POLITECNICO DI TORINO

Master of Science's Degree in Biomedical Engineering

Master of Science's Degree Thesis

Estimation of parameters to evaluate asymmetries in movement in patients affected by multiple sclerosis during activities of daily life

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Abstract

Multiple sclerosis is one of the most prevalent causes of neurological disability in young and middle-aged adults. It manifests through a diverse range of symptoms, including primarily motor disruptions such as fatigue, spasticity, coordination issues and even paralysis in some cases. The latter impairments lead to a deterioration of the individual quality of life, safety, and autonomy. In everyday life upper limbs motor abilities play a crucial role in performing typical activities of domestic environments and the ability to complete specific tasks is synonymous with individual functional independence. In several studies, the assessment of upper limb motor functions relies on the use of clinical scales such as the Action Research Arm Test and the Nine-Hole Peg Test. However, these methods present some limitations as they are based on standard clinical tasks conducted in a laboratory setting, and above all, not fully reflecting daily-life activities performances. Alternative solutions for the evaluation of upper limb function rely on conventional methods such as optoelectronic systems, which are also limited to operate under standardized settings, diverging from real-life scenarios. To overcome these limitations, the use of wearable devices such as magneto-inertial sensors (MIMUs) has gained increasing prominence, becoming relevant for assessing motor performances of the upper limbs. The practicality and ease of use of wearable MIMUs allows to move the analysis of movement from standard clinical settings toward conditions that closely resemble real life. However, more efforts should be made in refining protocols which, in most cases, involve the use of MIMUs for activity recognition or, alternatively, assessing range of motion during highly specific and well-defined tasks. The aim of the thesis is to investigate the feasibility of an original protocol based on MIMUs for detecting mobility changes trough quantitative evaluations of one-time or periodic performances in various conditions during real-life activities in individuals with multiple sclerosis. In this case-study, a set of parameters has been proposed to extract information from a complex protocol including different tasks and to quantify any differences before and after a multi-factorial training intervention. The analysed cohort comprehends 33 subjects (7 males; average age: 46 $\pm$ 12 years; EDSS: 1 - 6), equipped with three IMUs positioned on the lower back and right and left wrist. The motor assessment involved the execution of six activities of daily living in a predetermined sequence (wash floor, transfer light, laundry, meal management, clean surface and climb stairs) in two sessions, before and after undergoing an individualized rehabilitation training. Rehabilitation training consist of four types, one more comprehensive which includes both muscle strengthening and functional exercises, while the others primarily involve either muscular strength training, cardio training, or a combination of both. For each activity in every session, activity segmentation was automatically performed from wrist-acceleration signals. Then, for each activity several parameters were extracted to quantify right and left upper limb mobility: Standard Deviation of acceleration peaks, Peaks per Second, Peak Ratio, Mean Peak Acceleration, Acceleration Per Second, Log Dimensionless Jerk, Bilateral Magnitude and Magnitude Ratio. Various comparison was conducted, such as, for same subject and parameter, comparison between right and left limb in different tasks either before and after rehabilitation exercise, then, after setting an arbitrary threshold of improvement on inter-session variations, comparison was done between different subjects for the same task and parameter. Preliminary findings suggested that intervention based on functional exercises led to improvements in a greater number of activities, as expected. The proposed protocol has the potential to enable an ecological assessment of upper limb mobility during everyday activities using IMUs, providing a quantitative and clinician independent evaluation. Results generalization should be confirmed by increasing the number of participants.

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Acronyms

ADLs
Activities of Daily Living

IADLs
Instrumental Activities of Daily Living

MS
Multiple Sclerosis

EMSP
European Multiple Sclerosis Platform

ARAT
Action Research Arm Test

9HPT
Nine-Hole Peg Test

ICF
International Classification System

WHO
World Health Organization

MIMU
Magneto-Inertial Measurement Unit

CNS

Central Nervous System

RRMS

Relapsing-Remitting Multiple Sclerosis

CIS

Clinically Isolated Syndrome

SPMS

Secondary-Progressive Multiple Sclerosis

PPMS

Primary-Progressive Multiple Sclerosis

PRMS

Progressive-Relapsing Multiple Sclerosis

EDSS

Expanded Disability Status Scale

MSFC

Multiple Sclerosis Functional Composite

ROM

Range Of Motion

APA

Adaptive Preventive Activity

STD

Peak Standard Deviation

PPS

Peak Per Second

RATIO
Peak Ratio

MPA
Mean Peak Acceleration

APS
Acceleration Per Second

LDLJ
Log Dimensionless Jerk

Chapter 1

Introduction

1.1 Motivation and clinical relevance

Nowadays, evaluating person's mobility in real-life conditions has grown in importance to obtain a comprehensive understanding of typical motor skills. Monitoring the nature and intensity of motor activity is essential to gather valuable insights into the individual's overall well-being and functional capabilities. Mobility of both upper and lower limbs, indeed, has a greatly impact on health status, playing a crucial role in accomplishing both basic and instrumental activities of everyday life: the incapacity to perform essential activities of daily living (ADLs), may lead to unsafe conditions and reduced quality of life [1]. Moreover, the ability to perform ADL such as bathing or dressing, instrumental activities of daily living (IADL) like housekeeping or meal management, and mobility – the ability to walk without assistance- are essential to remain independent.
Various types of motor disorders, such as multiple sclerosis or Parkinson disease, might affect person's psychophysical stability, constraining their capacity to accomplish a specific task. Furthermore, as the disease progresses, these disorders can gradually diminish the person's autonomy, limiting the ability to carry out activities and creating dependence. According to European Multiple Sclerosis Platform (EMSP), Multiple Sclerosis (MS) affects over 2.8 million people around the world, and among these, there are currently more than 1,2 million people living with MS in Europe. MS is one of the most prevalent causes of neurological disability in young and middle-aged adults [2]. It manifests through a diverse range of symptoms, which mostly involve motor deficits, such as fatigue, paralysis, and coordination

issues. Although MS can be diagnosed at any stage of life, it is most identified between the ages of 20 to 50, with a significant number of individuals receiving the diagnosis during their 20s and 30s [3]. Given that the disease often starts in early adulthood, individuals with MS are confronted with the possibility of a lifelong disability which greatly impacts their career advancement, family dynamics, and social integration. Understanding the development of disability on the individual ADL, IADL and mobility is important for health care professionals to develop and apply targeted interventions.
From this perspective, it is essential to have tools capable of assessing one-time or periodic performances (e.g., following a treatment), potentially allowing the quantification of changes in mobility to evaluate progress or deterioration, in settings different from the standard laboratory environment, but closer to real life. These instruments can also be valuable aids to clinicians, helping in verifying the effectiveness of a treatment and assisting in maintaining the patient's health status, ensuring an appropriate level of quality of life.

1.2 Upper limb mobility: towards out-of-lab analysis

It is widely recognized that walking impairment is one of the most prominent and significant symptoms, which can manifest even in the early stages of the disease and in patients with lower EDSS scores [4]. Consequently, more emphasis has been placed on addressing walking impairment, while relatively little attention has been directed toward the upper extremities, which are highly involved in real-life activities. As a result, upper extremity dysfunction has only recently started receiving the recognition it deserves. The use of both upper extremities is necessary for the completion of many everyday tasks and importance of upper limb function in MS is increasingly recognized, especially for evaluating progressive patients with a reduced mobility [5, 6].
In clinical settings, upper extremity function is generally assessed through standardized ordinal scales or timed tests, such Arm Research Arm Test (ARAT) or Nine-Hole Peg Test (9HPT). These approaches rely on performing standardized tasks within typical clinical settings and are clinician-dependent. Additionally, they not fully reflect daily-life activities performances.
An alternative approach could involve opto-electronic systems, despite their inherent complexity in measurements, which, coupled with their elevated costs and time-consuming nature, can restrict their widespread adoption in

numerous laboratory settings.
In last decades, the use of wearable magneto-inertial measurement units (MIMU) have become increasingly popular. These technologies incorporate miniaturized accelerometers, gyroscopes, and magnetometers, ensuring rapid responsiveness and portability. This enables the processing of their data on a microcontroller unit, also integrated into the MIMU. These devices present several advantages due to the fact that are relatively low-cost, lightweight, self-contained (despite other approaches such as optical/ ultrasonic/ electromagnetic trackers) and low powered [7]. Moreover, their practicality allows patients to mount them directly without requiring any technical knowledge. In light of these considerations, MIMUs are well-suited for monitoring the follow up of patients with movement disorders or evaluate changes in movement, both in clinical assessments as well as during ADL and over extended periods of time [7], enabling to conduct movement analysis outside the limitations of specialized laboratories.

1.3 Aim of the thesis

The aim of the thesis is to investigate the practicality of an innovative protocol based on wrist-acceleration signals gathered through MIMUs to detect changes in upper limb mobility, providing a quantitative assessment of upper limb motor function in MS patients, while performing their daily activities. In this case-study, a set of parameters has been proposed to extract information from a complex protocol including different tasks and to quantify any differences before and after undergone various training intervention. The results are compared for different rehabilitation exercises, intending to assess of rehabilitation treatment efficacy. The proposed protocol could lead to achieve a quantitative and objective evaluation of upper extremities, since it is based on parameters directly derived from signals recorded, allowing for the extraction of valuable information even from complex tasks.

1.3.1 Thesis Outline

- **Chapter 1** presents general introduction and clinical relevance of the topic of the thesis, explaining motivation and purpose of the work. In the end, the general structure of the thesis is outlined.

- **Chapter 2** provides an overview of multiple sclerosis, its characteristics, and related challenges. The second part discusses ADL and potential methods for assessing ADL performance.

- **Chapter 3** addresses the importance to evaluate upper limb motion and describes various available technologies used for upper limb movement analysis.
- **Chapter 4** presents material and methods. In first section dataset and experimental protocol are briefly described. In second second section, data processing and further analysis are reported.
- **Chapter 5** reports the main outcomes for the parameters considered. In the first part, a comparison is made considering the four rehabilitation groups separately, comparing the dominant and non-dominant limbs within each group. In the second section, the evaluation of inter-session variations is reported, considering only two rehabilitation groups.
- **Chapter 6** sums up the main achievements of the thesis and resume principal limitations of the new proposed protocol.

Chapter 2

Background

2.1 Multiple Sclerosis

Multiple Sclerosis is a disabling neurological disease, frequently manifesting in young adults and affecting approximately twice as many women as men [1]. It is an idiopathic inflammatory disorder of central nervous system (CNS), characterized pathologically by demyelination and subsequent axonal degeneration [1]. In individual with MS, the immune system cells, which typically safeguard us against viruses, bacteria, and abnormal cells, erroneously target the myelin in the CNS (comprising the brain, optic nerves, and spinal cord). Myelin, the protective covering encasing nerve fibres (axons), becomes the unintended focus of these misguided attacks (Figure 2.1). Because of this damage, the transmission of electrical impulses within various parts of the nervous system is disrupted, leading to variety of signs and symptoms. These manifestations encompass physical, mental, and occasionally psychiatric issues. The sites where the myelin is lost appear as scars. This is why multiple sclerosis means, literally, many scars.

There are four main subtypes of MS, named according to the progression of symptoms over time [9, 10]:

- **Relapsing-remitting MS** (RRMS): typically, the relapsing-remitting subtype of MS commences with a clinically isolated syndrome (CIS). In CIS, an individual experiences an attack that indicates demyelination, but doesn't meet the full criteria for multiple sclerosis. Notably, 30 to 70% of people who have CIS eventually progress to a diagnosis of MS.

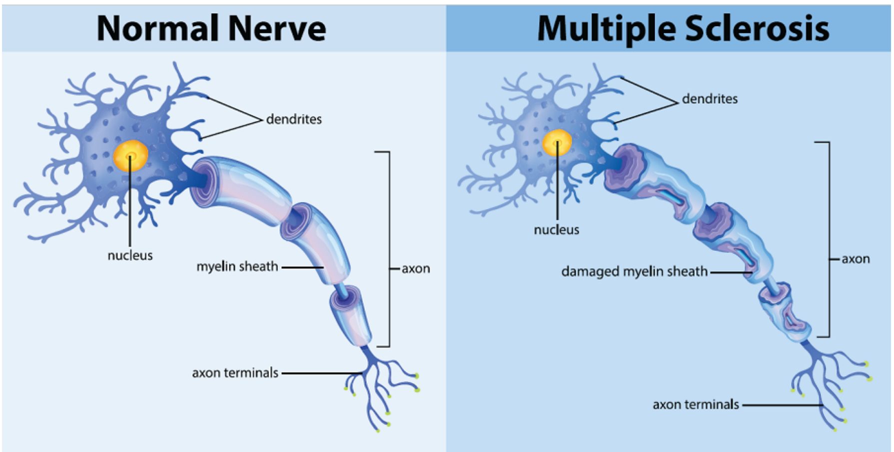

Figure 2.1: Effects of demyelination process. Adapted from [8].

RRMS is characterized by unpredictable attacks, followed by periods of relative calm with no new signs of disease activity. During these attacks, individuals may experience symptoms, also known as relapses or exacerbations. However, they often recover or return to their usual level of disability after each episode. The periods of disease inactivity between these attacks are referred to as remissions, and they can persist for varying duration, ranging from weeks to months, or even years before another attack occurs. This initial course of MS is experienced by approximately 80%.

- **Secondary-progressive MS** (SPMS): approximately 65% of individuals diagnosed with initial RRMS experience progressive neurological decline without definite periods of remission. This form of MS typically manifests in those who previously had MS attacks, but they eventually develop a gradual and consistent deterioration in their functional abilities over time. If left untreated, many individuals with severe RRMS may progress to a SPMS. On average, the conversion from RRMS to SPMS occurs around 19 years after the initial onset of the disease.

- **Primary-progressive MS** (PPMS): this variant of MS is less prevalent, affecting approximately 10-20% of individuals diagnosed with the disease. It is distinguished by a continuous and gradual worsening of symptoms from the onset, without any noticeable relapses of the condition, although there might be occasional temporary or minor relief from symptoms. The typical age of onset for this primary progressive subtype is later than that of the relapsing-remitting subtype. It closely aligns with the age at which secondary progressive MS typically emerges in RRMS, which is around 40 years of age.

- **Progressive-relapsing MS** (PRMS): the most uncommon variant of MS, with only 5% of patients with MS diagnosed with this form. It is characterized by a constant deterioration of symptoms from the outset, coupled with occasional acute relapses that may happen at different points throughout the course of the disease.

In addition to the four traditional MS subtypes, there exists an additional clinical presentation known as Benign MS. Benign MS is a rare form of MS that refers to a disease course in which patients experience very mild or no attacks, separated by long period with no symptoms, and make an excellent recovery. They are diagnosed with MS, but they show minimal impairments or disability even after a lengthy disease course

2.1.1 Risk Factors

The precise cause of MS remains uncertain. Despite its complexity, a range of acknowledged risk factors has been associated with an increased vulnerability to developing the condition. It is important to say that the existence of one or more risk factors does not definitively signal the onset of MS, as the disorder arises from several interplays encompassing genetics, environmental influences, and immune responses [11, 12].

- *Age*: typical age of MS diagnosis lies between 20 and 50 years. Even though it can manifest at any age, risk increases with advancing age.
- *Gender*: prevalence of MS is higher in females compared to males, with a gender ratio of approximately 2:1.
- *Genetic influences*: family history plays a role in MS. Individuals who a have close family member (such as a parent, sibling, or child) affected by MS, bear a slightly increased susceptibility.
- *Geographical distribution*: epidemiological patterns have identified geographical regions with increased MS prevalence, particularly at higher latitudes. People from regions near the equator, where there is a great deal of bright sunlight, generally have a much lower risk of MS than people from temperate areas such as the U.S. and Canada.

- *Ethnicity/Race*: white people, particularly those of Northern European Caucasian descent, are at highest risk of developing MS. People of Asian, African or Native American descent have the lowest risk.

- *Vitamin D deficiency*: low vitamin D levels have been associated with augmented MS risk. Vitamin D synthesis upon sunlight exposure may help regulate the immune system in ways that reduce the risk of MS or autoimmunity in general.

- *Autoimmune correlations*: presence of other autoimmune disorders, such as type 1 diabetes or autoimmune thyroid disease, may increase the chance to MS occurrence.

- *Viral implications*: specific viral infections, such as Epstein-Barr virus (EBV), the virus that causes mononucleosis, has received significant attention in recent years. A growing number of research findings indicate that previous infection with EBV contributes to the risk of developing MS.

- *Smoking habits*: plays an important role in MS. Studies have shown that smoking increases a person's risk of developing MS and is associated with more severe disease and more rapid disease progression.

- *Living in obesity*: in childhood and adolescence, particularly in girls, obesity increased the risk of later developing MS. Other studies have shown that obesity in early adulthood may also contribute to an increased risk of pathology development. Furthermore, it may contribute to inflammation and heightened MS activity in individuals already diagnosed with MS.

As a result of the widespread nature of the myelin lesions and axonal injuries, symptoms can vary among individuals. Symptoms can include motor, cognitive, and neuropsychiatric disruptions. They can be divided into:

- **Primary symptoms**, resulting from a demyelination in the CNS, are a direct consequence of MS and may include bowel and bladder problems, fatigue, pain, sexual problems, spasticity, speech and swallowing difficulties, tremors, visual and cognitive problems.

- **Secondary symptoms**, resulting from primary symptoms, may include pain, loss of balance, anxiety, and depression, decrease in ADLs and IADLs.

Among principal physical symptoms, according to [9]:

- **Spasticity and weakness**: in muscle functions are central features of MS which manifest itself in weakness of the limbs and involuntary muscle actions. Lower limbs are most often affected in an asymmetric way.
- **Sensory Deficits**: include numbness in feet and/or hands leading to affected individuals often not being unable to feel the floor, feel their own movement, or feel objects they hold.
- **Balance issues**: may result in awkward gait, or limp, even in patients who appear healthy in other ways. Balance problems typically result in a swaying and "drunken" type of gait known as ataxia. People with severe ataxia would benefit from using an assistive device (e.g., cane, walker).
- **Vision problems**: are a common symptom of MS. Actually, some individuals may only experience visual problems. One very common visual problem in MS is optic neuritis, which may result in blurring or graying of vision, or blindness in one eye. A scotoma or dark spot may also occur in the centre of the visual field.
- **Incontinence**: affects many MS patients throughout the course of the illness. Patients may suffer from bladder or bowel dysfunction, or both. This symptom is caused when MS lesions block or delay transmission of nerve signals in areas of the central nervous system that control the bladder and urinary sphincter.
- **Sexual problems**: are commonly reported amongst both men and women as the CNS is crucial to human sexuality.
- **Fatigue** is one of the most common and functionally limiting symptoms of MS, occurring in about 80% of MS patients. Fatigue is often accompanied by a desire to sleep and a lack of motivation to do anything else. Fatigue is often considered a state of exhaustion which interferes with a person's ability to function at home and at work and often leads to difficulty in maintaining employment

2.1.2 Assessment of MS impairments

From a clinical point of view, the severity and progression of the disease is determined based on two widely accepted standards, provided by the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC).

Expanded Disability Status Scale
The EDSS scale is the most popular and widely used instrument of clinical assessment in MS. It provides information about disease progression and assess the effectiveness of therapeutic interventions in clinical trials. The original scale, known as Disability Status Scale (DSS) had 11 grades ranging from 0 to 10 [13]. Subsequently, this scale was enhanced in the form of the Expanded Disability Status Scale (EDSS), wherein each of the grades from 1 to 10 was subdivided into two, thus augmenting sensitivity. This expansion effectively resulted in a refined scale with twenty distinct gradations. This ordinal rating system ranging from 0 (normal neurological status) to 10 (death due to MS) in 0.5 increments interval (when reaching EDSS 1) (Figure 2.2). This advancement was attributed to the work of the neurologist Kurtzke in 1983 [13].

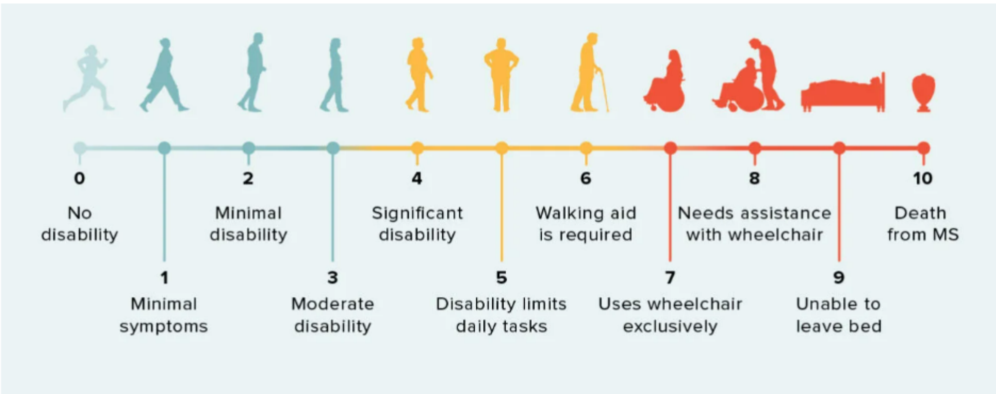

Figure 2.2: Illustration of Expanded Disability Status Scale. Adapted from [14].

In detail, it is a clinician-administered assessment instrument evaluating the functional systems of the CNS. In the EDSS, patients are assessed based on their medical history and the observations made during a standardized neurological examination within the relevant categories of the functional

system. An overall score describing the patient's disability is then obtained by combining the different functional system grades and the ability to walk, which must be assessed separately, to provide a score on the full 20-point scale [13]. The lower values on the EDSS scale quantify impairments primarily through a neurological assessment, closely linked to the functional system. Conversely, the upper range of the scale (EDSS > 6) evaluates the degree of handicaps encountered by patients. The assignment of EDSS scores within the range of 4 to 6 is significantly influenced by factors related to the individual's walking capability [15, 13].
Despite its widespread use, the EDSS poorly captures MS related cognitive dysfunctions and upper limb impairments, both of which are common symptoms in MS and are equally significant as walking impairment.

Multiple Sclerosis Functional Composite
MSFC is a comprehensive, three-part, standardized, and quantitative evaluation tool intended for application in clinical trials related to MS. Developed by the National MS Society (NMSS) Clinical Outcomes Assessment Task Force in 1994, the MSFC reflects the progression of neurological disability through three separate assessments targeting lower limb function/ambulation, upper limb/hand function, and cognitive function.
In more detail (Figure 2.1):

- Time 25-foot Walk (T25W) evaluate leg function and walking;
- 9-Hole Peg Test (9HPT) measures arm and hand function in terms of manual dexterity;
- Paced Auditory Serial Addition Test (PASAT-3) assesses cognitive function, specifically information processing and speed, working memory, and attention.

Measure	**Description**	**Time Limit**	**Function**
9HPT	Minimum time needed to do all replacements with dominant and non-dominant hand (each 2 trials)	5 min/trial	arm/hand function
T25W	Minimum time needed to walk 25m (2 trials)	3 min/trial	leg function/ambulation
PASAT-3	Mental addition of each two consequents digits heard every 3 seconds, and saying it	60 stimuli with 3-s intervals	auditory, cognitive function

Table 2.1: Multiple Sclerosis Functional Composite. Adapted from [16].

Regarding the evaluation of upper limb functionality, the 9HPT stands as the gold standard. It calculates an average score from both the right and left arms, even though individuals with MS frequently exhibit a lateralization of neurological impairment. The MSFC score is generated by transforming the scores of each individual test into Z-scores. In cases where tests cannot be completed due to disability or fatigue, a designated score (not necessarily zero) is assigned following MSFC guidelines. These Z-scores, computed using standardized formulas, are subsequently averaged to establish a comprehensive composite score [17]. This approach facilitates the evaluation of not only lower extremity function but also upper extremity and cognitive functions. Its effectiveness is attributed to its multidimensional nature, which aims to encompass the wide-ranging clinical manifestations of MS among patients and over different periods. This has resulted in a higher sensitivity to changes compared to the EDSS [18].

2.2 Activities of Daily Living

Activities of Daily Living (ADLs) is a term used to collectively describe fundamental skills requires to independently care for oneself, such as eating, bathing and mobility. The term "activities of daily living" was first coined by Sidney Katz in 1950 and is used as indicator of a person's functional status. These functionals skills are typically acquired early in life and tend to remain relatively intact even as cognitive abilities decline, unlike more complex tasks at higher cognitive levels.
ADLs are usually classified into basic ADLs and Instrumental ADLs (IADLs) [4]:

- Basic ADLs or physical ADLs are those skills require to manage one's basic physical needs, including personal hygiene or grooming, dressing, toileting, transferring or ambulating and eating.
- IADLs include more complex activities related to the ability to live independently in the community, such as i.e. managing communication with others, transportation, shopping, food preparation, housekeeping, laundry .

Changes in the performance of ADLs, particularly altered daily activity levels or even inability to accomplish essential tasks, provides important insight regarding an individual's functional and cognitive capacities. These modifications also highlight the loss of autonomy and decline in health status, in addition to contributing to a diminished quality of life. Eventually, this can lead to unsafe living conditions, heightened healthcare expenses, increased mortality rates, and a higher likelihood of requiring institutional care [19].

2.2.1 Assessment of ADL performance

Current assessment of limbs motor function of patients with disability or injury is primarily achieved using visual assessment and through quality of life questionnaires that assess pain, functional abilities in ADLs, emotional well-being and physical strength. Direct observation of performance is often considered one of the most accurate ways to assess someone's abilities or skills, as it personally provides information about their actions, behaviours, and outcomes. However, there are indeed situations where direct observation might not be practical or feasible due to various limiting factors, e.g. time constraints, space limitations or medical conditions. Given these limitations, researchers and clinicians often turn to alternative assessment methods, such as self-reports, questionnaires, simulations, interviews, and performance by proxy.
Within self-reported measurements, various clinical scales are utilized to assess an individual's capacity to complete both basic ADLs and IADLs. Among these, the most frequently employed scales include:

- **The Katz Index of Independence** in ADL typically includes six essential functions: bathing, dressing, toileting, transferring (in and out of bed or chairs), continence (control of bowels and bladder), and feeding. Each function is rated by assigning a value of 1 (fully independent) or 0 (dependent). The total score is calculated by adding up all the points obtained. The Katz Index allow to monitor the prognosis and treatment of older adults and chronically ill people, measuring a person's independence in common ADL. Nevertheless, this scale presents some limitations, such as its inability to detect changes at low levels of disability [1, 20].

- **The Bathel Index** comprehends ten items, such as grooming, dressing, feeding, transferring, bathing, and mobility on level surfaces, among others basic ADLs. The ten items are scored with several points, and then a final score is calculated by summing the points awarded to each functional skill. This allows the examiner to measure a patient's functional disability by quantifying their performance. This indicator exhibits strong reliability and sensitivity in detecting changes in ADL ability. However, there are shortcoming, as the index doesn't account for environmental factors, and certain improvements in ADL capability might not be fully captured in the scoring [21].

- **The Lawton & Brody Scale** is used to evaluate independent living skills related to IADLs. It assesses a person's ability to perform tasks in eight domains of functions, including food preparation, housekeeping, laundering. Individuals are scored according to their highest level of functioning in that category. A summary score ranges from 0 (low function, dependent) to 8 (high function, independent). Each ability measured by the scale relies on either cognitive or physical function, though all require some degree of both. It provides self-reported information about functional skills necessary to live in the community. The shortcomings of this scale lie in its reliance on self-administration as opposed to the direct demonstration of the functional task [1, 22].

These tools are sensitive to gross functional changes, but less sensitive in measuring small and more specific changes [23]. As seen, the use of clinical scales carries some inherent limitations in their application, which do not allow for a comprehensive assessment of the patient's motor condition. They also suffer from subjectivity dependent on the operator who administers them, and this can impact the final evaluation [24].

In the context of this thesis work, after completing each task, patients were provided with a questionnaire designed to evaluate the effort perceived by the patient in relation to the recently completed activity. This assessment tool, referred to as the **Borg Scale** or **Rating Perceived Exertion (RPE)** (Table 2.2), consists of 15 increasing numerical values (ranging from 6 to 20) that are associated with heart rate measurements: the lowest value ideally corresponds to 60 bpm (beats per minute), while the highest corresponds to 200 bpm. It is essential that the judgments expressed by the subjects remain as objective and truthful as possible, avoiding both overestimation and underestimation of the effort involved.

The upper limb exhibits significant functionality, thanks to the mobility of numerous joints capable of executing fine movements, driven by complex neuromuscular control. Therefore, objective measurement parameters and

Table 2.2: Borg Scale.

Borg Scale	Perceived Exertion	% FC MAX
6	Rest	20%
7	Extremely light	30%
8		40%
9	Very light	50%
10		55%
11	Fairly light	60%
12		65%
13	Somewhat hard	70%
14		75%
15	Hard	80%
16		85%
17	Very hard	90%
18		95%
19	Extremely hard	100%
20	Maximum exertion	Exhaustion

precise systems of movement analysis are necessary to enable an objective and quantitative assessment of the patient's performance, providing a more detailed and specific description of upper limb activities [23].
In this context, measurement instruments like opto-electronic systems find application. These systems utilize cameras and markers positioned at the anatomical reference points on the patient, enabling the recording of the subject while performing a movement or a basic activity. By analyzing the gathered data, it becomes possible to extract the kinematics of the specific body segment's motion. Kinematics analysis primarily involves the examination of individual movements, such as reaching and grasping movements, or, alternatively, simple daily activities like drinking from a glass or moving a box on a table [23, 25]. In the following, few example of application of this system are presented.

In the work by Koltz et al.(2013), the Range Of Motion (ROM) of the upper limbs in patients with cerebral palsy is evaluated. Specifically, they measured the ROM of the elbow, shoulder, and trunk during 10 ADLs to detect limitations in the ROM of the upper extremities. As reported in this paper, 3D motion capture was performed, applying the Heidelberg Upper Extremity model [25]. Participants were equipped with instrumentation by attaching reference markers to anatomical landmarks on the shoulder and elbow. They were instructed to complete 10 ADLs, which include unilateral and bilateral tasks (Figure 2.3). Before the examination, passive ROM of elbow, shoulder and trunk was measured. To facilitate the analysis of the ROM and limitations during the ADLs, it was introduced a parameter, called "Activity of daily living related range of motion" (AROM). For each subject and joint direction, the global maximum and minimum in joint position reached during the 10 ADLs were documented. The results obtained from

Figure 2.3: Example of a bilateral task. Adapted from [25].

the affected side were compared to those from the controlateral, unaffected side of the body and to an age-matched group of able-bodied individuals. Additionally, a correlation comparison was performed to correlated reduce ROM and Manual Ability Classification System (MACS).

In the work of Reyes-Guzman et al., opto-electronic system is used to evaluate upper limb functional impairments in individuals who have experienced cervical spinal cord injuries, by assessing their ability to perform the drinking ADL [24]. In this work, upper limb movement was recorded by using the Codamotion system based on active markers. A total of 18 markers were used, placed on the skin surface in the trunk and the right arm [24]. Three kinematics indices to asses UL ability and dexterity has been proposed to quantify movement accuracy, efficiency and coordination. These metrics have been computed by means of a mathematical formulation from the hand path during the performance of the drinking ADL.

This technology is certainly one of the most endorsed in the literature for its reliability and accuracy; however, it implies some limitations due to the fact that the experimental setup is quite complex, requiring initial preparation of the subject and the laboratory environment. Furthermore, it restricts measurements to specific environments. This method is well-suited for assessing the range of motion of specific movements or simple tasks, for which it is useful to evaluate the biomechanics of the movement, including trajectories and angles between different segments. However, when considering more complex tasks, such as the performance of a daily activity in its entirety, if the goal is to replicate a situation as closely as possible to real life, this tool would be challenging to implement due to the constraints imposed by the setup and the instrumentation itself.

A third option is represented by the use of MIMUs. In recent years, this technology has gained increasing popularity due to its practicability and ease of use. MIMUs are devices that contain within them an accelerometer, a gyroscope and a magnetometer. These are wearable devices for the patient, thus enabling the analysis of human movement to extend beyond laboratory standards. Previously, efforts were made to recreate within a laboratory environment what could happen outside, such as simulating situations in which daily tasks are performed. Now, it is possible to directly observe what happens in real life. This shift in paradigm from direct observation instead of simulation has also involved technological aspects that have led to the development and dissemination of these devices. Furthermore, these instruments, as well as opto-electronic systems, enable quantitative measures of human movement quality. These measures are significant in the field of rehabilitation for assessing treatment outcomes, distinguishing between healthy and pathological conditions, and aiding in clinical decision-making. However, more efforts should be made in refining protocols which, in most cases, involve the use of MIMUs for activity recognition or, alternatively, assessing range of motion during highly specific and well-defined task. In the following, few examples of these application of MIMUs to assess upper limb mobility are reported.

Liu et al. (2017) design and develop a wearable sensor-based activity recognition system to recognize housekeeping tasks and classify the activity level [26]. Subjects involved in the analysis were asked to wear sensors on six body position, including upper limb, wrist, thigh, shank, chest, and waist. Subjects were instructed to perform a series of activities with various utensils for 10 seconds each. In this work the accelerometer and gyroscope are utilized to collect and sense movement information. Subsequently, after pre-processing data, several features have been extracted from collected data and ability and capability of four different machine learning models used in gesture and activity recognition problems are compared [26].

K. Daunoraviciene et al. (2020) introduced a protocol for evaluating asymmetries between the upper and lower limbs in individuals with multiple sclerosis and comparing the findings to those of healthy subjects. Furthermore, they conducted a quantitative analysis of two standard tests, specifically Finger-to-Nose Test (FNT) and Heel-to-Shin Test (HTS) movements. Raw data from

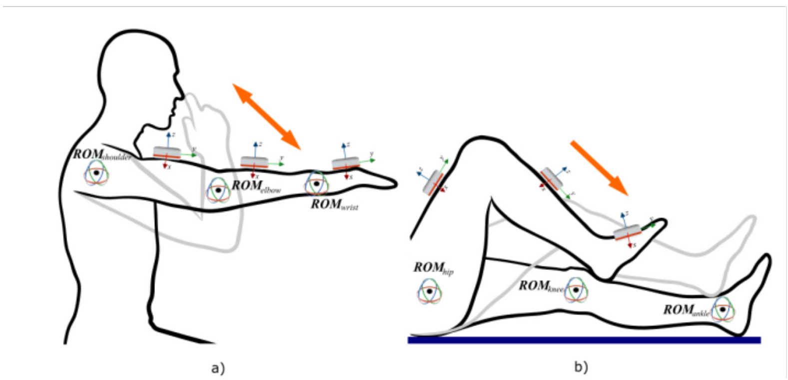

Figure 2.4: The standardized procedure of FNT (a) and HTS (b) test. Adapted from [27].

six IMUs positioned on the upper and lower extremities (Figure 2.4) were pre-processed in three dimensions according to Madgwick's Attitude and Heading Reference Systems (AHRS) algorithm. Both sides of the body were evaluated and respectively Euler's angles of the wrist, elbow, and shoulder joints (in FNT) or ankle, knee, and hip joints (in HST) were calculated. The range of motion (ROM) of joints was calculated in three dimensions and Symmetry was determined based on four usually used symmetry indices:

- Ratio Index (RI), which uses the ratio of the values for the two limbs
- Symmetry Index (SI) calculated from an average of the absolute maximal and minimal values for both limbs
- Gait Asymmetry (GA) index is a logarithmic transform of the RI
- Symmetry Angle (SA) is a factor calculated for the angle of the vector plotted from the right and left values of discrete gait parameters in relation to the OX axis.

Thereafter parametric or nonparametric statistical tests, including respectively one-way ANOVA or Kruscal-Wallis test, is performed to verify the existence of a possible relationship between the variables examined. Spearman correlation was also performed to determine the relationship between upper and lower limb symmetry [27].

Carpinella et al. (2014) proposed employing a single IMU (MTx, XSens) for the quantitative assessment of upper limb impairment in individuals affected by Multiple Sclerosis (MS). Data were collected during the execution of the (ARAT). The study included 21 MS patients and 12 healthy subjects. In MS patients, only the most affected arm was assessed. A clinician assigned a 4-point scale score to the performance of each task. The IMU was positioned near the wrist (Figure 2.5). Data analysis involved segmentation and the extraction of the following parameters for each task and submovement:

- Duration of the movement
- Jerk, calculated as the logarithm of the mean amplitude of first derivative of acceleration, normalized with respect to the duration and the mean absolute acceleration
- Z-score related to duration and jerk.

These parameters were characterized using median and range values and were subjected to nonparametric statistical tests, including the Kruskal-Wallis test. Additionally, a cluster analysis was utilized to identify distinct

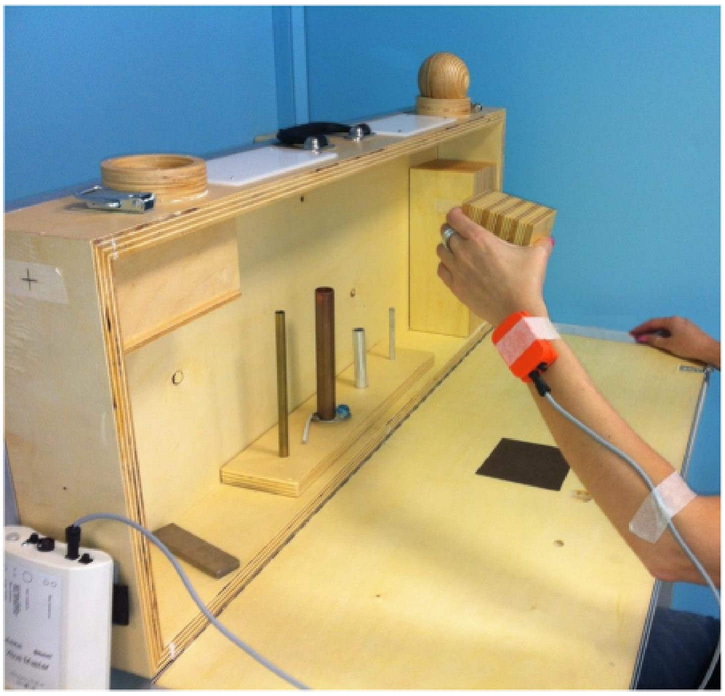

Figure 2.5: Positioning of wrist IMU. Adapted from [28].

subgroups among MS patients with varying levels of impairment, using the initial evaluation scores of the subjects as input. This approach effectively distinguished the motor performance of MS patients from that of healthy subjects [28].

Chapter 3

Upper limb motion analysis

3.1 Relevance of upper limb movement

Reaching with the arm and grasping with the hand and fingers is a complex behaviour that appears in utero, it is elaborated over the first few years of life, and serves essential everyday functions throughout the course of human life [29]. Upper extremity function, which refers to the abilities and movements of the arms, hands, and fingers, is crucial for performing a wide range of quotidian tasks. These tasks can include basic activities of daily living, work-related tasks, recreational activities. Given the importance of upper extremity function in daily life, any loss or impairment of this function can significantly impact a person's independence and quality of life. From this point of view, evaluating the functionality of the upper extremities becomes essential not only for gaining insights into their level of disability but also for handling clinical decisions to determine the most suitable rehabilitation approach. Additionally, it serves as a valuable tool to monitor the progress achieved by the patient and comprehend sensorimotor recovery. Even though impairments affecting arm and hand function can result in significantly debilitating motor limitations, as upper limb movements play a substantial role in everyday activities, greater emphasis has historically been placed on addressing walking impairments. As a result, dysfunction in the upper extremities has only recently begun to receive the acknowledgment it merits.

3.2 Availiable technologies for upper limb motion analysis

Neurological damages following neurological or neurodegenerative disorders can result in severe impairment of sensorimotor functions, affecting functional activities, independence, and eventually the quality of life. This is particularly true for the upper extremities, which are fundamental to interact with the environment and perform ADL. [30].
In 2001, the World Health Organization (WHO) provided a valuable reference for categorizing outcome measures utilized in the context of addressing functionality and disability among individuals with upper limb motor impairments by endorsing the International Classification of Functioning, Disability and Health (ICF)[1] as the globally recognized standard for describing and quantifying health and disability [31]. The ICF is widely used to classify the outcome measures according to three levels including "Body Functions and Structures", "Activity" and "Participation". Based on ICF framework, if there is a notable deviation or loss in a body function or structure, it is referred to as impairments. Outcome measures at the "activity" level are employed to comprehend the challenges individuals encounter when undertaking ADLs associated with the upper limb: within this level, a distinction is made between capacity and performance measures. Capacity measures evaluates the highest probable level of functioning of a person to perform a task or action within a specific domain at a particular instance, under standardized conditions. Conversely, performance measures appraise an individual's habitual execution of a task or action within their typical environment.

To evaluate capacity and performance measures, among the systems most reliable in the literature, the following can be listed:

- Clinical scales and questionnaries
- Standard instrumental tests, exploiting opto-electronic measurements

[1]The International Classification of Functioning, Disability and Health (ICF) is a well-established framework developed by the WHO to provide a comprehensive and standardized method to describe and classify the impact of health conditions on individuals' functioning and disability. It aims to provide a holistic perspective on health by considering not only the medical aspects of a person's condition but also the broader social and environmental factors that influence their well-being.

system and magneto-inertial measurement units (MIMUs).

3.2.1 Clinical Scales

In a clinical context, motor skills can be evaluated through various methods, and indeed, numerous clinical assessment tools have been introduced to measure upper limb functionality in task execution [32]. The commonly employed assessment tools in clinical settings for evaluating the upper limbs in MS include a collection of clinical scales, timed examinations, and questionnaires, all centred around the motor aspect to assess. They can be divided in two groups, namely self-reported measurements, in which the functional ability of the patients is evaluated by the clinician with a number of questions answered by the patient and by proxy or performance measures, where the clinician evaluates several tasks computed by the patient giving a score.
The attention is focused on performance metrics, which are employed utilizing clinical scales as tools for assessment. In following three of mainly used for testing upper limb motor function in MS are proposed:

- **9-Hole Peg Test (9-HPT)** stands as the commonly employed quantitative measure for assessing upper extremity function in MS. This brief, standardized, and quantitative test evaluates manual dexterity and is widely recognized as a gold standard in upper limb assessment [33, 34]. 9-HPT is a timed test in which the patients are asked to transfer pegs from container to a pegboard with 9 holes as quickly as possible. In each trial, there is a set maximum time limit of 5 minutes (300 seconds). The test is done on both the dominant and non-dominant arms twice consecutively and the time taken to complete the run is recorded. The mean time to complete the task, in seconds, is calculated for each hand with lower scores indicating quicker (improved) performance. The faster-performing hand was identified as the “less impaired hand”; the other hand was identified as the “more impaired hand”. The mean time for both hands was determined by calculating the average of all four trials [35]. The 9-HPT has high inter-rater reliability, high test-retest reliability, and high discriminative validity [35]. A limitation of the 9-Hole Peg Test is its susceptibility to practice effects. Thus, it is advised to conduct a few practice rounds before establishing a baseline assessment [34].

- **Action Research Arm Test (ARAT)** is a standardized observational measure used to assess upper extremity performance which evaluates the ability of handling and transporting objects of different weight and size and performing gross upper limb movements [36]. The 19 items included in ARAT are categorized into four subscales (grasp, grip, pinch and gross movement) and arranged in order of decreasing difficulty, with the most difficult task examined first, followed by the least difficult task. Task performance is rated on a 4-point scale, ranging from 0 (no movement) to 3 (movement performed normally) [28], for a total score of maximum 57 points each arm, with a higher score indicating better performance. This scale enables a thorough assessment of arm and hand function while performing tasks closely resembling everyday activities. Moreover, it can be utilized with individuals who might have difficulty grasping a peg or block [35].

- **Wolf Motor Function Test (WMFT)** quantifies upper extremities motor ability through timed and functional tasks. The test includes 15 items, involving timed functional tasks and an assessment of movement quality while completing various tasks, and 2 strength-related items. The 15 items are evaluated according to the Functional Ability Scale (FAS), i.e. a score between 0 and 5 is given to each exercise for a total score of maximum 75.

3.2.2 Opto-electronic system

Opto-electronic measurements systems - also referred to as optical motion capture (MOCAP) systems or stereophotogrammetry – are regarded as gold standard in MOCAP systems due to their high accuracy and reliability. These systems enable the tracking of position and orientation of body segments, allowing for the capture of human motion within a three-dimensional space. The setup is based on a set of fixed infrared cameras that can therefore acquire data only in a restricted area, depending on the number of cameras and the field of view of each. The cameras capture positions of markers, which are placed on the performer's body or clothing, and subsequently collected data is processed to obtain 3D trajectories of markers (Figure 3.1). In marker-based motion capture system, markers can be either active of passive: passive markers are covered in a reflective material which will reflect IR light coming from camera, while active markers are light emitter, This type of marker implies that the light has to travel the distance between

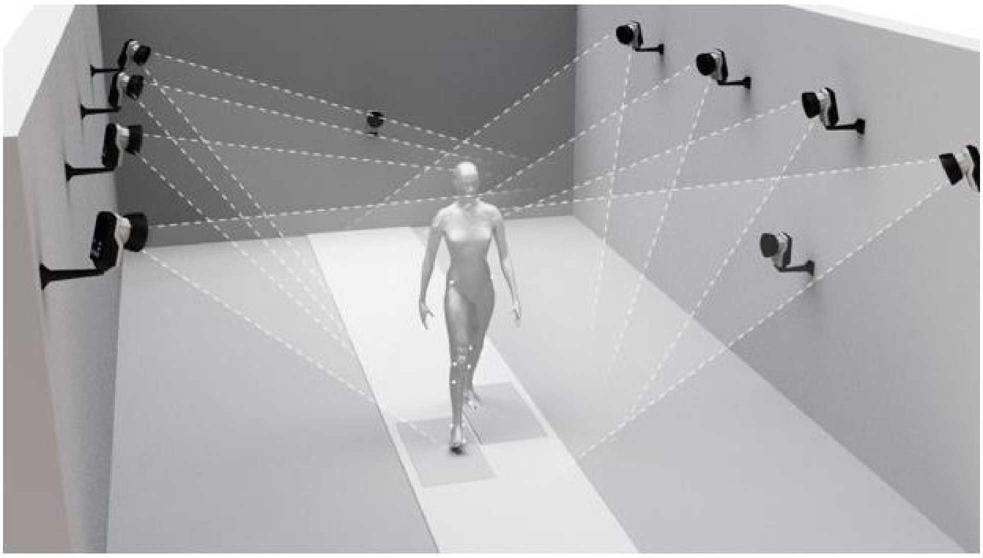

Figure 3.1: Illustration of a MOCAP system. Adapted from [37].

the camera and the marker only once, which results in an enlarged volume of acquisition in respect to the ones achievable through passive markers. The main drawback of this type of marker is that it requires an active power supply for each marker to allow the emission of the light. Optical systems can incur high costs, especially in cases involving a large number of cameras. Additionally, they necessitate a specialized laboratory setup, restricting motion analysis to limited observation periods.

3.2.3 Magneto-Inertial Measurement Unit

In recent years, ultimate advances in wearable technologies have opened new opportunities for development of practical and automated tools to perform clinical screening of real-time in the natural environment outside laboratory [19, 38]. In particular, the use of wearable magneto-inertial measurement units (MIMUs) for motor function assessment has grown significantly, since their cost-effectiveness and the practicability allow measurements outside of a motion laboratory, unlike optoelectronic or video-based systems [28]. Despite the common use of accelerometers to measure physical activity levels, their use to assess upper extremity movements is very recent, especially in persons with MS [39]. The device comprehends a tri-axial accelerometer, tri-axial gyroscope and tri-axial magnetometer.

Accelerometer

An accelerometer is a device which measures the proper linear acceleration, whereby the rate of change of velocity. The proper linear acceleration a_p is defined as the vectorial difference between the sensed acceleration - which is the rate of change of velocity of the sensor - and the gravity acceleration g.

$$\vec{a_p} = \vec{a_s} - \vec{g} \tag{3.1}$$

Considering an object in free-fall, sensor output measure will be 0 m/s^2, while if the object is stationary the output measure will be equal to $|\vec{g}| = 9.81\ m/s^2$.

Principle of functioning. An accelerometer can be modelled as a second order spring-mass-damper system, with a proof mass (m), elastic constant (k) and damping factor (b). When a force is applied ($F_{applied}$) to the proof mass, the spring and the damper tend to react with opposite forces to balance the movement. The force exerted on proof mass is equal to

$$F_{applied} = ma_{applied} \tag{3.2}$$

The force exerted by the spring correspond to

$$F_{spring} = kx \tag{3.3}$$

The force exerted by the damper correspond to

$$F_{damping} = b\dot{x} \tag{3.4}$$

According to the Newton's second law, the algebric sum of the applied force and the forces exerted by the spring and by the damper equals the inertial force acting on the proof mass:

$$F_{applied} - F_{spring} - F_{damping} = m\ddot{x} \tag{3.5}$$

Since the Equation 3.4 is a non-homogeneous second-order differential equation, it can be easily resolved in the Laplace domain.

$$ms^2(x) + bsx(s) + kx(s) = F(s) = ma(s) \tag{3.6}$$

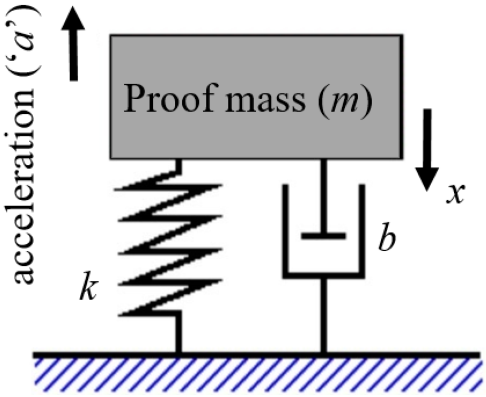

Figure 3.2: Dynamic of model of an uni-axial accelerometer. Adapted from [40]

Reordering the terms of Equation 3.6, it can readily calculate the ratio between the output displacement x(s) and the input acceleration a(s) as follow:

$$H(s) = \frac{x(s)}{a(s)} = \frac{1}{s^2 + \frac{b}{m}s + \frac{k}{m}} = \frac{1}{s^2 + \frac{\omega_0}{Q}s + \omega_0^2} \tag{3.7}$$

H(s) - also called *transfer function* - characterises the behaviour of a dynamic system by relating input and output. Q and ω_0 correspond respectively to the quality factor and to the resonance angular frequency:

$$Q = \frac{m\omega_0}{b} \tag{3.8}$$

$$\omega_0 = \sqrt{k/m} \tag{3.9}$$

Given that accelerometers work in low-frequencies domain, high resonant frequency is needed to achieved a large sensing bandwidth. This specific can be obtained by reducing size of the proof mass and increasing the stiffness of the springs. However, this reduces the sensitivity of the device; therefore, a compromise between sensitivity and bandwidth must be found.

Technical specification

- **Sensitivity**: this term is defined as the output voltage signal generated per unit input acceleration in a given direction:

$$S_x = \frac{\text{Output voltage generated (mV)}}{\text{Input acceleration along x-axis (g)}} \tag{3.10}$$

- **Dynamic range**: this represents the range between the smallest detectable amplitude that the accelerometer can measure to the largest one before distorting or clipping the output signal. It's measured in '±g'.
- **Bandwidth**: it indicates the range of vibration frequencies to which the accelerometer responds or how often a reliable reading can be taken. For human motion analysis, a bandwidth of 40 - 60Hz is adequate.
- **Zero-g-voltage**: this terms specifies the range of voltage that can be expected at the output under $0g$ of acceleration.
- **Non-linearity**: is a measurement of deviation from a perfectly constant sensitivity, specified as a percentage with respect to either full-scale range or ± full scale.

$$\%\ \text{Non-linearity} = \frac{\text{Maximum deviation (g)}}{\text{Full scale range (g)}} \times 100 \tag{3.11}$$

- **Noise Density**: this term is defined as the square root of the power spectral density of the noise out.

Several models of accelerometers are available on the market, such as piezoresistive devices, capacitive devices, tunneling devices, optical devices and piezoelectric devices, depending on specifics required (Figure 3.3).

Gyroscope

A gyroscope is a device used for measure and maintain of the angular velocity of a mass in motion. There can be composed by one, two, or three orthogonal axes, around which measurements were performed. Angular velocity are generally measure in degrees per second (dps). Depending on the application, it is possible to choose between several alternatives. There exist three fundamental categories of gyroscopes: traditional rotating gyroscopes, vibrating structural gyroscopes, and optical gyroscopes.

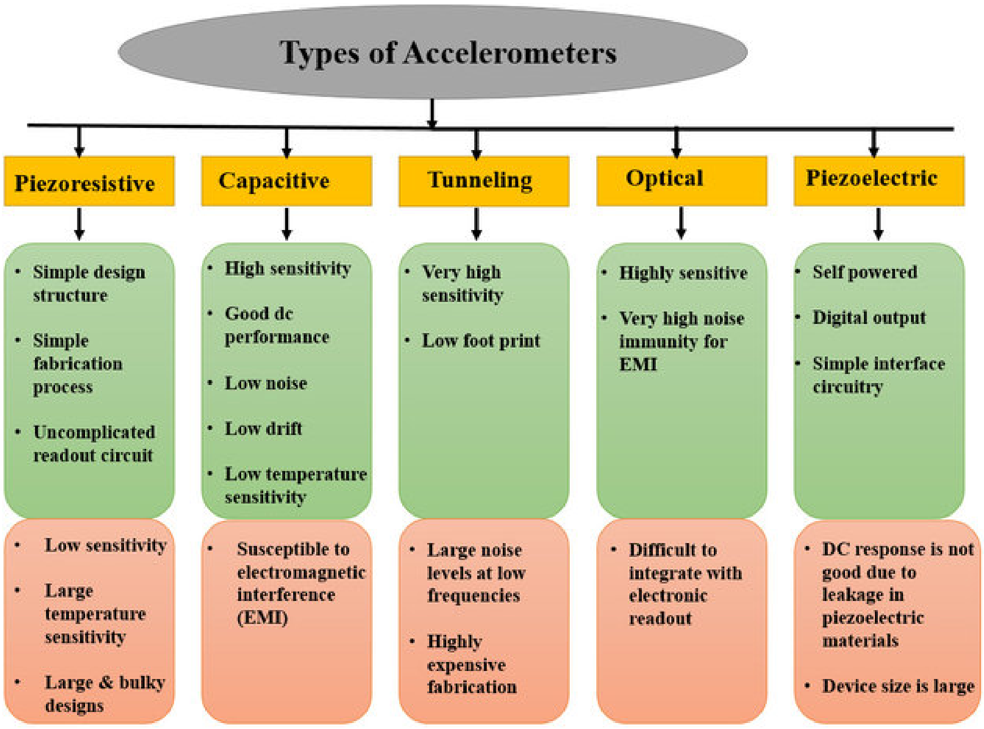

Figure 3.3: Advantages and drawbacks of various trasduction schemes. Adapted from [40].

Principle of functioning. Traditional gyroscope relies on the concept of conservation of angular momentum. When an object is in rotation, it possesses angular momentum, a property that leads it to resist alterations in its direction of movement. According to principle of conservation, the angular momentum of an object remains constant unless subjected to an external force.
The most common type of gyroscope works on the principle of Coriolis force. Considering an object with mass which is rotating with an angular velocity ω around vertical axis and translating with a velocity v_t perpendicular to angular velocity ω, a transversal force is produced. This force, known as the Coriolis force, tends to induce oscillations in the mass.

$$F_c = -2m \cdot v_t \times \omega \tag{3.12}$$

Hence, gyroscopes based on the Coriolis force are commonly referred to *Vibrating forks gyroscope* or *Coriolis vibratory gyroscope*. These technologies embedded a pair of proof masses which are oscillated with the same amplitude, but in opposite directions. Tines are triggered to resonate in anti-phase in he plane of fork. When the sensor rotate, the tines begin to oscillate along perpendicular direction to the plane. Thus, producing a torque that trigger the torsional mode around the stem.

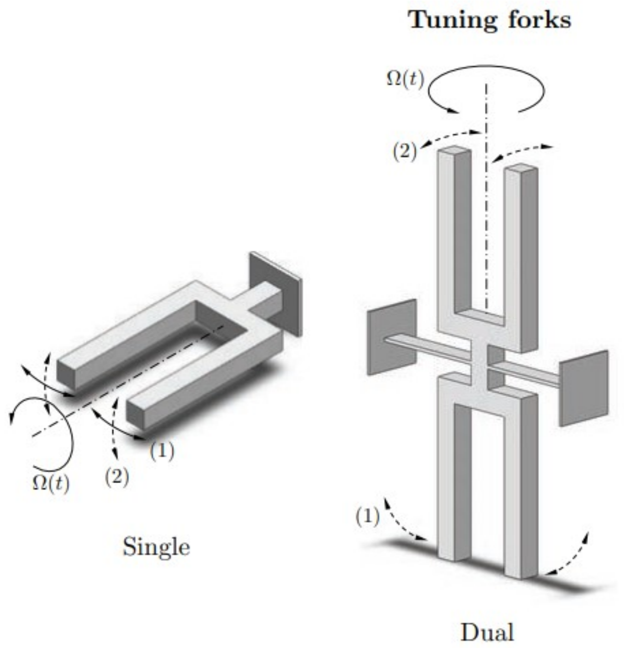

Figure 3.4: Common type of vibrating forks gyroscope. From left, single, dual and multi-tine configuration. In figure, $\Omega(t)$ is the input angular rate, (1) is the primary vibration mode, and (2) is the vibration response due to Coriolis forcing [41].

Technical specifications

- **Input range**: the extreme values of the input, generally plus or minus, within which performance is of the specified accuracy. Full scale input is the maximum magnitude of the two input limits [41]
- **Accuracy (or linearity error)**: the deviation of the output from a least-squares linear fit of the input-output data, generally expressed as percentage of the input full-scale [41].
- **Scale factor**: the ratio of a change in output to a change in the input intended to be measured [41].

- **Resolution**: the smallest change, for input greater than noise level, that can be reliably detected [41].

- **Drift rate**: the portion of gyro output that is functionally independent of input rotation. It comprehends *Bias* or *zero rate output (ZRO)*, the *Environmentally sensitive drift rate* - which considers acceleration, temperature, vibration, etc.) and the random component *Bias Instability* [41].

Magnetometer

A magnetometer is a device used to measure the magnetic field, particularly with respect to its magnetic strength and orientation [42]. A common magnetometer is the compass, which points to the direction of the Earth's magnetic.
Principally, magnetometers can be divided in two categories: scalar and vector magnetometers. Scalar magnetometers accurately measure the magnitude of the magnetic field. On the other hand, vector magnetometers are measures both the magnitude and direction of the magnetic field, detecting its vectorial components.

Principle of functioning There are many types of magnetometers which are based on different functional principles. For example, electronic compasses can indicate which direction is the magnetic north using phenomena such as the Hall effect, magneto induction, or magneto-resistance. The Hall effect is the production of a potential difference (the Hall voltage) across an electrical conductor due to the application of a magnetic field perpendicular to the current that flows in it. Thus,a Hall effect sensor consists of a metal strip through which a current flows. When a magnetic fields is applied, electrons move toward an edge and produce a voltage gradient. The force induced by the charged particles has to balance to the force generated by the magnetic field. It follows that the Hall voltage is a measure of the magnetic flux density.
At the basis of this principle, there is the Lorentz force which introduces an anisotropic conductive behaviour. The force exerting on a single charged carrier is:

$$F = q(E + (v_d \times B)) \tag{3.13}$$

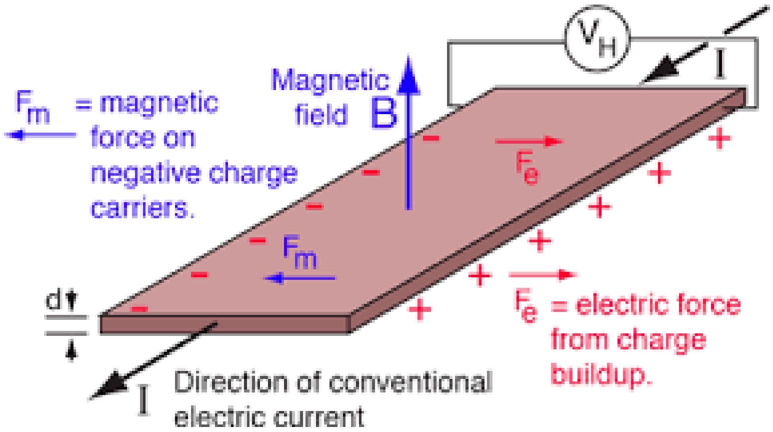

Figure 3.5: Hall Effect. Adapted from [43].

where F is the Lorentz force, q the charge of the elementary particle, $E$the electric field vector, v_d the velocity of the carrier, and B the magnetic field vector.
Knowing that current can be expressed as:

$$I = j \times A = nqv_dwd \tag{3.14}$$

where j is the current density, n the number of charged carries, A the area of the conductor (w is the width and d is the thickness), v_d the drift velocity. At equilibrium, the magnetic force will perfectly balance the electric force:

$$qv \times B = \frac{V_hq}{w} \tag{3.15}$$

The voltage caused by the accumulated charges is derived as

$$V_h = \frac{IB}{nqd} \tag{3.16}$$

Hence, a magnetometer evaluates how the current is altered or deflected by the magnetic field, and the voltage at which this occurs is known as the Hall voltage, which is directly proportional to the strength of the magnetic field.

Chapter 4

Materials and Methods

4.1 Dataset & Experimental Protocol

This project was funded by FISM (Italian Foundation Multiple Sclerosis) and carried out in collaboration with a group of neurophysiatrists from the *University of Sassari*.

4.1.1 Participants

A total of 33 MS subjects (26 female, 7 male) were recruited at *University of Sassari (Italy)* from February 2022 to March 2023 for participating to this study. The mean age was 46 $\pm$ 12 years and 4 out of 33 were left-handed. The EDSS score ranges from 1 to 6. All participants were informed about the experimental procedure before starting. Data recording occurred during two different sessions, among which participants underwent various rehabilitation treatments. These treatments encompassed the following alternatives:

- a cardiovascular training program;
- a muscle strengthening training program;
- a combined training program, which involves both cardiovascular and muscular component;
- a comprehensive rehabilitation program, named APA (Adapted Preventive Activity) incorporating elements such as upper and lower limb muscle reinforcement, proprioceptive exercises, balance training, gait re-education, postural adjustments, and cardiovascular exercises.

Figure 4.9 shows an example of typical program for each rehabilitation group.

Activities were recorded through the wearable INDIP system according to a well-defined experimental protocol. The INDIP (INertial module with DIstance sensors and Pressure insoles) system integrates multiple modular inertial units (MIMUs), including two plantar pressure insoles and two distance sensors, specifically designed for assessing gait in individuals with impaired mobility in real-world scenarios [44, 45]. In the standard reference configuration, this system utilizes three sensors placed on both feet and the lowerback, as well as pressure insoles and distance sensors. Additionally, for these data acquisitions, two sensors on the wrists and one on the head have been incorporated into the model. In subsequent analyses, only the signals collected by the lowerback and wrist sensors will be taken into account.

4.1.2 Experimental Protocol

The acquisitions were performed at the *University of Sassari*, in collaboration with a group of neurophysiologists.

The protocol is divided into four test, and it comprehends :

- **Static test** (Recording 1): the static test is performed to validate the accurate functioning of the sensors, assessing the quality of sensor performance. This procedure entails acquiring static signals of all MIMUs, which are placed on a flat surface and should not be moved for the duration of the acquisition (about 60 s). For ensure proper functioning of PI, recording of PI signal is performed while an operator exerts pressure on each sensing element of each PI. For sensors, the quality check verifies that signals acquire have an average value of zero, an accelerometer norm within expected range, a satisfactory standard deviation, and a proper full-scale range. For PI the quality check ensures the insole's condition has not degraded. If the quality check of one sensor fails, device must be replaced, and the procedure is performed again (Figure 4.1).

- **Standing test** (Recording 2): the standing test is performed to estimate correct MIMUs orientation with respect to global framework, to allow calculation of the rotation matrix that enables the reorientation

Table 4.1: Anthropometric data of patients recruits for the analysis. In the penultimate column is reported the corresponding rehabilitation program conducted: 0 = muscle strengthening program, 1 = cardiovascular training program, 2 = combined training program, 3 = comprehensive rehabilitation program. These data are property of *University of Sassari*.

ID	Gender	Age (y.o.)	Height (cm)	Weight (kg)	Dominant hand	Rehabilitation group	EDSS score
0004	F	29	163	92	Right	2	2
0020	M	44	174	85	Right	1	2,5
0022	F	60	169	89	Right	2	5,5
0024	F	51	158	69	Right	0	2
0025	F	37	168	49	Right	3	2,5
0026	M	43	168	68	Right	0	4,5
0028	F	69	157	72	Right	1	6
0029	M	33	171	97	Right	3	1
0030	F	56	158	77	Right	2	6
0033	F	61	152	65	Right	1	3
0037	F	61	155	57	Right	1	6
0038	M	41	173	67	Right	3	3,5
0040	F	54	164	65	Right	3	3,5
0044	F	28	153	58	Right	0	3,5
0045	F	54	161	68	Right	2	6
0046	F	26	154	66	Right	1	1,5
0049	F	31	159	60	Left	2	1,5
0050	F	43	166	50	Left	0	4
0051	F	27	168	67	Right	1	0
0055	F	31	158	51	Right	2	1
0057	F	40	168	77	Right	0	3,5
0058	M	49	175	65	Right	2	1
0059	F	51	15	76	Left	1	4
0060	F	44	158	50	Right	3	2
0061	F	35	149	48	Right	3	2
0062	F	57	149	45	Right	1	3,5
0063	F	55	156	70	Left	3	5
0065	F	54	155	50	Right	2	3,5
0066	M	40	194	90	Right	2	3,5
0067	F	35	167	70	Right	0	2,5
0078	F	58	149	45	Right	3	3,5
0080	M	60	183	85	Right	3	6
0083	F	65	146	77	Right	3	5

of MIMUs recordings during dynamic tests. During this test, the participant is asked to stay still in a standing position for at least 10s, while

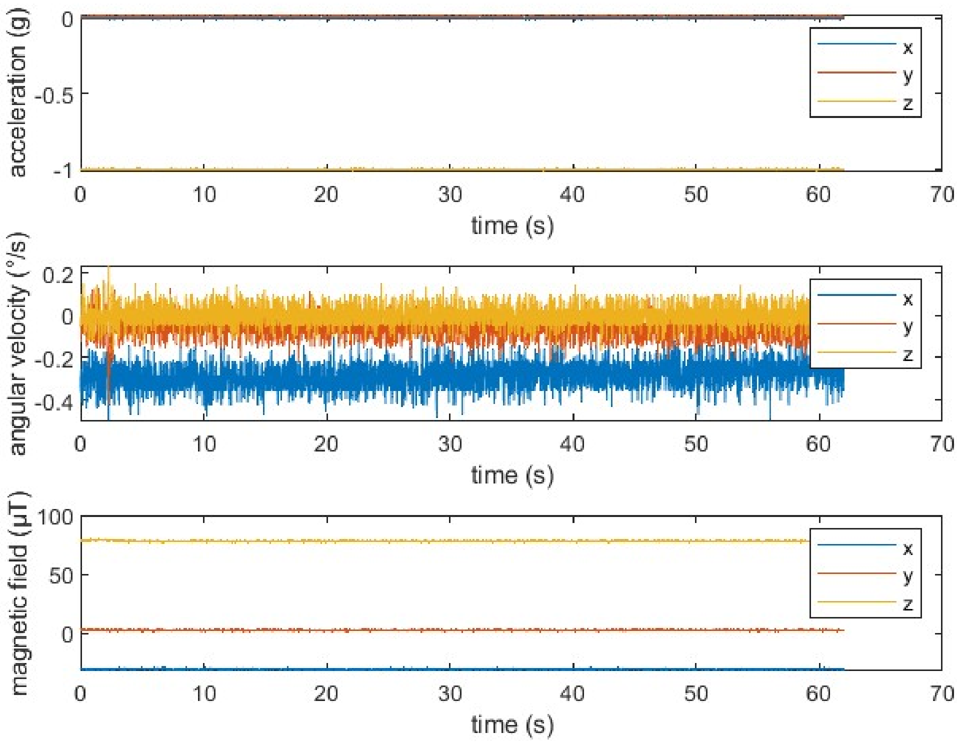

Figure 4.1: Left Wrist MIMU readings during Static acquisition (Recording 1) for subject 0024: first plot is from triaxial accelerometer signal, second plot is from the triaxial grysoscope, third is from the triaxial magnetometer signal.

wearing the whole INDIP configuration (Figure 4.2).

- **Data Personalization** (Recording 3): this test checks for correct placement and functioning of PI inside shoes (Figure 4.3). The procedure comprehends:
  - Standing still for 10-second;
  - Lift up the left foot for 5-second;
  - Stand still for 5-second;
  - Lift up the right foot for 5 s-second;
  - Stand still for 5-second;

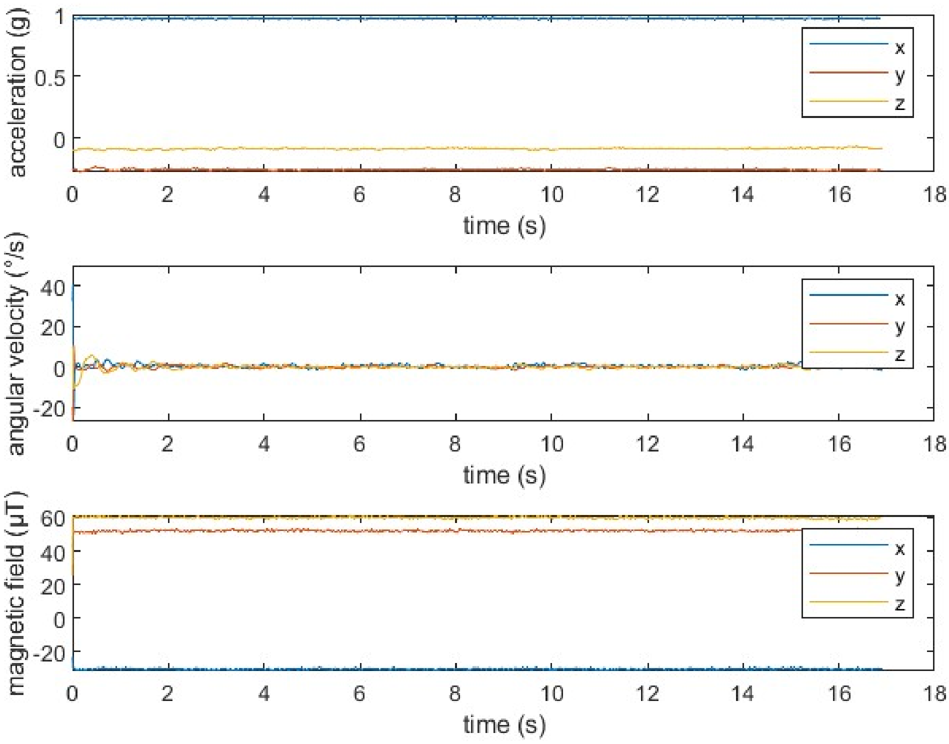

Figure 4.2: Left Wrist MIMU readings during Standing acquisition (Recording 2) for subject 0024: first plot is from triaxial accelerometer signal, second plot is from the triaxial grysoscope, third is from the triaxial magnetometer signal.

  - Raise and lower the left arm in the sagittal plane;
  - Raise and lower the right arm in the sagittal plane;
  - Walk at a comfortable speed along a 12 m path.

- **ADL Test** (Recording 4): in ADL test, the participant is required to simulate daily activities, started sitting on a chair and complete a series of tasks around a room. The patient is wearing 3 sensors, on the lowerback and one on each wrist. Activities are performed under the supervision of two operators and the participant is transported in a wheelchair to the starting positions of various activities. This approach ensures the preservation of the patient's resting conditions and provides

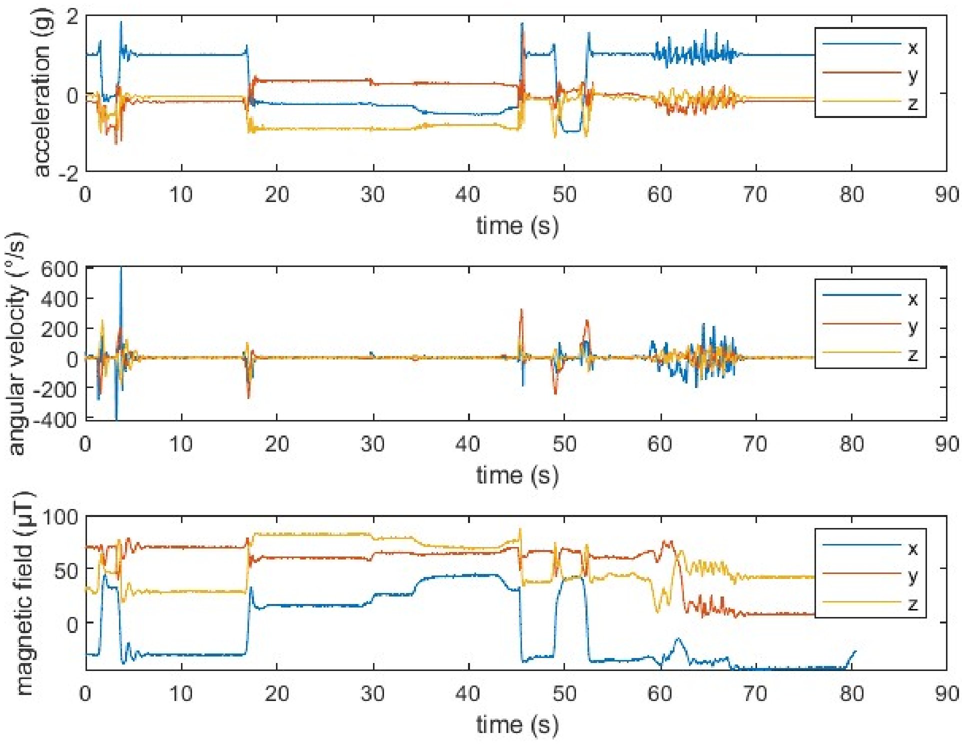

Figure 4.3: Left Wrist MIMU readings during Data Personalization acquisition (Recording 3) for subject 0024: first plot is from triaxial accelerometer signal, second plot is from the triaxial grysoscope, third is from the triaxial magnetometer signal.

them with the opportunity to recover.

The ADL test consists of a single recording that comprehends the completion of six consecutive tasks:

- *Wash Floor*: the participant is asked to add the detergent into the bucket with water, dampen the cloth, wring out excess water, and start cleaning the floor. After the initial pass, rinse the cloth, wring it out, and perform a second pass. Conclude the task by rinsing the cloth once more, wringing it out, and placing it on the rim of the bucket, then take a rest.
- *Transfer Light*: the participant is asked to stand up from the chair,

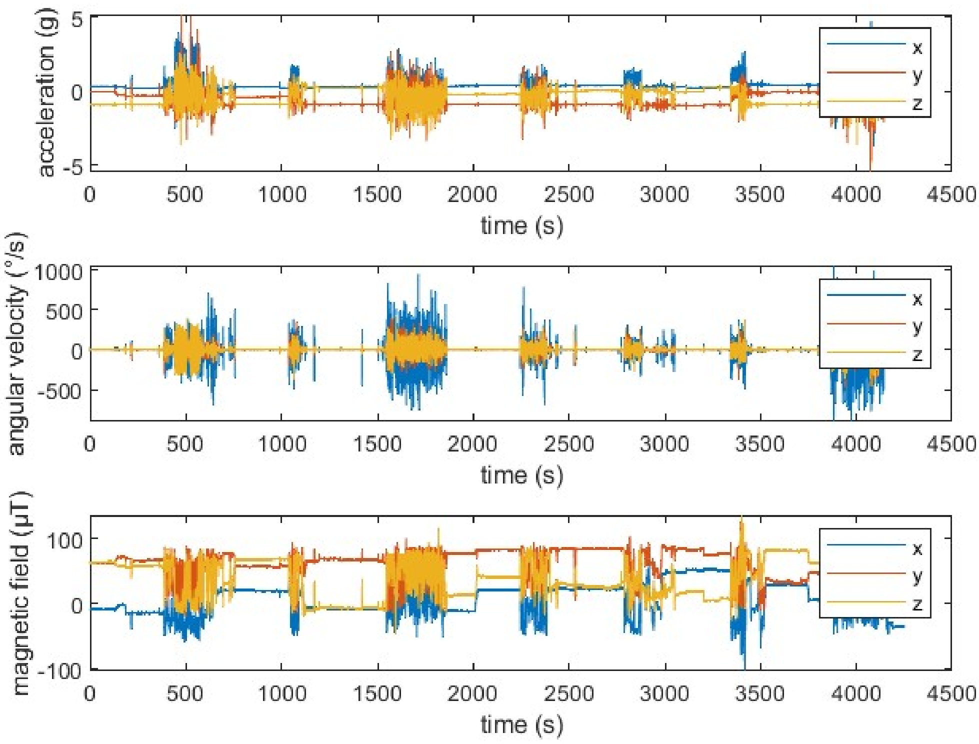

Figure 4.4: Left Wrist MIMU readings during ADL acquisition (Recording 1) for subject 0024: first plot is from triaxial accelerometer signal, second plot is from the triaxial grysoscope, third is from the triaxial magnetometer signal.

proceed along a 10-meter path, make a left turn, open a door, and continue along another 8-meter path. Afterwards, return, close the door, and take a break.

- *Laundry*: the participant is asked to put the clothes into the washing machine and shut the door; After a brief moment, open the door and hang all the clothes: open the drying rack and use clothespins to hang all the clothes on it. Afterward, take a break.

- *Meal Management*: the participant is asked to cut the fruit using hands or a knife; then garnish the pizza and slice it using the utensil of your choice. After they have to set the table with a tablecloth, glass, water, and pizza, therefore sit down and pour water into the glass. After finishing, clear the table and take a rest.

- *Clean Surfaces*: the participant is asked to stand up and clean the entire flat surface using a cloth, lifting any objects that are in the way. Thereafter, moving towards a vertical surface and clean it as if you were cleaning a window, attempting to reach as high as possible. Afterward, take a break.

- *Climb Stairs*: the participant is asked to stand up and ascend four flights of stairs, taking one step at a time. Upon reaching the top, they can either sit or take a break, before descending to the ground floor and sitting down, completing the task. Afterward, take a break.

4.2 Data preparation and Standardization

Upon the completion of free-living acquisitions, the recorded raw data from each sensor is accurately downloaded and saved as text (txt) files into the respective Participant's folder and prepared for further processing.
Once manually downloaded to the PC, the txt-format files are stored within the *ADL Test* folder and organized into subfolders according to the standards established in the Mobilize-d project[1] [46]. In the *Spot Check* subfolder, acquisitions related to the quality check (Recording 1) are placed, while in the "Experimental Protocol" subfolder, data of the other test/recordings (Recording 2, 3, 4) are stored. Subsequently, using a Matlab Renaming GUI, the files located within the subfolder "Experimental Protocol" are renamed based on the quality check data and both are saved inside a directory named *Free-Living*. This directory also contains an Excel sheet that encompasses the participant's personal and anthropometric details, sensor-related information, records of technical issues, and annotations.
Afterwards, data is standardized through a set of Matlab scripts and functions and stored within a structure named 'data.mat'. Each participant has their own corresponding data structure. The `data.mat` structure includes a field labelled `TimeMeasure1`, which contains four nested fields, each corresponding to a different recording. For each Recording, information regarding the corresponding acquisition and the signals acquired from individual sensors are stored separately (Figure 4.6). Precisely, the data obtained from each triaxial sensor is saved according to this convention:

- the first column represents the vertical component (VT);
- the second column the medio-lateral component (ML);
- the third column the antero-posterior component (AP).

Moreover, the unit of measurement for standardized data from accelerometer, gyroscope, and magnetometer sensors adheres to this convention:

- g per accelerations;

[1]an European project with the aim of producing real-world digital mobility outcomes (DMOs), to assess health status of individuals with mobility issues, aiming to enhance individualized care.

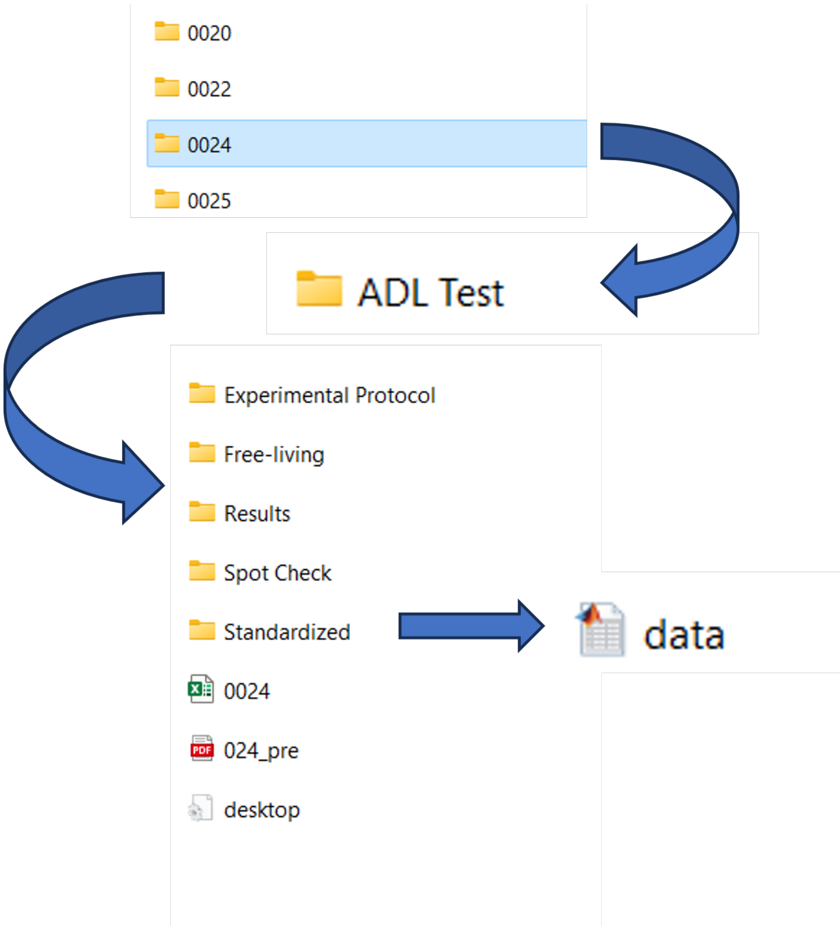

Figure 4.5: Example of how each subject's directory is organized. Inside each one, there is *ADL Test* folder in which several subfolders are nested. Standardized structure `data.mat` is contained in *Standardized* folder.

- *dps* for angular velocities;
- μT for magnetometric measure.

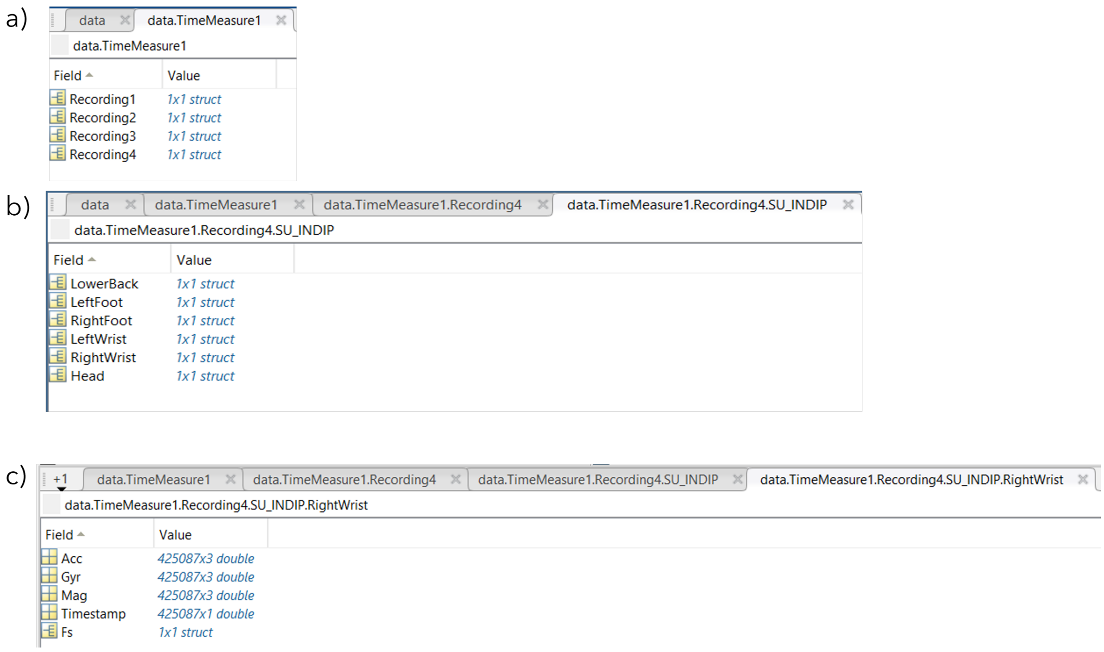

Figure 4.6: Example of how `data.mat` structure is organized. a) `data.Timemeasure1` contains, in addition to important information about the time the recording started, the data acquired from the MIMUs and the data acquired from PI and distance sensors. b) In `data.Timemeasure1.Recording4.SU_INDIP`, all the inertial signals acquired from MIMUs placed all over the body are listed separately. d) Different signals acquired by one single MIMU.

4.3 Data processing

Considering the evaluation of relative mobility in the upper limbs, the analysis comprehends acceleration signals from both the right and left wrists, in addition to the signal collected from the lowerback sensor. Activities involved in the analysis are those presented in previous section. All data processing was performed using MatLab R2022a (The MathWorks Inc., Natick, MA, USA).
Before proceeding with the extraction of kinematic parameters from wrist acceleration signals, the absolute acceleration vector is calculated for each signal using the Euclidean mean. The gravity component g, presented as a constant, is then subtracted from the calculated value, according to [38].

The resulted Absolute Acceleration signal is

$$Absolute\ Acceleration = \sqrt{x^2 + y^2 + z^2} - g \tag{4.1}$$

4.3.1 Preprocessing

Segmentation

For each patient, right and left wrist-acceleration signals and lowerback acceleration are extracted from the provided `data.mat` structure, and automatically segmentation is performed, trough which recording is divided into different tasks. In particular, a custom function called `getACTIVITY_interval` was used. This function, given the acceleration signals from both wrists and lowerback as input, returns the identified intervals as output. It relies on an algorithm that determines whether the subject is lying down or sitting (resting condition) or standing, while also assessing whether the subject is active or not. These two conditions are verified using two functions:

- `getFlagUp`: function used to determine if the subject is standing/sitting or lying. This is done looking at the scalar product between the vertical component of acceleration from lowerback sensor and the ideal gravity acceleration. If the subject is standing/sitting, the angle formed by the two vectors should be 0°; if the subject is lying, then the angle formed with respect to gravity direction should be 90°.

- `getFlagActive`: function used to determine if the subject is moving or not. This is obtained considering that the subject is moving only if the lowerback and at least one wrist are active. A threshold is imposed on the value of the total standard deviation - which is obtained as the sum of the standard deviations along the three axes - for each signal. The threshold values are determined experimentally and set at 2.2 $m/s^2$for the pelvis signal and 3.5 m/s^2 for the wrists signals. For standard deviations greater than these values, the subject is considered to be in activity.

This procedure allows for an initial selection of various intervals (Figure 4.7), which are then cross-checked and must match entries in an operator table that was compiled at the time of data acquisition, providing the start and end times for each activity. Once checked, the start and end times of each activity are saved within a Matlab structure.

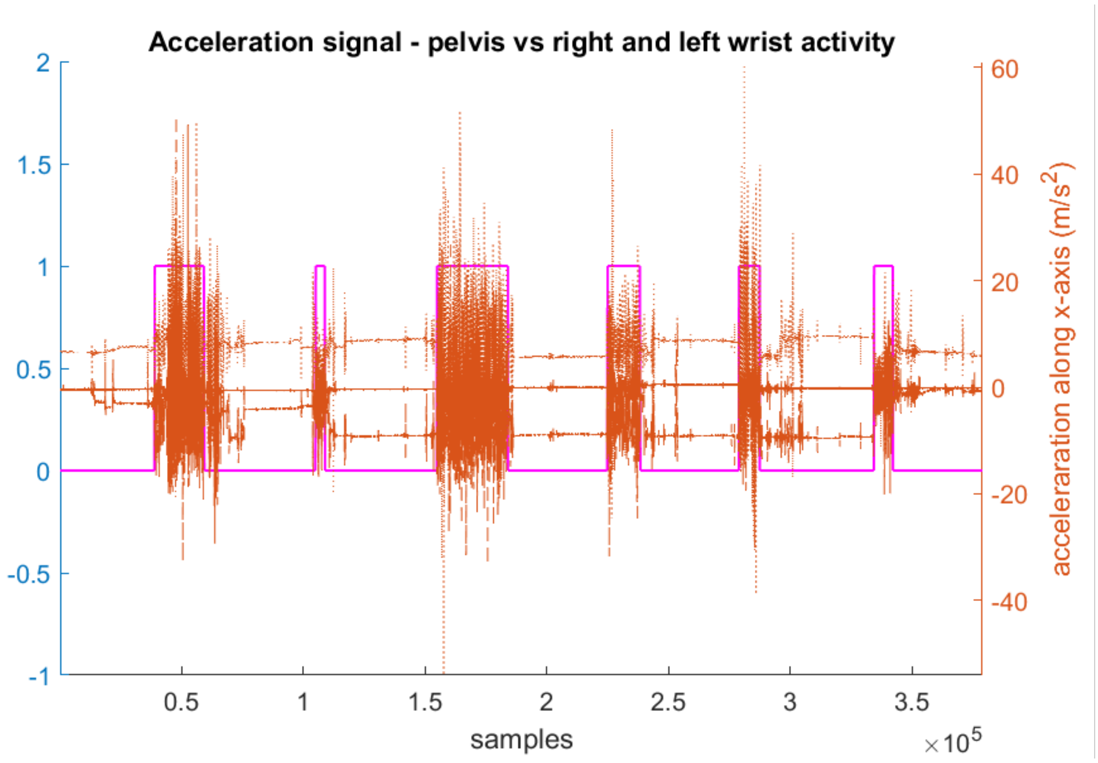

Figure 4.7: Activity segmentation for subject 0024.

Smoothing

Based on [38], raw acceleration data were smoothed using a local regression algorithm and a windows size of 420 ms (corresponding to 42 samples at sampling frequency of 100 Hz) through the Matlab function "*smoothdata*", for smoothing the signal, i.e. reducing the noise and retaining morphology of the original signal [47] (Figure 4.8).

4.3.2 Extraction of parameters

After signal preprocessing, according to [38], for each identified task, the following parameters were extracted from both right and left wrist-acceleration signals:

- **Peak Standard Deviation** (STD): standard deviation of all acceleration peaks (local maxima) in m/s^2 [38].
- **Peaks per Second** (PPS): number of acceleration peaks per second [38].

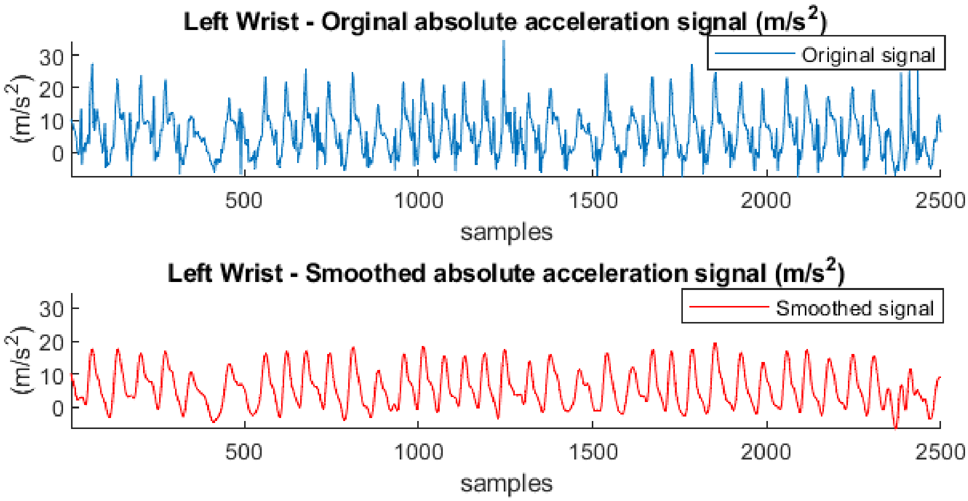

Figure 4.8: Comparison between original and smoothed signal.

- **Peak Ratio** (RATIO): Ratio between the number of acceleration peaks with a minimum prominence of 0.2 m/s_2 and the total number of acceleration peak [38].
- **Mean Peak Acceleration** (MPA): mean of acceleration peaks [38].
- **Acceleration per Second** (APS): absolute acceleration per second, measure of the rate of change in acceleration [38].
- **Log Dimensionless Jerk (LDLJ)**: logarithm naturalis of the sum of the squared acceleration multiplied with the trial duration to the power of three and divided by the squared peak acceleration [48, 49]. To compute this parameter, the initial acceleration signal underwent low-pass filtering with a 4th-order Butterworth filter set at a cutoff frequency of 3.5 Hz.

To quantify bilateral activity intensity and to investigate the contribution of both limbs and the contribution of the non-dominant limb compared to the dominant one, two additional parameters were include, according to [5]:

- **Bilateral Magnitude**: it reflects the intensity of activity across both upper extremities; it is calculated by summing the smoothed vector magnitude of the non-dominant and dominant upper limb for each second of activity

- **Magnitude Ratio**: it reflects the ratio of acceleration between upper limbs. It is calculated for each second of activity by adding one to activity count to the smoothed vector magnitude of both upper extremities, dividing the smoothed vector magnitude of the non-dominant arm by the smoothed vector magnitude of the dominant one, and log-transforming the calculated values.

To calculate these parameters, a different data processing approach is used. As reported [50], by utilizing open-source code, raw acceleration data is converted into activity counts (1 count = 0.016318 m/s^2). Then, for each second of data, activity counts across the three axes are combined into a single value, referred to as a vector magnitude, using the following equation $\sqrt{x^2 + y^2 + z^2}$. This process is performed individually for each upper extremity. Additionally, the vector magnitudes of each limbs are smoothed by applying a 5-sample moving average to minimize the variability in vector magnitude amplitude. Subsequently, bilateral magnitude and magnitude ratio are computed [5].

4.3.3 Data analysis

The previously mentioned parameters are computed for every session, both prior to and following the rehabilitation intervention. To evaluate the inter-session differences, the following criteria are employed:

- inter-session variations were quantified as difference between value obtained before and after the intervention $V_{post} - V_{pre}$
- since there were no reference values in the literature and it was not possible to define a minimum clinically detectable change, in agreement with the clinicians, it was decided to set a threshold of 0.30* V_{pre} to determine if there was a consistent improvement.

Statistical Analysis
Statistical tests are performed to assess if the obtained results were statistically relevant. The statistical test applied are:

- Shapiro-Wilk test

- T-test
- Wilcoxon Test

Shapiro-Wilk Test The Shapiro-Wilk test is a hypothesis test that evaluates whether a data set is normally distributed. It evaluates data from a sample with the null hypothesis that the data set is normally distributed. A large p-value indicates the data set is normally distributed, a low p-value indicates that it is not normally distributed. This test is necessary to decide whether to apply T-Test (parametric test) or Wilcoxon test (nonparamentric test) later. In this case it was applied for verifying if data obtained from the right and left arm of the same subject for a certain task were from a normal distribution. This test was utilized separately for each feature above mentioned. Matlab function **swtest** was used.

T-test T-test is a parametric test used for verifying the null hypothesis of continuous distribution of data with the same mean. In particular, it was used for comparing data obtained from left and right arm of a certain subject for each task separately and for comparing two rehabilitative groups. This verification was necessary to understand if the difference between data obtained from right arm and left arm and outcomes following different rehabilitative training ware statistically significants, hence, to this aim, unpaired t-test was used. Matlab function **ttest2** was used.

Wilcoxon test Wilcoxon test is a non-parametric test used for verifying the null hypothesis of continuous distribution of data with the same median. In particular, it was used for comparing data obtained from left and right arm of a certain subject for each task separately and for comparing two rehabilitative groups in order to know if the two samples were from the same continuous distribution. This verification was necessary to understand if the difference between data obtained from right arm and left arm was statistically significant and to assess statistical differences between two different rehabilitative groups. To this aim, Ranksum Wilcoxon test was used. Matlab function **ranksum** was used.

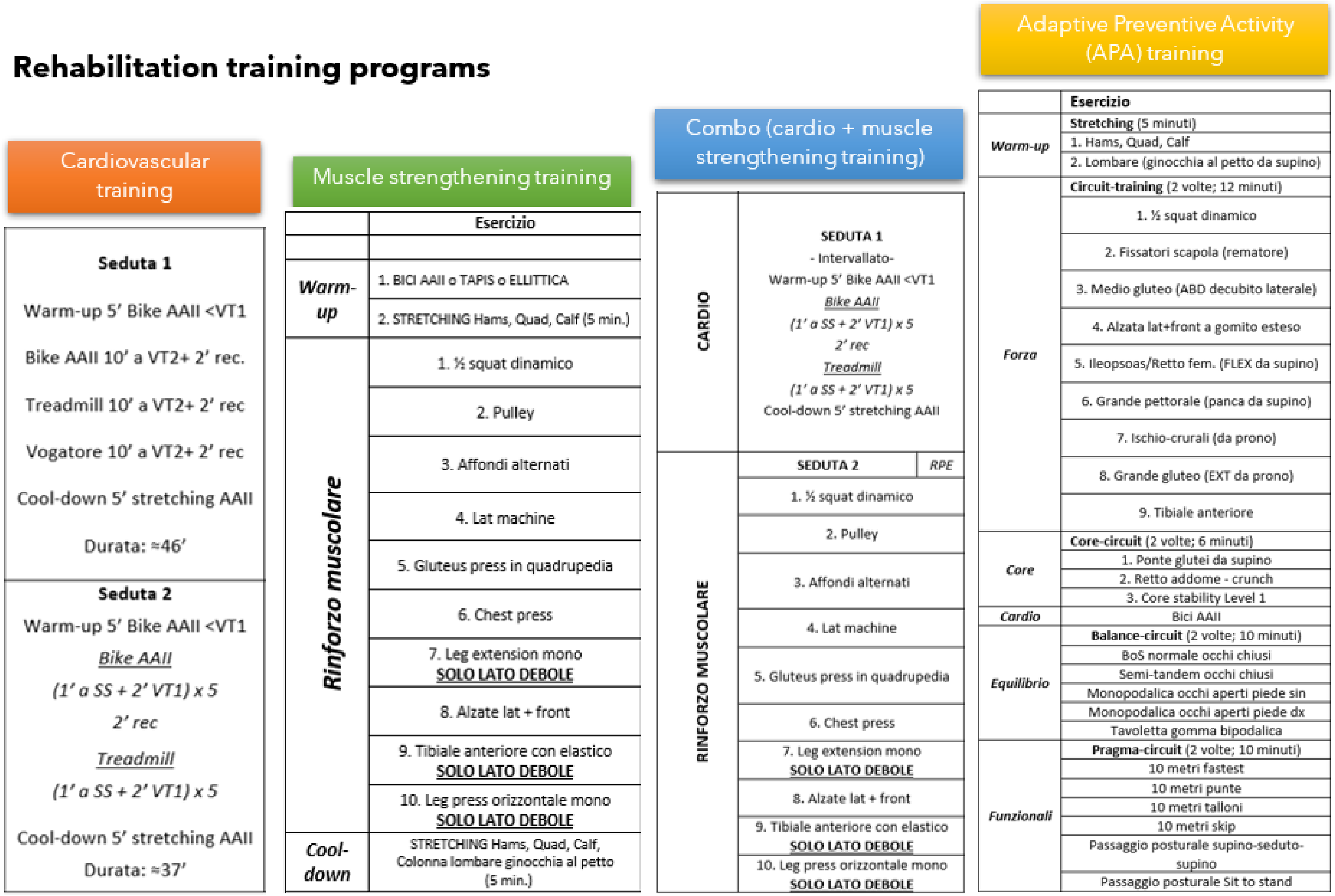

Figure 4.9: Examples of rehabilitation programs for each group.

Chapter 5

Results and Discussion

In this chapter, the results derived from kinematic analysis are presented. In the following various comparison are performed, in order to determine whether the extracted parameters indeed reveal differences, thereby characterizing distinct patient groups.

5.1 Kinematics outcomes

At first a comparison was conducted, considering both the dominant and non-dominant limbs of each subject before and after undergoing rehabilitative training for every training group.

5.1.1 Peak Standard Deviation

Outcomes obtained for STD parameter is reported in Figure 5.1 and Figure 5.2, respectively before and after the rehabilitative intervention, for both dominant e non-dominant limb. For each activity, mean value and standard deviation in m/s^2 are calculated across all subjects of each according group. According to [38], STD intends to reflect the intensity of actions, where higher values indicate more agile and dynamic movement execution, while lower values suggest a relatively monotonous and uniform behavior.

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.3. APA group shows significant differences in a greater number of activities (Transfer light, Meal management, Clean surface), while the other three groups only demonstrate differences in a single activity (Clean surface).

5.1.2 Peak Per Second

Outcomes obtained for PPS parameter is reported in Figure 5.4 and Figure 5.5, respectively before and after the rehabilitative intervention, for both dominant and non-dominant limb. For each activity, mean value and standard deviation in $1/s$ are calculated across all subjects of each according group. PPS can be considered a measure of the number of submovements, with higher PPS values indicating less smooth movement [38].

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.6. APA group exhibits statistically significant differences in one activities (Meal management), the combination group (b) exhibits statistically significant differences in Meal management, while the Cardio training shows statistically differences in Wash floor.

5.1.3 Peak Ratio

Outcomes obtained for RATIO parameter is reported in Figure 5.7 and Figure 5.8, respectively before and after the rehabilitative intervention, for both dominant and non-dominant limb. For each activity, mean value and standard deviation are calculated across all subjects of each according group. RATIO can be interpreted as a measure of movement smoothness, reflecting the proportion of distinct movements relative to all movements, including noise [38].

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.9. APA group exhibits statistically significant differences in three activities (Wash floor, Laundry, Clean surface), while the Cardio training group shows statistically significant differences in two activities (Meal management and Clean surface).

5.1.4 Mean Peak Acceleration

Outcomes obtained for MPA parameter is reported in Figure 5.10 and Figure 5.11, respectively before and after the rehabilitative intervention, for both dominant and non-dominant limb. For each activity, mean value and standard deviation in m/s^2 are calculated across all subjects of each according group. MPA is intended to represent the intensity of action, adapted from a similar measure of velocity [19, 38].

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.12. APA group shows statistical significance in two activities (Transfer light, Clean surface), combination of cardio and muscle strengthening group in three activities, while cardio and muscle strengthening in only one activity.

5.1.5 Acceleration Per Second

Outcomes obtained for APS parameter is reported in Figure 5.13 and Figure 5.14, respectively before and after the rehabilitative intervention, for both dominant and non-dominant limb. For each activity, mean value and standard deviation in m/s^3 are calculated across all subjects of each according group. APS is a jerk measure which expresses the rate of acceleration change.

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.15. Each of the four groups displays statistically significant differences in just one activity (Clean surface), with the exception of muscle strengthening, which also demonstrates significant differences in the Transfer light activity.

5.1.6 Log Dimensionless Jerk

Outcomes obtained for LDLJ parameter is reported in Figure 5.16 and Figure 5.17, respectively before and after the rehabilitative intervention, for both dominant and non-dominant limb. For each activity, mean value and standard deviation are calculated across all subjects of each according group. LDLJ aims to index and characterize the fluidity and hesitation in the executed actions [48].

Statistical Analysis
Statistical analysis was carried out through two distinct comparisons:

- Comparison between before and after rehabilitation session for the same limb. To this aim paired T-test or Wilcoxon Signed rank test was performed. Matlab function **signrank** was used.
- Comparison between dominant and non-dominant limb in pre e post rehabilitation session.

Results are presented in Figure 5.18. As reported in figure, each of the four groups displays statistically significant differences in just one activity (Clean surface).

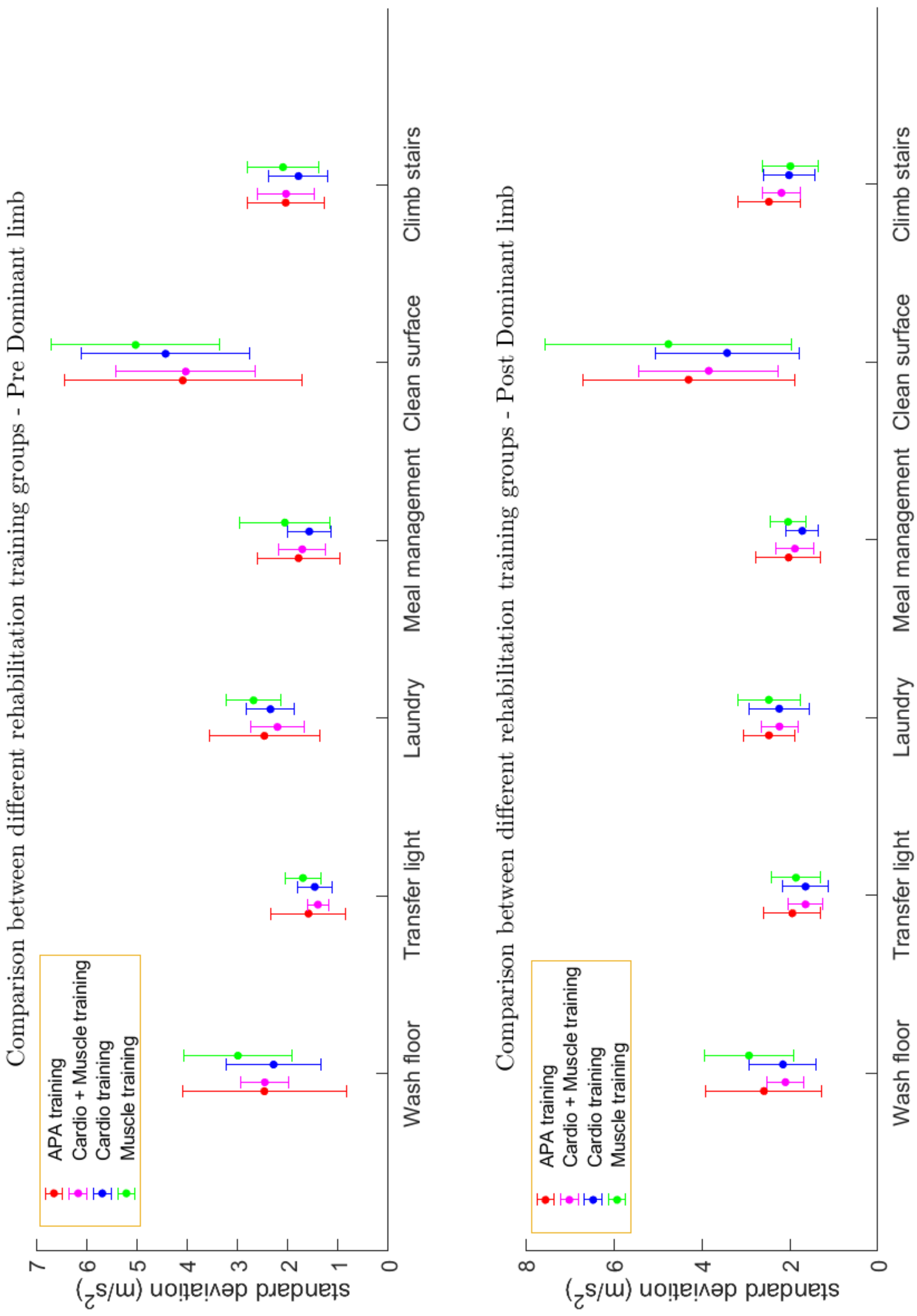

Figure 5.1: Mean and Standard Deviation for STD parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

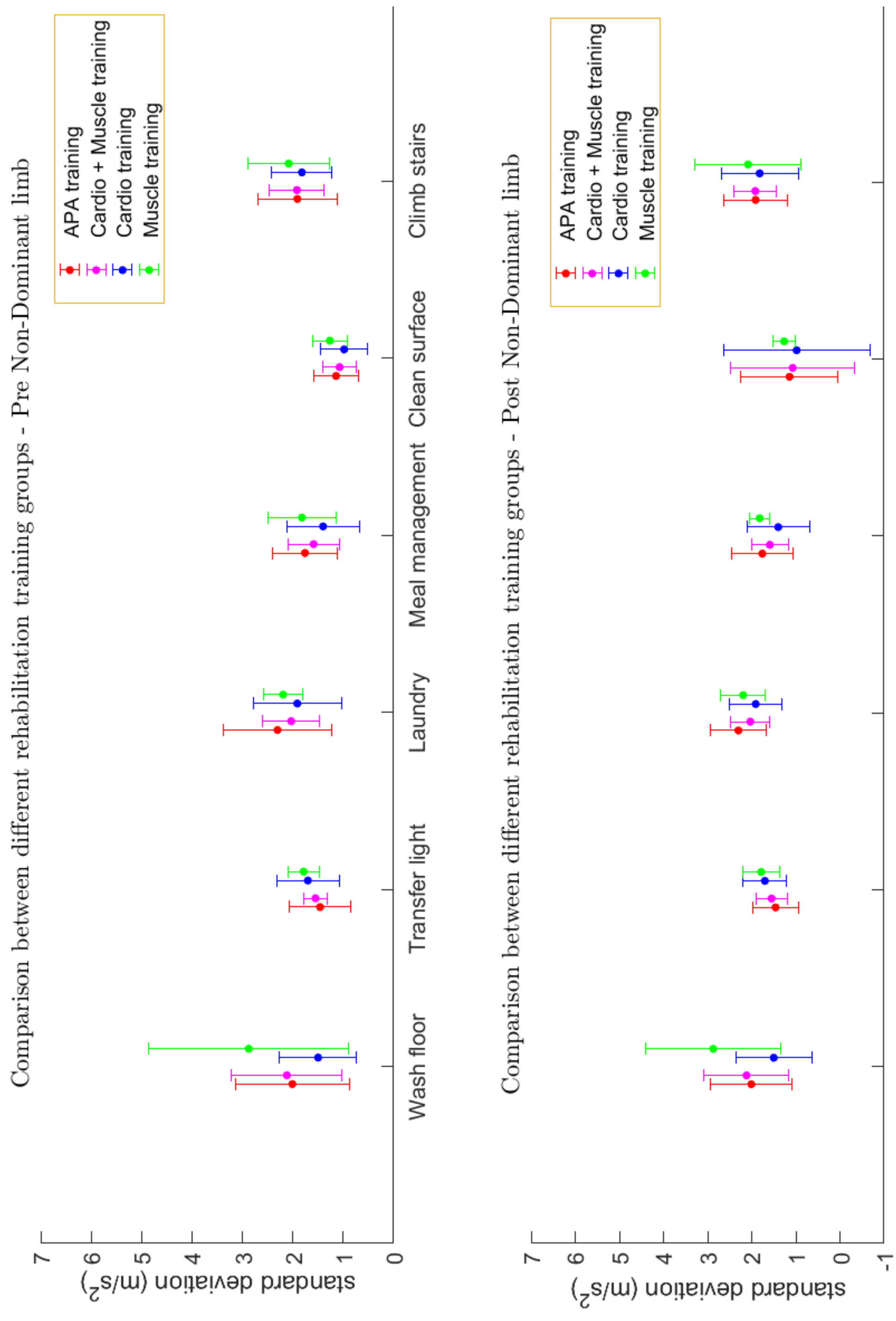

Figure 5.2: Mean and Standard Deviation for STD parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb.

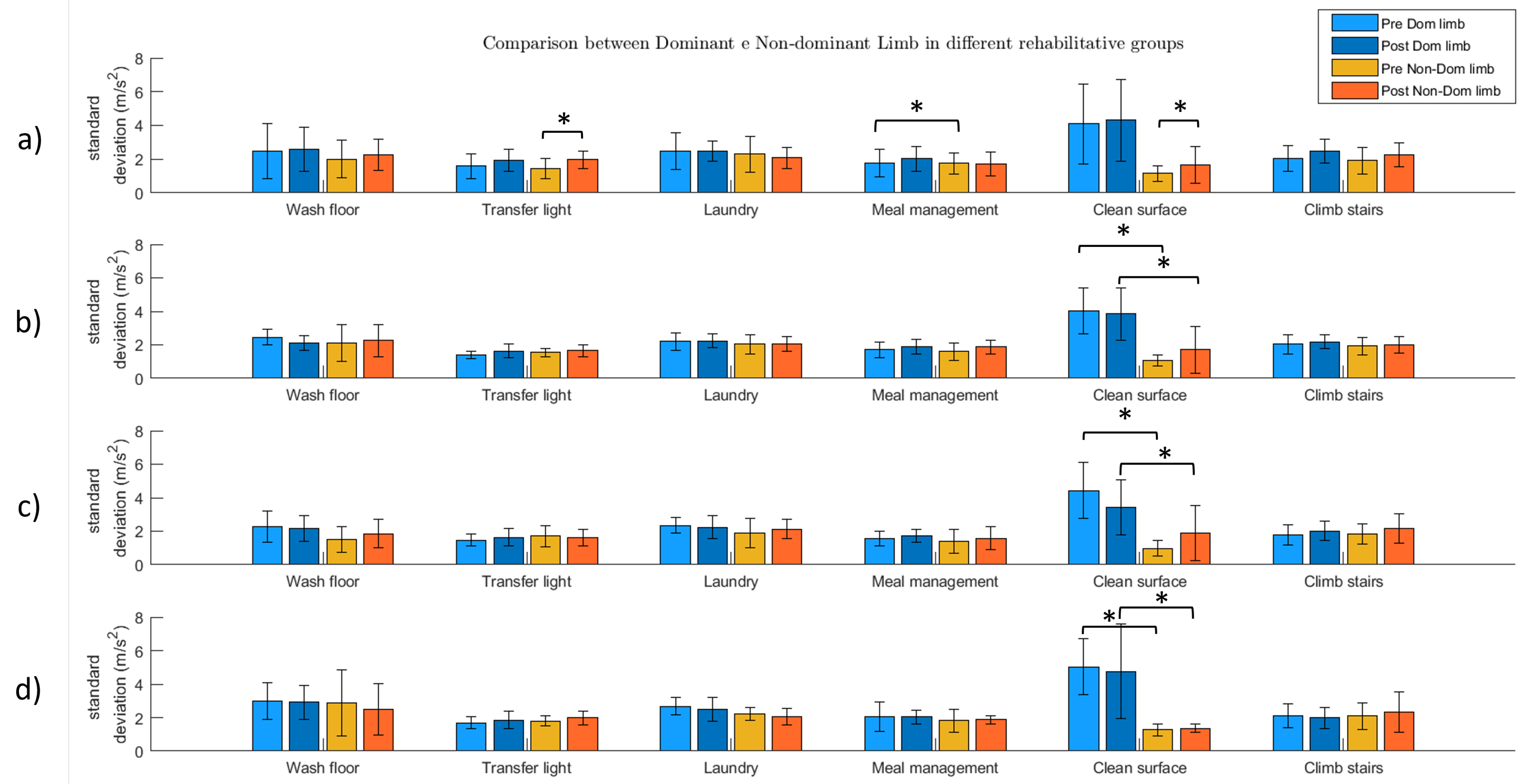

Figure 5.3: Comparison between different training group before and after rehabilitation intervention per STD parameters.a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

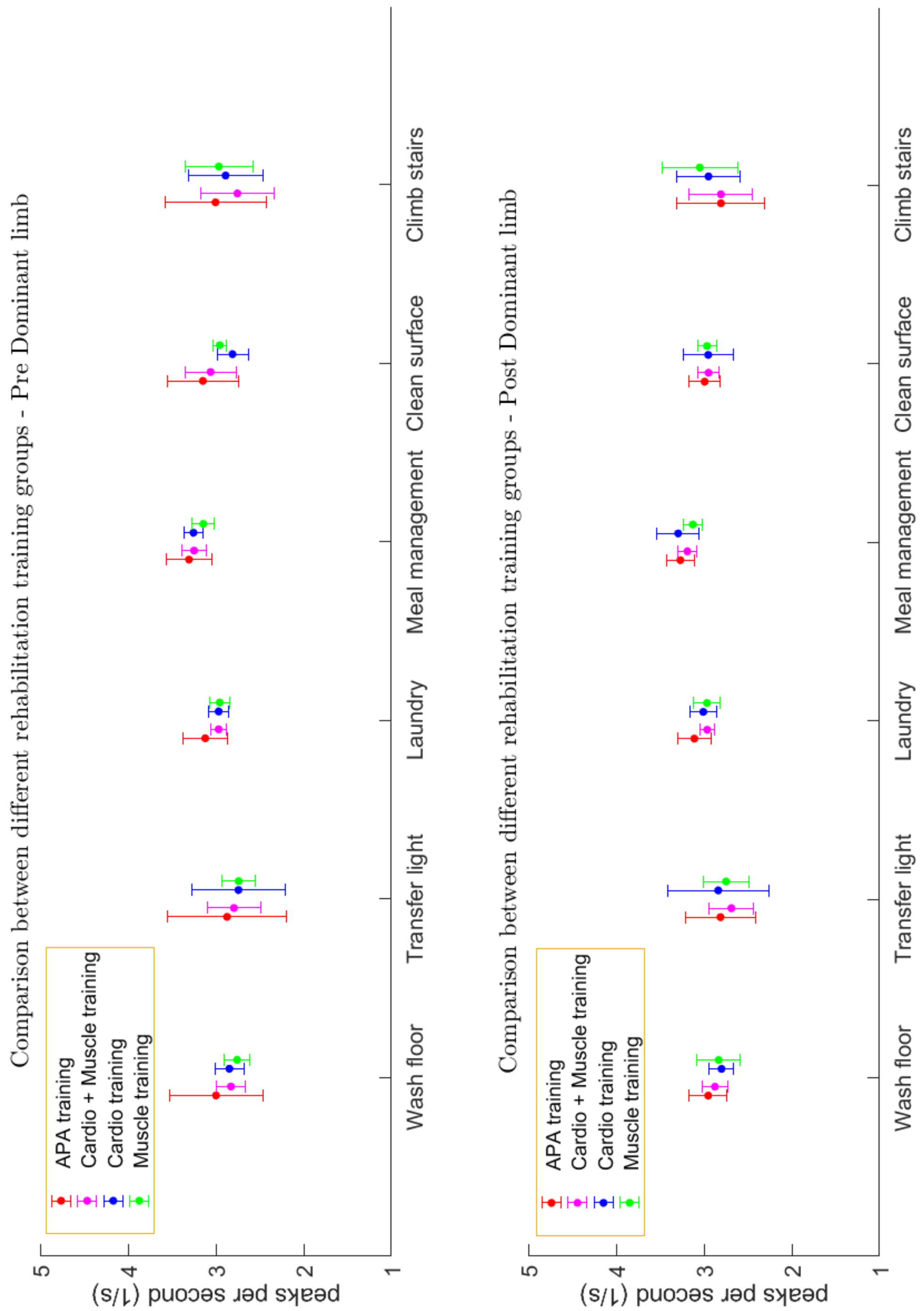

Figure 5.4: Mean and Standard Error for PPS parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

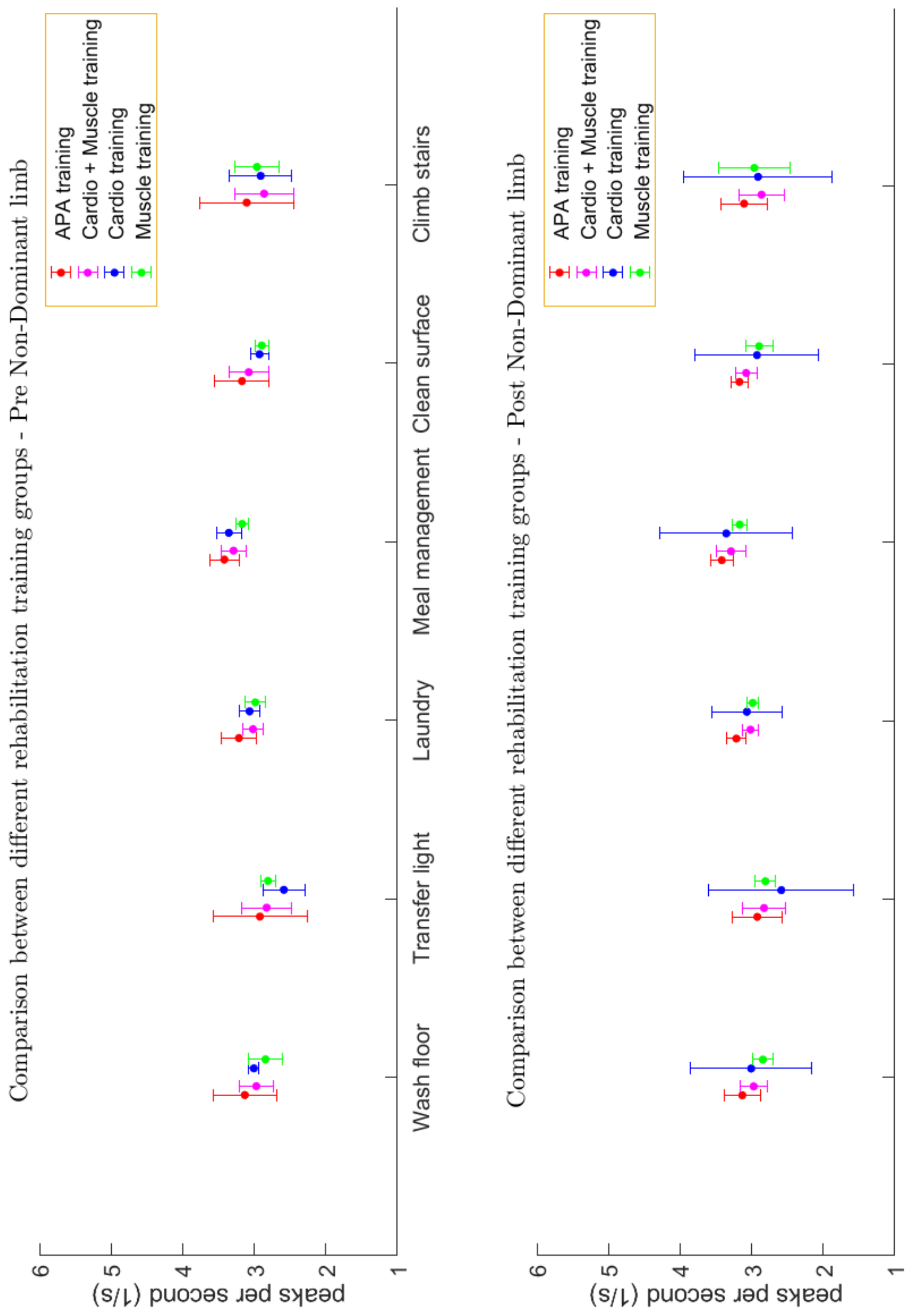

Figure 5.5: Mean and Standard Deviation for PPS parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb.

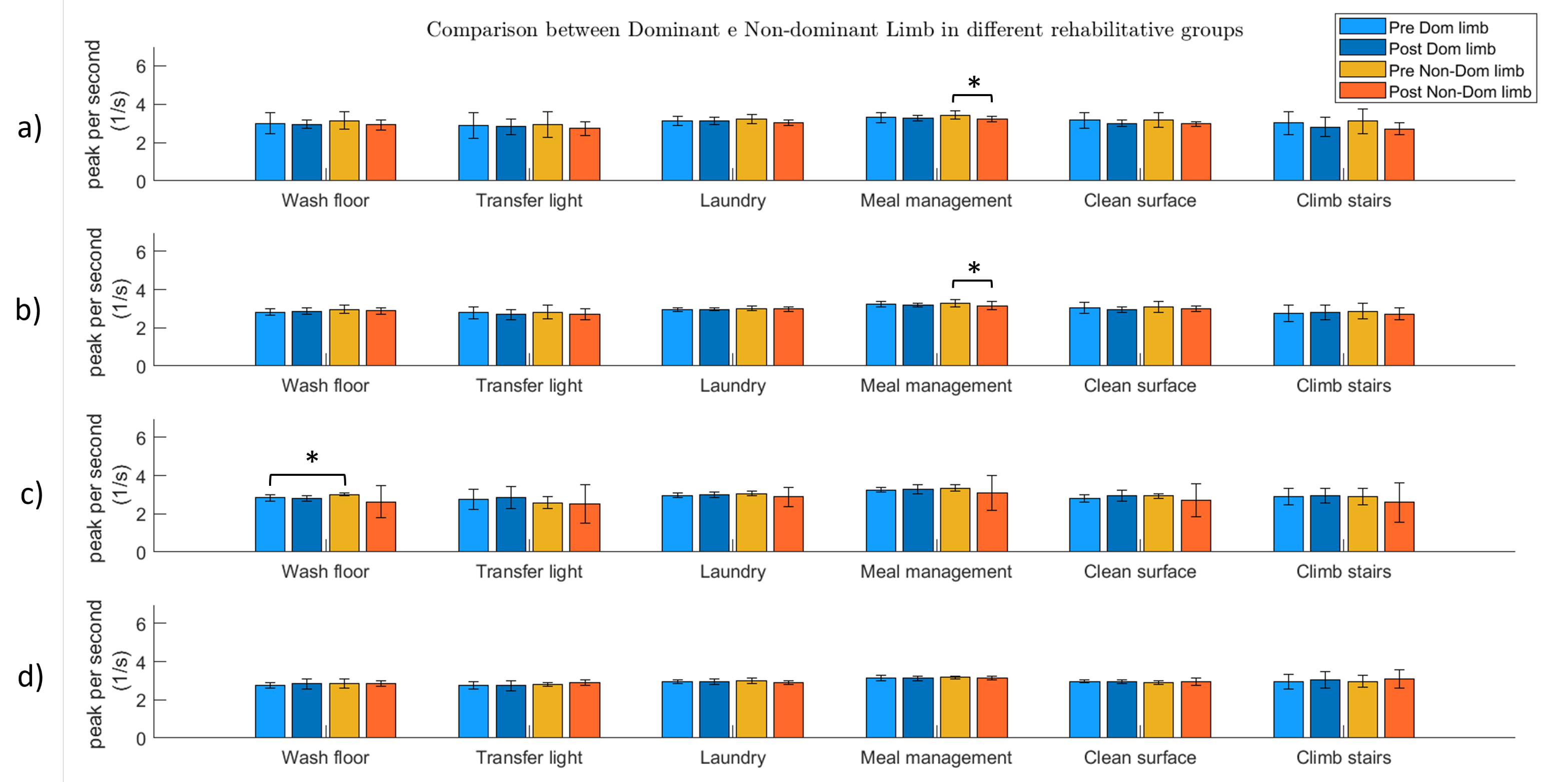

Figure 5.6: Comparison between different training group before and after rehabilitation intervention per PPS parameter.a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

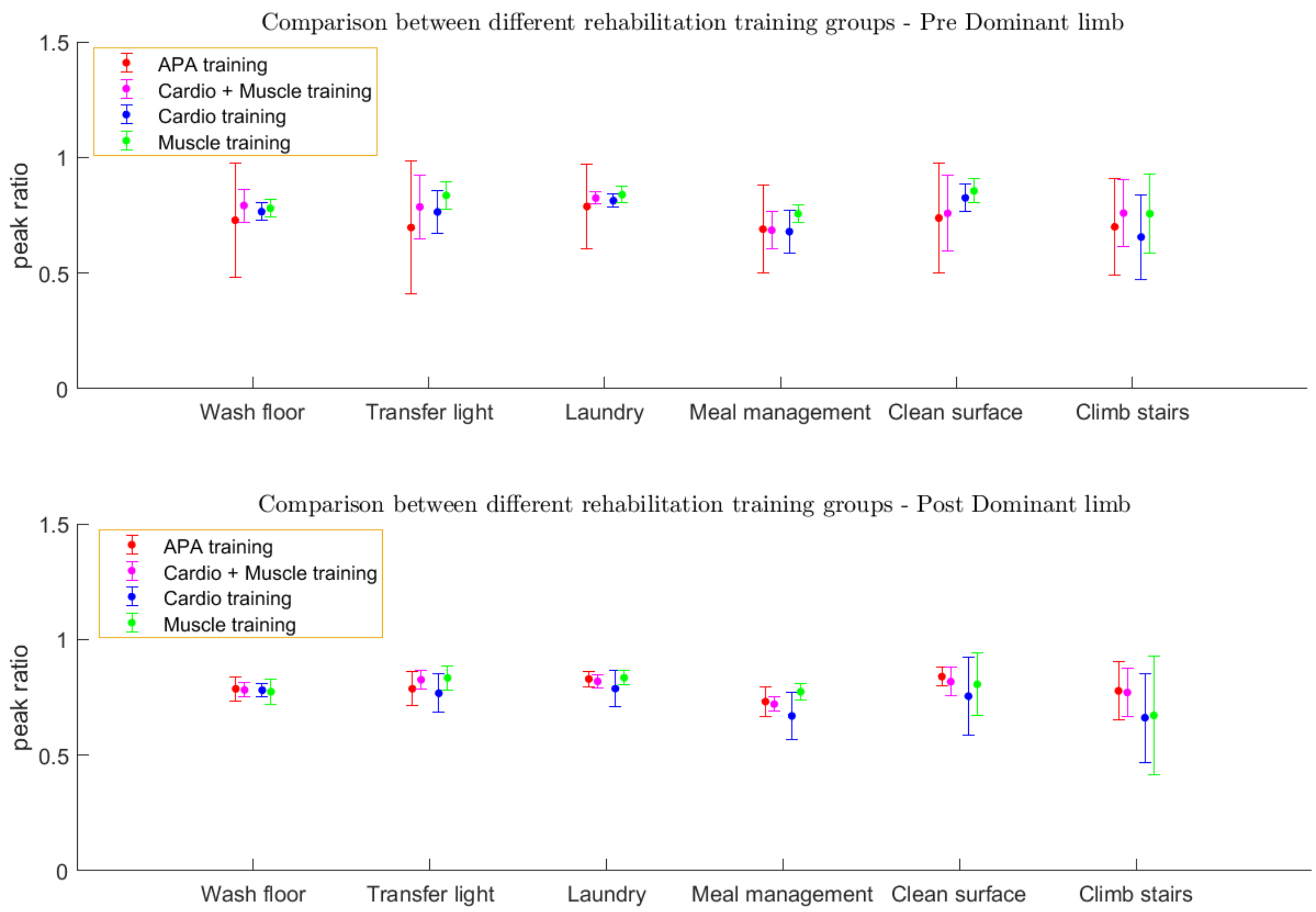

Figure 5.7: Mean and Standard Deviation for RATIO parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

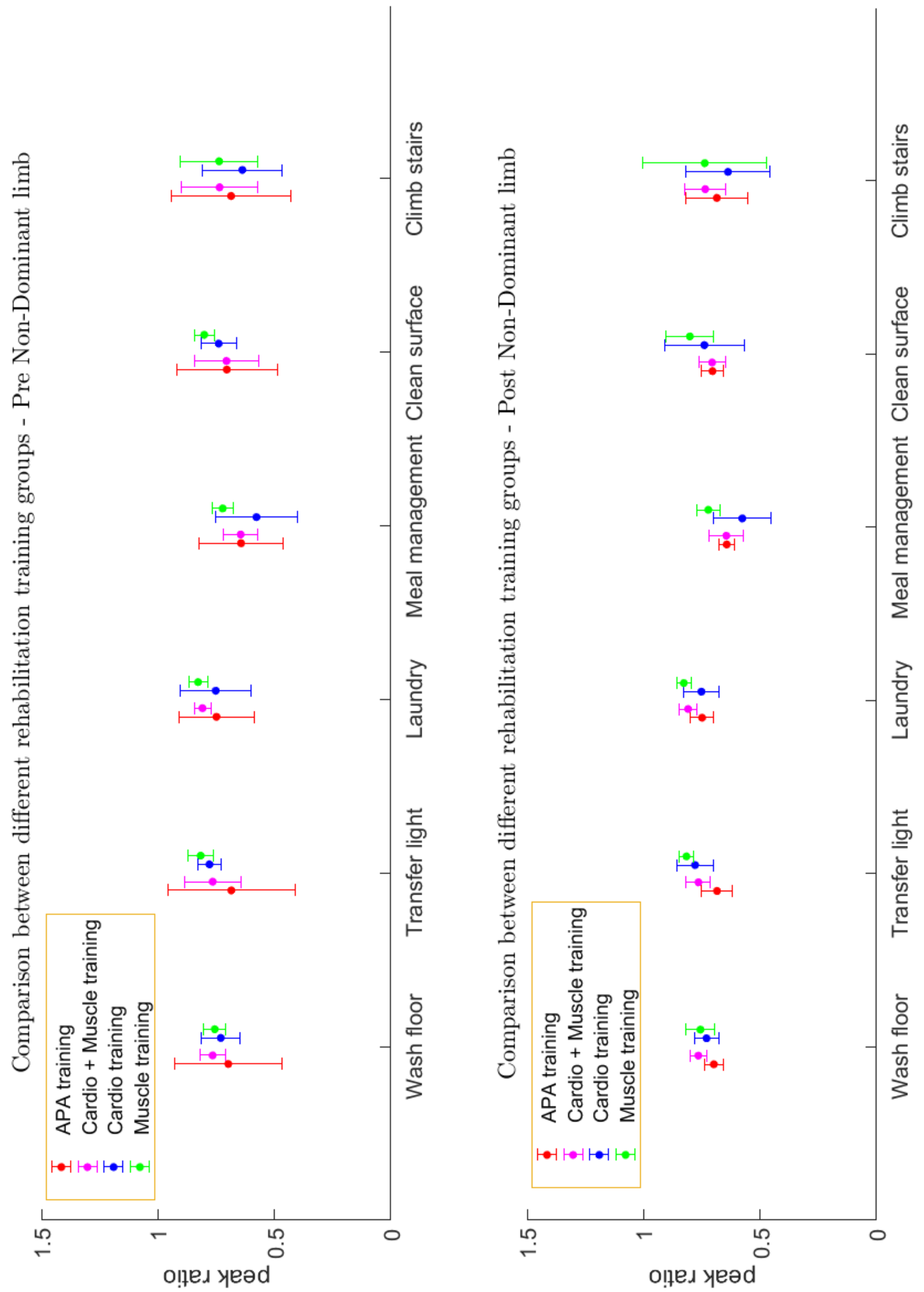

Figure 5.8: Mean and Standard Deviation for RATIO parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb.

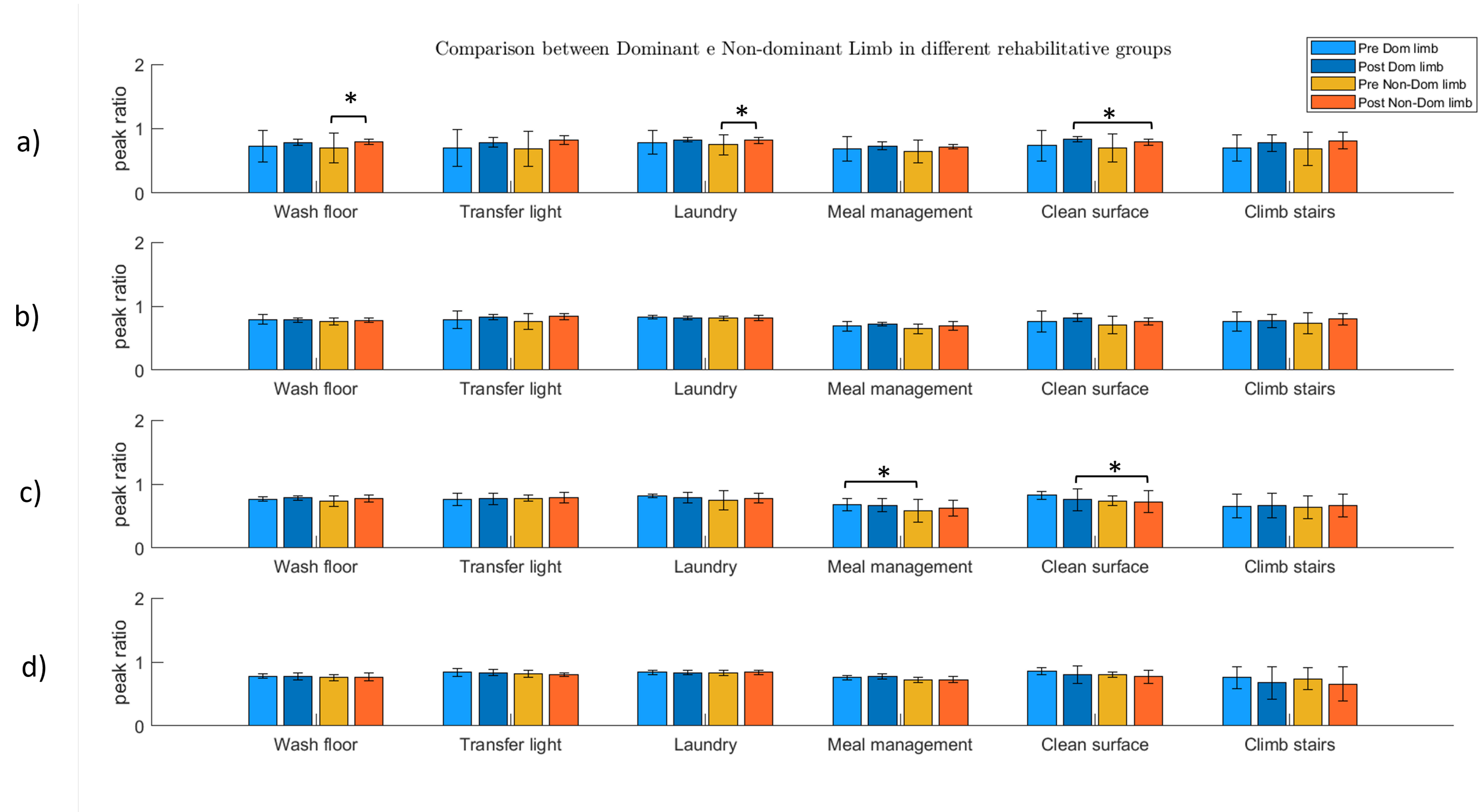

Figure 5.9: Comparison between different training group before and after rehabilitation intervention per RATIO parameter. a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

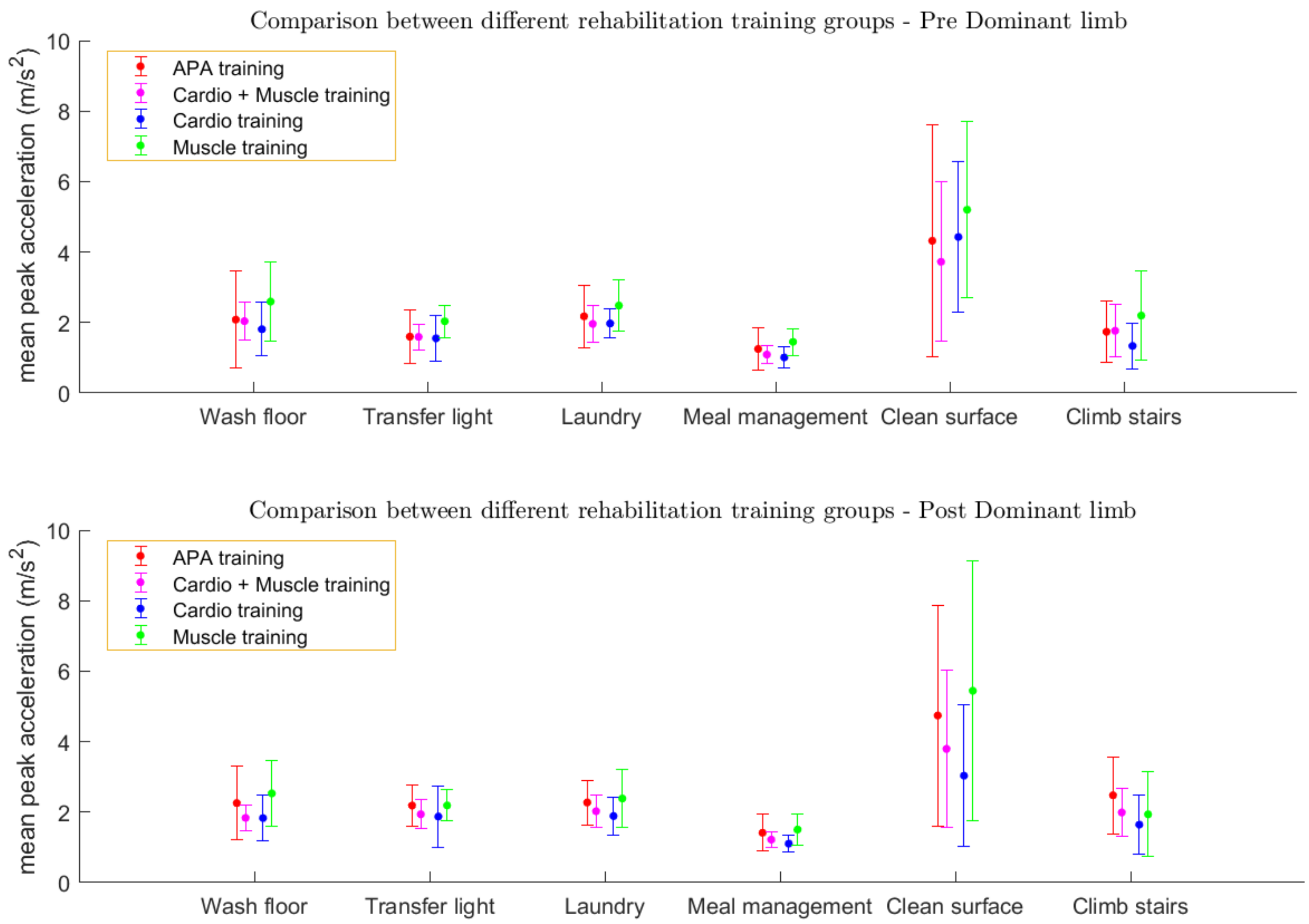

Figure 5.10: Mean and Standard Deviation for MPA parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

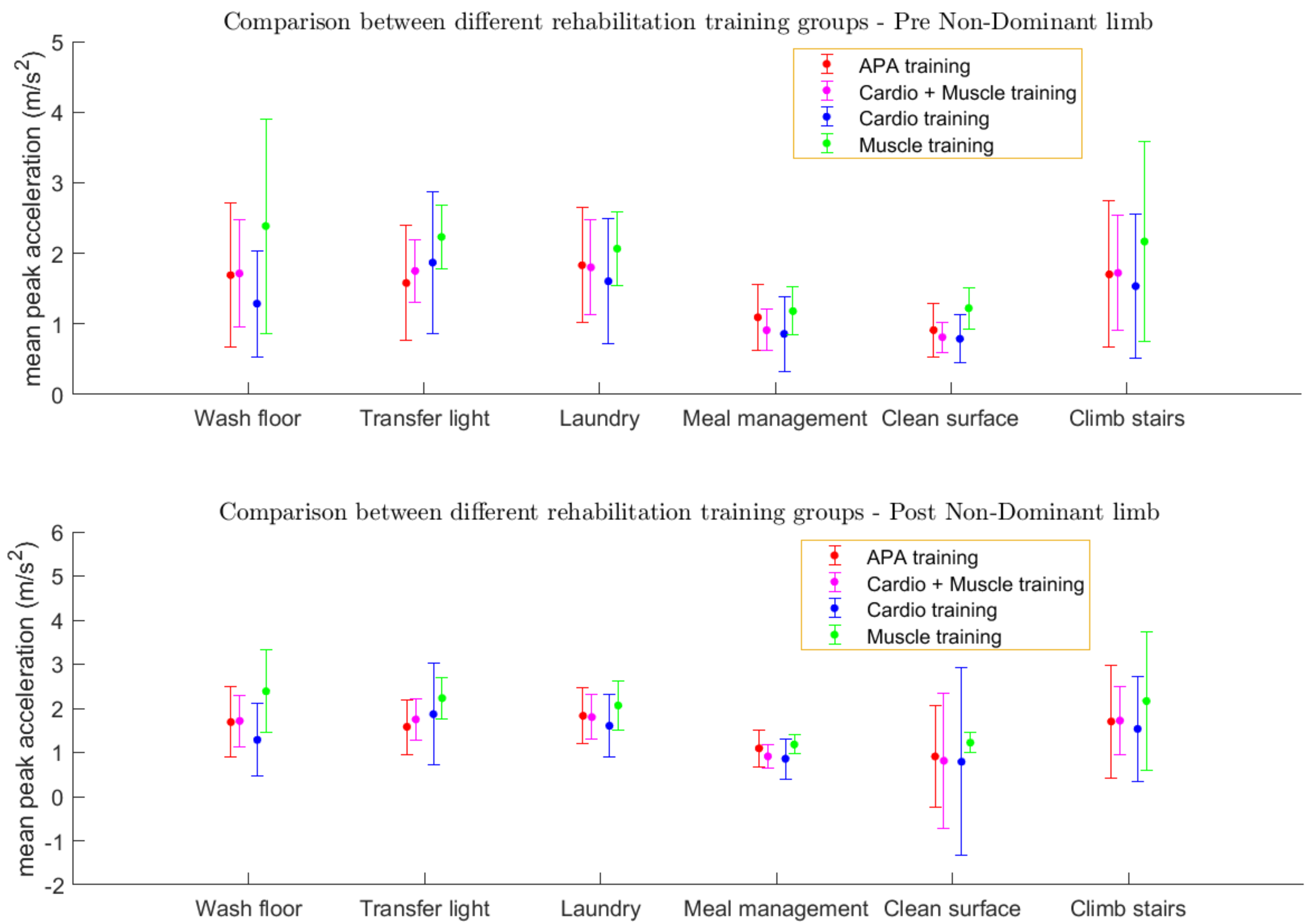

Figure 5.11: Mean and Deviation for MPA parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb.

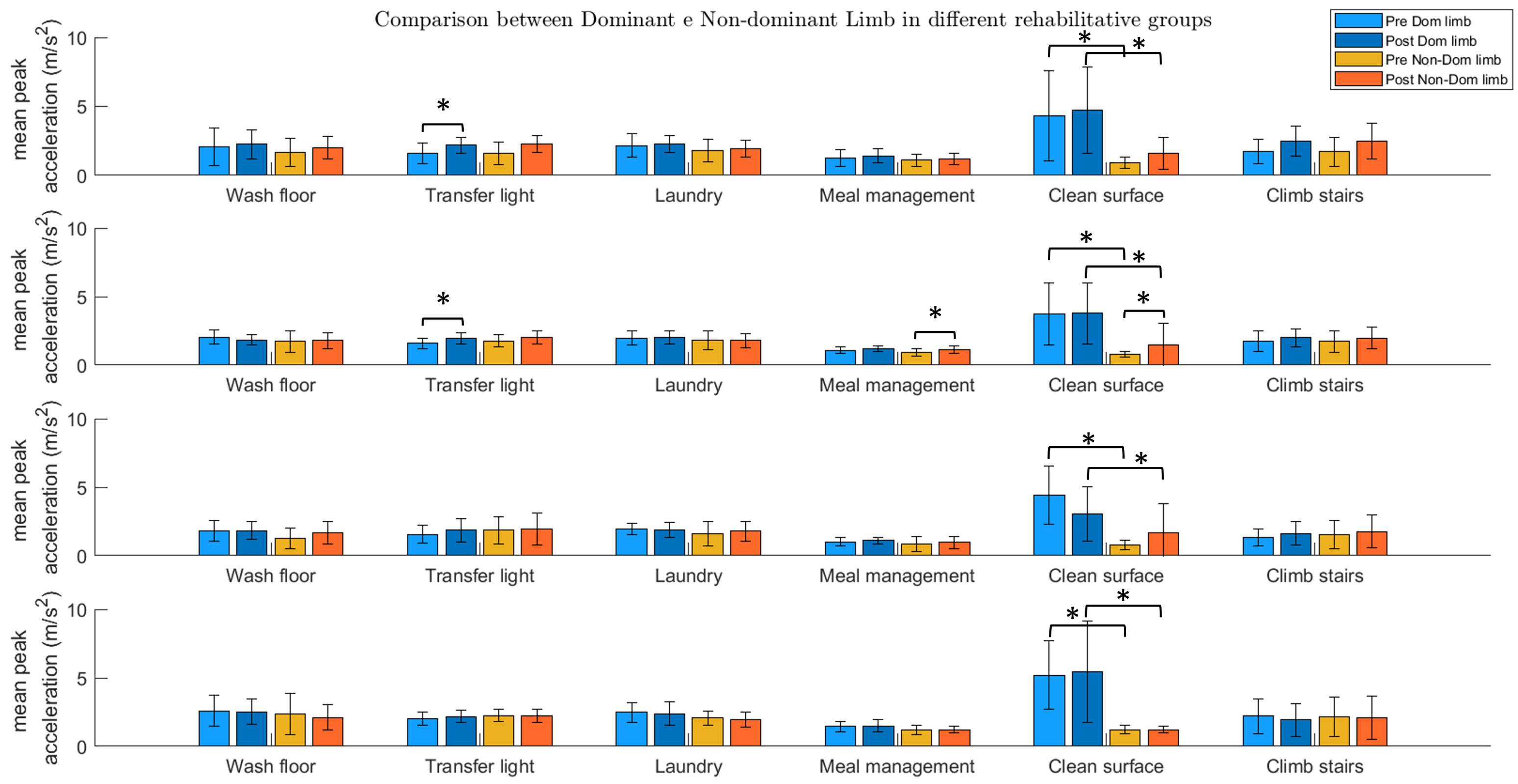

Figure 5.12: Comparison between different training group before and after rehabilitation intervention per MPA parameter. a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

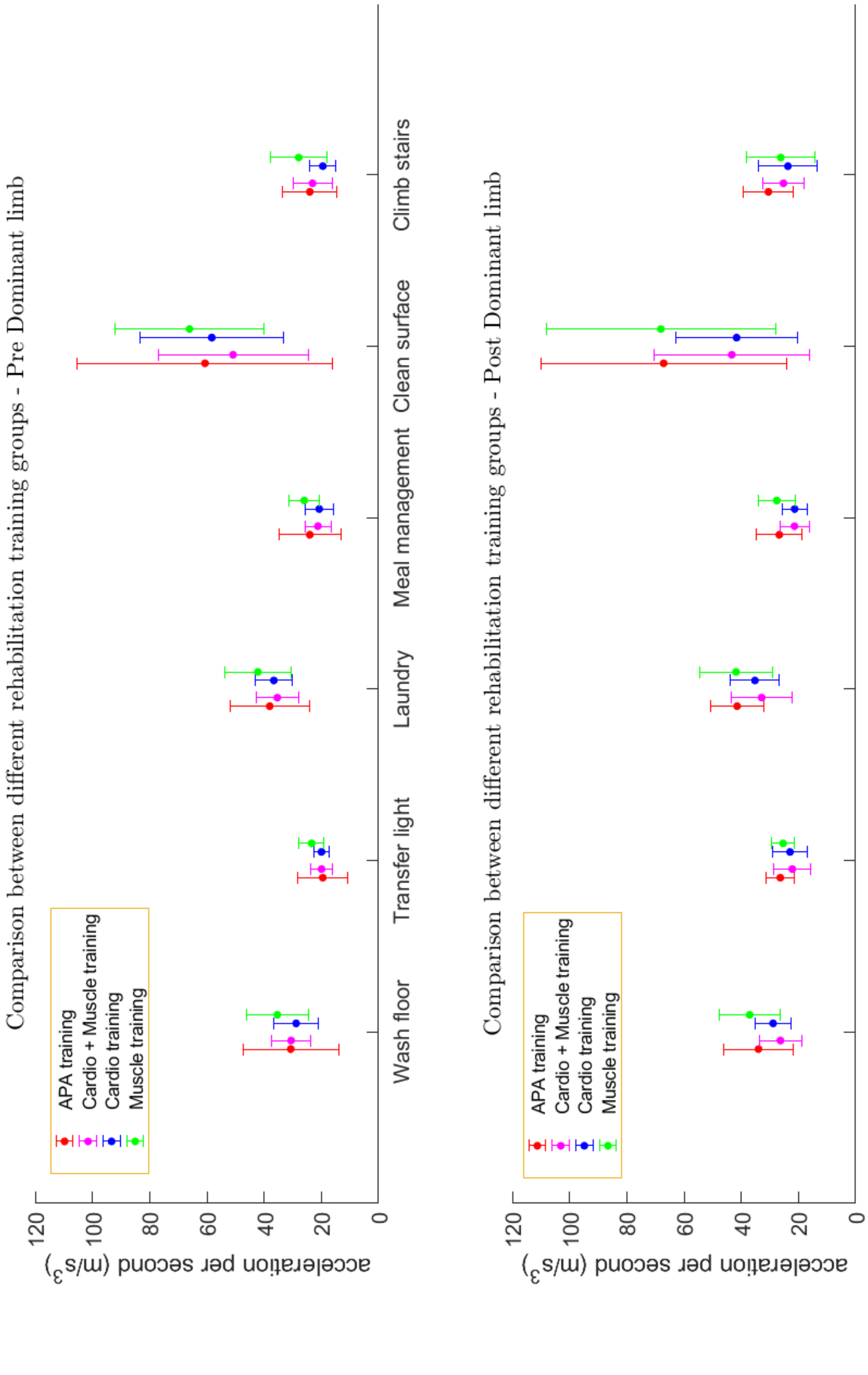

Figure 5.13: Mean and Standard Deviation for APS parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

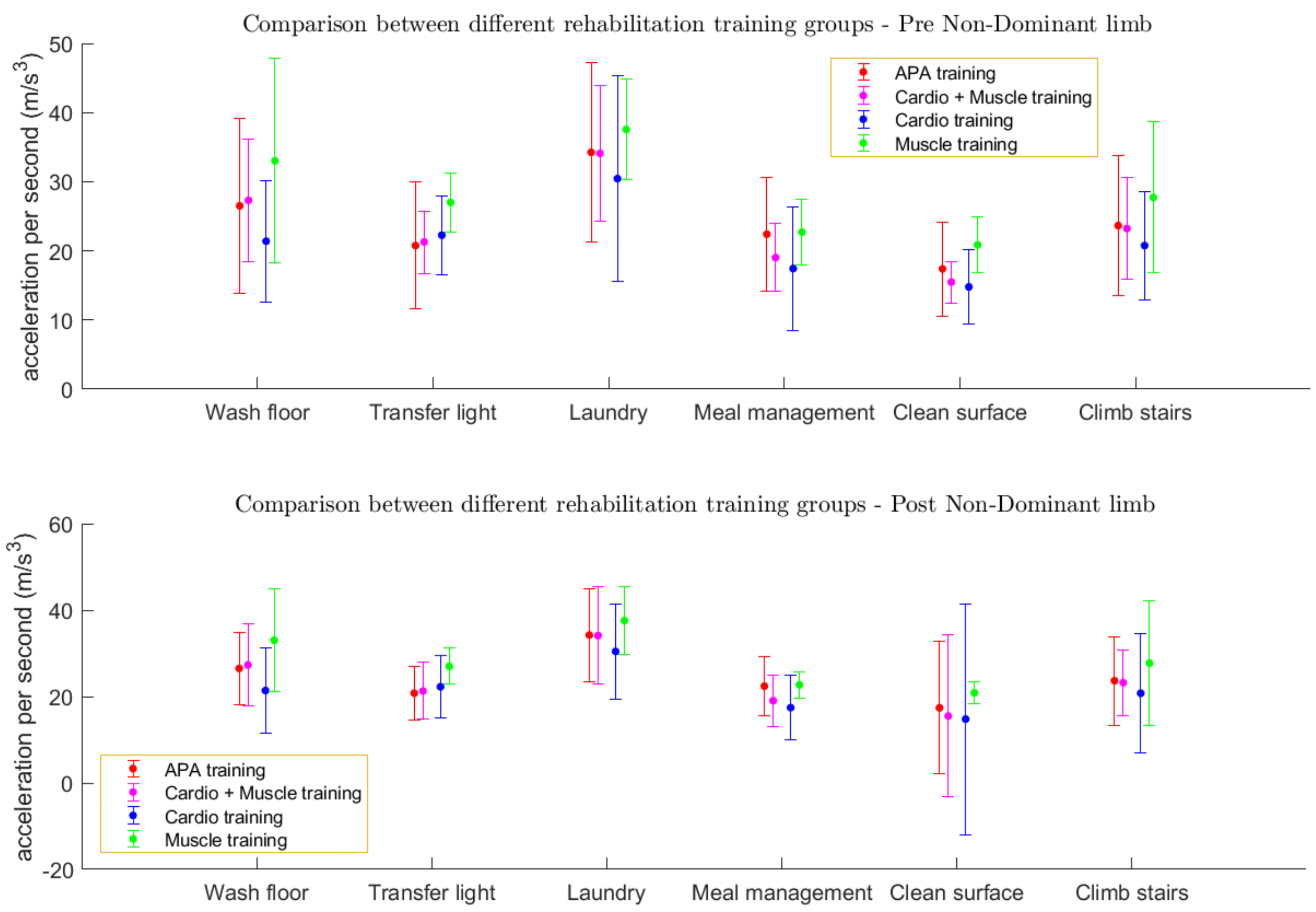

Figure 5.14: Mean and Standard Deviation for APS parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb.

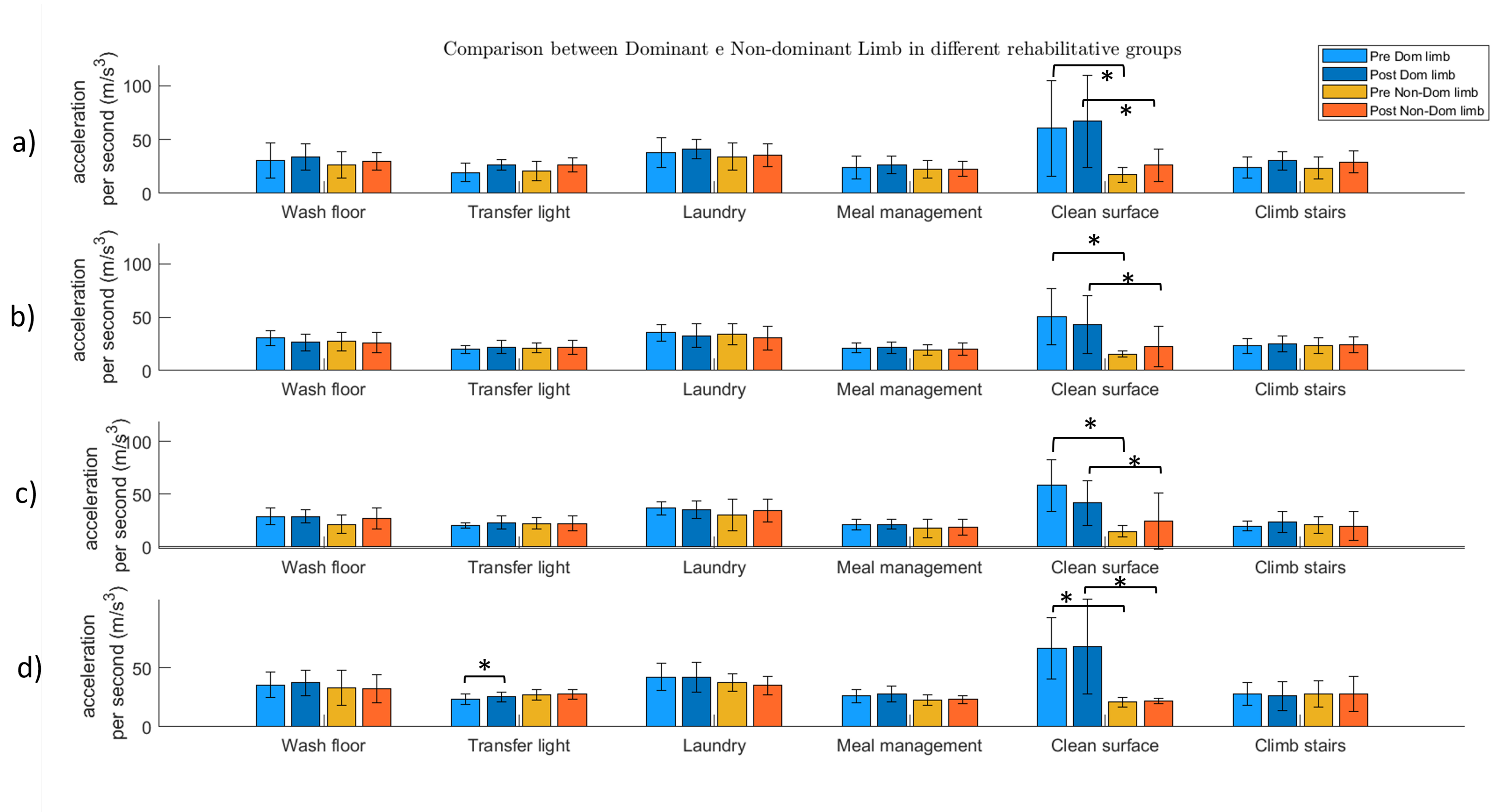

Figure 5.15: Comparison between different training group before and after rehabilitation intervention per APS parameter. a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

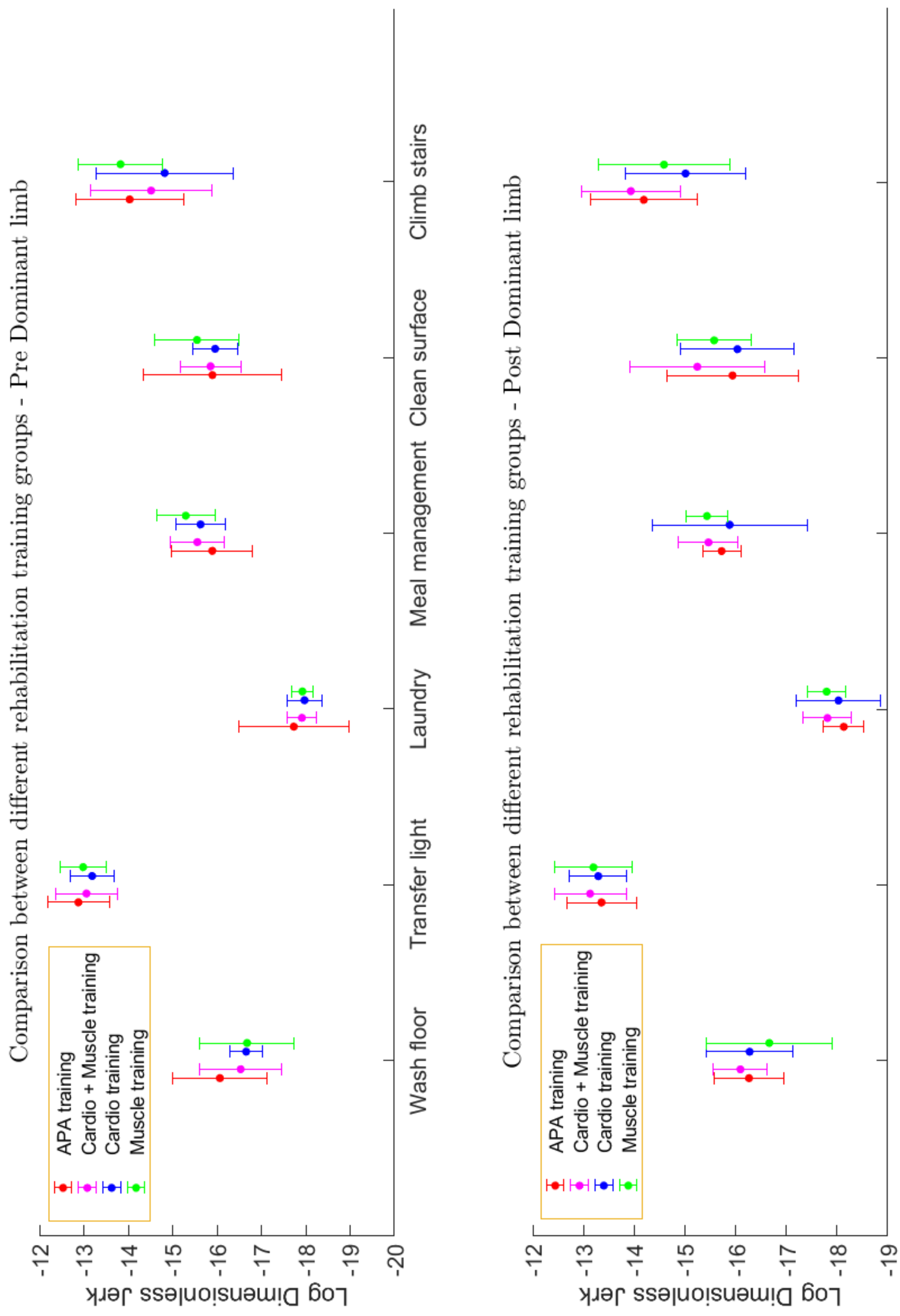

Figure 5.16: Mean and Standard Deviation for LDLJ parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for dominant limb.

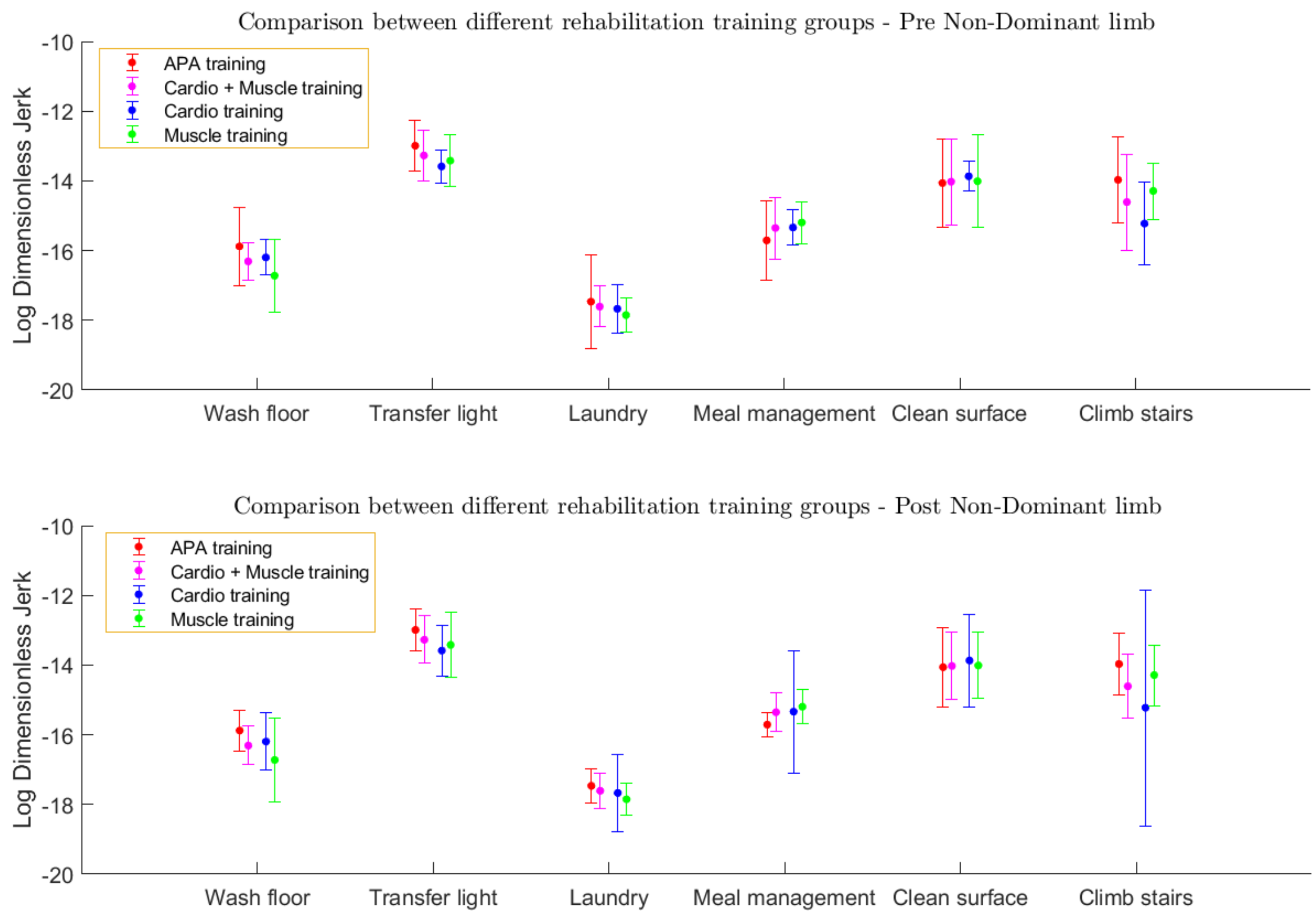

Figure 5.17: Mean and Standard Deviation for LDLJ parameter. Comparison between four rehabilitative groups in pre e post rehabilitation session for non-dominant limb

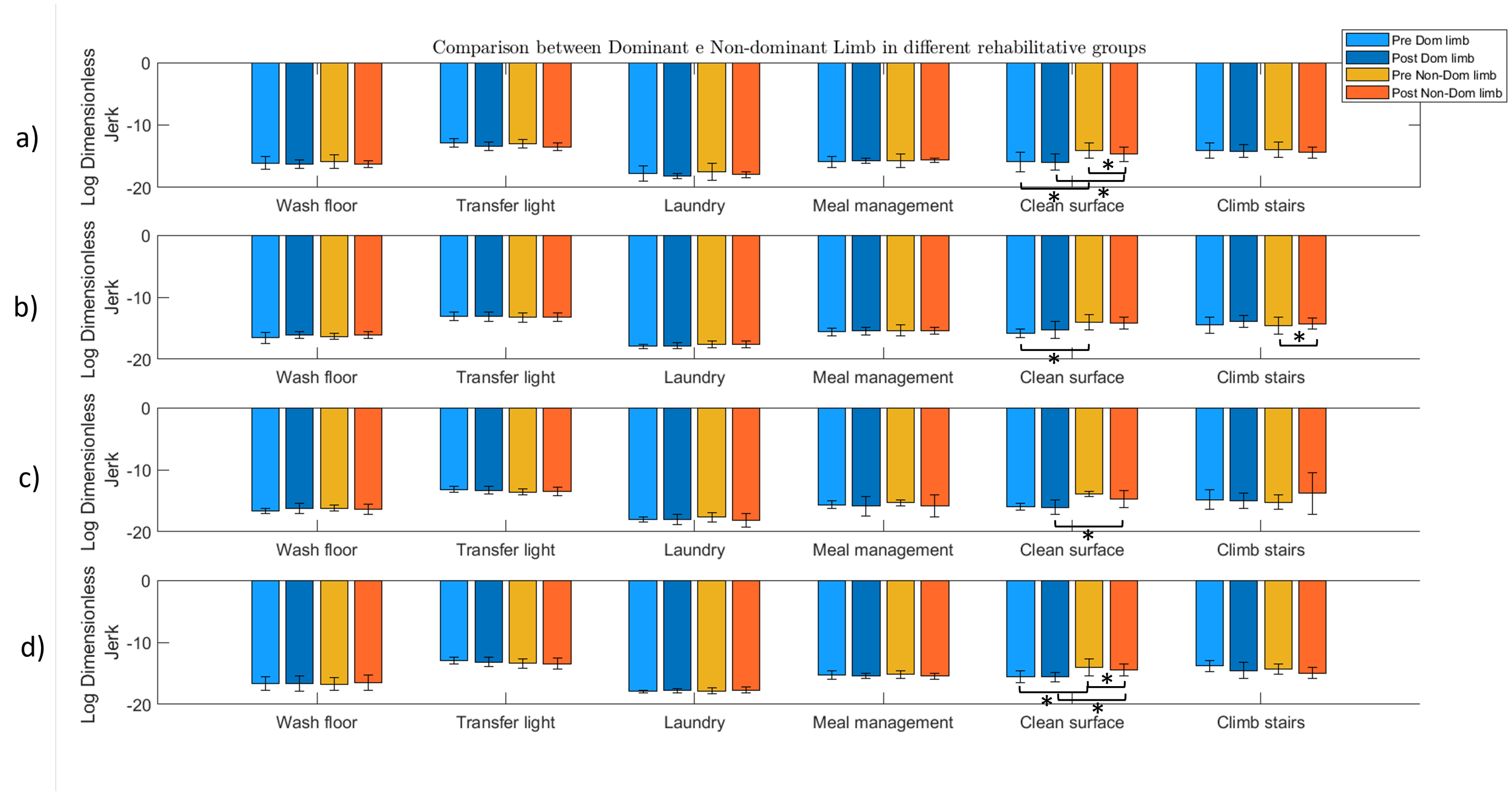

Figure 5.18: Comparison between different training group before and after rehabilitation intervention per LDLJ parameter. a) APA training group, b) Combination of cardio and muscle strengthening training group, c) Cardio training group and d) Muscle strengthening training group. Star indicates statistical significance.

5.2 Assessment of inter-session variations outcomes

For subsequent analyses, the cardio training group, muscle strengthening training group, and combination of both training groups have been merged into a single group referred to as *Others* group, which is then compared to the *APA* training group.
To assess inter-session variation, for each subject and activity, a parameter was considered "improved" if at least one or both limbs exhibited a positive change of 30% or more compared to the initial value. Number of improved subjects is evaluated for each activity and for every group and parameter. Radar plots in the following visually illustrate the comparison between the two groups for each parameter.

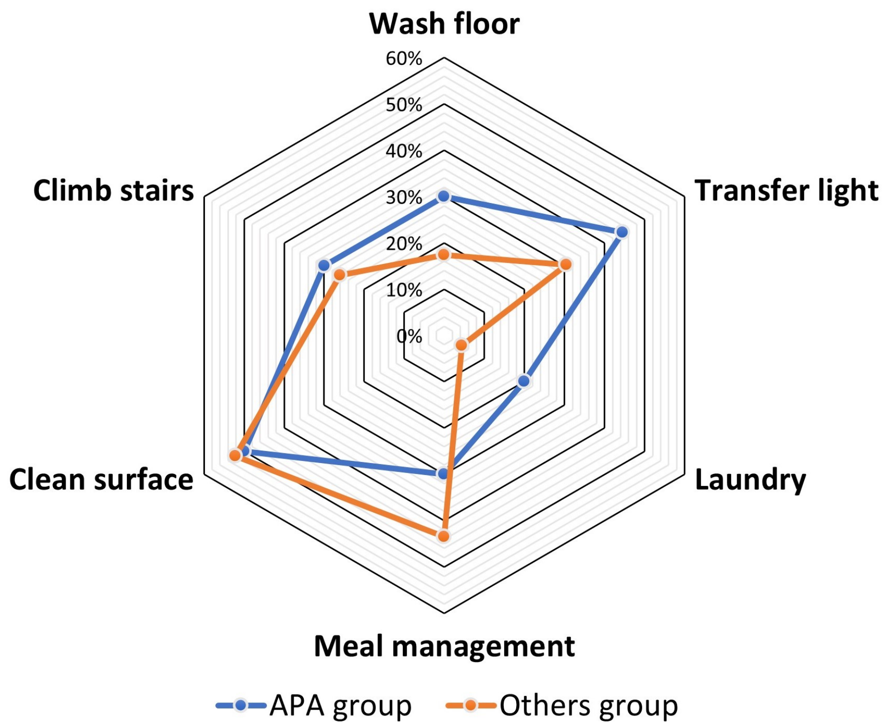

Figure 5.19: Radar plot summarizing the percentage of subjects for each activity that exhibited improvements in the STD parameter. This graph was created using Microsoft Excel®.

As shown in the Figure 5.19, generally, for the *APA* group, there is a higher percentage of subjects considered improved for all six activity respect to *Others* group.

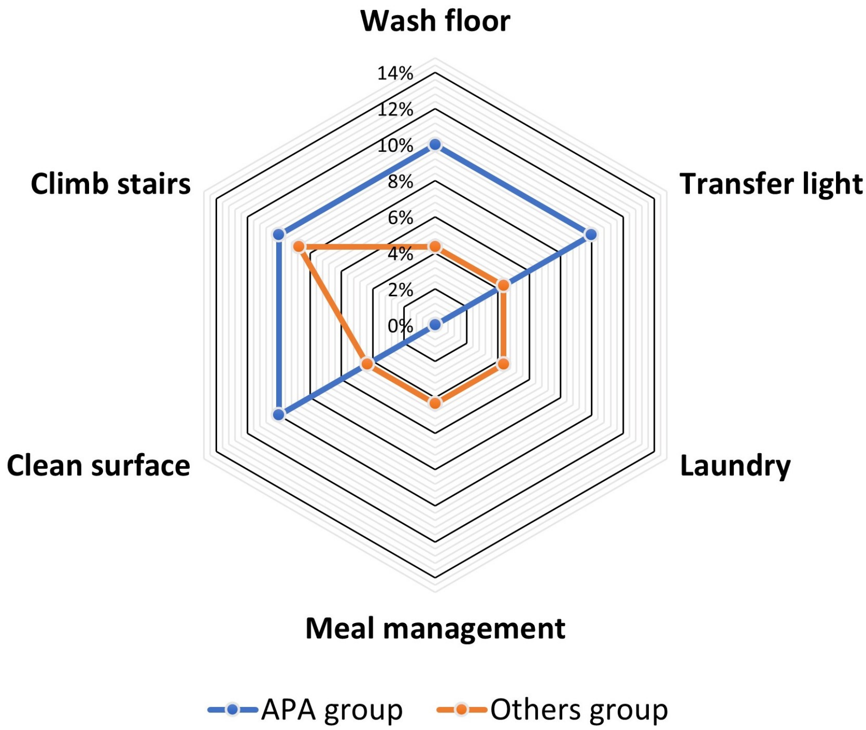

Figure 5.20: Radar plot summarizing the percentage of subjects for each activity that exhibited improvements in the PPS parameter. This graph was created using Microsoft Excel®.

As presented in the Figure 5.4, in this case as well, there is a greater number of activities with a higher percentage of patients considered improved in *APA* group. However, for two tasks (Meal management and Laundry), this percentage is higher in the *Others* group. This could be attributed to the difference in the sample sizes of the two groups being considered.

For PPS parameter (Figure 5.20, no improvement was observed in the subjects of the *APA* group. *Others* group, on the other hand, showed improvements in four activities (Transfer light, Meal management, Clean surface and Climb stairs). In Figure 5.22, it can be observed that even in the case

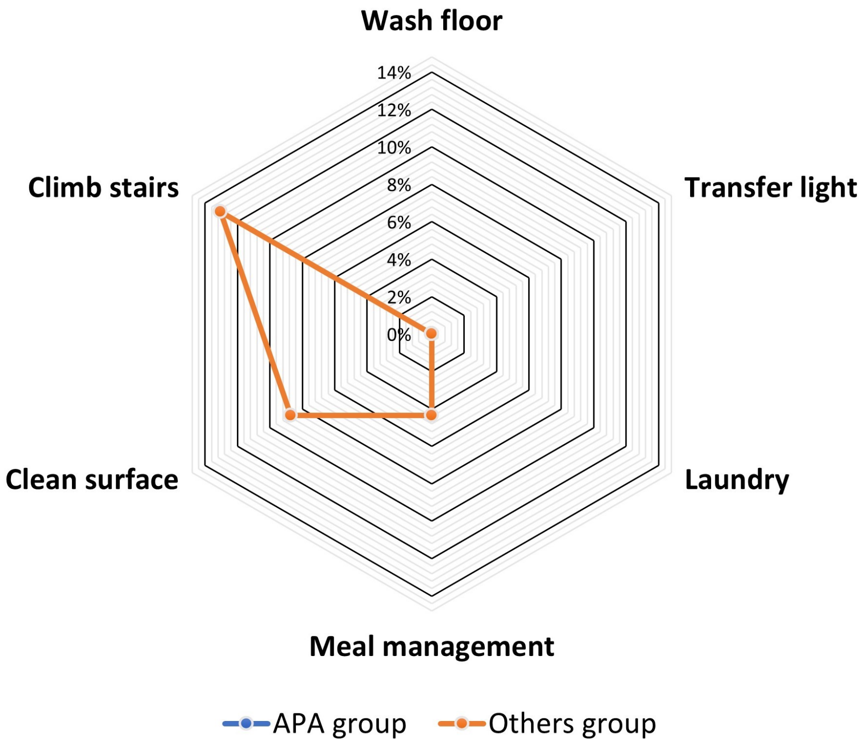

Figure 5.21: Radar plot summarizing the percentage of subjects for each activity that exhibited improvements in the RATIO parameter. This graph was created using Microsoft Excel®.

of the MPA parameter, there is a higher percentage of improved patients in a greater number of activities (Wash floor, Transfer light, Laundry, Clean Surface and Climb Stairs) for *APA* group, while the *Others* group exhibits a higher percentage in the case of Laundry and Meal Management task.
Lastly, similarly considering the APS parameter (Figure 5.23, a greater percentage of improved individuals is emphasized for every activity within the *APA* group.
However, the LDLJ parameter did not show any improvement for any subject in any group or activity. Nevertheless, it can be deduced that, based on the obtained results, it substantiates the assertion that a more comprehensive and functional treatment yields superior outcomes compared to a specific physical treatment.

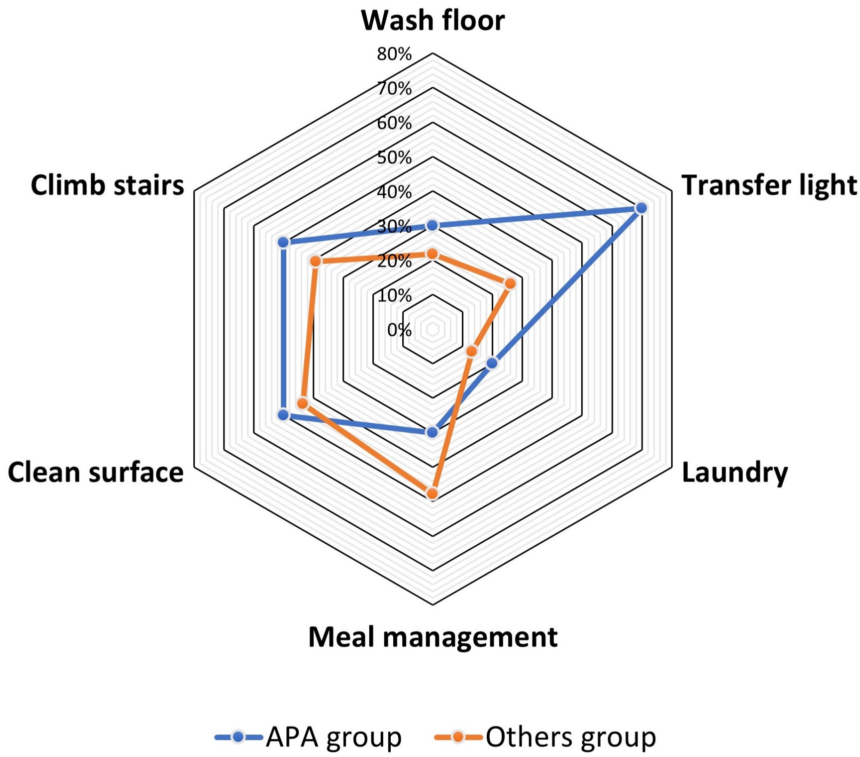

Figure 5.22: Radar plot summarizing the percentage of subjects for each activity that exhibited improvements in the MPA parameter. This graph was created using Microsoft Excel®.

Statistical Analysis

Afterward, the inter-session variations within the two studied groups underwent statistical analysis, and statistically significant differences were only found for one parameter (MPA) within a single activity (Transfer Light).

Finally, two additional parameters were considered to assess the contribution of both limbs in performing various tasks. Considering the activities performed, it was decided to treat all movement as functional for task performance. Specifically, in Figure 5.24, the comparison between pre- and post-assessment of both groups is represented for the Bilateral Magnitude parameter (the sum of contributions from both limbs) in various activities. Increasing values imply a greater involvement of the limbs, particularly an increase in the intensity of the activity.

Meanwhile, in Figure 5.25, the Magnitude ratio is depicted, expressing the

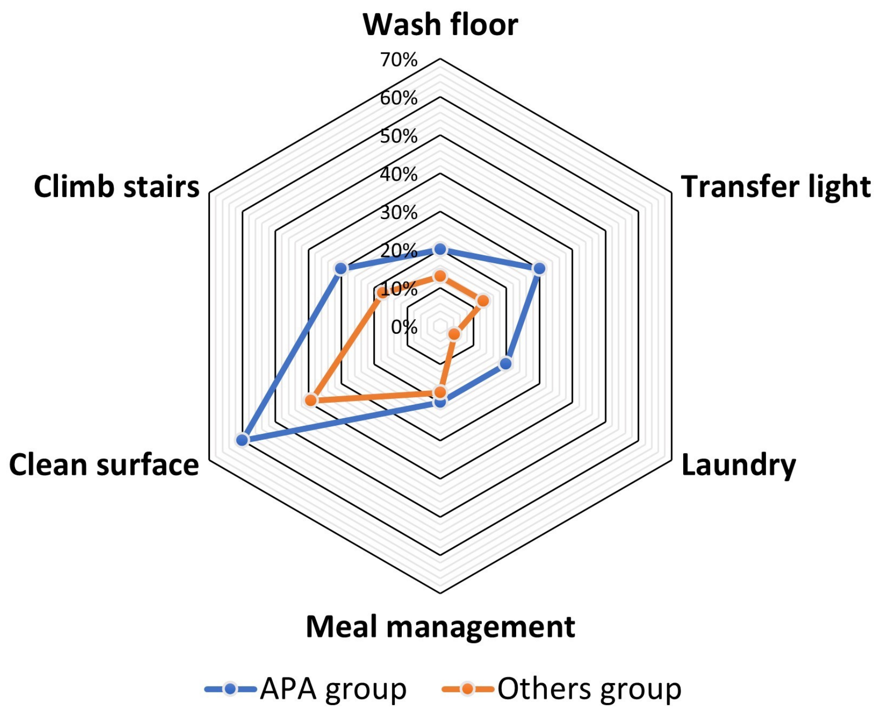

Figure 5.23: Radar plot summarizing the percentage of subjects for each activity that exhibited improvements in the APS parameter. This graph was created using Microsoft Excel®.

logarithmic ratio between the non-dominant and dominant limbs. Values close to 0 indicate symmetric limb involvement in movement, while results shifted towards positive or negative values imply a more asymmetric use of the non-dominant or dominant limb, respectively.

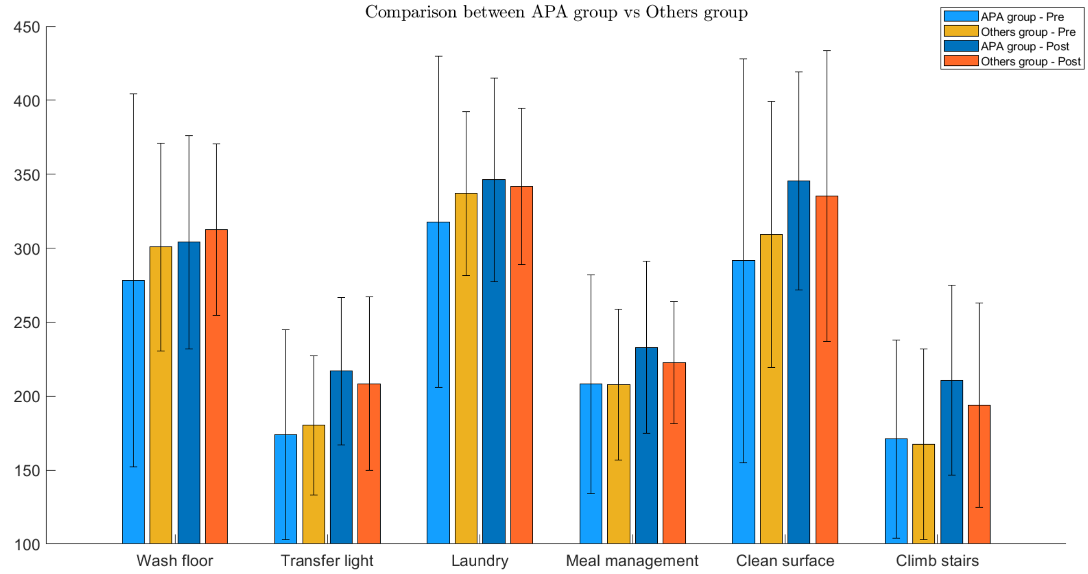

Figure 5.24: Comparison between APA and Others group for Bilateral Magnitude parameter.

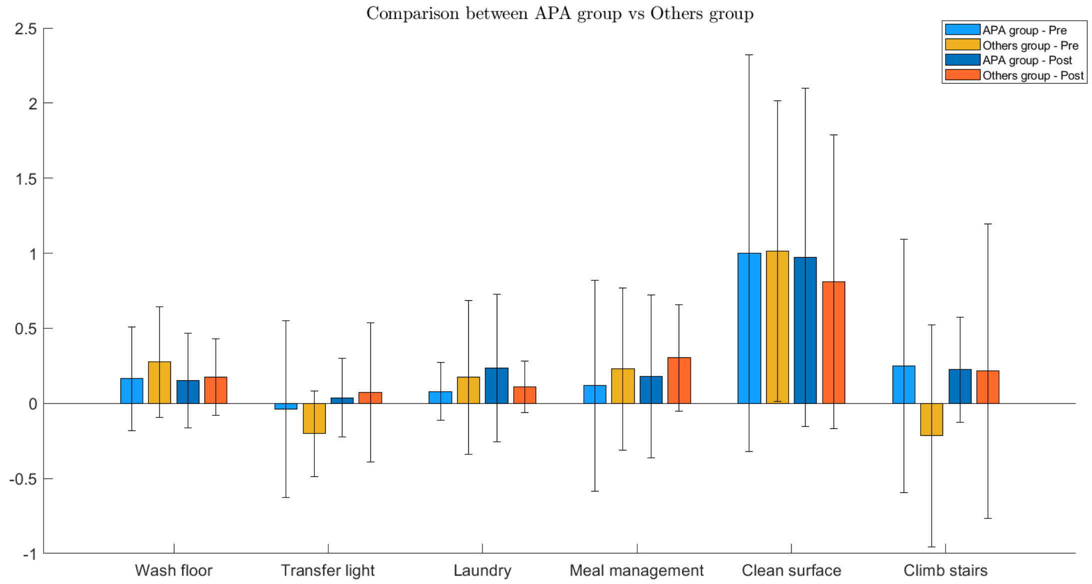

Figure 5.25: Comparison between *APA* and *Others* group for Magnitude Ratio parameter.

Chapter 6

Conclusion

The purpose of this thesis work was to explore the feasibility of a method, based on the use of wearable MIMUs, which could provide a quantitative assessment of upper limbs motor functions in patients with multiple sclerosis, during the execution of daily life tasks. By utilizing a set of extracted parameters, an effort was made to emphasize any potential changes, specifically improvements, that occurred as a result of a rehabilitation treatment, in upper limbs mobility, performing activity of daily life.
It is worth mentioning that physical, muscular training is effective and positively influences the execution of everyday tasks. In this study, four distinct rehabilitation groups were compared, consisting of multi-factorial specific rehabilitation training and three nonspecific groups that involved muscular strength training, cardio training, or a combination of both. The findings highlighted that the most functional and comprehensive treatment (APA group) resulted in improvements in a larger set of activities and parameters when compared to the other approaches.

The here presented protocol allows for the evaluation of changes in upper extremity motor functions, enabling an ecological evaluation of performance of patient, during activities of daily living. Furthermore, to date, and to the best of the author's knowledge, this the first time that such a comprehensive and complex protocol has been evaluated in individuals diagnosed with multiple sclerosis. The analyzed tasks did, in fact, involve gestures and movements of different levels of complexity and difficulty, all directed toward achieving the goal, occasionally requiring an asymmetrical use of the limbs, yet retaining functionality for the intended task.

This could be employed to overcome the constraints imposed by the use of clinical scales, which suffer from subjectivity in their administration, and standardized tests which are bound by the conventional laboratory setup, allowing only an assessment of the patient's capability.

Nevertheless, it is important to clarify that this work has some limitations. Within the existing literature, no prior research has tackled such a novel and intricate protocol in its activities. Consequently, there is a lack of reference values for the calculated parameters and a control group comprising healthy subjects for result comparison. This also explains the reason for a completely arbitrary choice of the improvement threshold, agreed upon with clinicians. In this regard, there is no evidence in works found in literature, to the best of author's knowledge, of values that define a minimum threshold of clinically detectable change considered as a reference point to determine whether a parameter has "improved" or not.
Another limitation arises from the unbalanced numbers of subjects belonging to the two groups considered for the final analysis (*APA* group vs. *Others* group). This disparity could, in part, account for some of the findings, including the observation that certain parameters (e.g., Peak Ratio) and activities exhibit greater improvement in the aspecific training group (*Others* group) when compared to the functional training group (*APA* group).

The first steps toward a more in-depth analysis may include balancing of the sample sizes of the two groups being studied and enlisting a cohort of healthy individuals for the purpose of comparing the extracted parameters and evaluating their reliability.

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