Analysis of body coordination with muscle synergies during robot-assisted exercise and therapy

March　２０２０

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ABSTRACT

Movement is one of the most fundamental, and probably the only way, for humans and animals to interact with the physical world. A control system in the body, known as the nervous system, utilizes actuating elements within the body to generate movement. There are suggestions that the nervous system is very closely coupled with movement and driven by physical needs. This implication could also apply to humans as well, from observations on stroke patients indicating that repeated non-use of paretic limbs will eventually cause that limb to be non-functional.

Gait deficits in post-stroke patients have been documented and the restoration gait functions is a clinically important goal pursued by therapists. To achieve this goal, proper measurement of gait is required, because without knowing what outcomes are to be expected, there is no way to design therapies for those outcomes. Physical measures, like kinematics and spatiotemporal measures, currently in use provides quite a good estimate of movement. However, it is not sufficient to evaluate the change neurological control of the limbs, as spatiotemporal measures can only measure the physical outcome of the movement. Previous work showing improvement in gait symmetry mainly evaluate kinematics and spatiotemporal measures but hypothesizes about neurological recovery. Since the human body is highly redundant, compensatory actions could also give results that could be interpreted as recovery. Although physical measures provide a good correlation with recovery, it might not be an indication of true neurological recovery.

As stroke is a neurological disease, this thesis proposes the evaluation of muscle coordination as a way to understand how the nervous system control movement. A muscle coordination index is developed in conjunction with studies evaluating the effects of EMG-triggered lumbar support robotic exoskeleton on healthy subjects, and also stroke patients undergoing robotic therapy with an EMG-triggered lower limb robotic exoskeleton. Additionally, an evaluation method of gait symmetry during walking was proposed for therapists to document gait symmetry visually.

Future directions for this avenue of research should be to clarify the relation between muscle synergies and kinetics of lower limbs. Another future direction that could be pursued is controlled longitudinal studies of patients utilizing robotic therapy. Although clear beneficial effects were observed in patients during in-patient therapy programs, it is still unknown whether such effects are maintained after patients are discharged and it would best for the patients if such effects were clarified.

DECLARATION

I, Tan Chun Kwang, declare that this thesis titled, **Analysis of body coordination with muscle synergies during robot-assisted exercise and therapy** and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed: Tan Chun Kwang

Date: 25 March 2020

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PUBLICATIONS

Some ideas and figures have appeared previously in the following publications:

[1] Chun Kwang Tan, Hideki Kadone, Hiroki Watanabe, Aiki Marushima, Yasushi Hada, Masashi Yamazaki, Yoshiyuki Sankai, Akira Matsumura, and Kenji Suzuki. "Differences in gait symmetry between subacute post-stroke patients during robot-assisted therapy and conventional therapy." In: (under review 2019).

[2] Chun Kwang Tan, Hideki Kadone, Hiroki Watanabe, Aiki Marushima, Masashi Yamazaki, Yoshiyuki Sankai, and Kenji Suzuki. "Lateral Symmetry of Synergies in Lower Limb Muscles of Acute Post-stroke Patients After Robotic Intervention." In: *Frontiers in Neuroscience* 12 (2018), p. 276. ISSN: 1662-453X. DOI: 10.3389/fnins.2018.00276. URL: https://www.frontiersin.org/article/10.3389/fnins.2018.00276.

[3] Chun Kwang Tan, Hideki Kadone, Kousei Miura, Tetsuya Abe, Masao Koda, Masashi Yamazaki, Yoshiyuki Sankai, and Kenji Suzuki. "Muscle Synergies During Repetitive Stoop Lifting With a Bioelectrically-Controlled Lumbar Support Exoskeleton." In: *Frontiers in Human Neuroscience* 13 (2019), p. 142. ISSN: 1662-5161. DOI: 10.3389/fnhum.2019.00142. URL: https://www.frontiersin.org/article/10.3389/fnhum.2019.00142.

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ACRONYMS

FAC	Functional Ambulation Category
FIM	Functional Independence Measure
FMA	Fugl-Meyer Assessment
BI	Barthel Index
BBS	Berg balance scale
EMG	Electromyography
MSA	Muscle Synergy Analysis

Part I

BASIS OF THESIS

1

INTRODUCTION

吾輩は人形である。身体は動かない。意識する必要はない
(I am a puppet. My body does not move. I have no need of consciousness)

A parody of "吾輩は猫である。名前はまだ無い。どこで生れたかとんと見当がつかぬ。"
From the book "吾輩は猫である", *1905-1907*
Natsume Sōseki

1.1 MOVEMENT AND THE BRAIN

Movement is one of the fundamental actions for humans to interact with the physical world. It involves the use of appendages to perform some task, like reaching or ambulation. Movement is also embedded in some languages, for example, in the Japanese language, the word for a puppet or doll is "人形", which can be directly translated as "human shape" or a human-shaped object, whereas a "human" is written as "人". This implies that without movement, a human is no different from a puppet or doll. Movement can be said to be related to consciousness, such that comatose patients are described as a "vegetative state" ([5]), although there has been a recent movement trying to change this definition, due to ethical issues of classifying patients as "vegetative" and to remove stigma associated with the term ([56]).

Another evidence for the importance of movement comes from biology. As a prominent neuroscientist, Daniel Wolpert famously said when describing the sea squirt (known as Ascidians), which digests its brain once it attaches itself to a rock: "So once you don't need to move, you don't need the luxury of that brain." ([67]). However, in this case, it is more accurately to say that the sea squirt reorganizes its brain and removes parts controlling locomotion. Research in Ascidian anatomy has shown that Ascidians undergoes metamorphosis during development and digests parts of its nervous system that control swimming ([75], [95]). They still maintain a brain and nervous system to regulate the internal organs of their adult forms ([115]). This implies the structure of the nervous system is driven by physical needs, which in this case is locomotion.

Carrying this implication further, if any animal, at any point in time, loses the need for locomotion, the parts of the brain controlling movement would probably degrade from disuse. This implication is particularly important in the field of neurorehabilitation, and there is even a study showing that repeated non-use of a paretic upper limb follow-

ing discharge from a rehabilitation program would cause the performance of the paretic limb to decrease ([71]). Other evidence suggest that exercise help the maintenance of brain executive and memory functions ([85], [96], [126]). This goes to show how movement and the brain is so closely coupled, and that it is possible to influence neural structures through the use of physical activity and exercise.

1.2 SYMMETRY IN NATURE AND IN HUMANS

Symmetry in locomotion could be said to have been noted in very early works by the Greek philosopher, Aristotle. He noted in his 350 B.C. work "On the Gait of Animals" [51], that animals can be naturally be divided into 6 parts, (superior and inferior, front and back, right and left). Aristotle also noted that animals with limbs have an even number of limbs for the purpose of walking, and animals with more legs increase their legs in progressions of even numbers. Subsequent work in zoology that studied evolution ([20]) postulated that bilateral symmetry in animals evolved from radial symmetry, with biradial symmetry as an intermediate form.

Humans are, and in general, are bilaterally symmetrical in structure, with the exception of some internal organs (e.g. stomach, liver, heart) ([108]). However, if we restrict ourselves to the shape of the human body, bilateralism hold. Similarly, the central nervous system is also symmetrical. An anatomical study of lateral symmetry in the human sulcus, brainstem and spinal cord ([19]) noted that there were only minor differences in structural symmetry. Similarly, there was also no significant lateral differences in the number of motor neurons in the spinal cord. The authors of the study ([19]) caution that in the context of the sensorimotor system, laterally specialized behaviors, like handedness, may not be supported by gross lateral differences in neural structures. A recent large scale by [86] with MRI scans of the brains of 106 left-handers and 1960 right-handers showed that there were no significant differences in the bilateral cortical surface areas between left and right-handers. And there was also no significant association of handedness to brain regions. A more recent review ([122]) also showed that although functional MRI reveal differences in brain structure relating to skill acquisition, neural correlates of handedness are ambiguious and difficult to pin down.

While limb dominance is clear in upper limbs, the limb dominance explanation for asymmetries in gait has been disputed in lower limb studies. An extensive review by [22] found that although limb dominance have been used as an explanation for gait asymmetries, several studies reviewed did not support the association between gait symmetry and limb dominance. [22] populates that limb dominance could be task specific, instead of reflecting underlying asymmetries. This is somewhat supported by [46] that skilled foot movements were executed more with the preferred foot, as compared with unskilled

foot movements. Also, [49] showed that vertical ground reaction forces were largely bilaterally symmetrical, with the exception that during faster walking speeds, propulsion forces of the dominant limb was slightly greater (7%) than the non-dominant limb.

Despite the ambiguity relating limb dominance and gait symmetry, restoring gait symmetry should be considered as an important clinical outcome. Hemiparesis, defined as weakness in one side of the body, is a common cause of gait asymmetries after stroke ([18]). Evidence has shown that asymmetry gait is energy inefficient and is associated with further complications, like joint pain, joint deformation, loss of bone mass in paretic hip ([76]). Asymmetry gait is also correlated with loss of bone density, usually in the paretic limb ([33], [123]), and also correlated to balance problems and falls ([90], [121], [129]). Therefore, effort should be made in understanding gait symmetry in stroke patients.

1.3 PURPOSE OF THESIS

With evidence of such tight coupling between the brain and body, there is no surprise to note that motor impairments are one of the most common ailments reported in stroke patients ([23]), which is associated with a lack of walking function in about 50% of stroke patients at the time of hospital admission ([16]). Hence, physical therapy programs are aimed at restoring gait functions using exercise and gait training. It is also worth to note gait training is the most prevalent activity, based on the amount of time spent on this type of training ([32], [81]).

In post-stroke patients, their gait patterns are markedly different from their healthy counterparts. Such changes include differences in gait velocity, kinematic profiles and spatiotemporal parameters (step length and stance time). Given the ease of implementation, gait velocity has been established as a clinical outcome measure to evaluate patients after therapy ([17], [24], [40]). However, recently, it has been suggested that gait velocity might not be sufficient as a marker for recovery, especially in stroke patients with hemiplegia, and that gait symmetry should be given more attention clinically ([48]). This points to a need to understand motor recovery from a neurological perspective.

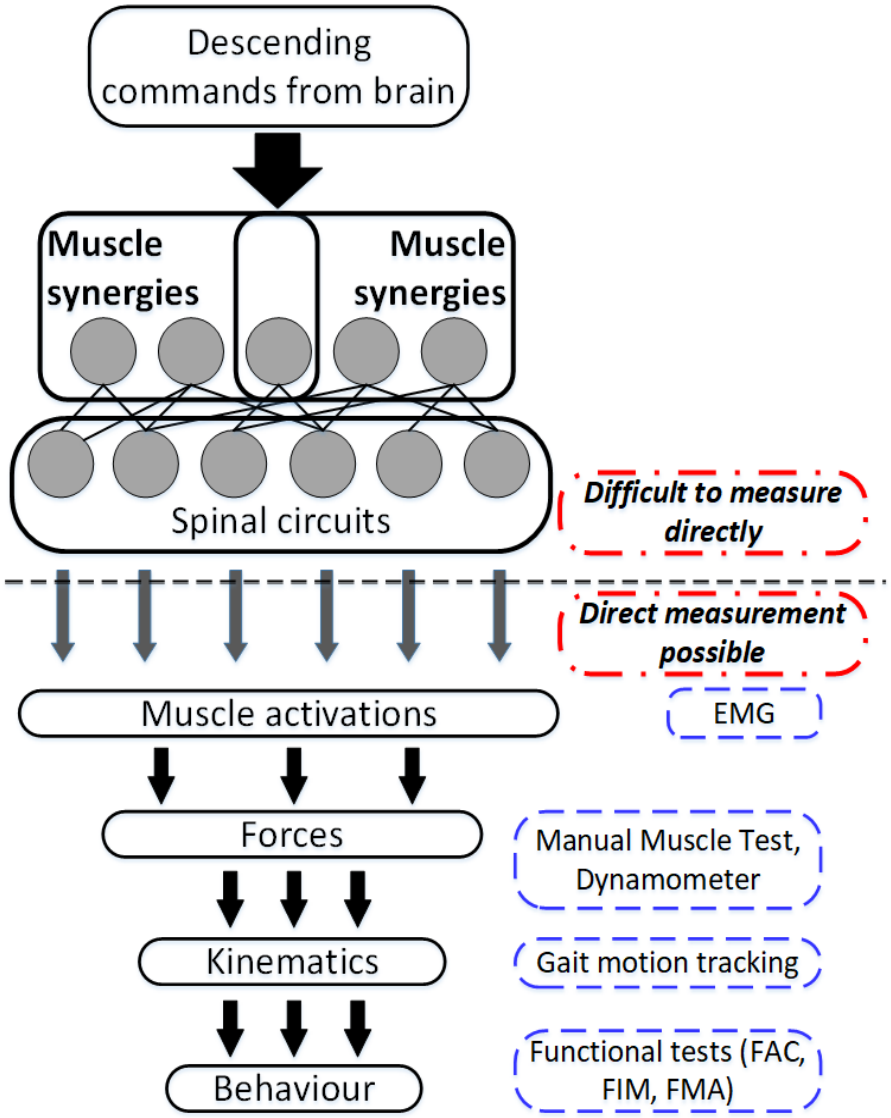


Figure 1.1: **Levels in human movement control** Adapted from [66]

The figure above (Figure 1.1) provides an overview about how human behaviour is generated. As stroke is a neurological disease, there is also a need to understand the reorganization of the nervous system after therapy. In this case, analyzing EMG would be a better alternative as compared to looking at kinematics, because it provides a better view on the state of the nervous system. However, EMG data is generally very high in dimension and difficult to analyze. To help reduce the dimension in data for analysis, muscle synergy theory proposes that spinal circuits are activated together at the same time to generate sufficient force to move the limbs.

In summary, to address the gap in knowledge about the neurological aspects of gait symmetry, this thesis presents:

- **The development of a measure of sEMG-based muscle coordination symmetry for gait**

- **The interpretation and translation of the analysis into a test that can be easily implemented by therapists, without specialized research equipment**

1.3.1 *Problem definition*

Functional stroke evaluation metrics such as the FAC ([9]), FIM ([11]), FMA ([6]), BI ([2]), BBS ([12]), Brunnstrom stages ([4]) have seen extensive use to assess the recovery in stroke patients. However, these scales measure motor recovery in terms of ability to function in daily living conditions, and only provides a gross overview of neurological health. Furthermore, spatiotemporal gait symmetries, like step length and stance time symmetry, were not adequately quantified with conventional functional stroke evaluation metrics ([58], [131]).

The correlation between gait velocity and gait symmetry is currently unclear, as this correlation changes, depending on the time where patients were evaluated. One study reported a correlation between increased gait velocity and step length symmetry (while other temporal gait parameters were not correlated with gait velocity) during inpatient rehabilitation over a mean length of stay of 30 days ([98]). As a note, the improvements in gait symmetry were not significant enough in the sample population, even there were correlations with gait velocity in one aspect of symmetry. The other study ([131]), who did followed stroke patients after discharge from a rehabilitation program for 6 months, found that gait velocity was significantly improved, spatiomtemporal gait symmetry was not significantly changed.

While spatiotemporal gait parameters represent another method to evaluate patients, it is still difficult to gain insight to the underlying neurological mechanisms affecting the control of limbs. The next step would be to examine muscle activations to evaluate the level of control in the limbs of stroke patients.

1.3.2 *Research Aims*

This thesis aims to evaluate muscle activation of stroke patients from the perspective of gait symmetry. One of the key questions addressed is whether muscle synergies are useful as an index to detect changes in muscle coordination symmetry in stroke patients. This would help provide some insight to the reorganization of the nervous system after stroke, since humans are bilaterally symmetrically, in terms of the number of limbs on each side of the body. The overall hypothesis is that muscle coordination analysis would reveal more about neuromuscular changes in the nervous system during rehabilitation, and gait symmetry provides some insight on whether the nervous system reorganizes in a symmetrical manner. The aims are summarized in a list below:

1. Examine which aspect of the muscle synergy method makes it suitable for analysis in stroke patients with healthy subjects
2. Examine the differences in gait symmetry of stroke patients before and after robotic therapy
3. Examine the differences in effect on gait symmetry by robotic therapy and conventional therapy
4. Develop a muscle synergy-based index to measure gait symmetry
5. Propose a simple gait symmetry measure for therapists without the need for specialized equipment to gather more data for future gait symmetry work

1.4 THESIS OUTLINE

Chapter 1 provides the overview of the research problem and aims of the thesis. Chapter 2 provides background on gait symmetry post stroke and current assessment methods. The chapter also relates how robots are deployed in therapy to aid therapists and finally provides some literature and related works on muscle synergies on how they have been used previously to evaluate the muscle coordination in stroke patients. Chapter 3, 4 and 5 can be read independently, as they describe separate studies. Chapter 6 proposes a simple evaluation method requiring minimal equipment for therapists to evaluate gait symmetry. The conclusion and future directions are also presented in Chapter 7.

2

BACKGROUND

Stroke, according to the World Health Organization (WHO) criteria, is defied as "rapidly developing clinical signs of focal (at times global) disturbance of cerebral function lasting more than 24 h or leading to death with no apparent cause other than that of vascular origin" ([130]). It is one of the leading causes of global mortality and disability, and is estimated to have a large economic burden, due to the costs of treatment and post-stroke care. ([130]). Given this large burden, it is important to understand the mechanism of stroke recovery and design better therapies to allow patients to regain functions quickly, without further negative complications.

2.1 HEALTHY AND POST-STROKE GAIT

2.1.1 *Healthy gait asymmetry*

Healthy gait symmetry, in terms of vertical ground reaction forces and stance time, can be defined as a deviation of around 4 to 14% from perfect symmetry ([13]). The study also noted that healthy gait is inherently asymmetric and cautions against using a single value threshold (e.g. 10% deviation) to decide between symmetric and asymmetric gait, as it might mistakenly misclassify a subject as asymmetric. A later study by Lathrop-Lambach et al. showed that joint angle asymmetry in the knee and hips of healthy subjects were higher than the predefined value of 10%, with median asymmetry ratios being around 20% ([89]). However, similar studies evaluating stroke patients showed that their joint angle asymmetries were typically of a much higher magnitude ([50]). As the threshold is currently unclear, joint kinematics results should not be used solely to determine the impairment level of a patient, but should be used in conjunction with other measures.

2.1.2 *Post-stroke gait asymmetry*

Hemiparesis, which is a common observance with stroke, generally cause gait asymmetries, due to weakness in one side of the body ([18]). It has been examined by researchers since the early 1980s due to its prevalence ([10], [15]). One finding is that step length asymmetry could be one compensatory mechanism after stroke ([61]). Recent evidence has shown that asymmetry gait is energy inefficient and is associated with further complications, like joint pain, joint deformation, loss of bone mass in paretic hip ([76]). Additionally, bone density in the paretic limb of stroke patients have been found to decrease after stroke. This could lead to further complications like fractures ([33],

[123]). Furthermore, there are significant correlation between balance (standing or dynamic) and gait asymmetry, which has been pointed out in various studies ([90], [129], [121])

However, despite much efforts that has been put into investigating gait symmetry, getting patients to recover gait symmetry is still not well understood, hampering the development of intervention methods. Also, gait asymmetry is considered to be difficult to correct in patients during therapy ([35], [47], [98]) and is predicted to worsen after discharge after 6 months ([131]). A longitudinal study showed that stroke patients actually had a worsening of gait symmetry years after discharge when evaluated with spatiotemporal measures of gait symmetry, but this worsening was not reflected in clinical scores and motor evaluation scores ([58]). Neurological studies also show that neurological symmetry is also an important factor to consider, as there is evidence that brain hemispheric asymmetry interferes with recovery ([57], [70]). This can be explained with interhemispheric inhibition, where activity on one side of the motor cortex can be inhibited by activity in the motor cortex on the opposite side ([25]), which also led to various studies examining how to utilize this neural mechanism in stroke recovery ([44], [111]). Taken together, this shows that symmetrical gait is an important factor to consider and should not be neglected when designing therapies to restore gait functions.

2.2 ROBOT-ASSISTED THERAPY

With the development and commercialization of technology, various robotic exoskeletons have been developed for therapy Some examples of them are the Hybrid Assistive Limb (HAL) ([29]), ReWalk ([77]), Lokomat ([27]) and the Lopes ([43]). These robots assist patients either by generating a pre-defined sequence of walking motion, or provide assistive torque on demand to joints in the lower limbs, via onboard sensors to detect the phase of gait. Studies evaluating the success of exoskeletons in general focus on clinical outcomes, like gait speed and functional recovery scores ([84], [93]), with one study further reporting on functional recovery scores being maintained after 2 months ([120]). [105] did an extensive review on various studies that looked into the effects of exoskeleton on therapy. However, their main conclusion is that it is too early to conclude that the benefits in rehabilitation is worth using powered exoskeletons, although they noted that clinical trials demonstrated the safety of such exoskeletons. In an earlier study, [62] also arrived at a similar conclusion that there is a need to develop standardized protocols to assess the effectiveness of powered exoskeletons in rehabilitation for stroke patients.

In general, while these studies show that robot-assisted therapy is beneficial to patients, it is difficult to use functional recovery scores to gain insights about what aspects of gait benefits from the use of robots. Coupled with the differences in control mechanism of each

robot listed above, it becomes even more difficult to draw any meaningful conclusions about neurological recovery in patients.

2.3 MUSCLE SYNERGY ANALYSIS

Muscle synergies theory proposes that co-activations of muscles involved in complex movement can be described with muscle synergies or motor modules. It was first suggested that the nervous systems of creatures requires some form of dimension reduction to deal with the complexity of controlling the many degrees of freedom in the body ([3]). This was noted as the sum of forces from different muscles ([7]). These co-activation of muscles to create movement was termed as motor primitives, as evidence from a frog spinal cord stimulation study showed ([14]). Subsequent studies hypothesized that muscle synergies are able to utilize a combination of motor primitives and generate different repertoires of movement with a small number of motor primitives ([14], [37], [39], [78]). This gave rise to an analysis method, called Muscle Synergy Analysis (MSA) has been used previously to describe postural or locomotion tasks in humans ([39], [42]). These synergies can be considered strategies that the human nervous system employs to facilitate control of limbs.

MSA is based on a mathematical method called the Non-Negative Matrix Factorization (NNMF) [21], used to factorize high dimensional data in order to simplify data processing. The figure below (Figure 2.1) illustrates generally how EMG can be decomposed into spatially grouped muscles (muscle synergies) and their corresponding activation (timing coefficients)

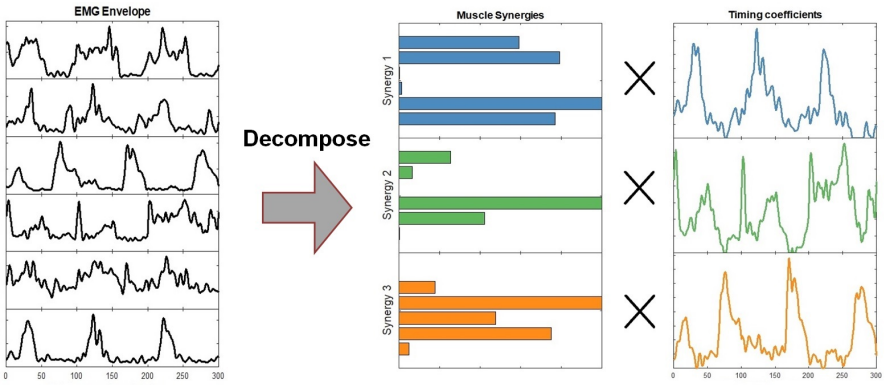


Figure 2.1: **Muscle synergy decomposition** An overview on how the method works

A generalized equation of muscle synergies can be seen below (Equation 2.1)

$$A_{ij} = (\sum_{x=1}^{r} W_{ix} T_{xj}) + \epsilon \tag{2.1}$$

with a constraint of $\epsilon = 0 : r = i$ where the error between the measured data and reconstructed data becomes zero when the number of

synergies match the number of dimensions in the data. Variables are listed below:

- A : Dataset (i rows and j columns)
- i : Rows (Channels in EMG)
- j : Columns (Data)
- x : Current number of synergies
- W : Muscle synergies
- T : Timing coefficients
- ϵ : Reconstruction error
- r : Maximum number of synergies selected

Muscle synergies have been shown to be useful in detecting pathological changes due to neurological disease, like stroke. For example, MSA has been used in various studies analyzing the gait of stroke patients ([53], [63], [80], [110]). Evidence from these studies show that muscle synergies are significantly different from healthy controls during walking, suggesting that stroke patients do indeed change the way they walk. More detailed analysis noted that the number of synergies that can be extracted from stroke patients were lesser, as compared to healthy controls, suggesting that the number of synergies could indicate the level of control in the limbs ([53]). The reduced number of synergies were also correlated with asymmetric step length and force propulsion ([53]).

Muscle synergies have also been shown to be robust between subjects ([69]) and even between days ([107]) making it a very useful tool to analyze EMG data. Also, muscle synergies are suggested to be invariant to gait velocity ([101]), which is further demonstrated in a computation model where it is possible to achieve a wide variety of gait velocity by modifying a few parameters ([128]). This is in contrast to joint kinematic analysis, which is showed to be affected by gait velocity ([36], [41]), which might make kinematic analysis difficult.

Because of the numerous advantages of using MSA, this thesis aims to develop this method into an index that could be easily used and understood by therapists.

Part II

MUSCLE COORDINATION SYMMETRY

3

MUSCLE SYNERGY DIFFERENCES IN HEALTHY INDIVIDUALS WHEN USING A LUMBAR SUPPORT EXOSKELETON

3.1 ABSTRACT

The human lower back is quite vulnerable to injury, as noted by the number of lower back problems in the world. This leads to several passive lumbar support devices available in the market. Recently, active lumbar support exoskeletons have developed to provide assistance via the use of motors. However, the effects of such devices on muscle use are not well understood, despite beneficial effects, like less back pain, being reported. In this study, we examined the short-term change in muscle coordination of subjects using a lumbar support exoskeleton in a stoop lifting task. The exoskeleton is triggered by bioelectric signals from the user's lower back muscles. Main muscle coordination changes observed were in the timing coefficients of muscle synergies as subjects fatigue, while minimal changes were observed in the contents of muscle synergies. One interpretation of the change in timing coefficients during fatigue could be that the dynamics of the motion is changed, where the angular velocity of the hip joint is generally faster when the lumbar exoskeleton is used. Understanding how muscle coordination change with the use of active exoskeletons would be helpful to design future generations of assistive exoskeletons.

3.2 INTRODUCTION

3.2.1 *Assistive exoskeletons for lumbar heath*

Lower back health issues are common globally and expected increase quite substantially ([72]). This problem affects productivity in various jobs and places a significant burden on the healthcare system ([45]). Even healthcare workers like nurses are also affected and, ironically, identified to be the most vulnerable to lower back pain ([83]).

In recent years, various assistive exoskeletons have been developed to alleviate this problem, mainly in the industrial sector. A review by Looze et al. ([104]) found that such devices were able to reduce back muscle activity when users were engaged in physical labour. Other versions of lumbar support exoskeletons were also developed for general use, for example, like the Hybrid Assistive Limb (HAL) for Lumbar Support ([54]) and the Smart Suit Lite, for the healthcare sector ([64]).

Researchers were also interested in the effects of lumbar support exoskeletons outside of the industrial sector. For example, [125] showed that that human performance in a snow-shoveling task was enhanced, while fatigue was reduced on the user. A longer term study by [113], evaluated changes in the human body when a lumbar support exoskeleton was worn continuously for a work day, over a 2-week period. They found participants did not experience any decrease in muscular strength, but had the benefit of a reduction in perceived fatigue. This suggests that wearing the lumbar support exoskeleton for longer periods of time did not produce any adverse effects in healthy subjects.

3.2.2 *Muscle coordination method*

Despite the beneficial effects of lumbar support exoskeletons on human task performance and general lumbar health, changes in muscle coordination of such device users were not studied in detail. This study is motivated by the lack of understanding on how muscle coordination change when lumbar support exoskeletons are used. We propose the use of muscle synergy analysis to study such changes. This is because muscle coordination is proposed to be modular in nature ([26], [31]). In these literature, such modules are known as muscle synergies and it is hypothesized that the central nervous system modulates the activation of muscle synergies to achieve movement. Although other studies pointed out limitations of using muscle synergies to understand how the central nervous system works ([94]), the muscle synergy framework has been a useful tool to characterize and describe quite a large range of human and animal movements ([37], [63], [68], [78], [102]).

More recent studies indicate that the use of active exoskeletons for the lower limbs does indeed change muscle coordination patterns in humans, when used in a locomotion task ([118], [92], [30]). We hypothesize that these changes can also be observed when a lumbar support exoskeleton is used, as wearing an exoskeleton is, in face, putting a foreign object on the human body. This leads to an immediate structural change to the shape of the human body, which could require users to adapt to the new kinematics and kinetic constraints imposed by the lumbar support exoskeleton. To summarize, we use muscle synergy analysis to evaluate changes in muscle coordination when the lumbar support exoskeleton is used by subjects in a stoop lifting task. A fatiguing protocol was used to exhaust the subject in trials with and without the lumbar support exoskeleton, so as to differentiate the effect of the lumbar support exoskeleton.

3.3 METHODS

This study was carried out in accordance with the recommendations of the University Guidelines for Clinical Trials, Institutional Review

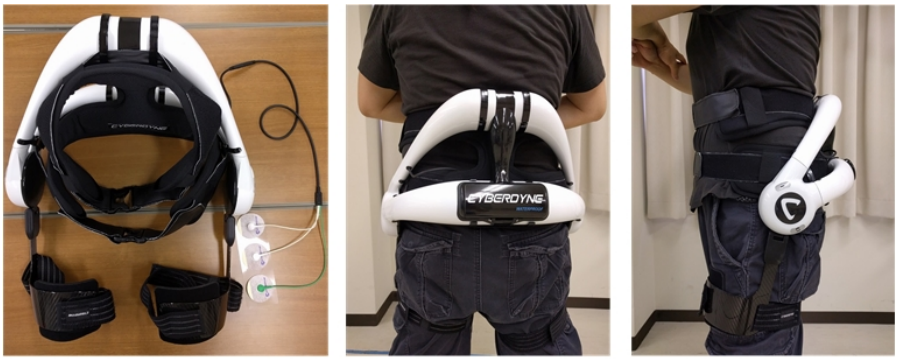
Board of University of Tsukuba Hospital, with written informed consent from all subjects. The protocol was approved by the Institutional Review Board of University of Tsukuba Hospital. The University Guidelines for Clinical Trials conforms to the ethical principles of the Declaration of Helsinki. All subjects provided written informed consent in accordance with the Declaration of Helsinki.

3.3.1 *Subjects*

20 healthy, right-handed subjects (13 male, 7 female), aged $22-43$ (31.5 ± 6.6) were recruited from the University of Tsukuba and University of Tsukuba Hospital. Subjects were screened before the study to ensure they are free from neurological and musculoskeletal disorders.

3.3.2 *Lumbar Assistive Device*

The commercial version of the lumbar support exoskeleton (Fig. 3.1), named HAL for Care Support (Cyberdyne, Ibaraki, Japan) [54] (will be referred to as Lumbar HAL in the rest of the study), was used in our study. This device consists of a frame and two motors attached to its sides. The frame is designed to restrict the movement of the lumbar vertebrae. Absolute angles of the user's trunk are measured with a triaxial accelerometer embedded in the exoskeleton, and relative joint angles are measured with potentiometers in the actuators. Straps and fasteners were wrapped around the user's trunk and thighs to secure the exoskeleton around the hips. The actuators provide assistive torque about the hips by applying force on the thigh and trunk. The assistive torque is triggered and controlled by muscle activations, measured by electrodes attached to the skin surface above the user's lumbar erector spinae muscles. A gain parameter on the muscle activations was manually adjusted until the user feels comfortable controlling the exoskeleton.



(a) HAL Lumbar Support Exoskeleton

(b) Back view of exoskeleton on subject

(c) Side view of exoskeleton on subject

Figure 3.1: **Lumbar HAL exoskeleton** Fitting of exoskeleton on body

3.3.2.1 *Electromyography (EMG)*

Skin preparation included wiping down the muscle bellies with alcohol swabs. 8 wireless, surface EMG electrodes (Trigno Lab, Delsys Inc., Boston, MA, USA) were placed bilaterally over the muscle bellies of: biceps brachii (BB), latissimus dorsi (LD), erector spinae (ES) and gluetus maximus (GM). EMG was sampled at 2000 Hz.

3.3.2.2 *Motion Capture system*

Motion tracking of subjects was achieved with the Vicon Motion Capture system (MX System, 16 T20S Cameras, VICON, Oxford, UK). 6 reflective markers were placed bilaterally on the acromion, great trochanter and lateral malleolus. Motion tracking was synchronized with EMG and sampled at 100 Hz.

3.3.3 *Experiment Protocol*

Subjects were asked to perform 2 trials (one with HAL and one without HAL) of stoop lifting/placing, until they feel they cannot continue. In each session, subjects were asked to lift and place a small box, (for males, 12kg, for females, 6kg). A metronome was used to regulate the speed of each lift cycle. The metronome was set to 30 beats per minute, which approximately allowed the subject to perform either one lift or place action every 2 seconds. A 15-minute break was given after each session to allow the subject to recover before starting the second session. Order of sessions were randomized for each subject (either starting with HAL or starting without HAL) to account for accumulated fatigue. Out of 20 subjects, We have 12 subjects that started the experiment without HAL, and the remaining 8 subjects, started with HAL.

Subjects were given time to familiarize themselves with the task and exoskeleton before each session until they feel ready. A silent observer counted the number of times the subject lifted the box. At the end of each session, subjects were also asked to evaluate their perception of fatigue on a Visual Analog Scale (VAS) from 0 to 10. The scale used is a 10 cm long continuous line, with the left end marked as '0' and the right end marked as '10'. Subjects indicated their perceived fatigue with a mark anywhere on the line. The distance of the mark to '0' was measured and recorded as the perceived fatigue.

3.3.4 *Data analysis*

3.3.4.1 *Software*

Data extraction, NNMF and the rest of the processing were performed with scripts on MATLAB 9.3 (Mathworks, Natick, MA, USA).

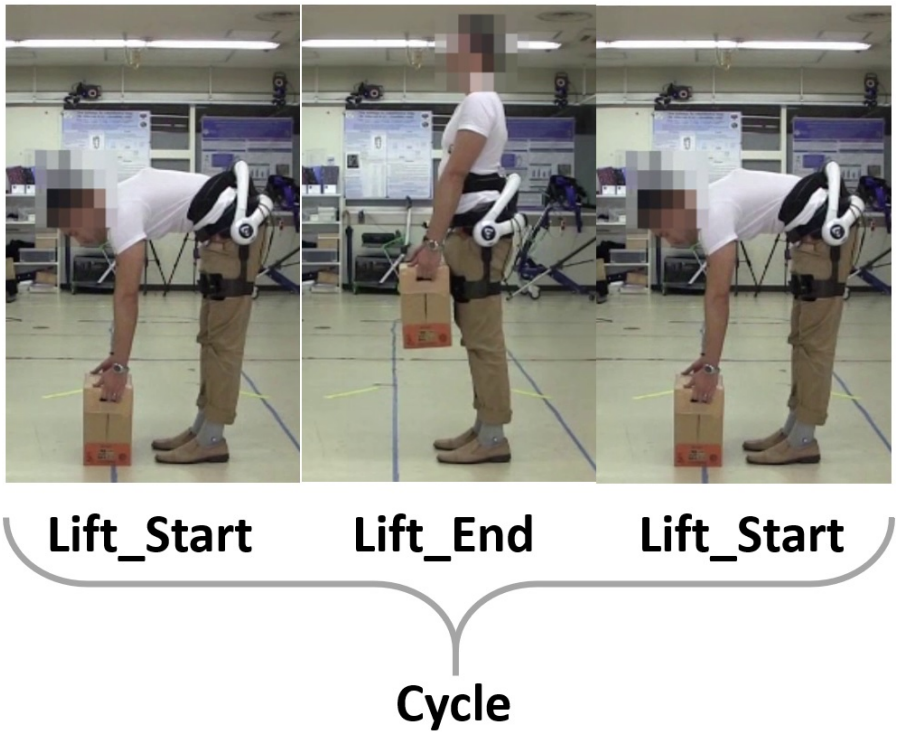


Figure 3.2: **Definition of a lifting cycle** A lifting cycle is a combination of box lifting and placement

3.3.4.2 *Preprocessing*

EMG data was first filtered with a 4th order, zero-lag Butterworth band-pass filter at 30 - 400 Hz. The bandpassed EMG was then filtered with a Hampel filter, with the parameters, time window, win $= 200$ and a threshold of $\sigma = 4$ (standard deviations), to remove artefacts. Finally, EMG data was fully rectified and low-passed with a 4th order, zero-lag Butterworth low-pass filter at 6 Hz to obtain the EMG envelope.

3.3.4.3 *Extraction of EMG based on kinematic data*

A lifting cycle consist of the subject lifting the box to an upright position, and placing the box back down again, as shown in the figure below (Fig. 3.2). 4 conditions were defined for analysis. They are:

1. No HAL Non-Fatigue
2. No HAL Fatigue
3. HAL Non-Fatigue
4. HAL Fatigue

The "Non-Fatigue" condition is defined to be 3 consecutive and consistent lifting cycles within the first 20% of the total number of lifting cycles for the session. This is to account for adaptation of subjects to the task. The last 3 consecutive lifting cycles for each session were defined as the "Fatigue" condition.

EMG envelope of 3 consecutive, consistent stoop lifting cycles were extracted. Each extracted cycle was normalized by its standard deviation and also interpolated to 100 time points per envelope. Finally, all extracted envelopes were concatenated to obtain a 300-by-8 matrix.

Consistency in peak angles and angular velocity were determined for the Non-Fatigue conditions by selecting 3 consecutive lifting cycles with the minimum total absolute difference in peak angles and angular velocities (Eqn 3.1). This is defined as:

$$i_{Non-Fatigue} = \mathrm{argmin}_i\left(\Theta_i^U + \Theta_i^D + \Omega_i^U + \Omega_i^D\right) \tag{3.1}$$

where the variables are defined as:

$$\Theta_i^U = |\theta_i^U - \theta_{i+1}^U| + |\theta_i^U - \theta_{i+2}^U| + |\theta_{i+1}^U - \theta_{i+2}^U| \tag{3.2}$$
$$\Theta_i^D = |\theta_i^D - \theta_{i+1}^D| + |\theta_i^D - \theta_{i+2}^D| + |\theta_{i+1}^D - \theta_{i+2}^D| \tag{3.3}$$
$$\Omega_i^U = |\omega_i^U - \omega_{i+1}^U| + |\omega_i^U - \omega_{i+2}^U| + |\omega_{i+1}^U - \omega_{i+2}^U| \tag{3.4}$$
$$\Omega_i^D = |\omega_i^D - \omega_{i+1}^D| + |\omega_i^D - \omega_{i+2}^D| + |\omega_{i+1}^D - \omega_{i+2}^D| \tag{3.5}$$

where $\theta_i^U, \theta_i^D, \omega_i^U$ and ω_i^D are the ith peak angles and angular velocities respectively of the hip joint projected to the sagittal plane, during lifting up and down. Θ and Ω are vectors representing the total absolute differences in peak angles and angular velocities. The superscripts represents the phase of the lifting cycle subject is in, with Θ^U and Ω^U representing transition from the Lift_Start to Lift_End phrase, and Θ^D and Ω^D representing transition from the Lift_End to Cycle_End phrase (Fig 3.2). Peak angles are additionally defined to be 95% of the actual peak values, so as to account for minute movements of the subjects when they are maintaining their posture. Figure 3.3 depicts how the threshold for hip angle values were applied to segment each lifting cycle

3.3.4.4 *Task and Kinematics Analysis*

Subjects were evaluated on the number of times they were able to lift the box and their perceived fatigue. Peak hip angles and angular velocities of each lifting cycle during each session were also evaluated. Instantaneous velocity profiles were first extracted by differentiation of the vector of hip angle values for each action. The velocity profiles were averaged over 3 actions for each subject and further averaged for all subjects for each condition. The obtained angular velocity profiles were then resampled to 100 time points for plotting. In addition, Root Mean Square (RMS) values of the EMG of each muscle were evaluated for each condition defined in Section 3.3.4.3.

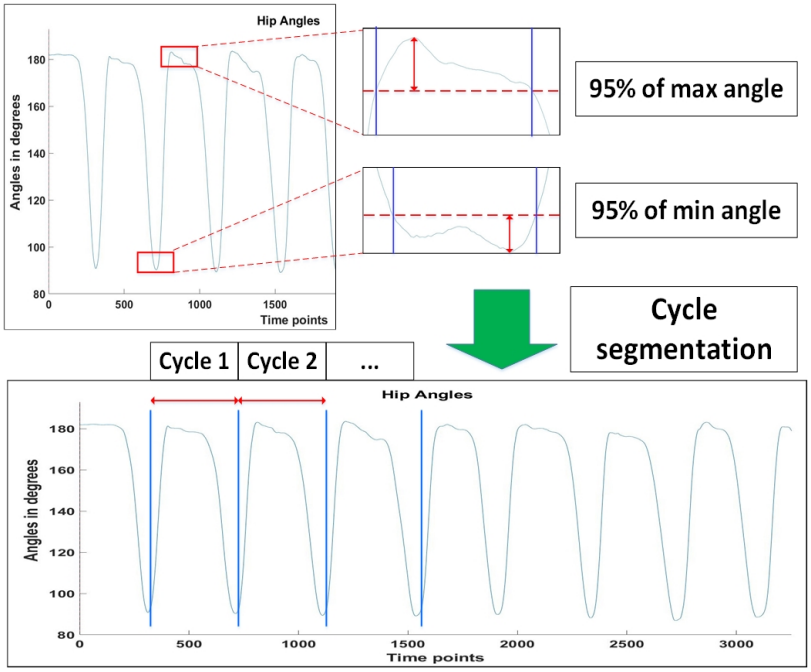


Figure 3.3: **Kinematic segmenting method** Thresholding of angle values and cycle segmentation of subjects

3.3.4.5 *Muscle synergy extraction with NNMF*

NNMF was then used to extract muscle synergies and timing coefficients from the concatenated EMG data. This was performed with Matlab's NNMF function (Matlab Version 9.3, 2017b), using the multiplicative update algorithm. Parameters for the tolerance for the residual (TolFun) was given as $1e-6$ and the tolerance for the relative change in elements (TolX) was given as $1e-4$. The algorithm was repeated 300 times with different random starting values of the synergies and timing coefficients. Results with the lowest root mean square residual were taken to be the best. Synergies were allowed to vary during the decomposition process.

The choice of number of synergies were determined with the criteria of when the variance-accounted-for (VAF_{muscle}) for each muscle vector was above 75% [42]. From our results below (Section 3.4), we fixed the choice of the number of synergies to be 3, as it is sufficient to represent the EMG profiles of all subjects.

The VAF is defined as $100 * (\text{uncentered Pearson correlation coefficient})$ [37]. This is given as:

$$VAF = 100 \cdot \left(\frac{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm} \cdot Y_{nm})^2}{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm}^2) \cdot (\sum_{j=1}^{m} \sum_{i=1}^{n} Y_{nm}^2)} \right) \tag{3.6}$$

where n is the number of datapoints for each channel, and m is the number of channels. For the single muscle vector case, m is simply 1. X_{nm} and Y_{nm} are the matrices containing the reconstructed and

original signal respectively. VAF calculation code is adapted from the "rsqr_uncentered" function in the file "PosturalData_NMFvsPCA_GUI_July2013" given in [106].

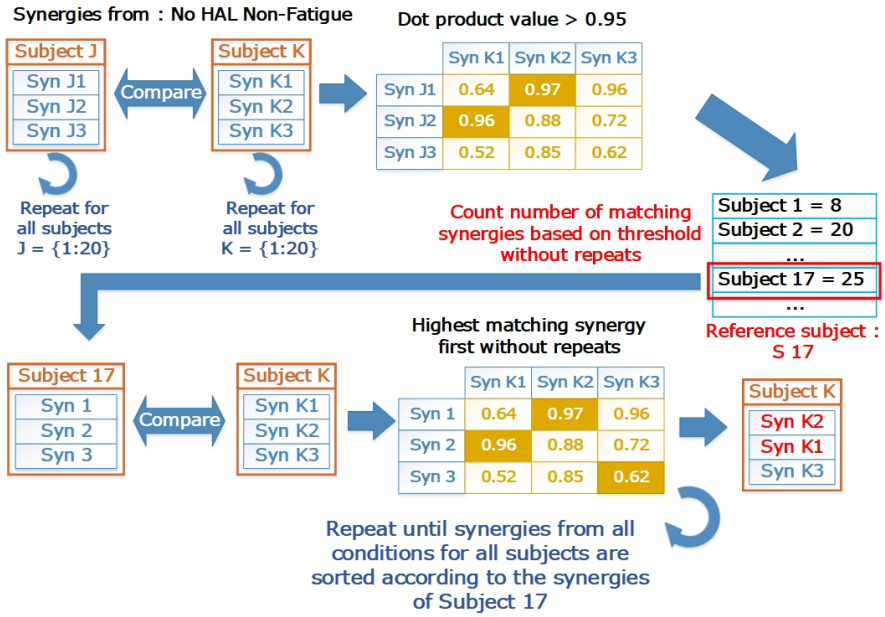


Figure 3.4: **Synergy sorting process**. The reference subject was selected by counting the number of matching synergies. Letters "J" and "K" refer to loop indices to indicate how the comparison is carried out in a loop to test all pairs of subjects. "J" are the indices for the outer loop, while "K" are the indices for the inner loop. The base condition for the subject (Subject 17, No HAL Non-Fatigue) was then selected as a reference where all other synergies from different conditions and subjects were matched with. After matching, the synergies were sorted according to the indices of the reference subject

To ensure that the synergies were in the correct order, we sorted the muscle synergy vectors, and their corresponding timing coefficients in relation to a reference subject, using a procedure similar to the greedy search procedure defined in [73]. We first chose a reference subject by comparing the synergies extracted from the base condition (No HAL Non-fatigue) for each subject. The subject with the highest number of matching synergies to the subject population was selected as the reference. After that, synergies and timing coefficients of all subjects from all the conditions were sorted according to the reference subject. Figure 3.4 provides a graphical view on the sorting process. Briefly, the sorting procedure compares a reference synergy vector (X, from Subject 17 in our case), with another synergy vector from a different condition/subject (Y), and pairs them such that the dot product value between X and Y is the highest. This pair is then removed from comparison. The procedure is repeated until all synergy vectors are paired. Indices of the vector being sorted (Y) were then arranged to match the order of the reference vector

3.3.4.6 *Synergy Analysis*

We first evaluated the reconstruction quality with the VAF for each condition. This is for deciding the number of synergies used for further analysis. As mentioned in the section above (Section 3.3.4.5), the reconstruction quality is considered sufficient when the VAF for all individual muscle vectors are above 75%. The use of the uncentered correlation coefficient is due to that it is proposed to be more stringent than the classic centered correlation coefficient, as it evaluates both the shape and magnitude of the data [37].

We also evaluated the magnitude of change when using Lumbar HAL by evaluating the similarity between sets of conditions with the centered Pearson correlation coefficient (R). Since we are interested in the overall difference, the centered correlation coefficient would be sufficient. Muscle synergy vector comparison with the scalar dot product [68] was also performed. This is to evaluate the difference in contents of the muscle synergy vectors, as the calculating the metric normalizes each vector prior to comparison. Each muscle synergy vector was compared with the corresponding vector in the same position for different condition. Timing coefficients were compared with the Uncentered Pearson Correlation Coefficient, in a similar manner as the muscle synergy vectors. This is for evaluating the shape and magnitude differences between timing vectors for different conditions.

To evaluate the significance of the change in synergies against the chance level, we extracted synergies from a random dataset. This dataset is generated by shuffling the data in each EMG muscle channel independently. This is done for every subject. Shuffled EMG data were extracted for processing based on the indices chosen in Section 3.3.4.3. The shuffling and extraction were repeated until 100 sets of raw EMG were obtained for all 4 conditions (4x100 dataset, each dataset containing 300 datapoints-by-8 channels), for every subject. Preprocessing as described in Section 3.3.4.2 was performed on the extracted data. Synergies and timing coefficients were extracted by NNMF described in Section 3.3.4.5, and compared in a similar way as the paragraph above (Section 3.3.4.6). Synergies with the highest similarity value from each of the 4 conditions (Best out of 100) were chosen to be the chance level for comparison.

Similar to [124], to evaluate the amount of mutual information between different conditions, synergy weights from one condition were used as a basis to decompose EMG from other conditions. The synergy weight was kept fixed during the entire decomposition process, while the timing coefficients were allowed to vary. This was achieved with a modified NNMF algorithm. Parameters for the modified algorithm was the same as the one described in Section 3.3.4.5 (Multiplicative update rule, TolFun : $1e-6$, TolX : $1e-4$, Replicates : 300). Evaluation of the timing coefficients were also performed in a similar

manner, with the modified algorithm using the same parameters, but with the timing coefficients fixed instead of the synergy weights.

3.3.4.7 *Statistical analysis*

Statistical comparison was performed on paired data with the Wilcoxon Signed-Rank Test. The 2-way ANOVA is used to independently compare the RMS values of muscles under different conditions. Significance was considered in comparisons with $p < 0.05$.

3.4 RESULTS

3.4.1 *Task related metrics*

Number of task repetitions and perceived fatigue

The figure (Figure 3.5) below depicts the difference in task repetitions.

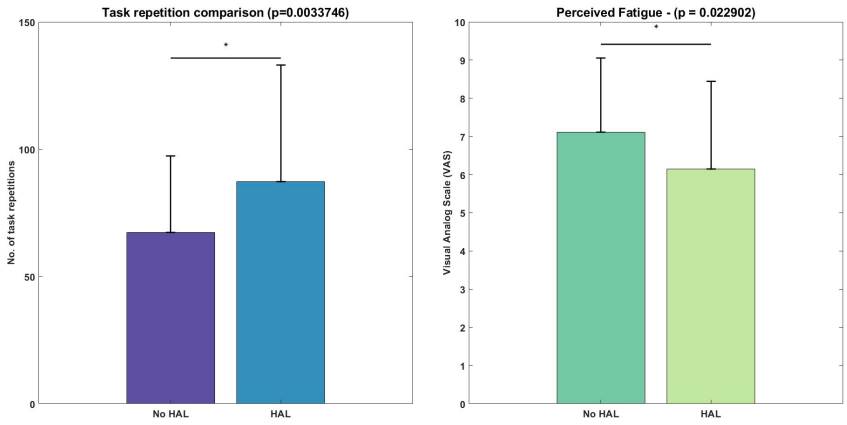


Figure 3.5: **Task and perceived fatigue** Difference in number of lifting cycles achieved and perceived fatigue, evaluated with the Wilcoxon Signed-Rank test. Asterisks denote significance level of $p < 0.05$

Figure 3.5 depicts the task metrics. Subjects were able to perform significantly more lifting cycles using the exoskeleton, as compared with not using the exoskeleton (HAL condition : 87.2 ± 45.93 vs No HAL condition : 67.25 ± 30.17, $p = 0.0034 < 0.05$). Perceived fatigue was significantly less when using the exoskeleton as compared to when they were not using the exoskeleton (HAL condition : 6.15 ± 2.30 vs No HAL condition : 7.12 ± 1.94, $p = 0.023 < 0.05$).

Kinematics

From the lifting cycle depicted in Figure 3.2, there were no significant differences in peak hip angles between conditions in the "Lift_End" phase (Figure 3.6). However, peak hip angles in the "Cycle_End" phase were significantly different when in the Non-Fatigue condition, both with and without HAL (*HAL* : 96.65 ± 7.74 vs *No HAL* 102.61 ± 12.62, $p = 0.025 < 0.05$). Similarly, significant differences were observed in

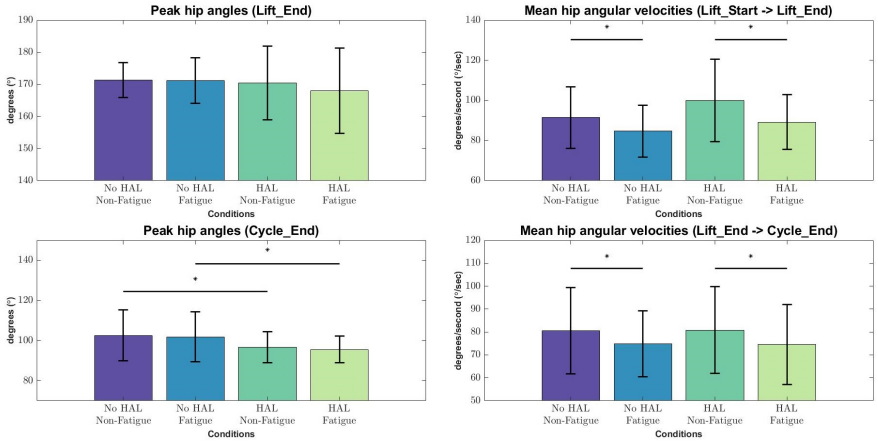


Figure 3.6: **Kinematics** Peak angles and velocities for each condition during each phase of the lifting cycle, evaluated with the Wilcoxon Signed-Rank test. Asterisks denote significance at the level $p < 0.05$

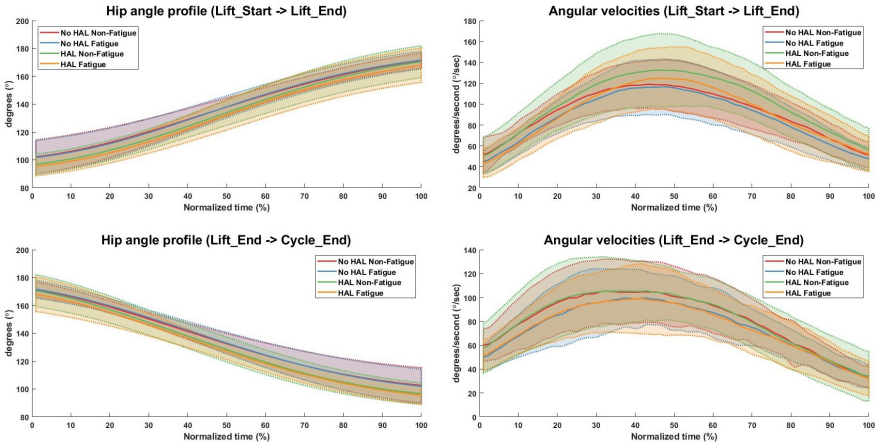


Figure 3.7: **Hip angle and angular velocity profiles** Bold lines indicate the mean velocity profile of all subjects, while shaded areas are the standard deviation. Dotted lines at the boundary of the shaded areas are drawn for better visualization.

the peak hip angles in the Fatigue condition, with HAL and without HAL (*HAL* : 95.61 ± 6.68 vs *No HAL* 101.90 ± 12.37, $p = 0.019 < 0.05$)

Angular velocities were significantly different in the "Lift_Start $\rightarrow$ Lift_End" phase, as subjects appear to slow down as they are fatigued, regardless of the exoskeleton (*No HAL Non-Fatigue* $\rightarrow$ *No HAL Fatigue* (91.51 ± 15.33 to 84.67 ± 12.84, $p = 0.0022 < 0.05$) and *HAL Non-Fatigue* $\rightarrow$ *HAL Fatigue* (100.03 ± 20.62 to 89.24 ± 13.56, $p = 0.00052 < 0.05$)). A similar trend can be also observed in the "Lift_End $\rightarrow$ Cycle_End" phase, where subjects slow down significantly when they become fatigued, both with and without the exoskeleton (*No HAL Non-Fatigue* $\rightarrow$ *No HAL Fatigue* (80.60 ± 18.83 to 74.80 ± 14.42, $p = 0.017 < 0.05$) and *HAL Non-Fatigue* $\rightarrow$ *HAL Fatigue* (80.83 ± 18.92 to 74.55 ± 17.50, $p = 0.028 < 0.05$)). Figure 3.7 provides a detailed view

of the mean instantaneous velocity profiles of the hip angular velocity under different conditions.

3.4.2 *EMG analysis*

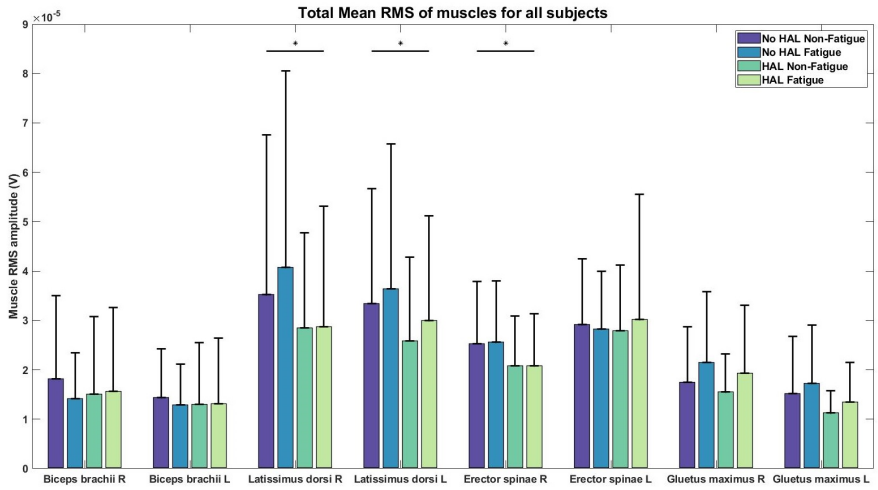


Figure 3.8: **RMS values of EMG**. Asterisks denote significance level of $p < 0.05$ for conditions involving HAL

Muscles \ Condition	HAL	Fatigue	HAL and Fatigue
BB Right	0.6002	0.1947	0.0586
BB Left	0.8117	0.3675	0.3172
LD Right	**0.0465**	0.2876	**0.0477**
LD Left	**0.0232**	0.1121	0.4223
ES Right	**0.0353**	0.9282	0.7894
ES Left	0.9113	0.7881	0.5426
GM Right	0.1538	**0.0140**	0.8872
GM Left	0.0528	**0.0211**	0.8808

Table 3.1: **Comparison of RMS** p-values of 2-way ANOVA analysis of RMS values for comparison between conditions

Figure 3.8 depicts the difference in RMS values in a graphical form while Table 3.1 provides a detailed view of the independent ANOVA comparisons between conditions. The RMS values are reported in the order of

1. No HAL Non-Fatigue
2. No HAL Fatigue
3. HAL Non-Fatigue

4. HAL Fatigue

There was a significant effect of the HAL on the RMS values of the Right LD ((**1.**)$3.5206e-05 \pm 3.2421e-05$ V, (**2.**)$4.0727e-05 \pm 3.9793e-05$ V, (**3.**)$2.8510e-05 \pm 1.9211e-05$ V, (**4.**)$2.8761e-05 \pm 2.4337e-05$ V) and Left LD ((**1.**)$3.3420e-05 \pm 2.3219e-05$ V, (**2.**)$3.6415e-05 \pm 2.9327e-05$ V, (**3.**)$2.5879e-05 \pm 1.6962e-05$ V, (**4.**)$2.9967e-05 \pm 2.1204e-05$ V) muscles, as well as, in the Right ES ((**1.**)$2.5311e-05 \pm 1.2528e-05$ V, (**2.**)$2.5587e-05 \pm 1.2384e-05$ V, (**3.**)$2.0858e-05 \pm 1.0023e-05$ V, (**4.**)$2.0784e-05 \pm 1.0576e-05$ V) muscles. For non-HAL changes, fatigue significantly changes the RMS values of both the Right GM ((**1.**)$1.7515e-05 \pm 1.1252e-05$ V, (**2.**)$2.1528e-05 \pm 1.4346e-05$ V, (**3.**)$1.5489e-05 \pm 7.6860e-06$ V, (**4.**)$1.9371e-05 \pm 1.3649e-05$ V) and Left GM ((**1.**)$1.5211e-05 \pm 1.1590e-05$ V, (**2.**)$1.7249e-05 \pm 1.1824e-05$ V, (**3.**)$1.1243e-05 \pm 4.5360e-06$ V, (**4.**)$1.3490e-05 \pm 7.9955e-06$ V) muscles, although marginal significance was observed for the Left GM muscles when HAL was used (Table 3.1).

3.4.3 *Number of muscle synergies and reconstruction*

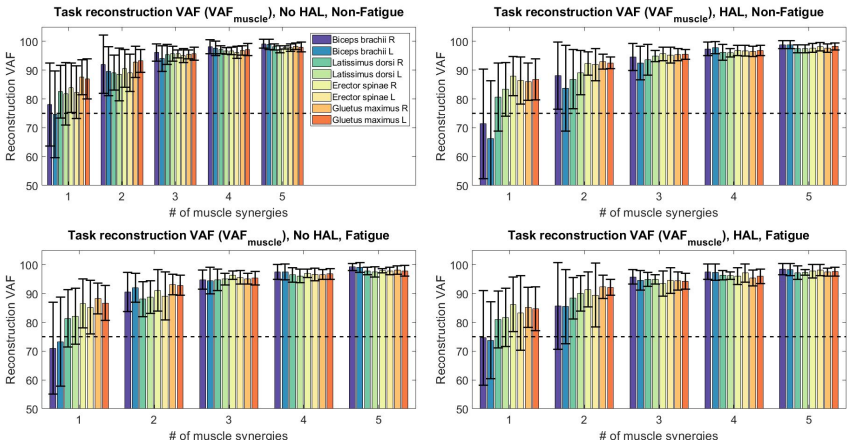


Figure 3.9: **Reconstruction VAF values for all sessions and conditions**. With 3 synergies, reconstruction quality of all subjects are above 75%

Figure 3.9 above depicts the reconstruction VAF in relation to the number of synergies used for reconstruction. With the threshold set at 75% (dotted lines in Figure 3.9), we can see that 3 synergies are able to reconstruct the EMG profiles under different conditions sufficiently for all muscle vectors.

For further analysis, we fixed the number of synergies to 3, as it would provide the best trade-off between reconstruction quality and number of synergies. All subjects were used for further analysis.

3.4.4 *Synergy changes during exoskeleton use*

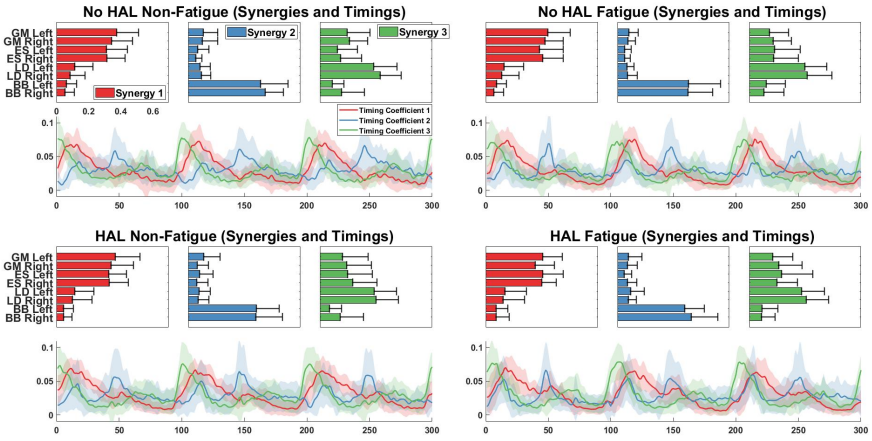


Figure 3.10: **Synergy vectors and timing coefficients from all conditions** Each triple subplot depicts the mean of each synergy vector across all subjects. Error bars indicate the standard deviation. Timing coefficients are depicted below synergies. The bold lines indicate the mean timing coefficients across all subjects while the shading indicates the standard deviation.

Figure 3.10 shows the extracted synergies and timing coefficients from different conditions for all subjects.

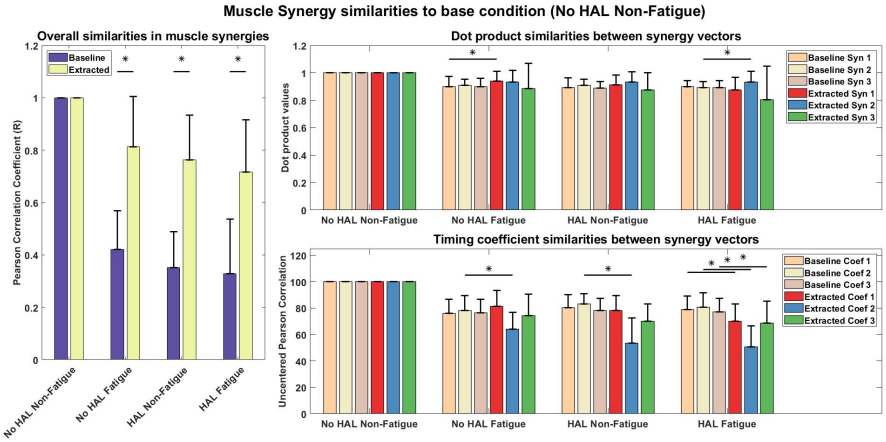


Figure 3.11: **Muscle synergy and timing coefficient comparisons** The Left plot compares overall difference of sorted muscle synergy vectors from all conditions with the base condition, which is the No HAL Non-Fatigue condition. The Top Right plot depicts the dot product differences for each muscle synergy vector against another muscle synergy vector with the same position in the baseline condition. Similarly, the Bottom Right plot compares each timing coefficient vector with the timing coefficient vectors in the same position of the baseline condition. Asterisks denote significance of $p < 0.05$ of the Wilcoxon Signed-Rank test. 'Baseline' indicate that the synergies were from randomly shuffled data, while 'Extracted' refer to synergies extracted from actual data

Figure 3.11 shows the comparison of synergies from different conditions with a chosen base condition, which is the No HAL Non-Fatigue condition. The overall difference of muscle synergy vectors between conditions extracted from subjects were significantly smaller than synergies extracted from the randomly shuffled EMG data. This is denoted by the higher similarity score of the baseline synergies, where (*No HAL Fatigue vs No HAL Non-Fatigue:* 0.42 ± 0.15 vs 0.81 ± 0.19, $p = 0.00014 < 0.05$), (*HAL Non-Fatigue vs No HAL Non-Fatigue:* 0.35 ± 0.13 vs 0.76 ± 0.17, $p = 0.00014 < 0.05$) and (*HAL Fatigue vs No HAL Non-Fatigue:* 0.33 ± 0.21 vs 0.72 ± 0.20, $p = 0.000088 < 0.05$)

A detailed look on the difference in muscle synergy contents with the scalar dot product showed that vectors in the 1st position of the No HAL Fatigue condition were significantly higher as compared to the baseline (0.90 ± 0.073 vs 0.94 ± 0.072, $p = 0.037 < 0.05$). Also, synergy vectors in the 2nd position of the HAL Fatigue condition were significantly more similar as compared to the baseline conditions (0.89 ± 0.045 vs 0.93 ± 0.077, $p = 0.0072 < 0.05$) (*Top Right*).

In the No HAL Fatigue condition, timing coefficients in the 2nd position were significantly different than the baseline (78.32 ± 11.27 vs 63.92 ± 12.96, $p = 0.0045 < 0.05$). For the HAL Non-Fatigue condition, timing coefficients in the 2nd position were also significantly different than the baseline (83.04 ± 7.80 vs 53.42 ± 18.99, $p = 0.00012 < 0.05$). Finally, in the last condition, all timing coefficients were significantly different to the baseline (1st position : 79.08 ± 10.19 vs 70.14 ± 13.04, $p = 0.014 < 0.05$, 2nd position : 80.78 ± 11.02 vs 50.66 ± 15.99, $p = 0.000089 < 0.05$, 3rd position : 77.26 ± 10.17 vs 68.70 ± 16.46, $p = 0.04 < 0.05$).

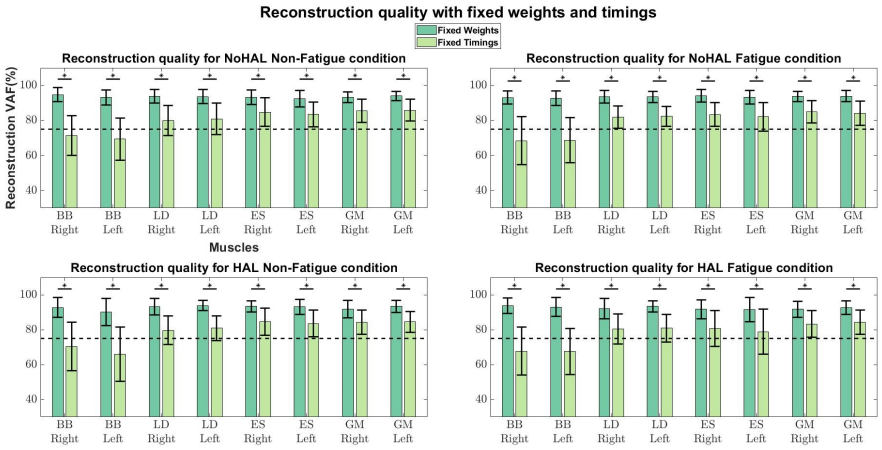


Figure 3.12: **Analysis of mutual information in different conditions** Synergy weights and timing coefficients were swapped between conditions. The bars on the left for each muscle shows the mean reconstruction quality (with the Uncentered Pearson Correlation Coefficient) for synergy weights from conditions different from the one being evaluated (e.g. For the No HAL Non-Fatigue condition, only reconstruction quality from the No HAL Fatigue, HAL Non-Fatigue and HAL Fatigue conditions were summed and compared). The right bars shows the reconstruction quality for timing coefficients different from the conditions as the synergy weights. Asterisks denote significance of $p < 0.05$ of the Wilcoxon Signed-Rank test.

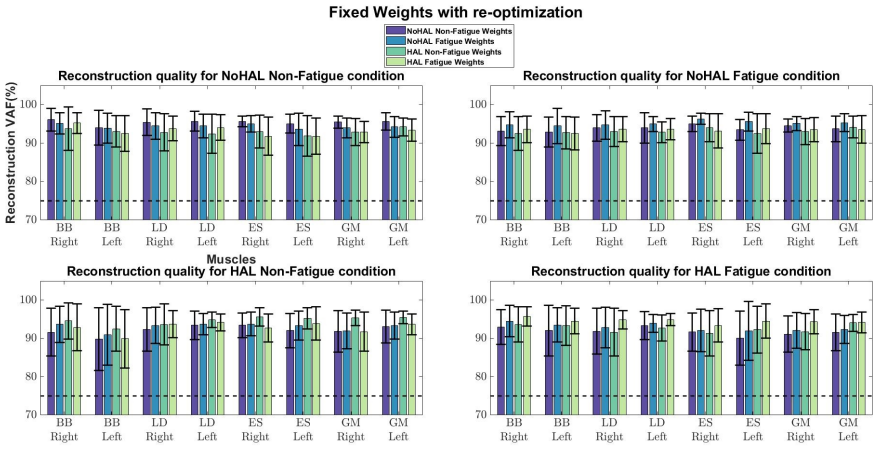


Figure 3.13: **Swapping synergies** Synergies from one condition was applied to other conditions to test if the muscle synergy weights were able to account for the variance in EMG from other conditions. Synergy weight was kept fixed during the entire decomposition process, while the timing coefficients were allowed to vary

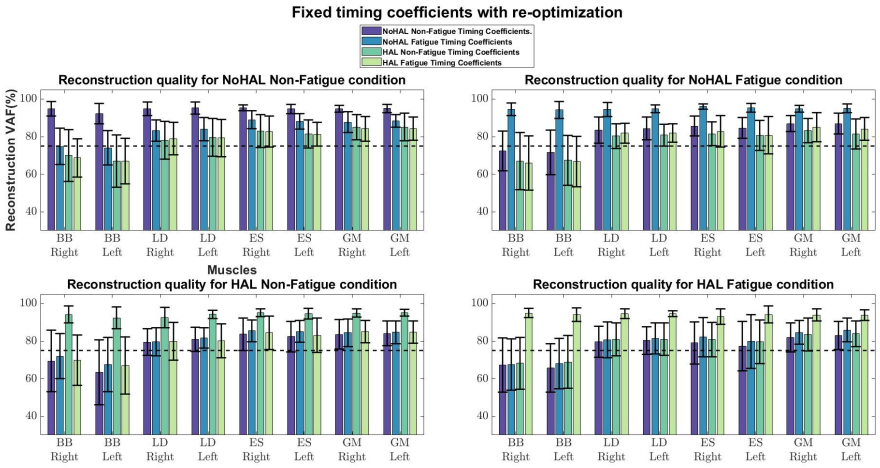


Figure 3.14: **Swapping timing coefficients** Timing coefficients from one condition was applied to other conditions to test if the timing coefficients were able to account for the variance in EMG from other conditions. Timing coefficients were kept fixed during the entire decomposition process, while the synergy weights were allowed to vary

Comparisons of reconstruction quality with fixed weights and timings (Figure 3.12) showed that when synergy weights were held fixed while the timings are free to vary, synergy weights gave a better reconstruction quality (values well above the 75% threshold), as opposed to the condition where the timings were fixed. A closer look at reconstruction qualities (Figure 3.13 and 3.14) indicated that the reconstruction quality for both the Right and Left biceps were consistently poor, when the timings from different conditions were held fixed.

3.5 DISCUSSIONS AND CONCLUSIONS

This current study examines the effect of an active lumbar support exoskeleton (Lumbar HAL) on muscle coordination in healthy subjects. For the experimental protocol, a fixed spatial set of muscle synergy weights were assumed, as there were strong evidence to indicate that modifications in movement can be attributed to variances in the recruitment of spatially-fixed muscle synergies. ([69]). Results from this study indicates that the recruitment times of the muscle synergies (known as timing coefficients) were significantly changed when the exoskeleton was used. However, there was only a slight change in the weights of muscle synergies. This change can be attributed to the Lumbar HAL, which generates assistive torque based on muscle activity in the ES muscles of the subjects. This assistance would cause changes in the kinetics of the movement, which can be noted in the velocity profiles (Fig. 3.7).

Task performance measures show that Lumbar HAL was able to increase the number of times subjects were able to lift the box before stopping. Additionally, perceived fatigue was also significantly lesser as compared to when Lumbar HAL was not used. Kinematic anal-

ysis showed that hip flexion angles were significantly lower in the stoop posture, when Lumbar HAL was used, regardless of fatigue levels (Figure 3.6 Bottom Left). This could be attributed to the design and fitting of Lumbar HAL, giving rise to a consistently smaller hip flexion angle in the stoop posture. Mean hip angular velocities were observed to decrease during posture transition (upright to stoop, stoop to upright), regardless of whether Lumbar HAL is used 3.6 Top Right, Bottom Right), suggesting that even with assistance from Lumbar HAL, subjects were unable to maintain their angular velocity at a non-fatigue level. Nevertheless, despite a decrease in angular velocity, subjects were still able to perform more lifting actions with Lumbar HAL, suggesting that angular velocity does not impact task performance.

Another interesting result noted was that back muscles which were not supported by Lumbar HAL (i.e. Latissimus Dorsi (LD)) was observed to have a reduction in activity when Lumbar HAL is used (Fig. 3.8). A 2-way ANOVA (Table 3.1) indicates that the reduction in activity can be attributed to the use of Lumbar HAL, with fatigue contributing to this reduction in the right LD muscles. The expected effect was that the ES muscles would show a reduction in activity when using Lumbar HAL, since this group of muscles are mainly responsible for straightening the back in stoop lifting. Torque assistance would help reduce the load on these group of muscles. However, this expected effect was only observed in the right ES muscles, but not in the left (Table 3.1). A possible explanation could be that the corset-like design of Lumbar HAL constrained the lower back to be straight, enabling the assistance to be transmitted towards the upper back. However, this would require further studies for verification. Another possible explanation could be that subjects had to modulate the timing of activity in their ES muscles in order to control Lumbar HAL, which is suggested by that change in timing coefficients (Fig. 3.11)

Differences in muscle coordination were dominated by timing coefficient. Although overall measures of muscle synergy similarity (Fig. 3.11 Left) indicate that muscle synery contents changed in different conditions, evaluating the synergies individually showed that the difference is not as great as expected, since most of the synergies were similar to the baseline random similarity to the base condition (No HAL Non-Fatigue). One notable differences were changes in muscle synergies in the "No HAL Fatigue", where the effects of fatigue was seen in the change in the 1st synergy (Fig. 3.11 Top Right, Red), against the change in 2nd synergy in the "HAL Fatigue" conditions (Fig. 3.11 Top Right, Blue). The interpretation of this result is that when subjects fatigue without using Lumbar HAL, coordination in back muscles (ES and LD) were changed, while when using Lumbar HAL, subjects change their arm muscle coordination (BB) when fatigued. From Fig. 3.10, the 1st synergy is mainly composed of the back muscles, while the 2nd synergy is mainly composed of the arm

muscles. Evaluation of timing coefficient differences individually revealed that the greatest change was observed in the "HAL Fatigue" condition, where the similarity index of all timing coefficients were significantly lower than the baseline random similarity. This could be that when subjects were fatigued, they relied more on the assistance provided by Lumbar HAL in order to move.

This change in muscle synergies and their timing coefficients were also observed in a recent study by [124], who examined muscle synergy change in walking with an ankle exoskeleton. They noted changes in both muscle synergies and timing coefficients when subjects were using the ankle exoskeleton. However, they also found that extracted synergies from the base condition were able to reconstruct EMG profiles better than random change, as compared to timing coefficients from the base condition, suggesting that synergy weights were able to account for the variability of EMG profiles in different conditions.

3.5.1 *Limitations of study*

A limitation of the study is that the gain parameter controlling the response of Lumbar HAL to the ES muscle activity was not recorded. This parameter was manually adjusted until subjects feel comfortable controlling Lumbar HAL during familiarization before the trial starts. Future studies could look into the relation of gain parameter of exoskeletons and the magnitude of change in muscle synergies. Another limitation to this study is that upper limb kinematics were not tracked in the study, making it difficult to interpret muscle activity change in the BB muscles. Future considerations could be to include full body tracking, instead of just the joints affected by the exoskeleton. Finally, the age range of subjects could be a possible factor affecting results, as there might be age-related differences in reported fatigue.

From the perspective of muscle synergy analysis, a limitation could be that the number of measured muscles were relatively small (4 per side). [82] showed in their study that the number of muscles could impact analysis results, and one interpretation of their study is that the number of muscles are similar to a form of resolution. An interesting figure to note in [82] is Figure 5, where an approximately logarithmic increasing similarity to the master set of muscles can be observed, as the number of muscles increase. One practical interpretation of this figure is that there is a diminishing return effect with each increase in the number of muscles. Having a fine resolution in our study might not be useful, since the task is a relatively simple task. Furthermore, [82] also noted that the size of the muscles also play a role in the analysis results, with larger muscles being able to contribute to the accuracy of the analysis, despite having a small number of muscles. Since large muscles relevant to stoop lifting were included in our

study, the number of muscles were considered to be sufficient for the needs of this study.

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4

SYMMETRY OF MUSCLE SYNERGIES IN SUBACUTE POST-STROKE PATIENTS AFTER ROBOTIC THERAPY

4.1 ABSTRACT

Impairment of gait is associated with stroke, and it has serious consequences impacting personal mobility of patients with this neurological disease. Physiotherapy and gait training are classic intervention methods to help stroke patients regain mobility. Recently, robotic exoskeletons have been developed to help provide therapy for patients, leading to various studies examining the effects of robotic exoskeletons on the recovery of stroke patients. Although these studies report improvement in stroke patients, they were usually reported with clinical assessment metrics, which only provide a gross overview on patient's gait, and unable to quantify gait symmetry. We hypothesize that muscle coordination can provide an objective view on gait symmetry after a course of therapy. To quantify improvement in gait symmetry, muscle synergy analysis was used to evaluate lower limb EMG data of stroke patients. Eight subacute stroke patients were evaluated before and after a course of robotic therapy with the Hybrid Assistive Limb (HAL), lasting three weeks. A significant increase in similarity between muscle synergies of both lower limbs was noted after robotic therapy. This was associated with significant improvement in spatiotemporal gait measures like walking speed, step cadence and stance duration. Clinical assessment metrics (FIM-Locomotion, FIM-Motor, FMA-LE) were also noted to have significant improvements as well. This study shows that muscle synergy analysis can be a good tool to quantify the change in neuromuscular coordination of lower limbs in stroke patients.

4.2 INTRODUCTION

4.2.1 *Stroke therapy with robotic exoskeletons*

Stroke is a serious neurological disease commonly associated with gait disturbance [76], [112]. This points to a need for assistive devices that can help in patients' therapy process and personal mobility. In reviews done by [62] and [112], there appears to be an increasing trend in the use of exoskeletons for therapy. This has led to the development of several commercially available exoskeletons for therapy. Some examples of these exoskeletons are the Hybrid Assistive Limb (HAL) [29], ReWalk [77], Lokomat [27] and Lopes [43]

4.2.2 *Difficulty assessing pathological gait*

Gait performance of stroke patients during therapy are typically assessed with clinical assessment metrics, like the Functional Independence Measure (FIM)([11]) and the Fugl-Meyer Assessment (FMA) ([6]). However one aspect of gait where clinical measures do not quantify well is gait symmetry. However, gait symmetry is turning out to be an important aspect to evaluate post stroke patients. Asymmetric gait has been identified as a feature of gait in stroke patients, which is attributed to weakness on one side of the body ([18]). An extensive review by [76] to characterize such asymmetries and found that asymmetries arise on the unaffected side due to compensation and adaptation. They also found that such asymmetries lead to inefficient energy expenditure, falls, abnormal joint loading, joint pain, deformity and pain. Since gait asymmetry is such a serious issue, having tools like muscle synergy analysis (MSA) would allow us to assess patient gait performance accurately, and thus, customize treatments. Further support for measuring gait asymmetries come from [58], who analyzed patient gait data up to a mean of 82 months, post stroke. They found that spatial and temporal gait symmetry parameters (stance time, swing time, step length symmetry), actually show a worsening of gait in those patients, whereas parameters like velocity, neurological deficit and lower extremity motor impairment did not reveal any significant worsening of gait. They conclude that gait asymmetry should be given more attention both in clinical situation and research.

Although improvements to stroke patients' gait can be clinically verified after robotic intervention, the effects of such interventions from the viewpoint of muscle activations are not well studied. Typically, studies involving the use of exoskeletons focus on clinical assessment metrics describing the performance of patients before and after a course of therapy. ([84], [93]). Diaz et al. also concluded that there is a need to develop standardized protocols to obtain reliable assessment data, as clinical measures are currently not sufficient and require many clinical trials in order to be widely accepted and implemented ([62]). Although clinical metrics are a good indication of the general wellbeing of patients, they are unable to reflect changes in the way muscles are coordinated in a task. However, despite such a lack in measurement protocols being pointed out, many later studies involving the use of robotic exoskeletons mainly reported clinical measures in patients after therapy ([105]).

4.2.3 *Muscle synergy analysis for neurological disorders*

Previous studies have proposed that co-activation of muscles, also known as muscle synergies or motor modules, are sufficient to describe various postural or locomotion tasks in humans [39], [42]. These synergies can be considered strategies that the human body employs

to facilitate control of limbs in various tasks. Such a method, known as muscle synergy analysis (MSA), has recently seen interest in the stroke therapy. Studies by [53], [110] and [63] used MSA to assess gait performance of stroke patients. One related work by [80] employed MSA to quantify walking performance of stroke patients before and after therapy. These studies highlight the importance of having such measures, in addition to clinical measures, in order to predict stroke patient performance and to customize therapies.

In our study, we investigate muscle activation changes with MSA in stroke patients who underwent a course of robotic therapy using the HAL Lower Limb exoskeleton [29]. Muscle synergies are extracted with Non-Negative Matrix Factorization (NNMF) [37] and compared to evaluate changes in muscle activation of stroke patients before and after robotic therapy. This study aims to quantify gait symmetry of post stroke patients with lateral symmetry of muscle synergies on both sides of the body, when they are walking.

4.3 METHODS

This study was carried out in accordance with the recommendations of the University Guidelines for Clinical Trials, Institutional Review Board of University of Tsukuba Hospital, with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Institutional Review Board of University of Tsukuba Hospital. The University Guidelines for Clinical Trials conforms to the ethical principles of the Declaration of Helsinki.

4.3.1 *Participants*

Eight post stroke patients in their acute phase after onset participated in the study (Table 4.1). Among the eight participants, there were four females and four males, aged between 43 and 80 (average: 59.3 $\pm$ 12.2) yrs. Four of them had hemiparesis on the left side, and the other four on the right side. Medical diagnosis included Atherothrombotic Cerebral Infarction (ACI), Subcortical Hemorrhage (SH), Brain Stem Infarction (BSI), Lacunar Infarct (LI) and Atherothrombotic Brain Stem Infarction (ABSI). Clinical evaluation of their Functional Ambulation Category (FAC) before starting the robotic intervention ranged from 1 (ambulation under substantial physical assistance) to 3 (independent ambulation under observation). These patients were included in the study 10-18 (average: 13.6 $\pm$ 3.4) days after onset.

ID	age (years)	gender	diagnosis	affected side	FAC before HAL	onset-HAL duration (days)
S1	67	F	ACI	L	1	10
S2	52	F	SH	R	2	17
S3	71	F	BSI	L	1	11
S4	55	M	LI	L	2	10
S5	55	F	ABSI	L	3	16
S6	43	M	LI	R	2	11
S7	51	F	ACI	R	2	18
S8	80	M	ACI	R	2	16

Table 4.1: **Participants characteristics** Diagnosis was Atherothrombotic Cerebral Infarction (ACI), Subcortical Hemorrhage (SH), Brain Stem Infarction (BSI), Lacunar Infarct (LI) or Atherothrombotic Brain Stem Infarction (ABSI).

4.3.2 *Robotic intervention*

Since all participants were hemiparetic, single leg version of Robot Suit HAL was used. The robot was composed of three rigid structures corresponding to lumbar, thigh and shank, and shoe, of the paretic side, weighing 9 kg in total. These parts were serially connected by joints allowing relative sagittal motion, realizing joint motion of hip, knee and ankle in the sagittal plane. Electric motors were embedded at the hip and knee joints, and controlled according to the bioelectric signals detected by surface electrodes attached on the skin surface of the relevant muscles. In equation, the hip and knee motors were controlled in real time to provide assistive joint torque as $T_{hip} = G_{hip,flex} * A_{hip,flex} - G_{hip,ext} * A_{hip,ext}$ and $T_{knee} = G_{knee,flex} * A_{knee,flex} - G_{knee,ext} * A_{knee,ext}$, where $A_{hip,flex}$, $A_{hip,ext}$, $A_{knee,flex}$ and $A_{knee,ext}$ are respectively filtered activation of Illiopsoas (hip flexor), Gluteus maximus (hip extensor), Hamstrings (knee flexor) and Vastus Lateralis (knee extensor) muscles. $G_{hip,flex}$, $G_{hip,ext}$, $G_{knee,flex}$ and $G_{knee,ext}$ are gain parameters adjusted according to wearer's comfort through the sessions.

Robotic intervention was started within the participants' acute period (Table 4.1). Intervention sessions were performed three times per week for three weeks, and therefore nine times in total, for each patient. An intervention session lasted approximately 60 minutes, including clinical examination, attaching the robot, 20 minutes of walking training using the robot including rest when necessary, and detaching the robot. During walking training, the patient walked repetitively in a 25 m course composed of two straight lines and two semicircles, on a flat surface. For safety reasons, a walking device (All-in-

One Walking Trainer, Ropox A/S, Naestved, Denmark) with a harness was used to prevent falls, and heart rate and oxygen saturation were monitored time to time.

4.3.3 *Data measurement*

Gait of the patients was measured during straight walking at a self-selected speed without wearing HAL, one to three days before the first HAL session (pre HAL) and after the last HAL session (post HAL). Lower limb muscle activity and foot motion were recorded using a measurement system. All-In-One Walking Trainer (Ropox A/S, Denmark), with a harness, was used during the walking test to prevent falls. The harness was adjusted so that it did not provide any weight support. The patients walked for 6 meters several times [55], until three consecutive steady steps were obtained. Data that did not fit the criteria of three consecutive steady steps were discarded. Also, the initiation and termination of walking during each 6 meters walking trial were discarded as well.

4.3.3.1 *Electromyography*

Skin preparation included wiping down the muscle bellies with alcohol swabs. 12 wireless, surface EMG electrodes were placed bilaterally over the muscle bellies of: Vastus Medialis (VM), Hamstrings (HAM), Tibialis Anterior (TA), Gastrocnemius (GAS), Adductor Longus (ADD), Gluteus Maximus (Gmax), using a TrignoTM Lab Wireless electromyography (EMG) system (Delsys Inc., Boston, MA, USA). EMG data was sampled at 2000 Hz.

4.3.3.2 *Motion Capture system*

Motion tracking of subjects was achieved with a motion capture system (VICON MX System with 16 T20S Cameras, Vicon, Oxford, UK), in synchronization with EMG and sampled at 100 Hz. 16 autoreflective markers were placed bilaterally on the anterior superior iliac spine, posterior superior iliac spine, lower lateral 1/3 surface of the thigh, flexion-extension axis of the knee, lower lateral 1/3 surface of shank, lateral malleolus for the ankle, posterior peak of the calcaneus for the heel and the lateral second metatarsal bone of the toe. These marker positions were used for gait phase detection during locomotion.

4.3.4 *Data analysis*

4.3.4.1 *Preprocessing*

From the synchronized tracks of EMG and motion data, three consecutive steady steps starting from a heel strike and ending with a succeeding heel strike were extracted in the middle of 6m walking for each leg (Right and Left), pre and post HAL, for each of the participants. EMG data was first band-passed with a 4th order, zero-lag

Butterworth band-pass filter at 30 - 400 Hz. The bandpassed EMG was then filtered with a Hampel filter, with the parameters, time window, win $= 200$ and a threshold of $\sigma = 4$ (standard deviations), to remove artefacts. Finally, EMG data was fully rectified and low-passed with a 4th order, zero-lag Butterworth low-pass filter at 6 Hz to obtain the EMG envelope. The EMG envelope is then time-normalized and resampled to 100 times points.

4.3.4.2 *Extraction of EMG based on kinematic data*

We segmented the EMG data into windows based on the phases of walking (Stance, Swing, Cycle). Stance is defined as the period starting from a heel strike and ending with toe off. Swing is defined as the period between starting from the toe off to heel strike. The Cycle is defined as starting from a heel strike and ending at the next heel strike.

Segmented data is further divided into sides (Affected and Unaffected). Each muscle vector in each segment was divided by its own standard deviation in that particular segment (e.g. Cycle muscle vectors are divided with the standard deviation of muscle vectors in the Cycle segment). This is based on the "UnitPer" definition (standard deviation per trial) of [109], who evaluated the effect of different EMG normalization methods with NNMF MSA. This provides a consistent effect size for varying muscle synergies and timing coefficients.

Data segments from 3 consecutive walking cycles were separated and concatenated, based on their phase in the gait cycle and side of the patient, thus obtaining 6 matrices in total (Affected_Stance, Affected_Swing, Affected_Cycle, Unaffected_Stance, Unaffected_Swing, Unaffected_Cycle). [91] noted that for intra-subject comparisons, muscle synergies extracted from concatenated signals yielded higher reconstruction quality, as compared to muscle synergies from averaged signals. This processing method was adopted as we would like extracted synergies to be representative of the subject's muscle activations. Also, we think averaging the EMG signals would mask step-to-step variability of muscle activations in hemiparetic patients.

4.3.4.3 *Muscle synergy extraction with NNMF*

NNMF was then used to extract muscle synergies from the concatenated EMG data. This was performed with Matlab's NNMF function, using the multiplicative update algorithm. Parameters for the tolerance for the residual (TolFun) was given as $1e-6$ and the tolerance for the relative change in elements (TolX) was given as $1e-4$. The algorithm was repeated 50 times and results with the lowest root mean square residual were taken to be the best. Synergies were allowed to vary per condition.

The choice of number of synergies were determined with the criteria

of when the variance-accounted-for (VAF_{total}) between the reconstructed and original EMG envelope was above 90% and subsequent increase of the number of synergies did not give more than a 5% increase in VAF. We also imposed a local criteria where the reconstruction VAF (VAF_{muscle}) for each muscle vector was above 75% [42]. The VAF is defined as $100 * (\text{uncentered Pearson correlation coefficient})$, which requires the total sum of squares to be taken with respect to zero [37]. This is given as:

$$VAF = 100 \cdot \left(\frac{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm} \cdot Y_{nm})^2}{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm}^2) \cdot (\sum_{j=1}^{m} \sum_{i=1}^{n} Y_{nm}^2)} \right) \tag{4.1}$$

where n is the number of datapoints for each channel, and m is the number of channels. X_{nm} and Y_{nm} are the matrices containing the reconstructed and original signal respectively. VAF calculation code is adapted from the "rsqr_uncentered" function in the file "PosturalData_NMFvsPCA_GUI_July2013" given in [106]

The mean muscle VAF was calculated for each extracted muscle synergy vector ($\frac{1}{n} \sum_{i=1}^{n} VAF_{muscle}^{i}$, where i = number of synergies and n = number of muscle channels), and were used as a basis in the sorting of muscle synergy vectors. Synergy vectors were sorted according to the mean muscle VAF in descending order (i.e. a synergy with highest mean reconstruction muscle VAF, as compared to other synergies, were placed as the first synergy).

4.3.4.4 *Synergy Analysis*

Lateral synergy symmetry was determined by comparing the sorted synergies (described in Section 4.3.4.3) from the affected side and unaffected side with the general Pearson correlation coefficient (r). Muscle synergy matrices were compared with the corresponding synergy matrix for the other side of the body (e.g. $Synergy_{affected}$ with $Synergy_{unaffected}$ and so on). Such comparisons were performed for muscle synergies extracted from the concatenated EMG data (Section 4.3.4.2) during different phases of gait. Note that only muscle synergies that belong to the same gait phase were compared (e.g. muscle synergies from the full cycle phase, on the affected side of the body, were compared only with the muscle synergies from the full cycle phase, on the unaffected side of the body). The motivation for this comparison is to provide a single value measure for similarity.

Synergy vector comparison with the scalar dot product [68] was also performed to evaluate the changes in contents of the muscle synergy vectors. Muscle synergy matching was also performed to discover the presence of similar muscle synergy vectors on both sides of the body. Muscle synergies with the highest scalar dot product score are selected, matched and removed from the pool of muscle synergies. This process continues until no more muscle synergies are left to match.

4.3.4.5 *Software*

Data extraction was done using scripts on MATLAB 8.4 (Mathworks, Natick, MA, USA). NNMF and the rest of the processing were performed with scripts on MATLAB 9.3 (Mathworks, Natick, MA, USA).

4.3.5 *Clinical assessments*

Physical therapists also evaluated the patients before and after the course of therapy. The below measures were used to evaluate patient motor functions:

1. Functional Independence Measure - Locomotion (FIM - Locomotion)
2. Functional Independence Measure - Motor (General) (FIM - Motor (General))
3. Fugl-Meyer Assessment, Lower Extremity (FMA - LE)

For the kinematics, we measured the walking speed, step cadence, absolute lateral difference of step length and the percentage of stance in relation to gait cycle. The absolute lateral difference of step length was derived from the step length variable. The absolute difference in step length between both sides of the body was calculated to account for the differences in compensatory walking strategies employed by the patients. Step length does not take into consideration the compensatory gait patterns hemiparetic patients exhibit. For example, some patients start their swing phase with their affected leg and bring their unaffected leg to their center for stabilization [76]. This causes the affected step length to be longer than the unaffected side. Similarly, patients who drag their affected leg during walking would have a longer step length on their unaffected side

4.3.6 *Statistical analysis*

Normality of the data were tested with the Shapiro-Wilk test, with the significance level set to 5%. Statistical comparison performed with the T-test (for normally distributed data) and the Mann-Whitney U-test (for non-normal distribution). For each paired dataset, both pairs would have to fulfill the criteria of the Shapiro-Wilk test before the T-test was applied. Otherwise, the U-Test was used instead. Significance was considered in comparisons with $p < 0.05$.

4.4 RESULTS

4.4.1 *Clinical Assessments*

Significant improvement in the kinematic measurements of the patients was observed (Figure 4.1). Statistically significant increase was observed in walking speed (Pre : 14.36 ± 12, Post : 31.47 ± 12.11 m/min, ($p <$

0.05)) and step cadence (Pre : 22.95 ± 9.04, Post : 35.32 ± 8.45 steps/min, ($p < 0.05$)), together with a decrease in the percentage of stance duration, in relation to the whole gait cycle (Pre Affected : 72.17 ± 6.12, Post Affected : 64.04 ± 4.51 %, ($p < 0.05$)) (Pre Unaffected : 80.89 ± 7.63, Post Unaffected : 70.76 ± 4.96 %, ($p < 0.05$)). There was no significant improvement in absolute lateral difference of step length. (Pre : 0.0783 ± 0.0473, Post : 0.0575 ± 0.0153 m, ($p > 0.05$)). Only the range of movement for the affected hip show significant improvement (Pre Affected Hip : 30.33 ± 10.15, Post Affected Hip : 39.63 ± 6.98degrees ($p < 0.05$))

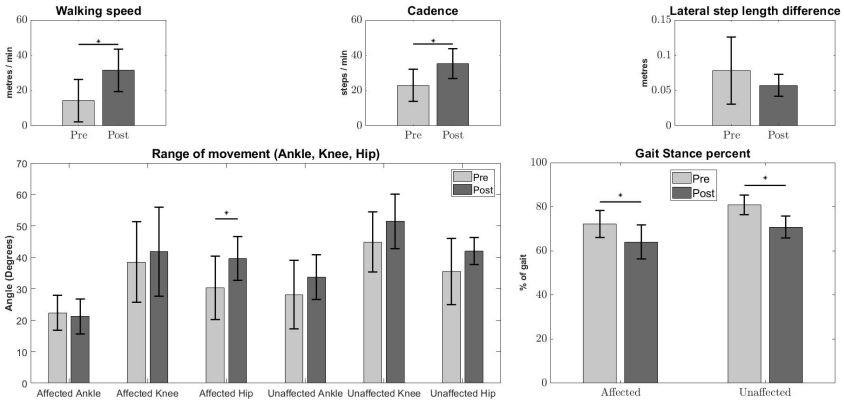


Figure 4.1: **Kinematic measures Pre-Post conditions** Error bars denote the standard deviation. Improvements were observed in walking speed (Top Left), Step cadence (Top Middle), Stance duration percentage of affected and unaffected side (Bottom Right), and Pre-Post affected hip angles (Bottom Left). The Lateral step length difference (Top Right) and other joint angles (Bottom Left) do not show any significant differences

The FIM-Locomotion (FIM-Loco) score, FIM-Motor (General) score, FMA-LE scores improved after robotic intervention. (Table 4.2). Only 1 patient (S7) did not show an improvement in FIM-Locomotion scores, however, other the other measures (FIM-Motor(General) and FMA-LE) showed improvement in the S7's condition.

	FIM-Loco (Pre)	FIM-Loco (Post)	FIM-Motor (General) (Pre)	FIM-Motor (General) (Post)	FMA-LE (Pre)	FMA-LE (Post)
S1	1	**3**	46	**73**	13	**18**
S2	1	**5**	40	**82**	19	**26**
S3	1	**2**	40	**55**	18	**28**
S4	2	**7**	52	**77**	26	**29**
S5	2	**7**	78	**90**	20	**27**
S6	1	**6**	66	**83**	21	**25**
S7	1	1	53	**62**	14	**22**
S8	1	**5**	50	**65**	17	**20**

Table 4.2: **Clinical Measures Pre-Post robotic intervention** Numbers in bold denote improvement in scores

4.4.2 *Number of muscle synergies in patients*

The figure below (Figure 4.2) details the mean overall reconstruction VAF and mean reconstruction VAF for each muscle vector (Figure 4.3) according to the number of muscle synergies for all subjects. Error bars denote the standard deviation.

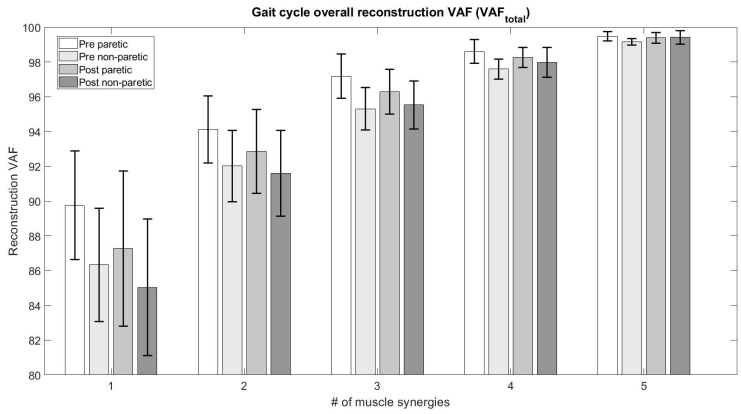


Figure 4.2: **Overall VAF** Total variability accounted for (VAF_{total}) based on the number of muscle synergies

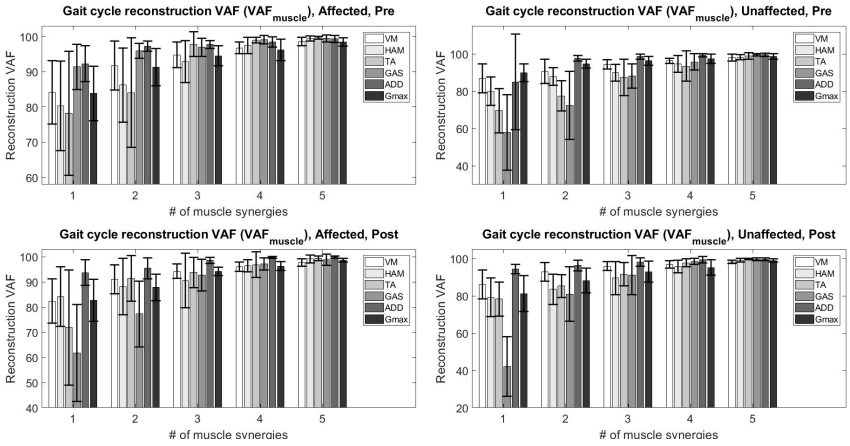


Figure 4.3: **Muscle VAF** Total variability accounted for (VAF_{muscle}) based on the number of muscle synergies and condition

The table below (Table 4.3) details the change in the number of muscle synergies per subject in different conditions. The number of synergies selected for each subject is based on both the overall reconstruction VAF ($VAF_{total} > 90\%$) and local reconstruction VAF ($VAF_{muscle} > 75\%$) [42] for each subject. We found that 3 subjects required an increase of the number of muscle synergies by 1, No change for 3 subjects, and 1 subject required a decrease in the number of muscle synergies for their affected side. The exception to this case is S3, reduced the number of muscle synergies by 1 after therapy. We also found changes in the unaffected side of patients, with S2, S3 and S4 showing a decrease in muscle synergies. The exception to this case were S5 and S6, who had an increase in the number of muscle synergies in the unaffected side.

	Affected			Unaffected		
	Pre	Post	Change	Pre	Post	Change
S1	1	**2**	+1	2	2	0
S2	2	2	0	3	**2**	-1
S3	3	**2**	-1	4	**2**	-2
S4	2	**3**	+1	3	**2**	-1
S5	3	**4**	+1	2	**4**	+2
S6	3	3	0	3	**4**	+1
S7	1	1	0	2	2	0
S8	1	**3**	+2	3	3	0

Table 4.3: **No. of synergies** Number of muscle synergies required pre and post robotic intervention for affected and unaffected sides. Bold numbers indicate the change in the number of muscle synergies

To determine the number of synergies for comparison between sides per subject, we selected the maximum number of synergy for both the affected and unaffected side in the comparison condition (e.g. In Table 4.3, the number of synergy for S2 is determined to be

3 for Side Similarity in the pre-intervention condition, and 2 for the post-intervention condition. However, for the same subject, the number of synergies for Pre-Post Similarity comparisons would be 3 for the unaffected side.).

4.4.3 *Muscle synergies, EMG waveforms and kinematics*

S2 was picked as the representative subject for reporting as this subject displays the greatest improvement in FIM (General) scores and reasonably good improvement in both FIM locomotion and FMA lower limb scores. Figure 4.4 and 4.5 shows the muscle synergy vectors, timing coefficients, original EMG envelopes and reconstructed EMGs, for the affected side of S2, during the pre-intervention and post-intervention conditions respectively. Raw EMG waveforms and joint angles for S2 in the pre-intervention and post-intervention conditions (Figure 4.6 and 4.7 respectively) were presented.

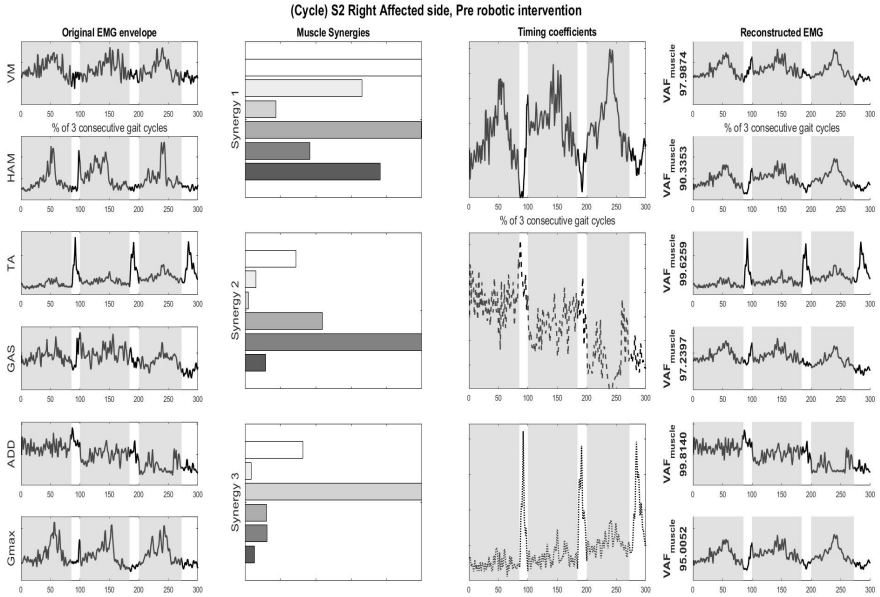


Figure 4.4: **Representative subject Pre therapy** Original EMG envelope, Muscle synergies, Timing coefficients and Reconstructed EMGs for affected side, pre HAL intervention, computed by NNMF with 3 synergies. Each bar of the synergy set is matched with the order of muscles in the 'Original EMG' (Left) column, namely (from top bar to bottom bar) VM, HAM, TA, GAS, ADD, Gmax. Similarly, each plot in the 'Individual Reconstructed EMG' column is matched with the order of the muscles in the 'Original EMG' (Left) column. Each line pattern represents the reconstructed EMG from each motor module. Shaded areas denote stance phases

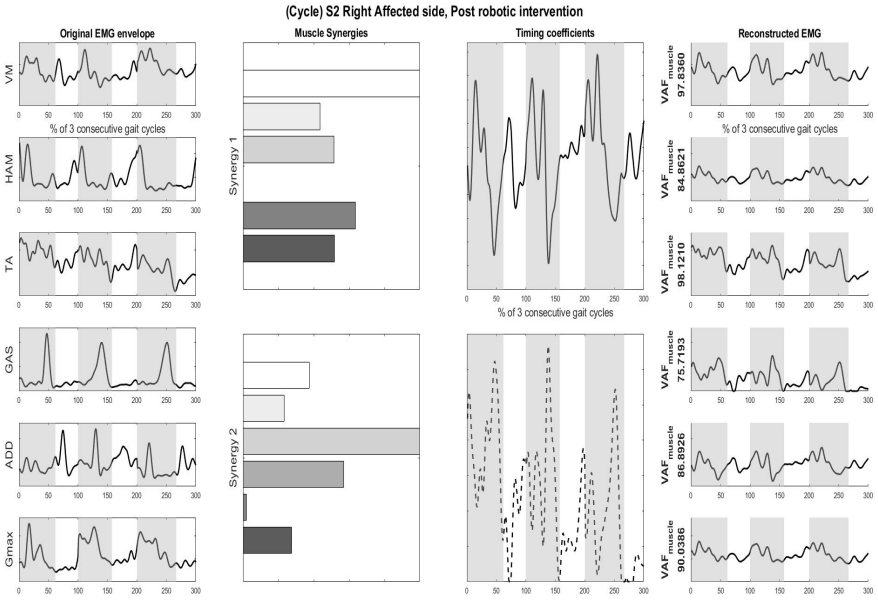


Figure 4.5: **Representative subject Post therapy** Original EMG envelope, Muscle synergies, Timing coefficients and Reconstructed EMGs for affected side, post HAL intervention, computed by NNMF with 2 synergies. Each bar of the synergy set is matched with the order of muscles in the 'Original EMG' (Left) column, namely (from top bar to bottom bar) VM, HAM, TA, GAS, ADD, Gmax. Similarly, each plot in the 'Individual Reconstructed EMG' column is matched with the order of the muscles in the 'Original EMG' (Left) column. Each line pattern represents the reconstructed EMG from each motor module. Shaded areas denote stance phases

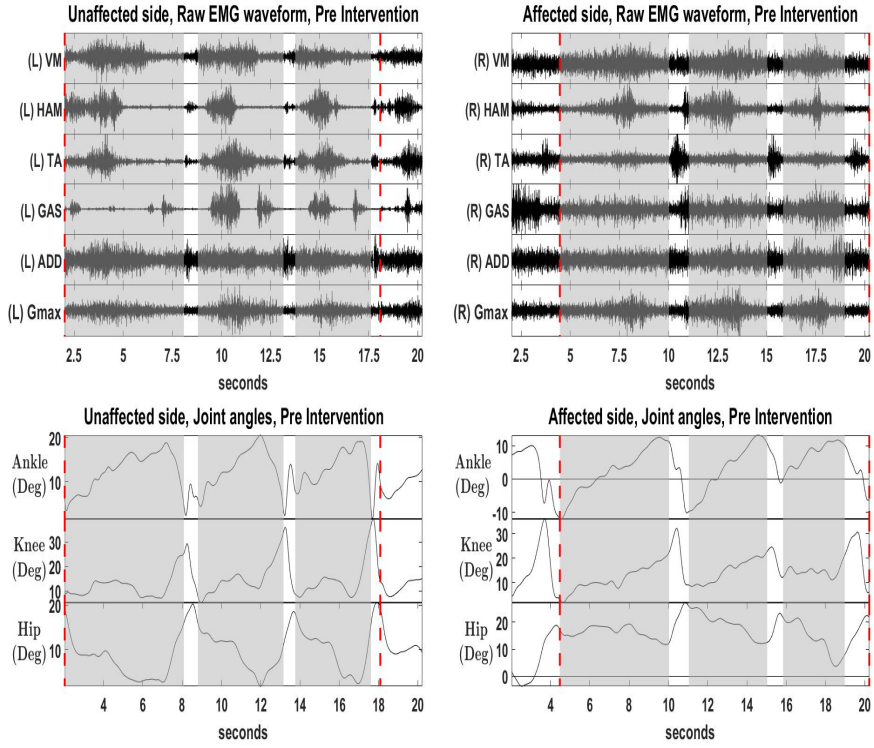


Figure 4.6: **Raw EMG waveform and joint angles, pre intervention** Positive values in angles indicate flexion, while negative values indicate extension

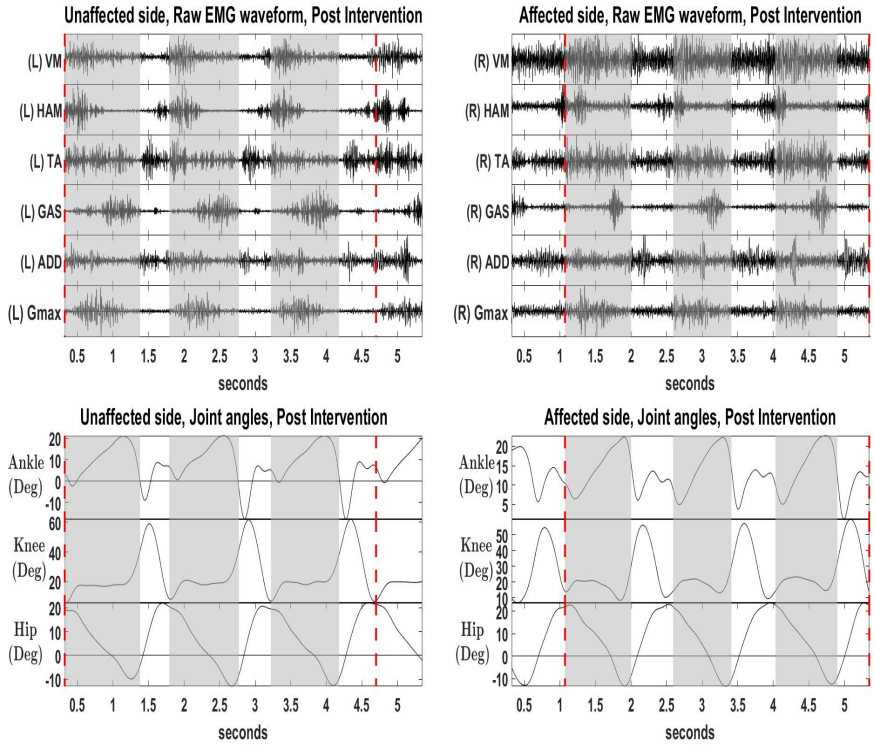


Figure 4.7: **Raw EMG waveform and joint angles, post intervention** Positive values in angles indicate joint flexion, while negative values indicate extension.

Overall reconstruction VAF for S2 is high (>90%) for both conditions, although certain abnormal looking EMG envelopes can be seen. To explain them, the raw EMG waveforms, and their corresponding joint angles, for both pre and post intervention conditions, are examined (Figure 4.6 and 4.7). Due to ethical reasons, we are unable to provide the raw EMG values, hence the vertical axes of EMG plots remain unlabeled. In the Pre-intervention condition (Figure 4.6, Affected side), subject's VM and GAS muscles are active for most of the gait cycle (**Stance percent**: 80.56 ± 7.24). This can be observed in the slow rate of increase in the knee angles. ADD muscles are also highly active in the pre-intervention condition, so as to provide stability for the hip joint, where hip angles hover around values between 10 to 20 degrees for most of the stance phase. In the post-intervention condition (Figure 4.7, Affected Side), the subject has an overly active TA post rehabilitation, contributing to abnormal dorsal flexion of the ankle throughout the gait cycle. We observed the VM muscles are active longer than usual in the stance phase. The timing of the GAS muscles were later, as compared to the unaffected side. The HAM muscles appear to be weaker than the unaffected side, where short activations were noted. The knee angle trajectory shows a slight parabolic curve on the Affected knee, as opposed to a relatively straight trajectory on the Unaffected knee.

4.4.4 *Synergy changes after robotic intervention*

Muscle synergy similarity was quantified with the Pearson correlation coefficient (r) to provide an overall view of the lateral symmetry of the muscle synergies.

A significant increase in the bilateral symmetry in the swing phase was observed. (Pre : -0.0987 ± 0.349, Post : 0.272 ± 0.291, $p < 0.05$) (Figure 4.8, Second column, Bottom). However, no significance were found for other phases of gait, although a upward trend can be observed. **Stance** (Pre : 0.251 ± 0.352, Post : 0.39 ± 0.514, $p > 0.05$), **Cycle** (Pre : 0.129 ± 0.368, Post : 0.344 ± 0.323, $p > 0.05$)

Pre-Post similarities between the affected and unaffected side for all phases were also not significant, although the variability in r for the affected side is much higher than the unaffected side, possibly indicating a greater change in muscle synergies after robotic intervention. **Stance** (Pre : 0.142 ± 0.548, Post : 0.443 ± 0.371, $p > 0.05$), **Swing** (Pre : 0.128 ± 0.257, Post : 0.393 ± 0.174, $p > 0.05$), **Cycle** (Pre : 0.0988 ± 0.41, Post : 0.446 ± 0.397, $p > 0.05$) (Figure 4.8, Top Row)

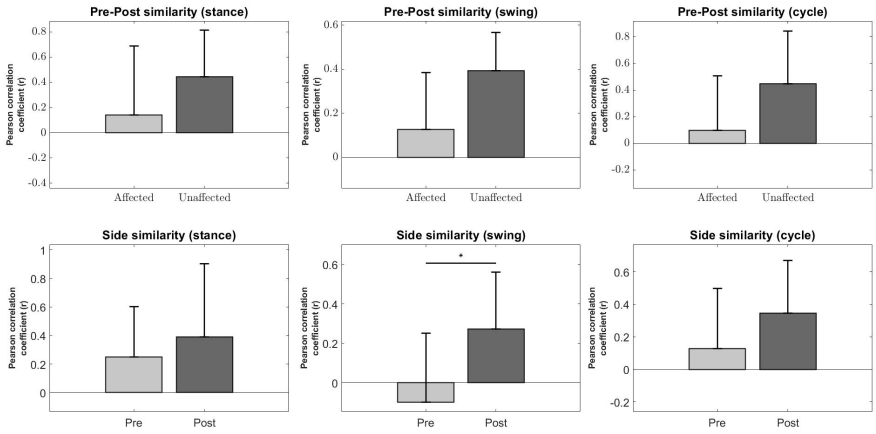


Figure 4.8: **Synergy comparison between conditions** Error bars denote standard deviation. Pre-Post comparison of r between affected and unaffected side during Stance, Swing and Full gait cycle (Top Row). Side comparison of r before and after robotic intervention during Stance, Swing and Fully gait cycle (Bottom Row).

We also evaluated muscle synergy vectors on an individual basis as well. Figure 4.10 and 4.11 show our results for Subject 2. Figure 4.9 labels the muscles shown in Figure 4.10 and 4.11.

Pre-intervention (Figure 4.10), it can be observed that muscle synergies on the affected side are different from muscle synergies on the unaffected side, when sorted by task contribution levels. For example, the first synergy on the affected side has that largest similarity to the second synergy on the unaffected side. This differences in task contribution levels of similar muscle synergies could lead to the observed asymmetric gait (Figure 4.6).

In the post-intervention condition (Figure 4.11), similar muscle synergies, denoted by a high scalar dot product value, now has similar task contribution levels, and this probably lead to a more symmetric gait (Figure 4.7).

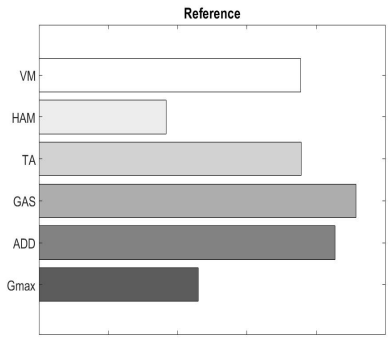
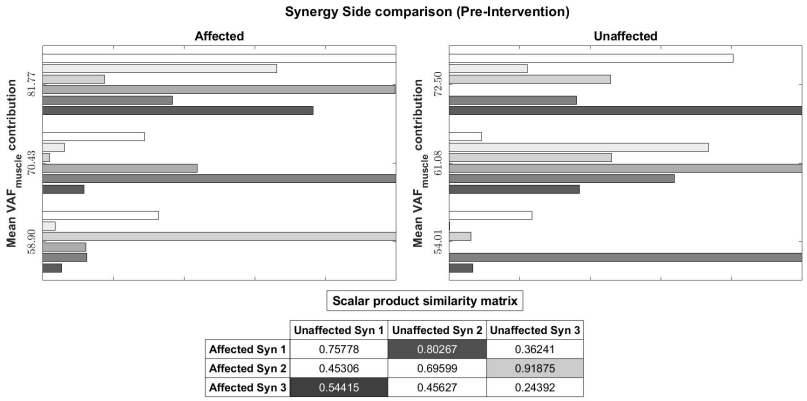
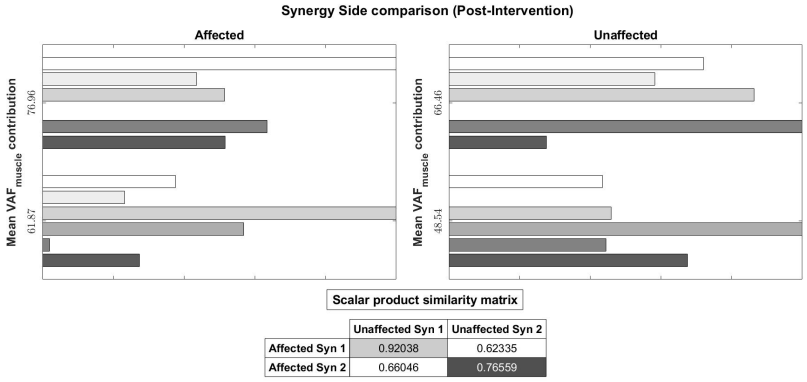


Figure 4.9: **Reference plot** Arrangement of muscles in Figure 4.10 and 4.11



	Unaffected Syn 1	Unaffected Syn 2	Unaffected Syn 3
Affected Syn 1	0.75778	0.80267	0.36241
Affected Syn 2	0.45306	0.69599	0.91875
Affected Syn 3	0.54415	0.45627	0.24392

Figure 4.10: **Muscle Synergy vectors of Subject 2, Pre intervention, Full Gait cycle** VAF to original states the contribution of each synergy to the original EMG. A higher value indicates a higher contribution. The scalar product similarity matrix shows results of comparing each synergy vector on the Affected side with all synergy vectors on the Unaffected side. Muscle synergies with the highest score are selected, matched and removed from the pool of muscle synergies. This process continues until no more muscle synergies are left to match. The synergies are matched in the sequence given by the color codes: 1st - Light grey, 2nd - Dark grey, 3rd, Black. The 1st synergy on the affected side is matched with the 2nd synergy on the unaffected side. Similarly, the 3rd synergy on the affected side is matched with the 1st synergy on the unaffected.



	Unaffected Syn 1	Unaffected Syn 2
Affected Syn 1	0.92038	0.62335
Affected Syn 2	0.66046	0.76559

Figure 4.11: **Muscle Synergy vectors of Subject 2, Post intervention, Full Gait cycle** With the same muscle synergy matching method, The order of muscle synergies for Subject 2 on the affected side was matched with the order of muscle synergies on the unaffected side (1st synergy on the affected side is matched with the 1st synergy on the unaffected and so on).

4.5 DISCUSSIONS AND CONCLUSIONS

Our current study attempts to provide a method to measure lateral symmetry by evaluating the number of synergies for each side of the body and contents of the muscle synergy vectors. This could be

a better representation of how the patient's gait is improving, since these synergies quantify muscle activations. By comparing muscle synergies, we can assess gait symmetries of patients. Although the usual method for previous studies to assess the performance of stroke patients is to compare them with healthy subjects ([63], [80], [52], [100], [87], [116]), we show that lateral symmetry can be used without healthy subjects, because gait symmetry, by nature, an intra-subject metric, where comparison is done between both sides of the same body. What is currently unclear at this point is the threshold where gait symmetry of patients could be considered similar to healthy people. Future considerations would be to analyze healthy subjects to test the accuracy of this method and define a threshold.

The increase in lateral symmetry is also associated with the improvement in clinical assessment and gait characteristics. This shows that robotic intervention is helpful for stroke patients (Figure 4.1 and Table 4.2). Among the kinematic measures, only absolute lateral difference of step length did not show significant improvement (Figure 4.1 Top Right). The reason could be due to the large differences in absolute step length between patients before therapy, which can be observed in the large standard deviations in the pre-therapy condition.

In our study, we utilized a sorting method to arrange muscle synergies according to their contributions for a particular task. One reason for the sorting is because the NNMF algorithm randomly orders the factorized synergies. Another reason is to account for the lack of age-matched controls. Although cluster analysis ([97], [102]) is also an important method to match muscle synergies and indicate the presence of similar muscle synergies on both side of the body, muscle synergies should also be evaluated in context of the task. Various studies have shown show that task-specific muscle synergies are dynamically recruited for different tasks, in addition to common muscle synergies found in all subjects ([114], [60]). Chvatal et al. noted that muscle synergies may be recruited by different neural circuits for a common motor task. ([78]) These studies suggest that the task might influence the recruitment of muscle synergies, hence analysis should be done in context of the task. We do not expect our subjects to possess similar muscle synergies, due to differences in descending neural commands from the motor cortex caused by stroke. Hence, sorting muscle synergies would help standardize comparison to the task level, allowing muscle synergies with similar contribution levels on both sides of the body to be compared.

4.5.1 *Change in number of synergies on both sides of the body*

Our results show that stroke patients have reduced number of muscle synergies on their affected side as compared to their unaffected side pre intervention (Table 4.3, Affected Pre and Unaffected Pre). This agrees with the previous studies on MSA of stroke patients ([53],

[68]). However, we have also observed patients who have decreased number of synergies on their unaffected side pre intervention (Table 4.3, S3 (Affected Side), and S2, S3, S4 (Unaffected Side)). Although this appears to be contradictory, Hashiguchi et al. found that subacute stroke patients exhibit both fractionation and merging of muscle synergies ([103]). They concluded that the number of muscle synergies do not consistently change with the recovery phase. They also found that the merging of synergies is associated with decrease in muscle strength and range of movement in the ankle joint, while fractionation is only related to improvement in the Barthel index.

Results from this study noted that the number of synergies on the unaffected side tends to match the number of synergies on the affected side, with S2, S3 and S4 showing a decrease in the number of synergies, and S5 and S6 showing an increase in the number of synergies. We think that the decrease in the number of synergies on the unaffected side could be due to the central nervous system trying to match the number of synergies on both sides of the body (Decrease in unaffected side of S2, S3, S4). Similarly, when the affected side sees an increase in the number of synergies, the unaffected side would probably require an increase in the number of synergies as well, in order to cater for the increased variety of movement (Increase in unaffected side of S5 and S6). A possible explanation for this phenomena is put forth by Graziado et al., who studied bilateral reorganization of the corticospinal system of stroke patients with hemiparesis ([70]). They found that the corticospinal system appears to prioritize symmetrical recovery, even if it is achieved at the expense of the non-lesioned side.

We think that once the affected side regains sufficient motor function, there is no need for the unaffected side to compensate for the affected side, hence leading to a change in the number and contents of synergies, thus, achieving gait symmetry. This could be beneficial for the patients, as gait asymmetries would lead to further complications in future if left untreated ([76]). We hypothesize that this might be the central nervous system's way of regaining symmetry. Indeed, results in a study by Clark et al. suggest that the organization of muscle synergies are similar in the legs of both healthy and post-stroke patients, with the only difference being the ability to activate muscle synergies independently, where reduction in this ability leads to merged synergies ([53]). This is also seen in the study by Cheung et al. ([68]). However, associating the number of degrees of freedom to number of muscle synergies seem to contradict our results, where we also observed a reduction in the number of synergies post robotic intervention. Another study also indicated that fractionation can also occur in post-acute stroke patients as they progress through therapy ([103]). A possible explanation for this contradiction could be that the studies by Clark et al. and Cheung et al. analyzed data from mainly chronic stroke patients (usually defined to be more than 6 months after stroke), while our study and Hashiguchi et al. analyzed data from subacute patients before and after therapy. This difference in the type

of patients could be the cause of this contradiction. Moreover, Clark et al. compared muscle synergies with healthy controls, whereas we compared muscle synergies within stroke patients. The difference in comparisons could also give rise to different results as the conditions were different. As Cheung et al. ([68]) pointed out, the motor system is a complex mix of descending and ascending neural pathways that interact with each other, and that changes occur in all parts of the nervous system after stroke. Therefore, more work in understanding muscle synergies in the context of both the cortical and subcortical neural circuits have to be done before any concrete conclusions can be drawn.

4.5.2 *Final remarks*

Our hypothesis of HAL was that, by its function of actually performing intended motion in real time based on the detected peripheral neuromuscular activity, it can assist neurorehabilitation of the original neuro-muscular motor function of the affected limb. This is in contrast to conventional physical therapy, in which the unaffected side was trained to perform compensatory motions, with orthoses and/or walking aids prescribed to help regain functional independence in daily life ([76]). They also noted that the adult human brain is capable of reorganization after stroke and can be manipulated with movement stimuli involving lower limbs. A recent study showed that recovery of neuromuscular activity is possible even in patients with chronic complete spinal cord injury with quadri/paraplegia ([117]). They used HAL to allow patients to trigger voluntary ambulation with residual muscle activations in their arms. This supports our hypothesis of HAL's effect on neurorehabilitation after stroke observed in this study.

It is also widely discussed that the synergy modules of muscular activation extracted by NNMF represents the way the central nervous system organizes the coordinated control of multiple muscles by descending commands to the peripheral system ([99]). The improvement of lateral synergy after robotic intervention using HAL shown in this study suggests possible contribution of HAL in the improvement of neuronal organization of gait by the central nervous system, in the acute phase post-stroke patients.

4.5.3 *Limitations of Study*

Limitation of the study includes the lack of control patients who did not receive HAL treatment. However, we do note that an extensive review of various clinical trials utilizing robotic intervention for post-stroke treatment had been performed, with findings that robotic intervention is safe and beneficial for stroke patients ([105]). Hence, this study is focused on developing methods to quantify the effects of robotic intervention. Nevertheless, comparison to control group and

investigation of synergy organization during sessions remain for future consideration.

We acknowledge that the variety of impaired gait in stroke patients cannot be fully captured with 8 subjects. However, our study would like to show that muscle synergies are able to quantify gait asymmetries in stroke patients and hope that this method would inspire others to use and refine our methods. That said, increasing the number of subjects remains a consideration for future studies.

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5

DIFFERENCES IN MUSCLE SYNERGY SYMMETRY BETWEEN SUBACUTE POST-STROKE PATIENTS DURING ROBOT-ASSISTED THERAPY AND CONVENTIONAL THERAPY

5.1 ABSTRACT

Spatiotemporal gait asymmetries are commonly observed in stoke patients due to hemiparesis. Gait asymmetries are known to cause long-term complications like joint pain and deformation. Recent studies have indicated that conventional clinical measures have difficulty in quantifying gait symmetry. Analysis with spatiotemporal measures in such studies showed that gait symmetry is difficult to correct and worsens after discharge. Recent advances in technology have seen the use of robotic exoskeleton during gait training of stroke patients. However, the improvement of patients who underwent robotic gait training was reported with clinical assessment metrics. Such metrics only provide a gross overview on the performance of the patient's gait, and is shown in other studies that they are unable to quantify gait symmetry. This study proposes evaluating muscle coordination symmetry between stroke patients undergoing robotic gait training (HAL group) and conventional gait training (Control group). This muscle coordination symmetry was obtained from surface electromyography (EMG) recordings of muscles in the lower limbs of stroke patients. Measurement for each patient was conducted at regular intervals over a course of gait training. An increasing trend of muscle coordination symmetry was observed for patients in the HAL group, whereas patients in the Control group did not exhibit this trend. Group comparisons showed that patients in the HAL group were more symmetrical in terms of muscle coordination after gait training. Analysis of muscle coordination reveals mechanisms of gait symmetry which could otherwise be difficult to observe with motor function tests. Similar to previous studies, it was noted that clinical scores are not correlated with muscle synergy symmetry and stance symmetry indices. Robotic gait training appear to provide an advantage over conventional gait training in restoring symmetrical neuromuscular control.

5.2 INTRODUCTION

5.2.1 *Stroke and gait asymmetry*

Gait impairment is traditionally associated with stroke, and hemiparesis is a common observance [18]. As a result of weakness in one side of the body, gait asymmetries are notable features in the loco-

motion of such patients. Gait asymmetries are known to cause long-term complications, like inefficient energy expenditure, together with joint pain and deformation [76]. Recently, studies indicated that gait asymmetries, like stance and swing symmetry are not adequately captured with conventional clinical measures, like gait velocity, motor deficit levels and impairment scores. Such clinical measures are uncorrelated with spatiotemporal measures of gait symmetry (e.g. step length, stance duration) ([58], [131]). Although the earlier study ([58]) tracked patients up to 6 years post stroke and reported that gait symmetry worsens, the more recent study by Rozanski and colleague did not find the worsening of gait symmetry to be as severe ([131]). However, Rozanski et al. noted that since the monitoring was only performed for 6 months, they hypothesized that the possibility of gait symmetry worsening is high ([131]). They also pointed out that the number of patients who improved their gait symmetry after therapy was lower than expected, which is an indication that gait symmetry is difficult to correct during in-patient therapy ([131]).

Evidence of the neurological basis of gait symmetry can be observed in studies evaluating the symmetry of cortical connectivity in both hemispheres of the brain. Through the use of a TMS (Transcranial Magnetic Stimulation) and MRI (Magnetic Resonance Imaging), Madhavan and colleagues provided evidence that stroke patients with greater ipsilateral cortical connectivity to the non-paretic lower limb suffered in accuracy when controlling their non-paretic ankle in a plantar and dorsiflexion task ([57]). Another similar study assessed side symmetry in the upper limbs by utilizing EEG (Electroencephalogram) and surface EMG (Electromyography) ([70]). They provided evidence that neural activity in the non-lesioned side drives asymmetry and only measures of symmetry were correlated with global recovery scores ([70]). Taken together with clinical observations, there appear to be a correlation between gait symmetry and the symmetry of the nervous system, which could suggest that improving gait symmetry could improve symmetry in the nervous system. However, due to the insufficient understanding of gait symmetry, design of effective interventions are difficult.

5.2.2 *Muscle synergy and its use in pathological gait analysis*

Muscle synergy analysis (MSA) is a method that has been previously applied in human gait and posture studies. It is used to characterize muscle activation patterns in humans ([39], [42]). The hypothesis is that a small number of spatially grouped muscles (known as muscle synergies), and their corresponding timing coefficients, are sufficient to describe various locomotion task, like walking. Muscle synergies has also been shown to be robust between subjects ([69]) and even between days ([107]). This method also serves as a dimension reduction method for further analysis. MSA has also been successfully applied on assessing gait performance in stroke patients ([110], [80], [63], [53]).

Hence, to allow better characterization of gait symmetry change, the use of MSA is proposed to analyze muscle coordination changes that occur over the course of different types of therapy, specifically in this study, the difference between robotic-assisted gait training and conventional gait training.

5.2.3 *Robotic gait training*

Recently, robotic suits have been developed for gait training and therapy for patients with neurological diseases ([29], [77], [27], [43]). Robotic therapy has been shown to be effective in therapy, with improved clinical scores observed in patients after robotic therapy ([105]). However, the mechanisms behind recovery were unclear and difficult to explain with clinical evaluation scores. A related study ([127]) showed that a course of robotic therapy was effective in restoring gait symmetry, as quantified by muscle synergies. However, that study was limited to accessing the outcome of patients after robotic therapy. Although post-therapy evaluations are useful to determine the effectiveness of robotic therapy, it is also important to evaluate muscle coordination symmetry change during the course of therapy, so as to provide additional information on the progress of the patients.

5.2.4 *Aims of study*

A related study ([98]), evaluated changes in spatiotemporal gait asymmetry during in-patient rehabilitation. This study was motivated by the lack of information about how patients change their spatiotemporal gait symmetry over the course of therapy. Their main findings was that a majority of patients did not significantly improve their gait symmetry during the course of therapy and after discharge. This current study would be a good complement to [98]'s study, since muscle coordination is evaluated over the course of physical therapy.

The current study aims to evaluate short-term changes in spatial and temporal muscle coordination symmetry, as quantified by the spatial organization of muscles used (muscle synergies) with their corresponding activation times (timing coefficients) in patients during a course of gait training therapy. This study is reported according to the TREND checklist ([28]). Please refer to the supplementary materials for details of the checklist.

5.3 METHODS

To evaluate the effects of robotic gait therapy on muscle coordination symmetry, subacute post-stroke patients were recruited and divided into 2 groups, with 1 group undergoing robotic gait training, while the other group undergoes conventional gait training. All patients were trained overground with a body weight support harness. Muscle coordination differences between groups were evaluated before and

after the course of therapy. Motor function test scores, stance duration and stance time ratio changes were also reported

5.3.1 *Participants*

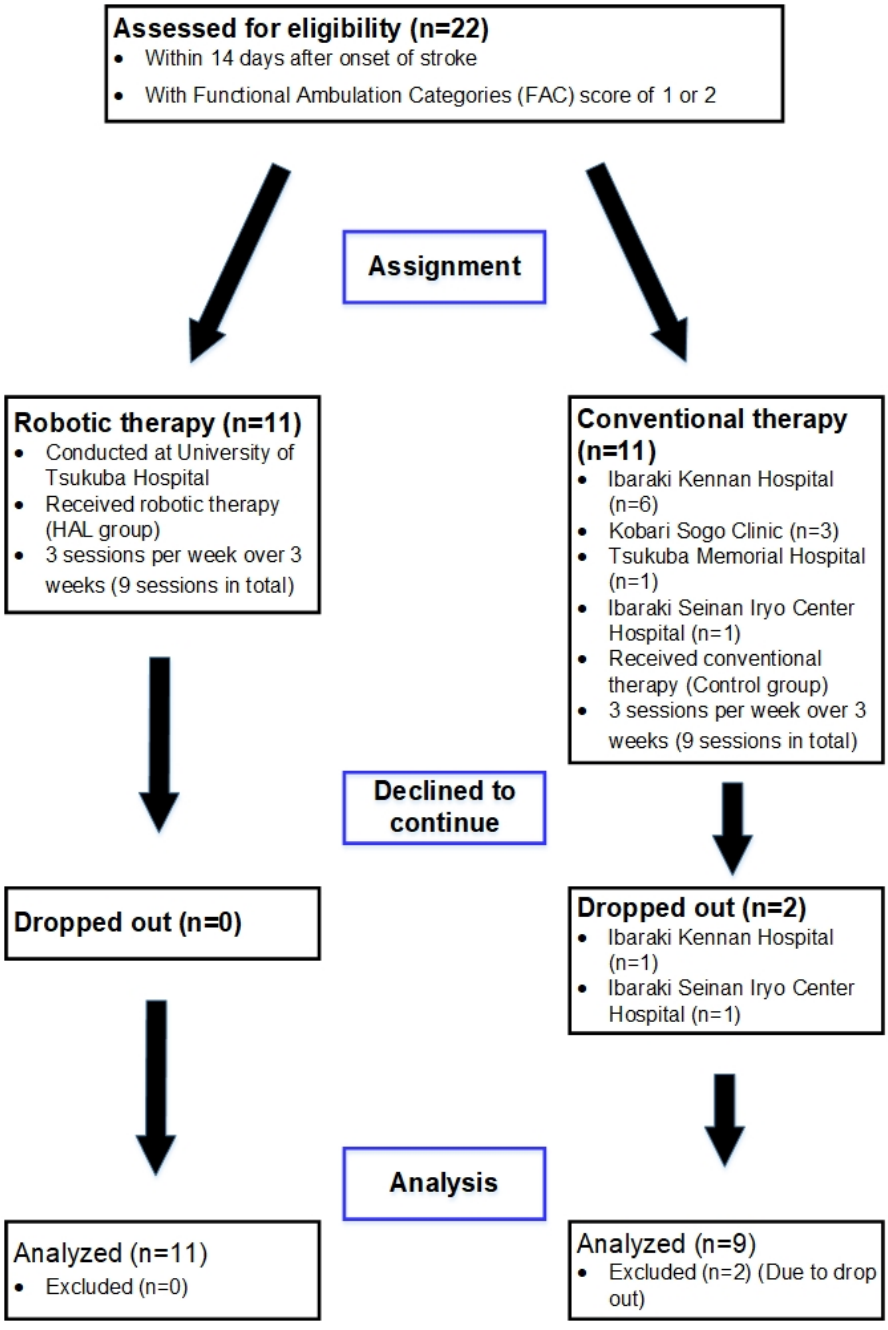

Figure 5.1: **Participant reporting flowchart:** Flowchart reporting on patient numbers, inclusion criteria and general overview of study protocol

Patients were recruited in a decentralized manner from the University of Tsukuba Hospital, Ibaraki Kennan Hospital, Kobari Sogo Clinic, Tsukuba Memorial Hospital and the Ibaraki Seinan Iryo Center Hospital. They were not randomized into groups and simply assigned based on the hospitals they were admitted to.

Patients recruited from the University of Tsukuba Hospital were assigned to the robotic gait therapy group (known as HAL group thereafter), while patients from the other hospitals were assigned in the conventional therapy group (known as Control group thereafter). Refer to the flowchart in Fig. 5.1 for details. Patients exhibiting hemiparesis after unilateral ischemic or hemorrhagic stroke, aged between 40 and 80, were examined by the Functional Ambulation Categories (FAC) criteria for inclusion (FAC score of either 1 or 2). Patients who had consciousness issues, cardiac disease (defined as myocardial infarction, severe heart failure, arrhythmia, or cardiomyopathy presenting abnormal blood pressure, heart rate or SpO2) or musculoskeletal problems were excluded. All patients arriving in the participating hospitals due to acute stroke were examined by the above criteria and recruited into the study if they fulfill the conditions. Numbers of patients recorded were only for those that fulfilled the criteria. Due to the difficulty in recruiting patients and matching intervention schedules between the groups across different hospitals, sample sizes were determined based on convenience, where at least 10 patients per group was set to be the target size.

Data of patients in the HAL group from the previous study [127] (Table 5.1 (R1 - R8)) were used for analysis in this current study. Data of new patients (Table 5.1 (R9 - R11)) that recently completed their course of therapy were included as well, making a total of 4 male and 7 female patients. HAL group patients were aged between 43 - 80 (60.27 ± 11.02) years old. They were included in the study about 10-18 (13.9 ± 3.2) days after the onset of stroke.

Initially, the Control group comprises of 7 male and 4 female subacute stroke patients. However, 2 patients dropped out of the study in the first session, citing stress due to attachment of EMG electrodes. Subjects that dropped out continued with their therapies at their respective hospitals, but no additional data was collected from them as they left the study. The remaining 6 male and 3 female stroke patients (Table 5.1 (C1 - C9)) underwent conventional gait training, with training schedules matched to the HAL group. Patients were aged between 49 - 76 (64.88 ± 8.79) years old. The control group were included in the study about 12-18 (15.6 ± 2.1) days after the onset of stroke.

Robotic gait training and all evaluations for the HAL group were performed in the University of Tsukuba Hospital, while conventional gait training and all evaluations for the Control group were performed at the following hospitals and clinics : Ibaraki Kennan Hospital, Kobari Sogo Clinic, Tsukuba Memorial Hospital, Ibaraki Seinan Iryo Center Hospital.

ID	Age (years)	Gender	Diagnosis	Affected side	Onset-Evaluation for eligibility	Onset-1st session (days)	FAC at 1st session
R1	67	F	CI	L	8	10	1
R2	52	F	ICH	R	13	17	2
R3	71	F	CI	L	7	11	1
R4	55	M	CI	L	8	10	2
R5	55	F	CI	L	14	16	3
R6	43	M	CI	R	8	11	2
R7	51	F	CI	R	15	18	2
R8	80	M	CI	R	14	16	2
R9	61	F	ICH	L	8	12	3
R10	72	F	ICH	R	12	14	1
R11	56	M	ICH	R	15	18	1
C1	76	M	ICH	R	15	17	1
C2	69	F	ICH	L	9	14	2
C3	64	M	ICH	L	14	15	1
C4	49	M	ICH	R	16	18	2
C5	69	F	CI	L	10	17	2
C6	66	F	CI	L	14	12	2
C7	73	M	ICH	R	10	16	2
C8	65	M	CI	R	15	18	2
C9	53	M	CI	L	15	14	2

Table 5.1: **Participants characteristics** Diagnosis was classified into Cerebral Infarction (CI) and Intracerebral Hemorrhage (ICH). HAL patients were labelled with the "R" prefix in their IDs (R1 - R11), while conventional therapy patients were given the "C" prefix (C1 - C9). Note that there is a difference of a few days between the evaluation for study eligibility and start of actual gait training.

5.3.2 *Gait training methods*

In addition to gait training described here, both groups of patients (HAL group and Control group) received a total of 160 minutes per week of conventional regular physiotherapy as part of their rehabilitation during their subacute phase, in their respective hospitals.

5.3.2.1 *HAL group*

The single leg version of Robot Suit HAL (Hybrid Assistive Limb) [29] was used for patients in the HAL group. Briefly, the robot was composed of 4 rigid segments (lumbar, thigh, shank and shoe), ac-

tuated with motors in the hip and knee joints. EMG signals were detected from the surface of the skin over the hip flexor (Iliopsoas) and extensor muscles (Gluteus Maximus), as well as, the knee flexors (Hamstring) and extensor muscles (Vastus Lateralis). The ratio between the flexor and extensor muscles determines the direction and amount of assistive torque that is to be generated in real time. Gain parameters can be set individually for each flexor or extensor muscle by the therapist until the patient is comfortable with controlling the robot. A more detailed description of the control paradigm of the robot suit is available in ([127]).

Patients followed the protocol detailed in [127]. Briefly, HAL therapy was started during the participants' subacute period (Table 5.1). For each patient in the HAL group, overground gait training were performed 3 times per week for 3 weeks, for a total of 9 sessions, using HAL. Each session lasted approximately 60 minutes, with 20 minutes devoted to walking training, and the remaining time for clinical examinations, wearing and removing the robot from the patient. Patients walked in a 25m course, composed of two straight lines and two semicircles, for several laps until accumulated walking time reaches 20 minutes. No specific instructions were provided to the patients, other than the encouragement to walk. For safety and fall prevention, a walking device (All-in-One Walking Trainer, Ropox A/S, Naestved, Denmark) with a harness was used.

5.3.2.2 *Control group*

For each patient in the Control group, the same amount of overground gait training as the HAL group was performed (3 sessions each week for a total of 9 sessions). Each session lasted approximately 60 minutes, with 20 minutes of walking and the remaining time for clinical examinations. However, the use of a walking device and harness during the training was not mandated and left to the discretion of the attending physiotherapist. No specific instructions were provided, other than the encouragement to walk

5.3.3 *Data measurement*

5.3.3.1 *Data collection protocol*

Lower limb movement of patients in the HAL group was measured with a motion capture system (detailed in Section 5.3.3.3). Lower limb muscle activity were measured with wireless EMG electrodes (detailed in Section 5.3.3.2). Measurement was conducted during straight-line walking, at a self-selected speed without wearing HAL. Measurement schedule are as follows: before the 1st session, before the 4th session, before the 7th session, and after the 9th session. The All-In-One Walking Trainer (Ropox A/S, Denmark), with a harness, was used during the walking test to prevent falls. The harness was adjusted such that it did not provide any weight support. The patients

walked for 6 meters several times, until at least 3 gait cycle per limb were obtained. Also, the initiation and termination of walking during each 6 meters walking trial were discarded as well.

Gait of patients in the conventional gait training group was measured with the same protocol as the HAL group (self-selected walking speed, 6m walking distance, All-in-One Walking training with harness for fall prevention, harness did not provide weight support, and at least 3 gait cycle per limb were collected). Measurement schedule was matched with the HAL group (Before course of therapy, before 4th session, before 7th session, after 9th session). Lower limb muscle activity were measured with the same EMG system defined in Section 5.3.3.2. However, due to the lack of a motion tracking system for this group, gait events (heel strike and toe off) were determined with foot pressure sensors, detailed in Section 5.3.3.4

5.3.3.2 *Electromyography*

Skin preparation included wiping down the muscle bellies with alcohol swabs. 12 wireless, surface EMG electrodes were placed bilaterally over the muscle bellies of: Vastus Medialis (VM), Hamstrings (HAM), Tibialis Anterior (TA), Gastrocnemius (GAS), Adductor Longus (ADD), Gluteus Maximus (Gmax), using a Trigno^{TM} Lab Wireless electromyography (EMG) system (Delsys Inc., Boston, MA, USA). EMG data was sampled at 2000 Hz. This data measurement protocol was applied on both groups of patients

5.3.3.3 *Motion Tracking*

For the HAL group, motion tracking of subjects was achieved with a motion capture system (VICON MX System with 16 T20S Cameras, Vicon, Oxford, UK), in synchronization with EMG and sampled at 100 Hz. Similar to our previous study ([127]), 16 autoreflective markers were placed bilaterally on the anterior superior iliac spine, posterior superior iliac spine, lower lateral 1/3 surface of the thigh, flexion-extension axis of the knee, lower lateral 1/3 surface of shank, lateral malleolus for the ankle, posterior peak of the calcaneus for the heel and the lateral second metatarsal bone of the toe. These marker positions were used for gait phase detection during locomotion.

5.3.3.4 *Foot pressure sensor*

For the Control group, gait phase was determined with foot pressure sensors, Trigno^{TM} 4-channel FSR (Force Sensitive Resistor) (Delsys Inc., Boston, MA, USA), sampled at 100 Hz. 2 FSRs were used, with a FSR pasted below the big toe and the other pasted below the heel of patients. Shoes from the same manufacturer were provided for the patients to ensure that FSR values were not affected by different shoe types. Gait phase detection was based on the pressure sensor values.

5.3.4 *Verification between Vicon and foot pressure sensors*

A small verification test was conducted to check the differences in measurement values between the motion tracking system and foot pressure sensors. Data from 3 healthy subjects were collected for over-ground walking. Similar to the Control group, foot pressure sensors (Delsys, Trigno^{TM} 4-channel FSR (Force Sensitive Resistor), sampled at 100 Hz) were used, with 1 FSR pasted below the big toe and the other pasted below the heel. Shoes, which have the same manufacturer as the Control group, were provided. The same motion capture system (VICON MX System with 16 T20S Cameras, Vicon, Oxford, UK, sampled at 100 Hz), was used. 6 reflective markers were placed bilaterally on the lateral malleolus for the ankle, posterior peak of the calcaneus for the heel, and the lateral second metatarsal bone of the toe. Subjects walked for 5 trials of 10m each, at a self-selected speed. Heel-strike and toe-off events were recorded for both legs in order to calculate stance duration for both legs. The absolute error between the values from both measurement systems were calculated.

5.3.5 *Clinical assessments*

Motor function evaluation were conducted at the 1st session and after the 9th session. These evaluation are listed below:

1. Functional Independence Measure - Locomotion (FIM - Locomotion)
2. Functional Independence Measure - Motor (General) (FIM - Motor (General))
3. Fugl-Meyer Assessment, Lower Extremity (FMA - LE)

Stance duration in relation to each gait cycle was recorded as it has been shown to be a relatively good indication of symmetry in other studies ([58]).

5.3.6 *Data analysis*

5.3.6.1 *Preprocessing*

The extracted EMG data was first band-passed with a 4th order, zero-lag Butterworth filter at 30 - 400 Hz. The bandpassed EMG was then filtered with a Hampel filter (parameters : time window - win $= 200$, threshold - $\sigma = 4$) to remove noise artefacts. Finally, the EMG data was fully rectified and low-passed at 6 Hz, with a 4th order, zero-lag Butterworth filter.

5.3.6.2 *Extraction of gait events*

For the HAL group the elevation of the heel markers were used to identify gait events. A heel strike is determined to be the point where elevation of the heel reflective marker is at the lowest point. A toe-off

is determined to be at the point right before a steep increase in elevation of the toe reflective marker.

A total of 3 consecutive gait cycles, bounded by a heel strike and ending with a heel strike, were extracted from the middle of each recording session from each leg, for each participant in both groups. The 3 gait cycles were labelled as Paretic and Non-paretic. The initiation and ending of gait are discarded. A total of 6 gait cycles, 3 gait cycles per side, were chosen because this was the minimum number of calculable gait cycles that can be extracted from a 6m walk test from all subjects, across all sessions.

A selection criteria was imposed to select consistent gait cycles from the data. This criteria would help filter out gait cycles where patients stumble. Selection criteria is as follows: Heel strikes were segmented into windows consisting of 7 consecutive heel strikes, starting from a paretic heel strike, ending on the paretic heel strike. The average duration between each heel strike, from paretic to non-paretic and vice versa, were calculated for each window. The window with the smallest average duration between heel all strikes were chosen as the most consistent gait cycle.

The process of extracting heel strikes from the control group is illustrated in Fig. 5.2. Similar to the HAL group, a selection criteria designed to extract consistent gait cycles. A heel strike is determined to be the start of the rising edge of heel pressure sensor values. Heel strikes were segmented into windows consisting of 7 consecutive heel strikes, starting from a paretic heel strike, ending on the paretic heel strike. The average duration between each heel strike, from paretic to non-paretic and vice versa, were calculated for each window. The window with the smallest average duration between heel strikes were chosen to have the most consistent consecutive steps. A total of 6 gait cycles, 3 gait cycles per side were chosen for the Control group as well, to keep the amount of data consistent between groups.

5.3.6.3 *Extraction of EMG*

Preprocessed EMG data (Section 5.3.6.1) of 6 consecutive gait cycles were separated into Paretic and Non-paretic windows, each having 3 gait cycles (Paretic side, Non-paretic side), using the best heel strike indices obtained from Section 5.3.6.2. EMG from each gait cycle was then normalized by dividing each vector with its standard deviation, following the definition of "UnitPer" described in [109]. The normalized EMG was then interpolated to 100 time points and concatenated together, giving a matrix of 6x300 (6 EMG channels by 300 time points), for each lower limb.

5.3.6.4 *Muscle synergy extraction with NNMF*

Non-negative Matrix Factorization (NNMF) ([21]) was used to extract muscle synergies from concatenated EMG data. This was performed

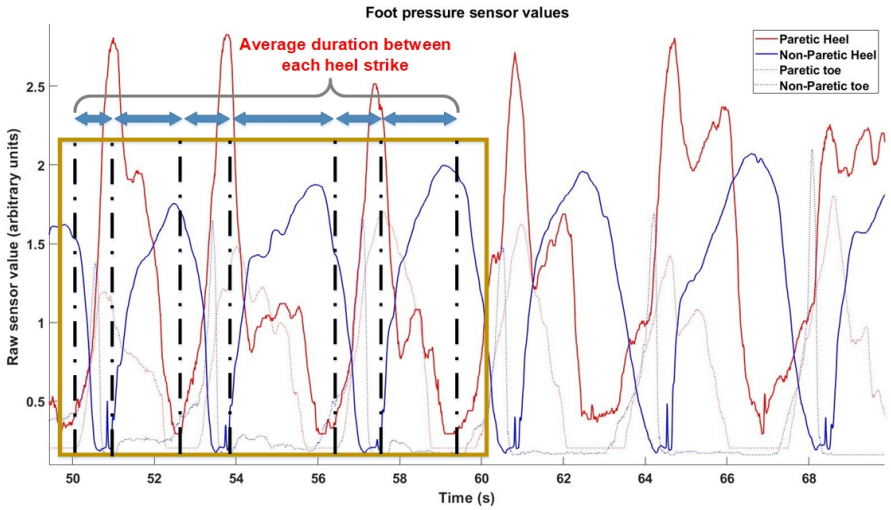

Figure 5.2: **Gait cycle extraction method:** Extraction of windows of consecutive steps for control group. Yellow box illustrates one of the windows consisting of 7 heel strikes, starting from the paretic heel strike and ending with a paretic heel strike. The average duration between each consecutive heel strike is calculated. The process is repeated until all possible windows are calculated. The window with the smallest average duration between heel strikes is considered to be the one with the most consistent steps. Note that the y-axis is in arbitrary units as it has been normalized to illustrate the pressure magnitudes

with Matlab's NNMF function, using the multiplicative update algorithm. Parameters for the tolerance for the residual (TolFun) was given as $1e-6$ and the tolerance for the relative change in elements (TolX) was given as $1e-4$. The algorithm was repeated 300 times and results with the lowest root mean square residual were taken to be the best. Synergies were allowed to vary per condition.

The choice of number of synergies were determined with the criteria of when the overall variance-accounted-for (VAF_{total}) between the reconstructed and original EMG envelope was above 90%. A local criteria imposed was that the reconstruction VAF (VAF_{muscle}) for each muscle vector was above 75% and that and subsequent increase of the number of synergies did not give more than a 5% increase in VAF [53]. The VAF is defined as $100 * (\text{uncentered Pearson correlation coefficient})$, which requires the total sum of squares to be taken with respect to zero [42]. This is given as:

$$VAF = 100 \cdot \left(\frac{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm} \cdot Y_{nm})^2}{(\sum_{j=1}^{m} \sum_{i=1}^{n} X_{nm}^2) \cdot (\sum_{j=1}^{m} \sum_{i=1}^{n} Y_{nm}^2)} \right) \tag{5.1}$$

where n is the number of datapoints for each channel, and m is the number of channels. X_{nm} and Y_{nm} are the matrices containing the reconstructed and original signal respectively.

5.3.6.5 *Synergy Analysis*

Prior to comparison, muscle synergy vectors on the paretic side were matched according to the muscle synergy vectors on the non-paretic side. The similarities of muscle synergies on the paretic side to the non-paretic side were calculated with the scalar dot product ([68]). The pair with the highest similarity score was removed from the pool and the process continues until all synergy vectors were matched. This matching process was repeated for all sessions and subjects. An infograph of the matching process is provided in Figure 5.3.

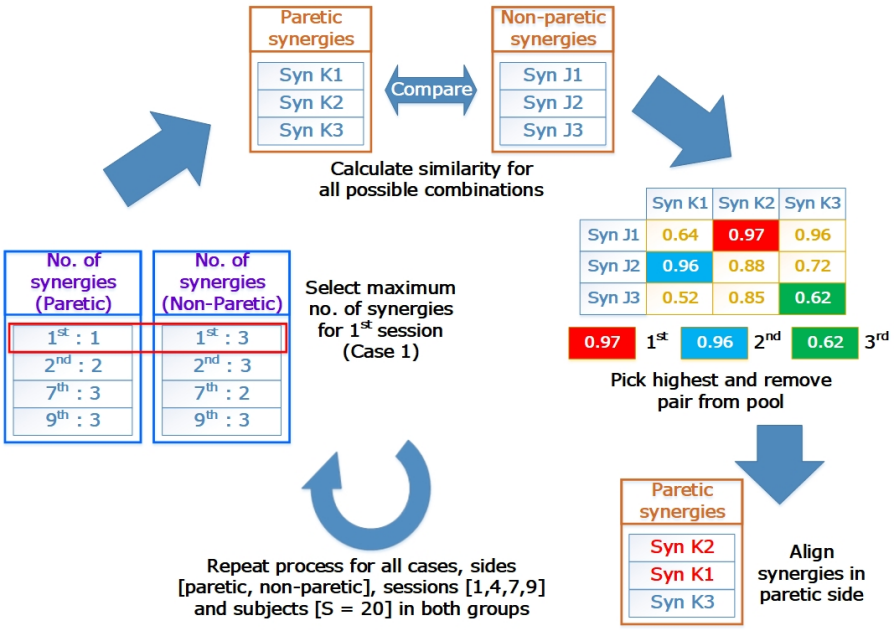

Figure 5.3: **Muscle synergy matching Infograph** Graphical representation of matching muscle synergies vectors on the paretic side to the non-paretic side. Similarity between each synergy is quantified with the scalar dot product

This matching process was carried out based on 2 parameters:

1. Comparison_{Max}: Maximum number of synergies within sessions

2. Comparison_{Min}: Minimum number of synergies within sessions

Typically, the number of synergies were chosen based on a threshold value of the VAF ([42], [53]). However, this would mean the paretic and non-paretic side will have different number of synergies, with the paretic side usually having a smaller number of synergies due to merging of synergies ([68]). This makes direct comparison between the synergies difficult. Hence, by imposing the same number of synergies on both the paretic and non-paretic side, direct comparison becomes possible. However, to prevent information loss with such a method, all possible number of synergies will have to be considered during analysis. For example, the "Maximum number of synergies within sessions", picks the side (either non-paretic or paretic) with the most number of synergies (as extracted with the criteria defined

in Section 5.3.6.4), and uses this selected number of synergy for both the paretic and non-paretic side for comparison. This process was then repeated until all synergies for all possible conditions and sessions were matched.

After the matching process, synergies on both sides of the body were compared with the scalar dot product and the mean of each comparison was recorded. Additionally, the similarity of the corresponding timing coefficients for the muscle synergies were evaluated with the Pearson correlation coefficient, R. Evaluation was done with the mean of the timing coefficients from each step to account for step-to-step variability.

5.3.6.6 *Muscle synergy symmetry and Stance duration*

It is also in the interest of this study to investigate whether muscle synergy symmetry has any relation to stance duration. The Pearson Correlation Coefficient (R) is used to evaluate if there are any linear correlations between muscle synergy symmetry and stance duration progressions through therapy. Linear correlation between muscle synergy symmetry and the stance duration ratio was also evaluated. The stance duration ratio was defined in ([59]):

$$\text{stance ratio} = T_{paretic}/T_{non-paretic} \tag{5.2}$$

where $T_{paretic}$ and $T_{non-paretic}$ are the stance duration of both the paretic and non-paretic side respectively, expressed in percentages of the gait cycle

5.3.6.7 *Software*

Data extraction from the Motion capture and EMG systems was done using custom scripts on MATLAB 8.4 (Mathworks, Natick, MA, USA). NNMF and the rest of the processing were performed with custom scripts on MATLAB 9.3 (Mathworks, Natick, MA, USA). Statistical tests were performed with R (version 3.5.3).

5.3.7 *Statistical analysis*

Statistical analysis of the data was performed with the Paired Wilcoxon Signed-rank Test for comparison of clinical scores, muscle synergy symmetry and stance duration within groups. Due to unequal group sizes, intergroup comparisons of muscle synergy symmetry and stance duration were evaluated with the Mann-Whitney U-Test. Significance was considered in comparisons with $p < 0.05$ with 95% confidence intervals reported. Statistical analysis was performed with non-parametric tests as normality of the distribution cannot be assumed.

A preliminary two-way ANOVA was used on the obtained symmetry values to check for interaction between the choice of number of synergies and therapy outcome (pre therapy or post therapy). This

is to check if selecting different number of synergies would cause gait symmetry to be estimated differently. There was no interaction between the different choices of number of synergies and therapy outcomes ($p = 0.5187$), indicating that selecting different number of synergies are not affecting therapy outcomes.

5.4 RESULTS

5.4.1 *Patient characteristics*

The age of patients between groups did not significantly differ (HAL group (60.27 ± 11.02) vs Control group (64.88 ± 8.79)) ($p = 0.4030$, $CI = [-14.0000, 6.0000]$). The duration from the onset of stroke to the first session of gait training did not differ as well (HAL group (13.9 ± 3.2) vs Control group (15.6 ± 2.1)) ($p = 0.2345$, $CI = [-5.0000, 1.0000]$). Group comparisons of FIM-Locomotion, FIM-Motor, and FMA-LE scores at the 1st session did not show significant differences (FIM-Locomotion: $p = 0.0923$, $CI = [-1.9999, 0.0000]$) (FIM-Motor: $p = 0.6209$, $CI = [-9.0000, 21.0000]$) (FMA-LE: $p = 0.7320$, $CI = [-8.0000, 10.0000]$)

5.4.2 *Clinical scores*

The FIM-Locomotion (FIM-Loco) score ($p = 0.0087$, $CI = [-4.9999, -2.4999]$), FIM-Motor (General) score ($p = 0.0038$, $CI = [-27.0000, -12.9999]$), FMA-LE scores ($p = 0.0038$, $CI = [-7.0000, -3.4999]$) increased in the HAL group. (Table 5.2 (R1 - R11)). Patients in the Control group (Table 5.2 C1-C9) had significantly increased clinical scores in all categories, pre and post therapy (FIM-locomotion ($p = 0.0206$, $CI = [-3.5000, -1.0000]$), FIM-Motor (General) ($p = 0.0091$, $CI = [-27.5001, -9.0000]$) and FMA-LE ($p = 0.0090$, $CI = [-9.0001, -3.4999]$)).

ID	FIM-Loco (Pre)	FIM-Loco (Post)	FIM-Motor (General) (Pre)	FIM-Motor (General) (Post)	FMA-LE (Pre)	FMA-LE (Post)
R1	1	3	46	73	13	18
R2	1	5	40	82	19	26
R3	1	2	40	55	18	28
R4	2	7	52	77	26	29
R5	2	7	78	90	20	27
R6	1	6	66	83	21	25
R7	1	1	53	62	14	22
R8	1	5	50	65	17	20
R9	2	5	68	82	29	30
R10	1	5	62	83	26	30
R11	1	1	60	72	14	20
C1	2	3	29	35	3	10
C2	3	5	55	64	12	24
C3	1	2	18	48	9	16
C4	1	1	54	76	24	25
C5	1	1	46	64	9	18
C6	5	6	62	86	27	33
C7	3	5	67	71	29	33
C8	3	5	65	83	25	27
C9	1	6	50	87	25	34

Table 5.2: **Clinical evaluation scores** At the 1st session (Pre) and after the 9th session (Post). Patients with the "R" prefix belong to the HAL group, while patients with the "C" prefix belong to the Control group

5.4.3 *Overview of EMG*

Fig. 5.4 below provides an graphical overview relating the change in the EMG and stance duration. The first 2 subfigures (Fig. 5.4 (A, B)) illustrates the changes in the HAL group, while the following 2 (Fig. 5.4 (C, D)) illustrates changes in the Control group

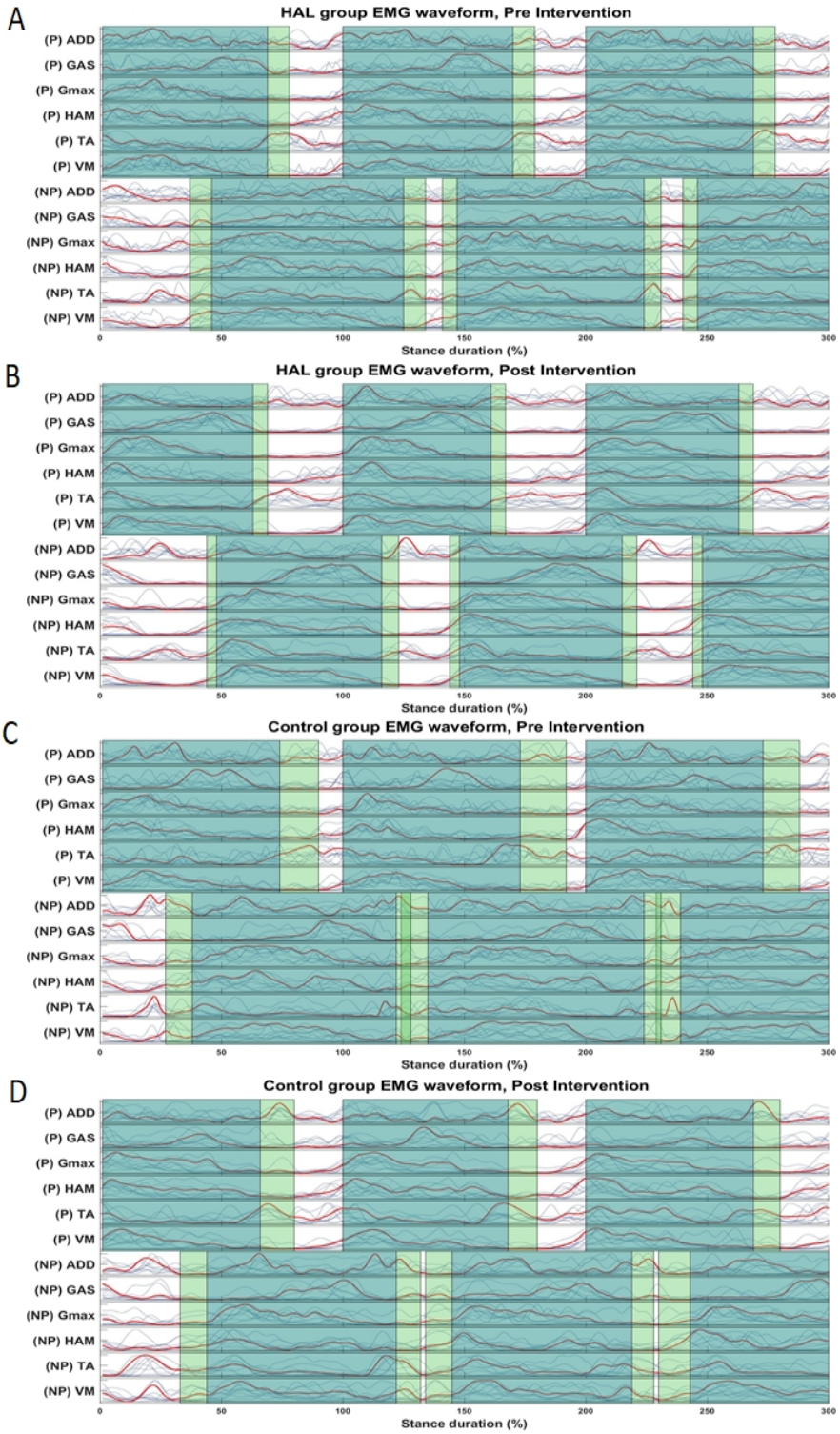

Figure 5.4: **Overview of rectified EMG and stance duration** Overview of changes in stance duration and EMG waveform for both HAL and Control group. Dark green shaded areas represent the mean stance duration for patients in their respective groups, while the lighter green areas represent the standard deviation. Red lines indicate the mean EMG amplitudes for the respective groups, while the faint blue lines represents EMG waveform from each patient. Stance durations for the non-paretic side are time-normalized according to the paretic heel strikes

5.4.4 *Stance duration*

Stance duration, expressed as a percentage of the gait cycle (heel strike to heel strike), was evaluated and shown in Fig. 5.5 (Left). A significant decrease in stance duration was observed in the HAL group for both legs after therapy (69.1 ± 8% -> 62.4 ± 5% ($p = 0.0029, CI = [0.0232, 0.1085]$) (Paretic leg), 77.4 ± 8% -> 68.2 ± 4% ($p = 0.000977, CI = [-0.0512, 0.1295]$) (Non-paretic). Marked with an asterisk in Fig. 5.5 (Left - Red Lines with asterisk)). However, a significant decrease in stance duration was only observed in the non-paretic leg of the Control group (86.9 ± 8% -> 77.3 ± 9% ($p = 0.0039, CI = [0.0552, 0.1431]$) (Non-paretic) Fig. 5.5 (Left - Blue Lines with asterisk)), while the stance duration of the paretic leg was not significantly decreased (73.4 ± 15% -> 67.9 ± 11 % ($p = 0.4258, CI = [-0.0474, 0.1823]$) (Paretic leg)). Significant differences was observed for non-paretic stance duration between the HAL group and Control group in both the 1st session ($p = 0.0159, CI = [-0.1880, -0.0129]$) and 9th session ($p = p = 0.0465, CI = [-0.1684, -0.0014]$) (Indicated with a diamond in Fig. 5.5 (Left)). However, no significant differences were observed in the paretic stance duration between groups before and after their respective therapies.

Direct comparison of stance duration percentages between the paretic and non-paretic limbs within the HAL group showed significant differences in stance duration percentages pre-therapy (1st session: $p = 0.0029, CI = [-0.1451, -0.0266]$) and after therapy (9th session: $p = 0.0068, CI = [-0.0991, -0.0207]$). The Control group also showed significant differences in stance duration percentages pre-therapy (1st session: $p = 0.0195, CI = [-0.2827, -0.0287]$), but not in the last session (9th session: $p = 0.1641, CI = [-0.2310, 0.0341]$)

As for Stance Time ratio, a stance symmetry metric, No significant differences were observed in both the HAL ($p = 0.5195, CI = [-0.0685, 0.0438]$) and Control ($p = 0.4961, CI = [-0.1868, 0.1101]$) group after the course of therapy (Fig 5.5 (Right)). Intergroup comparisons of stance ratio symmetry is also not significant pre-therapy (1st session: $p = 0.5027, CI = [-0.0679, 0.1769]$) and post-therapy (9th sessions: $p = 0.9408, CI = [-0.1017, 0.1698]$)

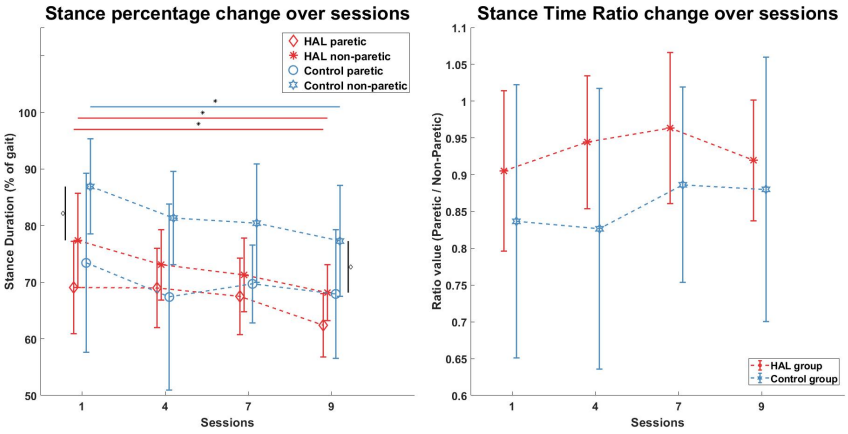

Figure 5.5: **Stance Duration and Stance Ratio** Mean stance duration in both the paretic and non-paretic lower limbs for the HAL group were significantly different before and after therapy (indicated by an asterisk). Only the non-paretic leg for the Control group showed significant differences. Non-paretic stance percentages differences were significant between the HAL group and Control group, before and after their respective courses of therapy (indicated by a diamond) (Left). Stance Time Ratios, however, were not significantly different from the 1st and 9th session, and also not significantly different between groups. (Right)

5.4.5 *Muscle synergy symmetry*

The figure below provides an example how would muscle synergies extracted with the comparison conditions described in Section 5.3.6.5 look like (Fig. 5.6). A representative subject, S10, was selected from the HAL group because the patient has the most number of muscle synergy change throughout therapy.

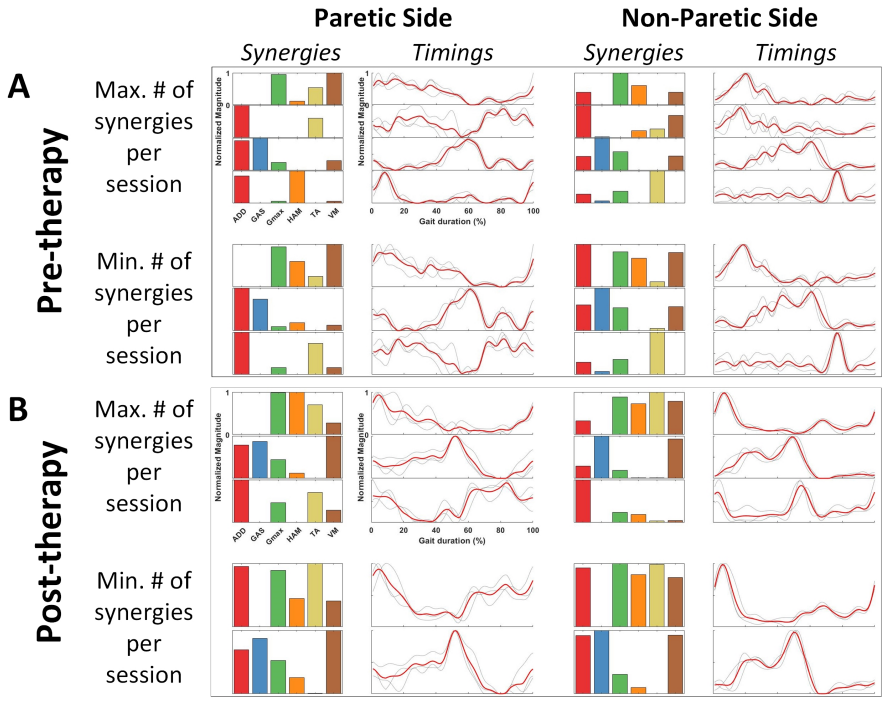

Figure 5.6: **Representative subject (S10) with all synergy extraction parameters** Figures are arranged as (A) Pre-therapy, Paretic Side (Left column) Non-Paretic Side (Right column) (B) Post-therapy, Paretic Side (Left column) Non-Paretic Side (Right column). Rows for both pre and post therapy conditions show the synergies extracted with comparison parameters: "Max number of synergies per session" and "Min number of synergies per session" respectively

Comparison of muscle synergy modules showed a trend of increasing symmetry for the HAL group, (0.76 ± 0.11 -> 0.88 ± 0.09, ($p = 0.0098, CI = [-0.2050, 0.0248]$)) (Fig. 5.7 (Left)). However, no significant differences were observed in symmetry values in the Control group ($p = 0.6523, CI = [-0.1491, 0.0979]$) (Fig. 5.7 (Right)).

For the symmetry in the corresponding timing coefficients of the matched synergies, increasing symmetry was also observed (0.3 ± 0.26 -> 0.58 ± 0.28 ($p = 0.0068, CI = [-0.5261, 0.0491]$)) (Fig. 5.8 (Left). No significant increase in timing coefficient symmetry was observed in the Control group ($p = 0.9102, CI = [-0.4435, 0.1886]$) (Fig. 5.8 (Right)).

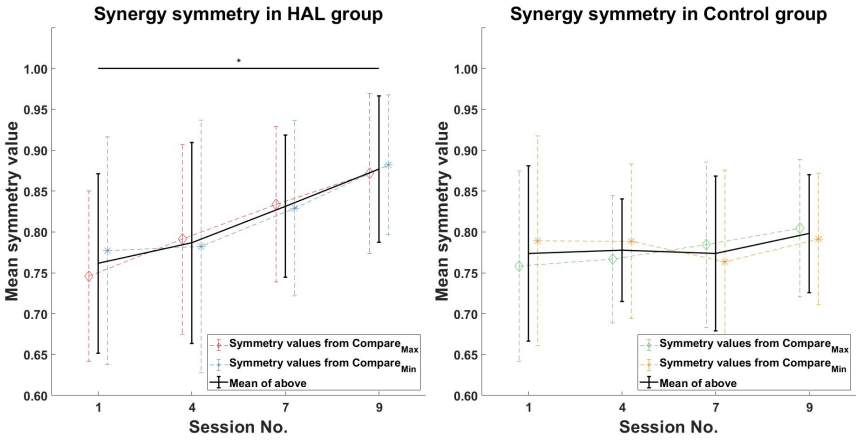

Figure 5.7: **Muscle synergy symmetry comparison** Increasing symmetry in muscle synergy modules in the HAL group observed, but not in the Control group. Black asterisks denote significant increases in symmetry from the 1st session to the 9th session. Lines with symbols denote the mean, while errorbars denote standard deviations

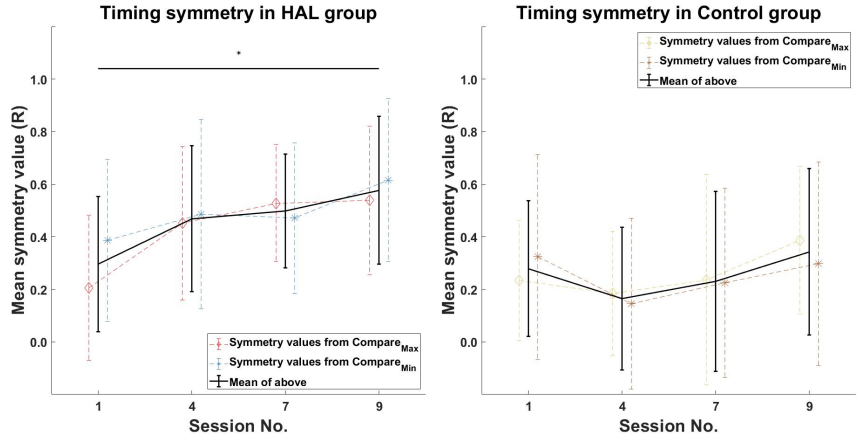

Figure 5.8: **Synergy timing symmetry comparison** Increasing mean symmetry in corresponding timing coefficients in the HAL group (Left). However, no significant improvement in the Control group can be observed. Black asterisks denote significant increases in symmetry from the 1st session to the 9th session, Lines with symbols denote the mean, while errorbars denote standard deviations

Between the two patient groups (HAL and Control), there were no significant differences in synergy symmetry ($p = 0.8238, CI = [-0.1164, 0.1213]$) and timing symmetry ($p = 0.7664, CI = [-0.2391, 0.2482]$) for both HAL and Control groups before gait training (Fig. 5.9, (Left PRE and Right PRE), 1st session). However, there were significant differences in symmetry indices post therapy in terms of synergy symmetry (0.88 ± 0.09 vs 0.8 ± 0.072, $p = 0.0381, CI = [0.0111, 0.1678]$)) (Figure 5.9 (Left POST)) and but no significant differences in timing symmetry (0.58 ± 0.29 vs 0.34 ± 0.32, $p = 0.0952, CI = [-0.0457, 0.5880]$) (Figure 5.9 (Right POST))

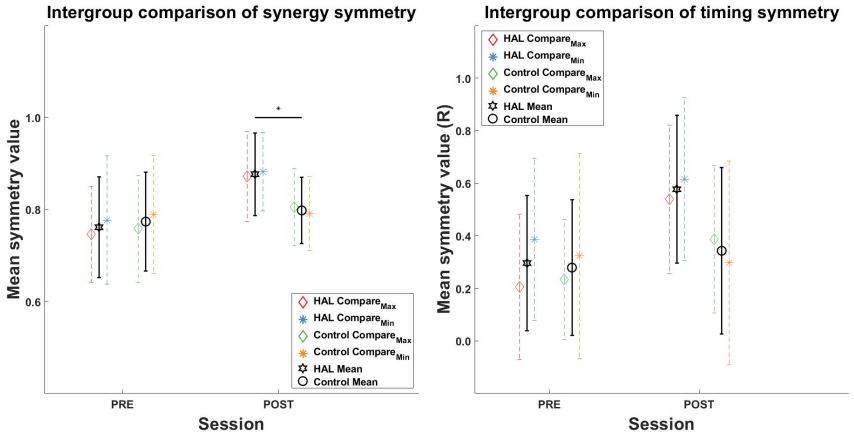

Figure 5.9: **Intergroup comparison of muscle synergy and timing, pre and post therapy** Muscle synergy symmetry between groups were not significantly in the 1st session. However, after their respective course of therapies, patients in the HAL group showed greater symmetry when compared with the Control group. Plotted symbols denote the mean, while errorbars denote standard deviation. Asterisks denote statistical significance

5.4.6 *Correlation between muscle synergy symmetry and stance duration*

Correlations between the stance duration, stance ratio and muscle synergy symmetry was explored and tabulated in the table below (Table 5.3).

Variables / **Symmetry conditions**	HAL Paretic	HAL Non-paretic	Control Paretic	Control Non-paretic	Stance Time Ratio (HAL)	Stance Time Ratio (Control)
Max. within session	−0.8645	−0.9896	−0.5597	−0.9061	0.3495	0.8303
Min. within session	−0.9650	−0.9061	−0.0396	0.1155	0.0557	−0.5641

Table 5.3: **Correlation between symmetry and stance duration** R values (Pearson correlation coefficient), relating muscle synergy symmetry with the paretic and non-paretic stance duration. Values are calculated with the mean values in each condition

5.4.7 *Verification of between sensor detection*

Figure 5.10 depicts the mean and standard deviation stance duration values of the 3 healthy subjects, from both measurement systems. Stance duration values were similar (Figure 5.10 Left) between both systems and the differences (Figure 5.10 Right) were within 1%

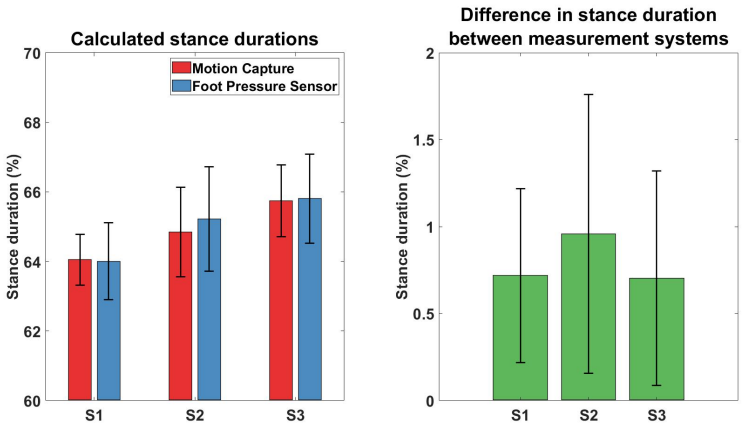

Figure 5.10: **Comparison of calculated stance duration between different measurement systems** Results of the stance duration from 3 subjects, measured with different gait tracking systems. Left plot depicts the mean and standard deviation of the values recorded from the two measurement systems, while the Right plot depicts the difference between the values from both systems

5.5 DISCUSSIONS

Our study aims to quantify gait symmetry changes with muscle synergies and evaluate differences in muscle coordination between patients undergoing robotic gait training and conventional gait training (HAL group vs Control group). Our results showed that this method is a good complement to clinical scores and reveal some key differences between patients in different groups.

5.5.1 *Comparison with multiple number of synergies*

Muscle synergies and their corresponding timings were compared using multiple number of synergies extracted from different conditions (Section 5.3.6.5). The key reason behind this comparison is to allow direct comparison between the paretic and non-paretic limbs, which typically have different number of synergies ([68]). However, imposing the same number of synergies on both the paretic and non-paretic limb would make estimation of the contents of muscle synergies difficult, since either too many or too few synergies were used. Our method attempts to resolve this by taking the mean of multiple comparisons with different number of synergies. The results obtained from such comparisons (Fig 5.7 and 5.8) allowed us to quantify the trend in muscle coordination change through in-patient rehabilitation. It is believed that this method has a few advantages over selecting a single number of synergy, first is the ease of direct comparison between contents of muscle synergies. Second, multiple comparisons with different parameters helps to validate trends in the data. If results using different parameters agree, then one can have a better confidence that a trend exist in the data.

5.5.2 *Lack of correlation between clinical scores and gait symmetry*

In our study, A lack of correlation between stance symmetry and clinical scores was observed, as was noted in a previous study ([58]). There was significant improvement in clinical scores of patients in the Control group (Table 5.2), while there is a lack of improvement in stance symmetry (Fig. 5.5 (Right)) and muscle synergy and timing symmetry (Fig 5.7 (Right) and 5.8 (Right)). This provides more evidence that clinical scores are not adequately evaluating gait symmetry in patients.

The lack of significant improvement in stance time and muscle synergy symmetry of patients in the Control group (Fig 5.5 (Control), and Fig 5.7 (Right)) was supported by studies that found patients do not significantly improve spatiotemporal gait symmetry over the course of conventional therapy ([98], [131]). Although our results show no significant differences in stance duration between groups for the paretic and non-paretic limbs (Fig 5.5), it is believed that it could be a result of the large standard deviations in stance duration found in the Control group. Nevertheless, there was a significant improvement in stance duration of both legs in the HAL patients after treatment, and stance duration of the non-paretic leg for the Control group.

5.5.3 *Improvement in muscle coordination in the HAL group*

The increase of symmetry values in muscle synergy comparisons indicate that patients in the HAL group learned how to coordinate their limbs in a symmetrical manner (Fig. 5.7 (Left)). The change in contents of the muscle synergies indicate significant reorganization of spatial muscle coordination. It is believed that the HAL exoskeleton achieves this by allowing patients to trigger movement based on detected peripheral neuromuscular activity, thus allowing movement and sensory stimuli from the lower limbs to propagate to the brain, aiding neurorehabilitation. Torque assistance by the HAL provided on demand helps patients identify voluntary movement, as no assistance will be provided if the patient decides not to move the limb. Since this is a study that focuses only on muscle coordination changes during therapy, it would be interesting for future work to examine if such improvement in muscle coordination would improve long-term gait symmetry after discharge from the therapy program.

5.5.4 *Muscle usage and body weight bearing on limbs*

Patterson et al. pointed out that improvement in swing symmetry could be correlated with increased body weight bearing on the paretic limb ([98]). Further support for this correlation comes from a study by Hendrickson et al. ([88]). They found a correlation between balance in quiet standing and gait, that is, patients that walked asymmetri-

cally had similar patterns of asymmetry during balance. Similarly, Yavuzer et al. found that balance training that compelled patients to bear more weight on their paretic side also improved gait symmetry ([38]). In such a context, it could be that paretic limb weight loading could be facilitated by the HAL exoskeleton during gait training, as the exoskeleton compensates for weakness in the paretic limb by providing compensatory torque around the knee and hip joints during walking in post-stroke patients. Although body weight loading on the paretic leg was not measured in our study, it is hypothesized that the spatial organization of muscle synergies are correlated with the increased use of the limb. Hence, if the muscle coordination is similar to the non-paretic leg, then increased usage of the paretic leg can be assumed. The increased symmetry of muscle coordination in the HAL group (Fig. 5.7 (Left)) appear to support this hypothesis. The lack of symmetry improvement in muscle coordination in the Control group (Fig. 5.7 (Right)) gives further support to this hypothesis. A negative correlation between muscle synergy symmetry and stance duration for the paretic and non-paretic limb for the HAL group was noted (Table 5.3). This negative correlation suggests that increased limb use contributes to an improvement in stance duration. However, this correlation is not strong in the Control group, suggesting that in addition to muscle coordination, there could be other factors influencing stance duration. Further work should explore this relation between muscle coordination and limb use.

5.5.5 *Relation between muscle coordination and stance symmetry*

Another point of note is that despite muscle synergy and timing symmetry improved significantly, stance time ratios are relatively unchanged after the course of therapy. This was observed for both groups of patients (Fig. 5.5 (Right)). Correlations between stance time ratio and muscle synergy symmetry were too varied to be regarded (Table 5.3). This is interesting because if patients were able to improve symmetrical muscle coordination, improvement in stance ratio symmetry would be expected. Although there was an increasing trend of stance time ratio in the HAL group from the 1st to 7th session (Fig. 5.5 (Right)), it does not seem to be sustained after the 7th session. This suggest that there might be other factors that could contribute to the improvement of stance symmetry. Future work could be to discover this underlying mechanism influencing stance symmetry.

5.5.6 *Limitations of Study*

One limitation of this study is that only 3 gait cycles per leg (6 cycles in total) were extracted for each patient. This is because 6 gait cycles were the minimum number of gait cycles of walking in a straight line that can be extracted from the 6m walk tests. This number of gait cycles was used as a criteria to keep the amount of data for analysis consistent.

The other limitation could be that the Control group was recruited from hospitals that do not have access to motion tracking facilities, hence the use foot pressure sensors. There might be differences in tracking accuracy which could give rise to biases in data favoring the HAL group, which was captured using a motion tracking system. However, a small verification test comparing the data captured with motion tracking and the foot pressure sensor showed that the accuracy did not differ much (1% difference, Figure 5.10). Hence, the use of different methods of tracking stance duration would not affect our results much. However, future considerations should include capturing spatiotemporal gait parameters using the same type of sensors.

One more limitation could be that stance duration asymmetry were not considered during recruitment, which resulted in the patients from the Control group having a higher stance duration that the HAL group for the non-paretic limb. However, as this current study focuses on the relative improvement of gait symmetry, the absolute values of stance duration was not considered. Future studies should try to recruit patients with similar spatiotemporal gait parameters.

A final limitation could be that the exact details of the exercises performed by the patients during conventional regular physiotherapy sessions were not tracked. This is a current difficulty in data entry which requires tremendous effort by each individual therapist and therapy center, which is currently difficult to implement. Future studies should consider designing tools to ease data entry.

5.6 CONCLUSIONS

In conclusion, robotic therapy appear to provide an advantage over conventional gait training to restore symmetry in muscle coordination during walking. This could be due to the consistency of assistance provided by the robot, in terms of the response time and magnitude of assistance according to the level of muscle activation. Also, muscle coordination symmetry appear to be quantifying a different aspect of gait symmetry, as compared to spatiotemporal measures, however, this is still unclear and future works should consider clarifying the differences and underlying mechanisms influencing gait symmetry to provide targeted therapies.

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Part III

CONTRIBUTIONS AND CONCLUSIONS

6

PROPOSED VISUAL GAIT SYMMETRY EVALUATION

6.1 RATIONALE

The significant correlation between balance (standing or dynamic) and gait asymmetry has been demonstrated in various studies ([90], [129], [121]). Various gait symmetry metrics, like spatiotemporal parameter symmetry, had been proposed for evaluating stroke patients, however, despite that, most of these proposed metrics have not seen widespread use in a clinical setting. Various practical reasons could be that they require the use of equipment, like motion tracking, or/and the lack of resources (e.g. space, monetary or trained personnel) to use such equipment, might contribute to the slow adoption of such metrics clinically.

With these practical concerns faced by the therapists in mind, this thesis proposes an evaluation method for gait symmetry which only requires simple tools that are easily available and inexpensive.

6.2 METHOD

6.2.1 *Required equipment*

1. Flat, white rectangular surface, measuring 2 by 1 meter (2m x 1m). A brightly coloured centerline is to be drawn lengthwise down the middle of the white surface

6.2.2 *Protocol*

The evaluation protocol is described in this section. The figure below (Fig. 6.1) provides an overview of how the protocol should be carried out.

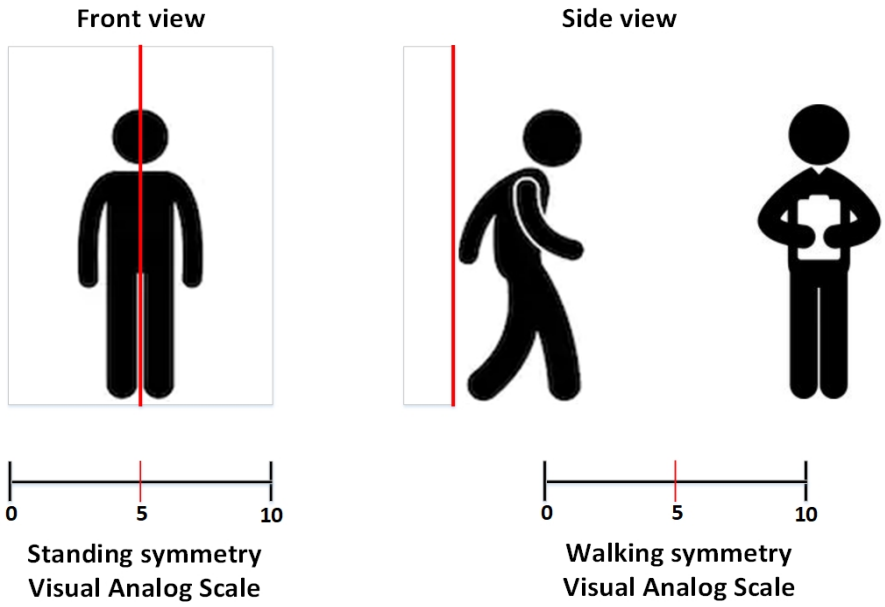

Figure 6.1: **Overview of evaluation protocol** Left side of the figure depicts the view of the evaluator facing the patient, while the Right side of the figure depicts the view of an observer

1. Prop the surface on a wall, such that it is vertical, with the centerline on the surface perpendicular to the ground
2. Patient stands in front of the surface, facing the evaluator, such that the imaginary centerline of the patient's hips coincide with the centerline of the white surface
3. Evaluator moves to about 6m away
4. Patient is asked to stand as straight as possible, while body deviation from the centerline is measured on a Visual Analog Scale (VAS) by the evaluator
5. Patient is then asked to move towards evaluator and stop after 5m. Evaluator visually inspects how much the body deviates during walking from the centerline and records it on the VAS
6. Evaluation ends

6.2.3 *Interpretation of results*

In standing symmetry (Item 4), the results would indicate the limb which is favored by the patient. This does not mean that the favored limb is the stronger limb, as there could be other various reasons, like compensatory movements. This metric is simply to indicate the direction of asymmetry, and visual magnitude of the asymmetry, and that intervention efforts should be taken to correct this asymmetry. Similarly, during walking symmetry (Item 5), the tilt indicates that is a visual indication of the favored side and magnitude, not the cause of asymmetry. The aim of this metric is to promote awareness of gait

asymmetry in patients and direct intervention efforts to correcting such asymmetries.

7

DISCUSSIONS AND FUTURE DIRECTIONS

7.1 DISCUSSIONS

Gait deficits in post-stroke patients have been documented and the restoration gait functions is a clinically important goal pursued by therapists. To achieve this goal, proper measurement of gait is required. As an old saying from software engineering goes "You cannot control what you cannot measure" ([8]). This phase holds true for gait analysis as well, because without knowing what outcomes are to be expected, there is no way to design therapies for those outcomes. Physical measures, like kinematics and spatiotemporal measures, currently in use provides quite a good estimate of movement. However, it is not sufficient to evaluate the change neurological control of the limbs, as spatiotemporal measures can only measure the physical outcome of the movement. Previous work showing improvement in gait symmetry mainly evaluate kinematics and spatiotemporal measures, but hypothesizes about neurological recovery. Since the human body is highly redundant, compensatory actions could also give results that could be interpreted as recovery. Although physical measures provide a good correlation with recovery, it might not be an indication of true neurological recovery. This thesis provides a better measure of neurological recovery by analyzing muscle coordination with EMG, which is an implementation of the nervous system's strategy.

Recovery of mobility after stroke is an important functional outcome of many therapy programs. However, contrary to the classic rehabilitation paradigm of functional recovery, neurorehabilitation, which is based on the theory of neuroplasticity, is guided by the general principle of reducing impairments ([79]), instead of teaching or reinforcing compensatory movements. This might become more important in future because functional recovery does not equate to the ability or confidence to use the paretic limb ([74]). Recovery of gait symmetry after stroke leans towards the neurorehabilitation principle, because compensatory movements in gait implies that the non-paretic limb would compensate for the loss of function in the paretic limb. This implication would most likely lead to gait asymmetries, and their expected long-term complications ([33], [76], [90], [123], [121], [129]).

Muscle coordination has been shown to be useful in previously to qualify impairment in stroke patients ([53], [63], [110], [80]). This thesis has shown that muscle synergies are indeed sensitive enough to detect changes in muscle coordination in pathological gait, as well as, to quantify neurological recovery. This thesis develops muscle synergy analysis further into an index to quantify gait symmetry. Studies conducted in this thesis has supported the observation that gait sym-

metry is difficult to quantify with functional ability tests ([58]) and gait velocity ([98]). Correlations between muscle coordination symmetry and motor evaluation test scores were weak for conventional therapy (Chapter 5), indicating that functional ability tests were indeed insufficient to quantify gait symmetry. Although there were strong correlations between muscle coordination symmetry and functional recovery test scores in the robotic assisted therapy group, functional ability test scores from both groups indicated that the patients were all rated to have recovered sufficiently, further reinforcing the evidence that functional ability tests were not sensitive enough to detect changes in gait symmetry.

One point to note is that robotic assisted gait training may speed up the improvement in gait symmetry, as compared to conventional gait training (Chapter 5). This could be that because of how robotic assistance is scaled with muscle activations from the patients, they were able to learn how to coordinate their muscles faster. However, this interpretation is currently difficult to verify and would require further controlled studies to examine this effect. On the other hand, although the conventional therapy group showed hints of regaining gait symmetry, the results were not significant. This could be due to the limitation that the study was conducted over a period of 4 weeks. However, it should be noted that intervention to correct impairment caused by stroke is recommended to be completed within 3 months after stroke, because there are indications that further interventions after that time would not provide any additional benefit ([79]).

Overall, the nervous system seems to tend towards symmetrical recovery, as evidence from previous studies showing how the non-paretic side could be maladaptive ([57], [70]). This thesis provides further evidence that the nervous system may be prioritizing symmetry over functional recovery, as the complexity of muscle corodination in the non-paretic limb tries to match the complexity of muscle coordination in the paretic limb (Chapter 4). This effect should be examined in more detail in future works because interventions based on recovering symmetry might be in conflict with historical rehabilitation aims of functional recovery and compensatory movements.

As a closing remark, although healthy gait, in terms of joint angle kinematics, has been shown to be asymmetric ([89]), this finding should not discourage interventions targetting gait symmetry. One reason is because the asymmetry in post-stroke gait is of a much higher magnitude, as compared to healthy gait, which causes long-term complications. The second reason is that encouraging compensatory movements might induce the more asymmetry as patients continue to rely more on the non-paretic limb.

7.2 FINDINGS AND CONTRIBUTIONS

This thesis has contributed by providing new evidence that muscle synergies are important neurological markers of gait symmetry recovery in stroke patients. A muscle coordination symmetry index was also developed to evaluate the gait performance of stroke patients. Additionally, a visual evaluation method of gait symmetry during walking was proposed for therapists. This method does not require specialized equipment and is simple to implement, which is important to speed up adoption. Subsequent subsections below discuss the contributions in more detail

7.2.1 *Chapter 3 - Muscle synergy differences in healthy individuals when using a lumbar support exoskeleton*

This chapter is based on the thesis author's publication ([132])

This study examines muscle coordination changes in healthy subjects in a stoop lifting task when a lumbar support exoskeleton is used. The aim is to evaluate whether muscles coordination is changed when an assistive force is provided by an exoskeleton, and if so, what type of changes should be noted. Muscle synergy analysis was used to perform analysis of muscle coordination in this study and is able to decompose raw EMG data into spatially grouped muscle modules and its corresponding activation values. The stoop lifting task is chosen because it is a relatively simple task in terms of kinematics, where the main change in the human body is restricted to the hip angle. This study shows that even in a relatively simple task, muscle coordination differs with the use of an active exoskeleton.

Overall, this study shows that muscle synergy analysis is indeed sensitive enough to detect changes in muscle coordination when an active exoskeleton is providing assistive force. It is also noted that in healthy subjects, the change in spatial organization of muscles (muscle synergies) are minimal, while most change occur during in the activation of the muscle synergies. What was also noted that when changes in muscle coordination is measured in a global manner (e.g. when evaluating all synergy modules together), the metric is unable to differentiate muscle coordination changes between conditions. However, when the evaluation is applied on each individual synergy, differences between conditions become detectable. Thus, development of a muscle synergy index should take into consideration of each individual muscle synergy and its corresponding activation so as not to mask differences with global measures.

7.2.2 *Chapter 4 - Symmetry of muscle synergies in subacute post-stroke patients after robotic therapy*

This chapter is based on the thesis author's publication ([127])

This chapter examines muscle coordination in lower limbs of subacute post-stroke patients before and after a course of robotic therapy. Gait asymmetries are commonly reported in stroke patients, usually due to hemiparesis, where one side of the body is weaker than the other. Previous work have shown muscle synergy analysis have shown it is possible to characterize changes in muscle coordination in stroke patients. It was noted that the spatial organization of muscles in the movement of stroke patients were different from healthy subjects, suggesting that neurological damage significantly changes how the nervous system controls movement. This difference in spatial organization of muscles were also observed in stroke patients after robotic therapy, suggesting it is possible to train patients to recover healthy gait with assistance from robotic exoskeletons.

This chapter also points out the need to investigate how should comparison between different number of synergies be determined. Muscle synergies are known to change over the course of therapy, described as merging and fractionation. This makes direct comparisons between muscle synergies difficult and limited to qualitative interpretations. The proposed method in this chapter fixes the number of synergies to the number extracted from the non-paretic EMG, and after that, sorts muscle synergies on each side of the body according to how much they were able to account for the measured EMG. This enabled direct comparison between muscle synergies possible, leading to the creation of an index for muscle coordination symmetry. Results showed that patients were more symmetrical, in terms of muscle coordination, after a course of robotic therapy.

What has been noticed in this study is that the number of synergies, which is thought to represent the degree of control in the limb, on the paretic side tends to match the non-paretic side

7.2.3 *Chapter 5 - Differences in muscle synergy symmetry between subacute post-stroke patients during robot-assisted therapy and conventional therapy*

This chapter is based on the thesis author's publication, which is currently under review since 06 December 2019 ([1])

This chapter is a follow up study of Chapter 4. A control consisting of stroke patients with similar diagnosis and demographics were added to the study. This control group underwent conventional gait training, with their session duration and schedule matched with the robotic therapy group. The main interest here is to compare the dif-

ferences in muscle coordination between patients that underwent different types of gait training and also to test if the muscle coordination symmetry is able to show differences in muscle coordination between different groups.

Previously, one of the limitations in muscle coordination symmetry index is that it is sensitive to the number of synergies selected. In this chapter, the refinement of the muscle coordination symmetry index is refined to include multiple comparisons with different number of synergies. To summarize, the mean value of muscle synergy symmetry were calculated with the number of synergies extracted from both sides of the body. First, a muscle synergy symmetry value was calculated based on the number of synergies on the paretic side, (e.g. X). Another muscle synergy symmetry value was calculated based on the non-paretic side (e.g. Y). The mean of these values (i.e. mean(X,Y)) was then taken to be the muscle coordination symmetry index.

The refined muscle coordination index was presented in this study and was applied on EMG data collected from both groups of stroke patients. Results showed that the robotic therapy group showed a trend of increasing muscle coordination symmetry within 4 weeks, whereas patients in the control group showed some indication of increasing muscle coordination symmetry, but was not significant within 4 weeks.

The lack of improvement in gait symmetry of the control group, from the perspective muscle coordination, agrees with previous studies that symmetrical gait is difficult to achieve during the course of conventional therapy ([98], [131]). Robotic therapy may be a way to speed up corrections to gait symmetry, however this would require further controlled studies to verify this effect and also to verify if the effect carries over after discharge.

7.2.4 *Chapter 6 - Visual gait symmetry metric*

This proposed evaluation method is based on the two correlation: limb weight bearing asymmetry and body sway ([34], [65], [119]), and also dynamic balance and gait asymmetry ([90], [129], [121]). One of key assumption behind the recommendation of this evaluation metric is that therapists or clinicians do not generally have access to expensive equipment for assessing patients, and they have limited time to perform their assessments.

While the direct relation between muscle coordination symmetry and posture sway during standing balance and gait is still unclear, the rationale behind the design of this evaluation metric is that the correlation between balance (both standing and dynamic) with gait symmetry would manifest itself visually as body sway during standing and walking. Also muscle coordination studies provided evidence that the

same muscle synergies are used in both standing and walking ([78]). Hence, as a first step, posture sway should be documented in a quantifiable manner. This will assist therapists to plan subsequent interventions. Data collected would help in further research help increase understanding between balance and muscle coordination symmetry

7.2.5 *Contribution to Human Informatics*

In this thesis, Human Informatics is defined as "the study of information the human body produces and how interactions with the environment changes information generation". Based on this definition, this thesis has contributed to the field of Human Informatics by providing a new method of quantifying changes in the neurological structure of humans after stroke. This method can be used as an estimation of how well can stroke patients recover gait symmetry after a course of therapy (robotic or conventional). The type of information generated by the human body (lower limb EMG) during walking (interaction with the environment) changes with neurological conditions (e.g. stroke). By observing how EMG changes in the lower limbs of patients with stroke when they are walking, it is possible to estimate the state of the nervous system. However, as EMG data is high in dimension and difficult to analyze, the use of dimension methods, like muscle synergy analysis makes interpreting EMG easier. By systemizing the way how EMG is interpreted, future studies involving the same type of data can be interpreted in a consistent manner.

7.3 FUTURE DIRECTIONS

Human gait appears to be comprised of two entangled tasks, one which is balance and the other related to the propulsion of the body. Hence, one future direction that can be pursued is the relation between muscle synergies and kinetics of lower limbs. While this correlation might be easy to examine in static balance, the kinetics of lower limbs during walking is much more difficult to quantify, due the inherent difficulty of obtaining physical properties (e.g. segment mass and segment center of mass). Deformation of muscles in the lower limbs during walking would also mean the segment center of mass changes depending on how the limb is moved, making model building difficult. A possible avenue to solve this measurement problem could be the development of good motion processing algorithms that can accurately estimate the kinetics of the limbs.

Another future direction that also should be pursued is controlled longitudinal studies of patients utilizing robotic therapy. Although clear beneficial effects were observed in patients during in-patient therapy programs, it is still unknown whether such effects are maintained after patients are discharged. Future studies should consider examining long-term effects of robotic therapy on stroke patients.

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