for this trial:
Chief Investigator: Dr Rui Loureiro
Principal Investigator Ms Emma Linley

		Please circle (and initial) one option	
1.	I confirm that I have read and understand the information sheet dated _____ Version_____ for the above study.	YES	NO
2.	I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	YES	NO
3.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	YES	NO
4.	I understand that relevant sections of any of my medical notes and data collected during the study, may be looked at by responsible individuals from the London Spinal Cord Injuries Unit at Stanmore, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	YES	NO
5.	I hereby grant the permission to record and use images of myself. I understand that the film footage taken will be anonymised and stored in a photo library for use in present and future publications and marketing materials. I relinquish any and all rights to said footage and consent to any and all uses of the film, picture and other recordings in which I may be portraying.	YES	NO
6.	I agree to take part in the above research study.	YES	NO

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

B-10: VIBROfocus clinical trial Spasticity and Pain Assessment, initial

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

SPASTICITY AND PAIN ASSESSMENT - initial

Level of Injury	Date of Injury	Spasticity side	Spasticity level (clinical)
Diagnosis:			
How many days/weeks/years since the injury have been since these started: Spasticity _____ Pain _____			
What triggers your spasticity (e.g. position changes, pressure)? *Details:*			
Have you received any spasticity treatment? Yes No *Details:*			
Are you currently taking any spasticity medications (e.g. baclofen, diazepam, dantrolene, clonidine or clonazepam)? Yes No *Details:* (include how long have been on prescription, dosage and when taken)			
How have you found the medication in treating your spasticity? *Very ineffective* *Very effective* 0 1 2 3 4 5 6 7 8 9 10			
Are you currently taking any pain medications? Yes No *Details*: (include how long have been on prescription, dosage and when taken)			
How have you found the medication in treating your pain? *Very ineffective* *Very effective* 0 1 2 3 4 5 6 7 8 9 10			

Researcher Name: _____ Sign: _____ Date:_____

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

Do you use an assistive device Yes No
Details:

Do you have any of the following symptoms?

Tight Limbs Yes No

Charley Horse/Cramps Yes No

Spasms (involuntary movement) Yes No

Details:

Please indicate which activities below are impacted by your symptoms

Feeding Yes No

Bathing Yes No

Toileting Yes No

Sleeping Yes No

Dressing Yes No

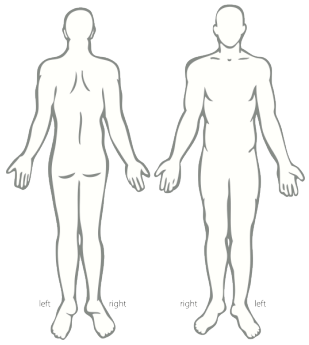
Walking Yes No

Details:

If you experience spasms, please indicate where and the severity of **the spasm**:

Penn's Spasm Rating Scale (PSRS)*

0 = No spasm
1 = Mild spasms induced by stimulation
2 = Infrequent full spasms occurring less than once per hour
3 = Spasms occurring more than once per hour
4 = Spasms occurring more than 10 times per hour



Head	Arms
Neck	Hands
Face	Legs
Trunk	Feet

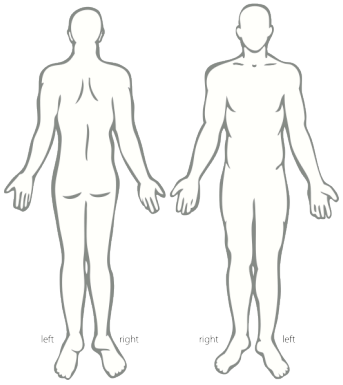
Details (include specification for the arm and hand):

*© Penn et al, 1989. From 'Intrathecal baclofen for severe spinal spasticity', The New Eng Jour of Medicine, 23, 1517-1521

Researcher Name: _____ Sign: _____ Date:_____

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

Please mark, on the drawing below, the areas where you feel the **pain associated with spasticity or tight, stiff muscles**. (Put E if external, or I if internal near the areas which you mark. Put EI if both external and internal)  	**Pain numeric rating scale**** *No Pain* *Worst Pain* 0 1 2 3 4 5 6 7 8 9 10 Rate the pain in your **arm** over the last _____ (day, week, month) Rate the pain in your **forearm** over the last _____ (day, week, month) Rate the pain in your **hand** over the last _____ (day, week, month) *Details:*

Which word or words would best describe the **pattern** of your pain?

Continuous	Yes No	Rhythmic	Yes No	Brief	Yes No
Steady	Yes No	Periodic	Yes No	Momentary	Yes No
Constant	Yes No	Intermittent	Yes No	Transient	Yes No

Details:

**© Melzack, 1975. From 'The McGill Pain Questionnaire: major properties and scoring methods', Pain, 1, 277-299

Notes:

Researcher Name: _____ Sign: _____ Date:_____

B-11: VIBROfocus clinical trial Spasticity and Pain Assessment, session beginning

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

SPASTICITY AND PAIN ASSESSMENT – session beginning

This questionnaire should be taken at the beginning of each session. Please answer each question in respect to the last visit (describe perceptions since the last visit).

Spasticity level (clinical measure)	Your spasticity is: Improved The Same Worse

Did you have any of the following symptoms?

Tight Limbs Yes No

Charley Horse/Cramps Yes No

Spasms (involuntary movement) Yes No

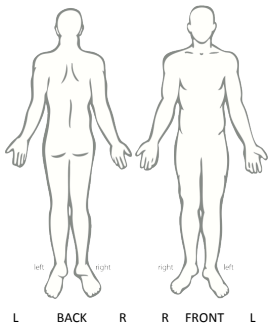
Details:

If you experienced spasms, please indicate where and the severity of the **spasm:**

Penn's Spasm Rating Scale (PSRS)*

0 = No spasm
1 = Mild spasms induced by stimulation
2 = Infrequent full spasms occurring less than once per hour
3 = Spasms occurring more than once per hour
4 = Spasms occurring more than 10 times per hour

Head	Arms
Neck	Hands
Face	Legs
Trunk	Feet



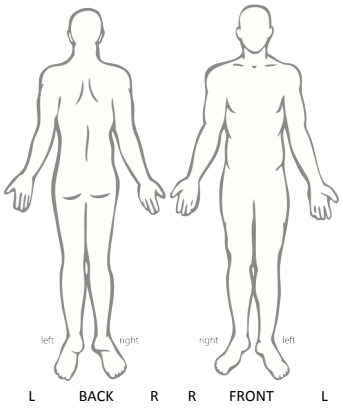
Details (include specification for the arm and hand):

*© Penn et al, 1989. From 'Intrathecal baclofen for severe spinal spasticity', The New Eng Jour of Medicine, 23, 1517-1521

Researcher Name: _____ Sign: _____ Date:_____

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

Please mark, on the drawing below, the areas where you felt the pain associated with spasticity or tight, stiff muscles. (Put E if external, or I if internal near the areas which you mark. Put EI if both external and internal) 	**Pain numeric rating scale**** *No Pain* *Worst Pain* 0 1 2 3 4 5 6 7 8 9 10
	Rate the pain in your **arm**
	Rate the pain in your **forearm**
	Rate the pain in your **hand**
	Details:

Which word or words would best describe the **pattern** of your pain?

Continuous	Yes No	Rhythmic	Yes No	Brief	Yes No
Steady	Yes No	Periodic	Yes No	Momentary	Yes No
Constant	Yes No	Intermittent	Yes No	Transient	Yes No

Details:

**© Melzack, 1975. From 'The McGill Pain Questionnaire: major properties and scoring methods', Pain, 1, 277-299

Notes:

Researcher Name: _____ Sign: _____ Date:_____

B-12: VIBROfocus clinical trial Spasticity and Pain Assessment, session end

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

SPASTICITY AND PAIN ASSESSMENT – session end

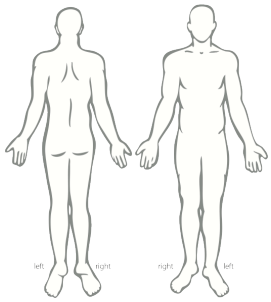
This questionnaire should be taken at the end of each session. Please answer each question in respect to today's session (describe the perceptions during todays session).

Spasticity level (clinical measure)	Your spasticity is: Improved The Same Worse
Did anything trigger your spasticity during this session? Yes No *Details:*	
Did you have any of the following symptoms? Tight Limbs Yes No Charley Horse/Cramps Yes No Spasms (involuntary movement) Yes No *Details:*	

If you experience spasms, please indicate where and the severity of the spasm:

Penn's Spasm Rating Scale (PSRS)*

0 = No spasm
1 = Mild spasms induced by stimulation
2 = Infrequent full spasms occurring less than once per hour
3 = Spasms occurring more than once per hour
4 = Spasms occurring more than 10 times per hour



Head	Arms
Neck	Hands
Face	Legs
Trunk	Feet

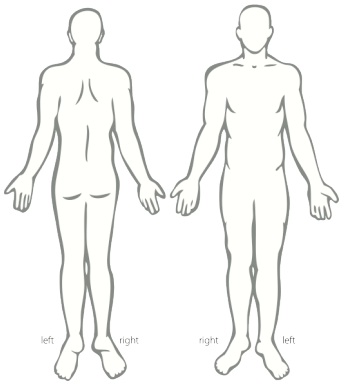
Details (include specification for the arm and hand):

*© Penn et al, 1989. From 'Intrathecal baclofen for severe spinal spasticity', The New Eng Jour of Medicine, 23, 1517-1521

Researcher Name: _____ Sign: _____ Date:_____

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

Please mark, on the drawing below, the areas where you feel the **pain associated with spasticity or tight, stiff muscles**. (Put E if external, or I if internal near the areas which you mark. Put EI if both external and internal) 	**Pain numeric rating scale**** *No Pain* *Worst Pain* 0 1 2 3 4 5 6 7 8 9 10
	Rate the pain in your **arm** over the last _____ (day, week, month)
	Rate the pain in your **forearm** over the last _____ (day, week, month)
	Rate the pain in your **hand** over the last _____ (day, week, month)
	Details:

Which word or words would best describe the **pattern** of your pain?

Continuous	Yes No	Rhythmic	Yes No	Brief	Yes No
Steady	Yes No	Periodic	Yes No	Momentary	Yes No
Constant	Yes No	Intermittent	Yes No	Transient	Yes No

Details:

**© Melzack, 1975. From 'The McGill Pain Questionnaire: major properties and scoring methods', Pain, 1, 277-299

Notes:

Researcher Name: _____ Sign: _____ Date:_____

Participant Number: _____ Sign_____ Date _____

Session Number: _____ Date/Time: _____

Please answer following questions in respect to the overall participation in VIBROfocus project.

Since the beginning, of your participation in VIBROfocus project, how would you describe the change (if any) your condition related to:

Patient's Global Impression of Change (PGIC) Scale***

0 = No change (or condition has gotten worse)
1 = Almost the same, hardly any change at all
2 = A little better, but no noticeable change
3 = Somewhat better, but the change has not made any real difference
4 = Moderately better, and a slight but noticeable change
5 = Better, and a definite improvement that has made a real and worthwhile difference
6 = A great deal better, and a considerable improvement that has made all the difference

Activity limitations	Symptoms	Emotions	Overall quality of life

Details:

Please tell us the degree of change since the beginning of participation in VIBROfocus project:

Much Worse *No Change* *Much Better*

0 1 2 3 4 5 6 7 8 9 10

Details:

***©Hurst et al. 2004. From "Assessing the clinical significance of change scores recorded on subjective outcome measures" *J of Manipulative Physiological Therapeutics* (IMPT);27,26-35.

Notes:

Researcher Name: _____ Sign: _____ Date:_____

B-13: VIBROfocus clinical trial participation Ghantt chart

Participation weeks	Days of the week	Participant 1 Mr R	Participant 2 Mr G
Week 1	Monday		
	Tuesday		
	Wednesday		
	Thursday		
	Friday		
	Saturday		
	Sunday		
Week 2	Monday		
	Tuesday		
	Wednesday		
	Thursday		
	Friday		
	Saturday		
	Sunday		

Appendix C: VIBROfocus hardware design

C-1: Maxon motor datasheet

maxon motor

maxon motor control	ESCON Servo Controller
Hardware Reference	Edition November 2015

ESCON 50/5

Servo Controller

P/N 409510

Hardware Reference

escon.maxonmotor.com

Document ID: rel5536

maxon motor ag Brünigstrasse 220 P.O.Box 263 CH-6072 Sachseln Phone +41 41 666 15 00 Fax +41 41 666 16 50 www.maxonmotor.com

2 Specifications

2.1 Technical Data

ESCON 50/5 (409510)		
Electrical Rating	Nominal operating voltage $+V_{CC}$	10…50 VDC
	Absolute operating voltage $+V_{CC\ min}$ / $+V_{CC\ max}$	8 VDC / 56 VDC
	Output voltage (max.)	0.98 x $+V_{CC}$
	Output current I_{cont} / I_{max} (<20 s)	5 A / 15 A
	Pulse Width Modulation frequency	53.6 kHz
	Sampling rate PI current controller	53.6 kHz
	Sampling rate PI speed controller	5.36 kHz
	Max. efficiency	95%
	Max. speed DC motor	limited by max. permissible speed (motor) and max. output voltage (controller)
	Max. speed EC motor	150'000 rpm (1 pole pair)
	Built-in motor choke	3 x 30 µH; 5 A
Inputs & Outputs	Analog Input 1 Analog Input 2	resolution 12-bit; −10…+10 V; differential
	Analog Output 1 Analog Output 2	resolution 12-bit; −4…+4 V; referenced to GND
	Digital Input 1 Digital Input 2	+2.4…+36 VDC (R_i = 38.5 kΩ)
	Digital Input/Output 3 Digital Input/Output 4	+2.4…+36 VDC (R_i = 38.5 kΩ) / max. 36 VDC (I_L <500 mA)
	Hall sensor signals	H1, H2, H3
	Encoder signals	A, A\, B, B\, (max. 1 MHz)
Voltage Outputs	Auxiliary output voltage	+5 VDC (I_L ≤10 mA)
	Hall sensor supply voltage	+5 VDC (I_L ≤30 mA)
	Encoder supply voltage	+5 VDC (I_L ≤70 mA)
Potentiometers	Potentiometer P1 (on board) Potentiometer P2 (on board)	240°; linear
Motor Connections	DC motor	+ Motor, − Motor
	EC motor	Motor winding 1, Motor winding 2, Motor winding 3
Interface	USB 2.0 / USB 3.0	full speed
Status Indicators	Operation	green LED
	Error	red LED

ESCON 50/5 (409510)			
Physical	Weight	approx. 204 g	
	Dimensions (L x W x H)	115 x 75.5 x 24 mm	
	Mounting holes	for M4 screws	
Environmental Conditions	Temperature	Operation	−30…+45 °C
		Extended range *1)	+45…+85 °C Derating ➔Figure 2-1
		Storage	−40…+85 °C
	Altitude *2)	Operation	0…10'000 m MSL
	Humidity	5…90% (condensation not permitted)	

*1) Operation within the extended range (temperature and altitude) is permitted. However, a respective derating (declination of output current I_{cont}) as to the stated values will apply.
*2) Operating altitude in meters above Mean Sea Level, MSL.

Table 2-4 Technical Data

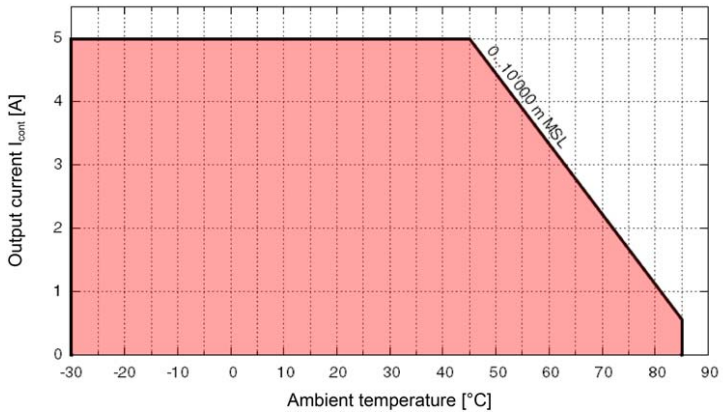


Figure 2-1 Derating Output Current

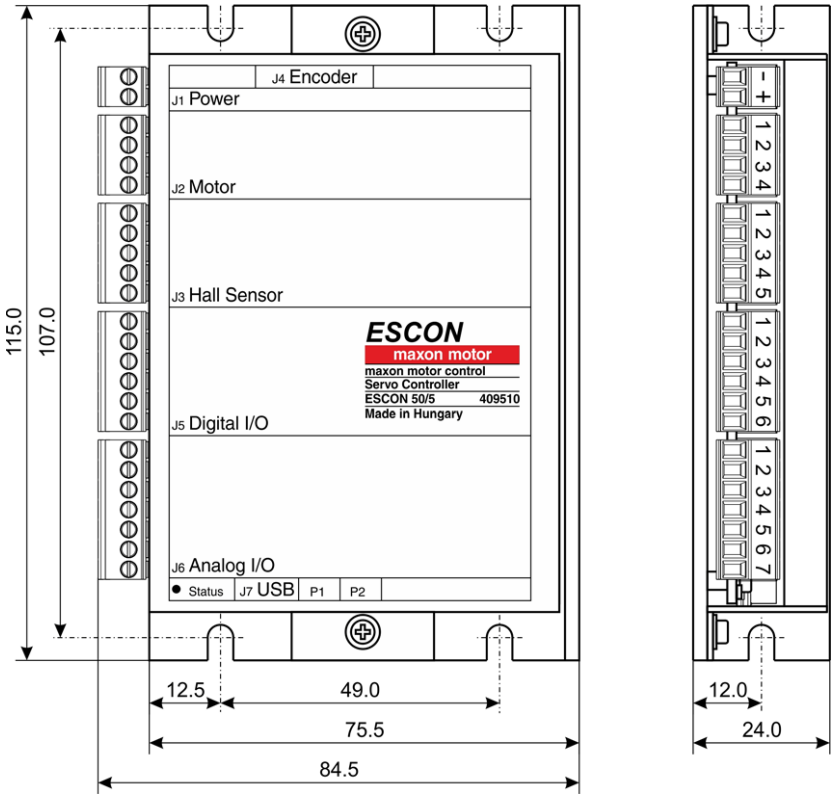


Figure 2-2 Dimensional Drawing [mm]

3.2 Determination of Power Supply

Basically, any power supply may be used, provided it meets the minimal requirements stated below.

Power Supply Requirements	
Output voltage	$+V_{CC}$ 10…50 VDC
Absolute output voltage	min. 8 VDC; max. 56 VDC
Output current	Depending on load • continuous max. 5 A • short-time (acceleration, <20 s) max. 15 A

1) Use the formula below to calculate the required voltage under load.
2) Choose a power supply according to the calculated voltage. Thereby consider:
   a) During braking of the load, the power supply must be capable of buffering the recovered kinetic energy (for example, in a capacitor).
   b) If you are using an electronically stabilized power supply, make sure that the overcurrent protection circuit is configured inoperative within the operating range.

Note
The formula already takes the following into account:
- *Maximum PWM duty cycle of 98%*
- *Controller's max. voltage drop of 1 V @ 5 A*

KNOWN VALUES:
- Operating torque M [mNm]
- Operating speed n [rpm]
- Nominal motor voltage U_N [Volt]
- Motor no-load speed at U_N, n_0 [rpm]
- Speed/torque gradient of the motor $\Delta n/\Delta M$ [rpm/mNm]

SOUGHT VALUE:
- Supply voltage $+V_{CC}$ [Volt]

SOLUTION:

$$V_{CC} \geq \left[\frac{U_N}{n_O} \cdot \left(n + \frac{\Delta n}{\Delta M} \cdot M\right) \cdot \frac{1}{0.98}\right] + 1\,[V]$$

C-2: Force sensor datasheet

FC22

Compression Load Cell

SPECIFICATIONS

- **10 – 100 lbf Ranges**
- **High Level or mV Outputs**
- **Interchangeable**
- **Compact Easy to Fixture Design**
- **CE Compliance**

FEATURES

- Small Size
- Low Noise
- Robust: High Over-Range Capability
- High Reliability
- Low Deflection
- Essentially Unlimited Cycle Life Expectancy
- Low Off Center Errors
- Fast Response Time
- 10 to 100 lbf Ranges
- Reverse Polarity Protected

APPLICATIONS

- Medical Infusion Pumps
- Robotics End-Effectors
- Variable Force Control
- Load and Compression Sensing
- Exercise Machines
- Pumps
- Contact Sensing
- Weighing
- Household Appliances

The FC22 is a medium compression force sensor that creates new markets previously unrealizable due to cost and performance constraints. The FC22 offers normalized zero and span for interchangeability and is thermally compensated for changes in zero and span with respect to temperature.

The FC22 incorporates MEAS' proprietary Microfused technology which employs micromachined silicon piezoresistive strain gages fused with high temperature glass to a high performance stainless steel substrate. Microfused technology eliminates age-sensitive organic epoxies used in traditional load cell designs providing excellent long term span and zero stability. The FC22 measures direct force and is therefore not subject to lead-die fatigue failure common with competitive designs which use a pressure capsule embedded within a silicone gel-filled cavity. Operating at very low strains, Microfused technology provides an essentially unlimited cycle life expectancy, superior resolution, and high over-range capabilities.

Cost-optimization of the FC22 brings your OEM product to life whether you need thousands or millions of load cells annually. Although the standard model is ideal for a wide range of applications, our dedicated design team at our Load Cell Engineering Center is ready to provide you with custom designs for your OEM applications.

Please refer to the FS20 for lower force applications or the FC23 for higher force applications.

FC22
Compression Load Cell

STANDARD RANGES

Range	lbf
0 to 0010	•
0 to 0025	•
0 to 0050	•
0 to 0100	•

PERFORMANCE SPECIFICATIONS

Supply Voltage: 5.0V, Ambient Temperature: 25°C (unless otherwise specified)

PARAMETERS	MIN	TYP	MAX	UNITS	NOTES
Span (Unamplified, FC2201)	24	30	36	mV/V	1
Span (Unamplified, FC2211)	19	20	21	mV/V	1
Span (Amplified)	3.8	4.00	4.2	V	1
Zero Force Output (Unamplified, FC2201)	-1	0	1	mV/V	1
Zero Force Output (Unamplified, FC2211)	-0.5	0	0.5	mV/V	1
Zero Force Output (Amplified)	0.45	0.5	0.55	V	1
Accuracy (non linearity, hysteresis, and repeatability)		±1		%Span	2
Output Resistance (Unamplified)		2.2		kΩ	
Input Resistance (Unamplified)		3		kΩ	
Temperature Error – Zero	-1.25		1.25	%Span	3
Temperature Error – Span	-1.25		1.25	%Span	3
Long Term Stability (1 year)		±1		%Span	
Maximum Overload	2.5X			Rated	
Compensated Temperature	0		50	°C	
Operating Temperature	-40		+85	°C	
Storage Temperature	-40		+85	°C	
Excitation Voltage (Unamplified)			5	Vdc	
Excitation Voltage (Amplified)	4.75	5	5.25	Vdc	
Isolation Resistance (250Vdc)	50			MΩ	
Deflection at Rated Load			0.05	mm	
Humidity	0		90	%RH	
Weight		18.41		grams	

For custom configurations, consult factory

Notes

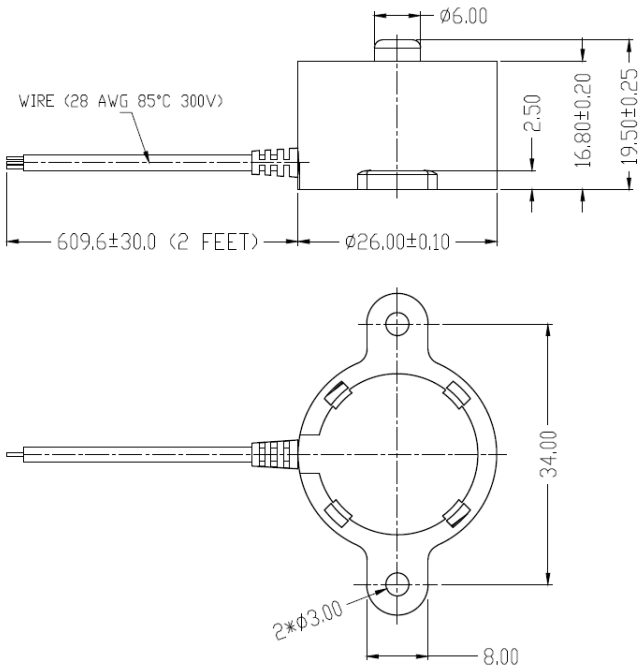
1. Ratiometric to supply.
2. Best fit straight line.
3. Maximum temperature error over compensated range with respect to 25°C.

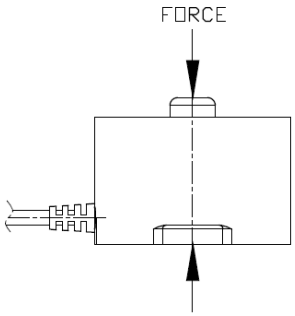
CE Compliance

IEC61000-4-2 [4 kV/ 4kV (Air/Contact)]
IEC61000-4-3 (3 V/m)
IEC55022 Class A

DIMENSIONS

FC2201:
FC2211:
FC2231:



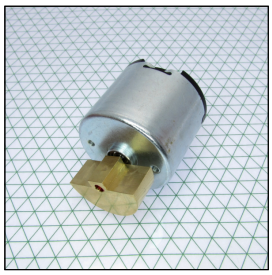


WIRE NOTE:

P/N	WIRE CONNECTIONS
FC2201 FC2211	4 CORE WIRE (28 AWG 85°C 300V) 1: YELLOW: +OUTPUT 2: WHITE: -OUTPUT 3: RED: +INPUT 4: BLACK: -INPUT
FC2231	3 CORE WIRE (28 AWG 85°C 300V) 1: YELLOW: +OUTPUT 2: RED: +INPUT 3: BLACK: COMMON

C-3: Vibration motor datasheet

334-401



34mm Vibration Motor - 30mm Type
Shown on 6mm Isometric Grid

PRECISION MICRODRIVES™

Product Data Sheet
Uni Vibe™
34mm Vibration Motor - 30mm Type

Model: 334-401

Ordering Information

The model number 334-401 fully defines the model, variant and additional features of the product. Please quote this number when ordering.
For stocked types, testing and evaluation samples can be ordered directly through our online store.

Datasheet Versions

It is our intention to provide our customers with the best information available to ensure the successful integration between our products and your application. Therefore, our publications will be updated and enhanced as improvements to the data and product updates are introduced.
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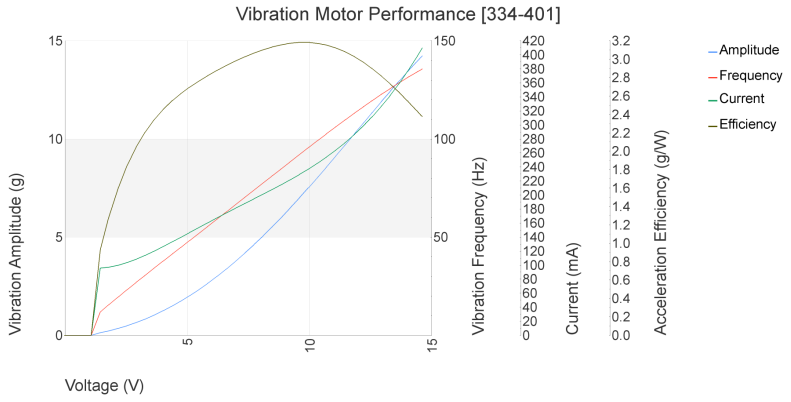
If you have any questions, suggestions or comments regarding this publication or need technical assistance, please contact us via email at:
enquiries@precisionmicrodrives.com or call us on +44 (0) 1932 252 482

Key Features

Body Diameter:	34 mm [+/- 0.2]
Body Length:	29.5 mm [+/- 0.3]
Ecc. Weight Radius:	12.8 mm [+/- 0.2]
Ecc. Weight Length:	10.5 mm [+/- 0.2]
Rated Operating Voltage:	12 V
Rated Vibration Speed:	6,800 rpm [+/- 1,350]
Typical Rated Operating Current:	180 mA
Typical Norm. Amplitude:	110 G

Typical Vibration Motor Performance Characteristics



Physical Specification

PARAMETER	CONDITIONS	SPECIFICATION
Body Diameter	Max body diameter or max face dimension where non-circular	34 mm [+/- 0.2]
Body Length	Excl. shafts, leads and terminals	29.5 mm [+/- 0.3]
Unit Weight		75 g
No. of Output Shafts		1
Ecc. Weight Radius	Radius from shaft for non-cylindrical weights	12.8 mm [+/- 0.2]
Ecc. Weight Length		10.5 mm [+/- 0.2]

Construction Specification

PARAMETER	CONDITIONS	SPECIFICATION
Motor Construction		Iron Core
Commutation		Carbon Brush
No. of Poles		3
Bearing Type	Front & rear bearings	Ball Bearing

Operational Specification

PARAMETER	CONDITIONS	SPECIFICATION
Rated Operating Voltage		12 V
Rated Vibration Speed	At rated voltage using the inertial test load	6,800 rpm [+/- 1,350]
Max. Rated Operating Current	At rated voltage using the inertial test load	320 mA
Max. Start Voltage	Certified starting voltage. Measured at no load, where applicable	3 V
Rated Inertial Test Load	Mass of rated load standard test sled	1,000 g
Max. Operating Voltage		14.4 V
Min. Vibration Amplitude	Peak-to-peak value at rated voltage using the inertial test load	6.7 G
Max. Start Current	At rated voltage	3,000 mA

Important: The characteristics of the motor is the typical operating parameters of the product. The data herein offers design guidance information only and supplied batches are validated for conformity against the specifications on the previous page.

Typical Performance Characteristics

PARAMETER	CONDITIONS	SPECIFICATION
Typical Rated Operating Current	At rated voltage using the inertial test load	180 mA
Typical Vibration Amplitude	Peak-to-peak value at rated voltage using the inertial test load	11 G
Typical Start Current	At rated voltage	2,700 mA
Typical Vibration Efficiency	At rated voltage using the inertial test load	5.1 G/W
Typical Norm. Amplitude	Peak-to-peak vibration amplitude normalised by the inertial test load at rated voltage	110 G
Typical Start Voltage	Measured at no load, where applicable	1.25 V
Typical Terminal Resistance		4.5 Ohm
Typical Terminal Inductance		3,650 uH

Typical Haptic Characteristics

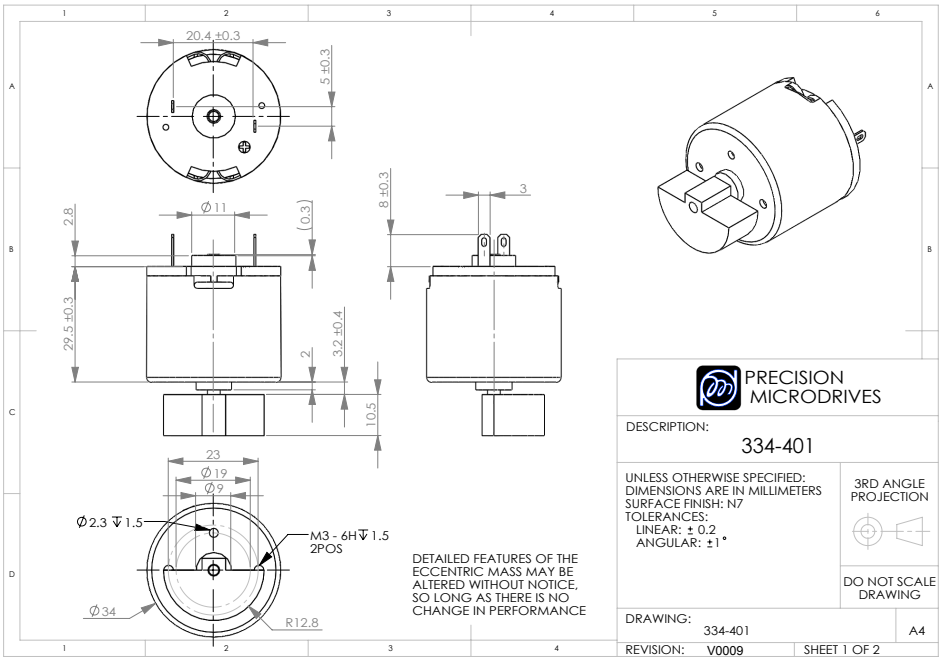
PARAMETER	CONDITIONS	SPECIFICATION
Typical Lag Time	At rated voltage using the inertial test load	6 ms
Typical Rise Time	At rated voltage using the inertial test load	77 ms
Typical Stop Time	At rated voltage using the inertial test load	176 ms
Typical Active Brake Time	Time taken from steady-state to 0.04 G under inverse polarity at max. voltage	72 ms

Environmental Characteristics

PARAMETER	CONDITIONS	SPECIFICATION
Max. Operating Temp.		60 Deg.C
Min. Operating Temp.		-10 Deg.C
Max. Storage & Transportation Temp.		70 Deg.C
Min. Storage & Transportation Temp.		-20 Deg.C

334-401

Product Dimensional Specification



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2. A critical component is any component of a life support device or system whose failure to perform can be reasonably expected to cause the failure of the life support device or system, or to affect its safety or effectiveness.

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