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Controlling cyclic motor tasks for movement rehabilitation after spinal cord injury

PhD Dissertation

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Abbreviations

CoP Center of Pressure. 39, 40, 55, 79, 83, 86

EMG Electromyogram. 12, 14, 29, 30, 33, 40, 69, 73, 77–79, 84, 87

ES Electrical Stimulation. 19

FES Functional Electrical Stimulation. 16, 17, 20, 84, 85

FES cycling Functional Electrical Stimulation assisted leg cycling. 17–20, 69, 84

FIM Functional Independence Measure. 20

GRF Ground Reaction Force. 24, 39, 40, 55, 61, 62, 79, 86

hybrid FES cycling hybrid Functional Electrical Stimulation cycling. 5, 20, 21, 24, 38, 82, 84, 86, 87

ICU Intensive Care Unit. 16

iSCI incomplete Spinal Cord Injury. 14, 19–21, 77, 84, 86, 87

MAS Modified Ashworth Scale. 20, 66, 80

MEPs Motor Evoked Potentials. 14

NNMF Non-Negative Matrix Factorization. 5, 14, 35, 84, 87

ROM Range of Motion. 12, 13

SampEn Sample Entropy. 41, 77–80

SCI Spinal Cord Injury. 17, 19, 66, 72

SCIM Spinal Cord Independence Measure. 20

2 Introduction

The natural human locomotion can not be discussed without the understanding of the cyclic human limb movements. In running, crawling, swimming, climbing and even in case of walking or hopping, the arms have also an important roles alongside the legs.

Even those, who have "just" partially malfunctioning limb or limbs, have many difficulties to carry out everyday tasks, including locomotion as well. Therefore the rehabilitation or the substitution of the limbs are in the focuses of the clinical rehabilitation and bionics studies.

An interdisciplinary field of clinical rehabilitation and bionics focuses on studying the motor control of cyclic upper and lower limb tasks, as well as their combinations, to gain insights for improving movement rehabilitation and the engineering design of neuromorphic control.

The human cyclic limb movements are also interesting from the biological point of view. The human gait, both walking and running are unique among the bipedal locomotions across all the living creatures. Even the apes have dynamically different fashion of walking from the humans [1]. This difference had a strong influence on anatomy and role of the the upper limbs as well. In case of the human arms, muscle architecture of the arms differ from the other primates [2]. These results suggest that there are human specific movement control strategies for the arms, including cyclic motions. Although, there are clear differences of the human anatomy from other creatures, the mechanism of how exactly this special system is controlled is still debated.

In recent decades, it has frequently been questioned to what extent human upper and lower limb movements are differentially or independently controlled by the central nervous system, in contrast to other vertebrates, which in many cases exhibit coupled or dependent motor control between limbs during locomotion.

In this thesis, this question is addressed from the perspectives of both motor control and the clinical implications for the medical rehabilitation of patients with incomplete spinal cord injury.

2.1 Arm Cycling

The arm cycling exercise, also known as hand cycling or cranking, generally refers to the various pedaling movement of the arms. In the literature, two special types are usually distinguished: synchronous and asynchronous cycling modes. Synchronous cycling means that the left and right arm cranks move in the same phase relative to each other. In case of asynchronous cycling, the left and the right cranks are out of phase with each other and there is 180° phase difference between them. In order to maintain asynchrony or synchrony, the cranks are usually mechanically coupled according to the task.

The arm cycling exercise is an important form of the cyclic human limb movements partly because it plays a significant role in the locomotion of wheelchair users. One limitation of a conventional non-motorized hand rim wheelchair is that manually propelling the wheels is physically demanding for the user when covering longer distances [3], [4].

A possible solution to the problem is to attach an extra wheel on the front of the wheelchair, which is propelled by arm cycling, via a bicycle chain. This locomotion has a better physiological efficiency compared to the simple wheelchair use [5].

Partly this limitation of the hand rim wheelchairs has directed attention to arm cycling, in order to optimize the efficiency of arm cycling driven locomotion. The importance of this form of movement is also highlighted by the fact that, the arm/hand cycling has been the part of the Paralympic games since 2007 [6]. Furthermore, it is an ideal form of combined arm movements for scientific research of the movement control of the upper body [7].

The following sections briefly summarize the knowledge gained over the past recent decades.

Bafghi et al. showed that the mechanical efficiency of pedaling at synchronous arm cycling is greater and has lower metabolic cost compared to asynchronous arm cycling. Furthermore, it has been shown that certain forearm and trunk muscles are more active during asynchronous spinning [8]. In line with this work is the study by Kraaijenbrink et al. [9], who also provided a detailed description of the magnitude of the 3D forces acting on the crank. This shows that asynchronous cycling has less efficiency but more gradual power delivery compared to synchronous cycling.

Faupin et al. described the kinematic characteristics of the upper limbs and shoulder during hand cycling. As part of this work, they described the Range of Motion (ROM) and the angular acceleration of the trunk, shoulders, elbows and wrists. They compared the angular parameter changes of the joints with each other [10]. Furthermore, they displayed the variation of the velocity of the propelled hand bike which has strong fluctuations. For the asynchronous cycling in sitting position, the joint angle changes were also displayed by Ceglia et al. [11].

Description of the Electromyogram (EMG) activity patterns of synchronous cycling movement is given by the work of the following authors: [12], [13], [14]. Quittmann et al. note that the several on-set times of muscle activity occurs earlier during high-intensity cycling compared to low intensity cycling [13].

Interestingly, Kraaijenbrink et al. note in their work that leg muscles are also activated when healthy people perform arm cycling [12]. In the later part of the thesis, this gains importance in the context of other parts of the literature and our work.

Arm cycling as a training for able-bodied persons

Although it is less researched but arm cycling can be interesting as a training task for sports for able-bodied persons as well [15]. Elmer and his colleagues demonstrated the possibilities of this on a special asynchronous hand ergometer [16], [17].

Beaven et al. showed that asynchronous eccentric arm cycling is less demanding (cardiovascular stress) at the same working load compared to concentric cycling, therefore this exercise is more effective to build muscle volume [18]. Hill et al. examined and compared the effect of asynchronous arm cycling and asynchronous arm cycling exercise on elderly people. They found similar effectiveness of the two types of the exercises on the balance and cardio-respiratory functions. Both exercise improved the measured functionalities. The authors also highlighted that the arm cranking improved the directional functional reaching movements of the participants as well [15].

Arm cycling as clinical training

Arm cycling in clinical practice is mostly associated with walking disability. Arm cycling aims to provide a cardiovascular training of the participants to substitute the positive effect and demand of the everyday walking. [19]. It is especially true, in case of SCI participants [20], [21].

A recent review highlights the potential application of arm cycling exercise as an early training exercise form for those patients who have to stay in bed for weeks. Beside the cardiovascular effects, it describes the danger of decreasing volume of muscle mass and also the importance of arm swinging during the walking [22].

Beside the aerobic training of the participants it is debated that arm cycling can be used as rehabilitation training to improve any impaired functionality of the wheelchaired people. In case of stroke, Diserens et al. found that the 3 weeks long intensive (5 sessions/week) stationary asynchronous arm cycling training increases the cycling muscle force and the range of motion (ROM) of the participants' joints [23]. In contrast, they found no significant changes in spasticity of the participants' limbs. It requires further investigation, whether the improved ROM and forces of cycling are the results of recovery of the motor control or the outcomes of the everyday physical training.

Kaupp et al. studied the effect of arm cycling on the walking ability and muslce spasticity of stroke survivors who have impairment in both their arms and legs. In line with the findings of Diserens et al., the participants' arm cycling performance improved and sporadic reductions in spasticity were recorded. Interestingly, they found that, the arm cycling significantly improves the walking ability of the participants [24].

Similarly to the treatment of stroke, the utilization of pure arm cycling exercise application in SCI treatment is questionable. Chiou et al. found no strong evidence to the application of arm cycling training as a rehabilitation technique [20].

Although a more recent research article suggests the application of arm cycling as a low-cost rehabilitation technique for improving trunk motor control in cases of chronic incomplete Spinal Cord Injury (iSCI). Both Motor Evoked Potentials (MEPs) and muscle activity of erector spinae muscle increased after arm cycling training. However, it must be noted that these parameters also increased in the healthy control group after similar arm cycling training [25].

Motor Control of Arm cycling

In section "Arm cycling", many biomechanical and performance related results are enumerated. Since most of these studies focused on the performance improvement of the arm/hand propelled cycling, the motor control phenomena and strategies of the cycling tasks were less highlighted. Kraaijenbrink et al. studied the effect of short term practicing of asynchronous or synchronous arm cycling on phase dependent biomechanical parameters. They found that participants rapidly learned the tasks, improving their force and power output during cycling, which implies an adaptation of motor control strategies [9]. Cartier et al. showed that long term (4 weeks) arm cycling training has also effect on the biomechanical parameters and improve the power and performance of the task [26]. Importantly, the authors showed that the muscle activity of the arms were also changed, not just in EMG amplitude but also in the co-activation of the muscles.

Muscle synergy analysis is a common method for investigating muscle co-working and control. This approach is based on matrix factorization, where the recorded muscle activity time series are organized into a matrix and decomposed into two smaller matrices: a weight matrix (W) and a coefficient (or control) matrix (H). Mathematically, muscle synergies are represented by these common control signals (H) and weights (W), where the product of these two matrices provides an estimation of the original muscle activity. The number of synergies refers to the number of control signals which are contained in the H matrix. There are several types of matrix factorization [27], but one of the most common algorithm for muscle synergy calculation is the NNMF [28], [29]. The detailed mathematical description of this method is written in Subsection 4.2.8.

Botzheim et al. found that both the asynchronous and synchronous arm cycling require four synergies for the sufficient reconstruction of the EMG channels accounting for 90% variance of the original data. They found that the two cycling modes have different synergies and the synchronous cycling is less complex than the asynchronous cycling, from the motor control point of view. Furthermore, they investigated that the sitting and supine position have different muscle synergies, which means that the central nervous system takes into account the direction of the gravitational field respect to the body position. In this paper it is also presented that the length of the arm crank does not affect significantly the muscle synergies. They also suppose some weak connection between the cycling and reaching movement tasks as well [30].

Cartier et al., in their previously mentioned study, also investigated electromyography profiles and the synergies of the arm muscles. Similar to Botzheim et al., they found four muscle synergies. The number of synergies did not change significantly after the 4 weeks training. They found strong variance of the posterior deltoid and triceps brachii muscle activity in the weights vectors of synergy 1. and 2. They expressed the idea, that the four synergy vectors (which form the W matrix) can be matched to the forward, backward, lifting and lowering actions of the control. Among these four the forward and backward directional movements are the most dominants [26].

Parallel with this results, Mravcsik et al. investigated that, the variance of the electromyograms of the arm muscles during asynchronous cycling increase quadratically with the amplitude of muscle activation. Form the aspect of neural control, interestingly, Mravcsik et al. found that, the volume of angular variance of the arms during the cycling did not change [31]. These results indicate that the central nervous system tries to keep the trajectory of the arms in the joint space configuration restricted. Meanwhile the compensation to the external mechanical changes are performed at the level of muscle activities.

Beside the muscle coordination, another interesting question is what kind of excitatory or inhibitory effect the central nervous system exerts on the descending neural pathways at the cortical, brainstem, and spinal cord levels during a movement task. In other words, how the information propagates through the central nervous system. This information can not be extracted from muscle synergy analysis.

Corticospinal excitability describes how much amplification or damping was occurred on the transmitted signals of the corticospinal neural pathway. This pathway is associated to the transmission of the cortical motorcontrol signals to the limbs and trunk. To quantify the excitability of this pathway, the motor evoked potentials (MEPs) are measured.

Forman et al. found that, the arm cycling exercise has higher corticospinal excitability at the dominant biceps brachii of the participants if they perform asynchronous arm cycling compared to intensity-matched tonic contraction [32]. This higher corticospinal excitability is evoked by supraspinal neural networks. Furthermore, the authors found not just the increased excitability, but also that, this excitability is phase dependent. It means that the amplitude of the motor evoked potentials (MEPs) are high at knee flexion and low at knee extension phases of the arm cycling. This means that, the arm cycling requires more cortical activity (primary motor cortex activity) and probably more complex regulation than the intensity-matched tonic contractions.

Since the corticospinal pathway has a decussation in the brainstem and axons in the spinal cord [33], therefore these anathomical regions could potentially influence the motor evoked potentials. One possible way, to distinctively examine the mechanism of the cortical (MEPs) and other activities (cervicomedulary motor evoked potentials or shortly CMEPs), is the additional application of transmastoid electrical stimulation (TMES) [34].

The arm cycling exercise is explicitly connected to the periodical motion, so the investigation of the cadence and power or resistance dependence of the corticospinal excitability are obvious questions. The corticospinal MEPs and CMEPs changes of the arm cycling regarding the cadence is discussed by Forman et.al. [35] while Spence et al. [36] focused on the observation of the power dependency of the corticospinal excitability. Spence et al. involved in the investigation the triceps brachiimuscle as well. They found different modulations of the MEPs and CMEPs for the two muscles.

The explanatory model of these results is still an open question but the investigation of the cortical level modulation of the corticospinal excitability has started [37].

2.2 Leg cycling

Leg cycling has a broad application in rehabilitation. I distinguish three subtype of leg cycling, these are the following: active, passive and Functional Electrical Stimulation (FES) assisted or evoked leg cycling.

Passive leg cycling

In case of passive leg cycling the pedaling movement of the participant is not performed by himself, but by a special ergometer. Usually the user is in sitting or supine position and his feets are attached to the pedals of a special ergometer and the ergometer rotates the pedals with the help of a built in motor, thus the person participates in a pedaling movement but does not actively propel the ergometer.

Phadke et al. reviewed several scientific databases and found a total of 11 relevant articles on passive pedaling tasks for spinal cord injured people. Based on the reviewed articles, they concluded that passive pedaling has beneficial effects on the cardiovascular, musculoskeletal and neurological systems and recommend the use of the method [38].

Besides the group of patients with spinal cord injuries, it naturally raised the question of whether this exercise could be beneficial for other patient groups as well.

Holms et al. evaluated the feasibility of using home passive pedaling ergometers in individuals with cerebral palsy. They found that home use of passive leg cycling improved the quality of life of the individuals examined [39]. While Lo et al. showed that passive leg cycling reduced spasticity in stroke patients [40]. It is worth mentioning that all three publication [38], [39], [40] highlight the beneficial effect of passive leg cycling on reducing spasticity.

However, there are also patient groups where passive leg cycling does not have relevant positive effect. For example, Sosnoff et al. examined the effect of passive cycling in multiple sclerosis but did not find significant improvement [41].

Takaoka et al. examined the use of passive leg cycling on Intensive Care Unit (ICU) patients in a review paper. In their work, they examined exercises performed in different positions, such as sitting, in-bed semirecumbent or supine cycling sessions. They were interested in whether passive leg cycling had any positive effects on the patients' health status, such as physical function or muscle strength. They concluded that passive cycling was safe but did not provide any significant benefits compared to the reference groups [42].

Active leg cycling

Active leg cycling involves the user cycling voluntarily with their own muscle force. It has been also investigated as a therapeutic method. Rahimibarghani et al., using a conventional stationary bike, showed that regular cycling improved walking ability in patients with multiple sclerosis [43]. Chieffo et al. found that leg cycling exercise combined with magnetic stimulation reduced spasticity in patients compared to reference measurements where magnetic stimulation was not applied [44].

FES assisted leg cycling

Functional Electrical Stimulation assisted leg cycling (FES cycling) refers to a special exercise type of cycling. In order to achieve leg cycling, external, specially timed electrical stimulation is applied to the muscle groups, such as (knee extensors or flexors) or neural pathways that can produce the target movements. So, external artificial control was applied on the participants' muscles but they actively use their FES generated own muscle strength to perform the task.

According to our best knowledge, this is the only broadly available technology which evokes active and not passive muscle forces to perform leg cycling exercise of those participants who lives with paraplegia or more extended and sever disability.

The relevance of this technology is also reflected in the large number of scientific articles published in this scientific topic. FES cycling as a therapy or training is used in the treatment of patients with stroke and spinal cord injury. Scientifically, the most common use of FES cycling is to train and maintain the cardiovascular system and muscle mass [45], [46], [47], [48], as well as to reduce muscle spasticity.

Lo et al. found that the FES cycling has additional benefits in reducing spasticity in case of stroke survivor participants with high muscle tone scores compared to passive leg cycling training [40]. In line with the previous results, Yeh et al. showed that the spasticity related hypertonia is decreased in stroke participants who received FES cycling training [49].

In case of Spinal Cord Injury (SCI), similar results are investigated by Alshram et al. In their review paper, they enumerate many articles which report improvements of spasticity of participants. They imply that, it is likely to improve the spasticity in various injury levels of SCI patients by FES cycling, although it has not been clearly proven that it is more effective than passive cycling [50].

The improvement of the cardiovascular functions, muscle mass and decreased spasticity by FES cycling, has huge impact on the quality of life of the paraplegic people. For those stroke survivors and incomplete spinal cord injured participants, who have some remained walking abilities, these positive effects can beneficially influence their gait rehabilitation as well.

In stroke survivors, Ambrosini et al showed that the FES cycling may improve patients walking ability [51]. To investigate whether these improvements are induced by the muscle volume and spasticity changes and/or by neural control recovery of the participants, Ambrosini et al. followed up the walking ability of subacute stroke injured patients by muscle synergy analysis who received FES cycling training. They found that the number of synergies did not changed but the weights and coefficients of muscle synergies are changed [52]. These results suggested that the motor control of the neural system has also changed during the FES cycling training. Also Ambrosini et al. have done a review of the impact of FES cycling training on the rehabilitation of walking ability of stroke injured patients. They found that, the FES cycling improves significantly the walking ability of the stroke injured participants but its clinically not relevant improvement [53].

Motor control of leg cycling

There are several models for describing lower limb movements, including pedaling movements. Ambrosini et al. and Torichelli et al., along with many other publications, presented a synergy-based description of pedaling movements [52], [54], [55], [56]. As Ambrosini et al. pointed out, the number of muscle synergies is 3 or 4 for pedaling movements, based on previous studies [52].

Both synergy-based models assume that one-one synergy is responsible for knee extension and flexion, while the remaining one or two synergies are responsible for describing the transient muscle coordination between the flexor and extensor states. The work of Ambrosini et al. was to monitor the FES cycling training effect to the walking rehabilitation of stroke survivor patients [52]. In a previous section, this work was already mentioned.

While Torrichelli et al. investigated how muscle synergies develop when able-body participants are asked to perform pedaling with a time-shifted phase of muscle activation instead of the their own natural cycling cadence and mode of muscle work. Their research results showed that the amplitude of muscle activity changes significantly in relation to the phase shift, but muscle synergies will show a similarity to the muscle synergies before the phase shift. They hypothesize that this result extends the idea that cyclic movements use synergy-based control in the case of short-term learning [54].

The use of neural oscillators to describe pedaling movements is an alternative to the synergy-based methodology, but with less emphasis [57]. The essence of this is that mutually inhibiting neuron groups can evoke periodic neural bursts. Members of these neuron groups can be associated with the extensor and flexor muscles. By connecting neural oscillators corresponding to the joints of the legs and parameterizing them appropriately, similar muscle activity and joint flexion changes can be modeled as during real cycling. This approach is a much abstract way of describing movement than synergies, but it is biologically inspired. An actively researched question in recent decades is the understanding of the existence and function of the central pattern generator pathways in the spinal cord. This modeling method provides a possible mathematical description of central pattern generators by modeling them with neural oscillators.

2.3 From cycling to walking rehabilitation

Restoration of lost walking abilities after spinal cord injury is one of the main goals of SCI treatments and research. According to the literature, approximately 2/3 of the patients with SCI had iSCI [58], [59]. In these cases, partial functionalities of the legs are observed, and the residual neural connections might be utilized for gait rehabilitation. The improvement of walking of iSCI persons would have a beneficial influence on the personal lives of the patients and social and economic systems.

Walking training for the patients requires sufficient force to stand up the body and keep it in motion. Furthermore, it demands realistic proprioception and balance. Many SCI persons lack these abilities. Thus, rehabilitation aims to strengthen and train the musculoskeletal system while protecting and enhancing the activity of the remaining neural pathways through neural plasticity. The earlier and the more efficiently we start to train the musculoskeletal system and stimulate the remaining neural pathways, the better recovery is expected. It is crucial to find the most effective rehabilitation protocols. The use of limb cycling training may be a good choice as it may improve walking functions [60].

In the gait rehabilitation of stroke survivors, the application of cyclic and pedaling movements was addressed to mimic similar movements to walking as soon as possible during the rehabilitation therapy [61].

There are other publications which also highlighted the analogy of walking and leg cycling [62] or "arm & leg" cycling [63]. These exercises can be performed in sitting or even in a supine position and in these cases, they do not require much muscle strength as the body weight does not have to be supported by the patients' muscles. So, the application of arm and leg cycling in the process of gait rehabilitation of iSCI patients seems to be a beneficial choice and it is essential for the spinal cord injured population to do such exercises to train walking functions.

Cycling exercises can be assisted or driven by electrical stimulation techniques as well. The application of Electrical Stimulation (ES) enhances the involvement of the remaining sensorimotor pathways of the participant during leg cycling.

For example, Piazza et al. showed that the transcutaneous ES of the legs and foot during leg cycling, significantly increased the soleus H-reflex of moderate iSCI patients which indicates that ES leg cycling facilitated spinal sensorimotor excitability [64].

Gomez et al. highlights the potential of sensorimotor pathway's electrical stimulation to gait rehabilitation of iSCI patients [65].

Another common application of electrical stimulation with leg cycling is Functional Elctrical Stimulation assisted leg cycling (FES cycling). While it is commonly used as a training method for complete SCI patients where the patients perform involuntary cycling [66], [67], [68], [69], it is less frequently studied in the case of iSCI patients.

Our recent study shows [J1] that even in the early subacute phase of iSCI, FES cycling can have a beneficial effect on improving the power output of the participants during cycling. Since walking also demands significant muscle strength and motor control, this technique appears to be a useful in gait rehabilitation as a supplementary training.

Yaşar et al. studied the effects of FES cycling in the case of chronic iSCI participants ($n = 10$). Each participant had 1 hour-long training session, 3 days per week for 12 weeks. They found that the Functional Independence Measure (FIM) significantly increased [70]. Gait parameters such as gait velocity, cadence, and step length increased but these changes were not significant [71].

The study of Duffell further developed this method with the modulation of the stimulation pattern according to the crank torque, during pedaling. This system was extended with biofeedback based virtual reality [72]. Their study involved 11 sub-acute iSCI participants. The training of all participants consisted of $3 \times (20 - 45)$ minutes of FES cycling training sessions per week. The training lasted 4 weeks for each participant. The participants also had sporadic improvement according to the Modified Ashworth Scale (MAS) and a slight improvement in the mobility score of Spinal Cord Independence Measure (SCIM).

If FES cycling is supplemented by simultaneous voluntary arm cycling, it may be a more efficient form of training than conventional FES cycling performed only with the legs. This combined exercise of the arms and legs is called hybrid FES cycling.

The paper of Zhou et al. showed that hybrid FES cycling improves more the walking abilities of iSCI participants compared to simple FES cycling [60]. In their study, they involved seven ($n = 7$) iSCI participants in the hybrid FES cycling and eight ($n = 8$) iSCI participants in the FES cycling. All participants received intensive training: 5×1 hour training sessions per week for 12 weeks. Their results proved that a significantly better improvement in walking ability can be achieved with hybrid FES cycling compared to FES cycling. The underlying reason behind the beneficial impact of upper limb cycling on gait rehabilitation remains unclear, but the authors hypothesize that rhythmic movement of the upper and lower limbs shares common neural pathways, and their activation may induce favorable changes in walking patterns.

The intensity of the cycling training differs when the above-mentioned studies are considered. When planning training protocols for cycling, the intensity is an important question. Should we need high-intensity training (frequent and long training sessions) to get walking improvements as a result of arm and leg cycling training?

2.4 Common motor control of the arms and legs during cycling

Zehr et al. [73] investigated the effect of leg cycling on the arm H-reflex and on the activation of corticospinal neural projections to the arm. They found that leg cycling suppressed the H-reflex of the lower arm muscle, the flexor carpi radialis, even when the arm was relaxed or isometrically contracted during foot pedaling. Furthermore, this suppression is not phase-dependent, i.e. it does not depend on the current position of the pedaling legs. Another interesting relationship is that the activation of the corticospinal tract projection to the lower arm is enhanced when the legs perform pedaling movements. This is true both during relaxed and isometric contraction of the arms. Based on their results, the Zehr et al. concluded that the regulation of corticospinal excitability increased by pedaling may have a subcortical cause.

Sakamoto et al. found that during simultaneous arm and leg cycling, the changes of the arm cycling speed had no effect on the pedaling speed of the legs, but if the pedaling of the legs was slowed or accelerated, the pedaling speed of the arms also changed [74]. Also in the same year, Sakamoto et al. investigated how arm and leg cycling in a sitting or standing position modulates the cutaneous reflexes of the arms and legs in a phase-dependent manner. They found that the magnitude of the reflexes in both arms and legs was modulated by the position of the pedals. Furthermore, the magnitude of the reflexes correlated with the background EMG amplitude measured during static performance, while this correlation disappeared during arm and leg cycling. In addition, there was no difference in the reflex changes occurring between the lower and upper limbs and the amplitude of the ipsilateral limb reflexes between in-phase and anti-phase arm and leg cycling [75].

Zhou et al. [76] demonstrated in a complex study that the motor activation potential (MAP) evoked by transcranial magnetic stimulation of the corticospinal tract, in the vastus lateralis leg muscle is significantly greater when the participant does arm cycling with resting legs than when all four limbs are relaxed in a static position. In contrast, for the same exercise comparison, no significant difference was found in case of participants with iSCI who had very limited walking ability (less than 0.31 m/s). From this results, they concluded that arm cycling movements modulate corticospinal motor control of the lower extremities and this control is impaired in incomplete spinal cord injured participants.

In the second part of the same publication, the authors investigated the effects of 12 weeks of FES-assisted simultaneous arm and leg cycling training (1 hour/day, 5 days/week). They found that patients had significantly higher motor activation potentials (MAPs) through the corticospinal tract in the vastus lateralis leg muscle after training than before. So, hybrid FES cycling has a beneficial effect on the functional recovery of corticospinal neural pathway.

Klarnen et al. investigated whether cycling with arms and legs affects stretch and cutaneous reflexes in individuals with stroke. They found that pedaling movements with all four limbs modulated the intensity of the reflexes both from the legs towards the arms and from the arms towards the legs [77].

Balter et al. investigated that the cutaneous reflex evoked by the tibialis anterior, when electrical stimulation of the superficial peroneal nerve at the ankle occurs, then the modulation of this reflex is also influenced by the pedaling movement of the arms, but this effect is regulated (enhanced or suppressed) by the knee extension or flexion state of the legs. This means that, the arms and legs participate in the modulation of the reflex simultaneously and this modulation is phase dependent [78].

Brass et al. [79] found that the amplitude of the left soleus H-reflex evoked at the tibial nerve depends on whether the arms are pedaling or statically stimulated, and whether the cervicospinal tracts are stimulated by transcutaneous spinal cord stimulation (tSCS). This means that external surface electrical stimulation at the C3, C6 level of the spinal cord also modulates the amplitude of the H-reflex. Brass et al. also observed that this modulation is similar to the effect exerted by pedaling arms, as both methods suppress the soleus H-reflex. Interestingly, the researchers also applied tSCS at the beginning of the lumbar and the end of the thoracic spine (T11, L1), but this did not produce a significant effect.

These studies highlight strong connections between upper and lower limb cycling at the level of reflex pathways, as well as the descending (corticospinal, cervicospinal) and ascending (cervicospinal) pathways of the spinal cord. However, to the best of our knowledge, no study has yet investigated this question at the organizational level of muscle synergies. Namely, it remains unclear whether the upper and lower limbs influence each other at the level of neuromuscular coordination.

3 Objectives

Question 1,

Is there a detectable neural interlimb coordination between the arms and legs during simultaneous arm cranking and leg cycling motor tasks?

To investigate this question, I applied two different approaches. In the first, I examined whether the neural interlimb coordination between the arms and legs could be replaced by artificial control. In the second approach, I examined how the synergistic coordination of the arm muscles during arm cycling depends on whether the task is performed without leg cycling or simultaneously with leg cycling.

Objective 1a,

- Collect and process Electromyographic (EMG) and kinematic data from healthy individuals performing arm and leg cycling simultaneously.
- Implement a regression-based estimation method using neural network training to predict the EMG activity of selected knee flexor and extensor muscles from EMG signals recorded from the arm muscles.
- Apply threshold-based methods to compute unipolar control signals suitable for FES cycling.

Objective 1b,

- Collect and process Electromyographic (EMG) and kinematic data from healthy individuals performing cycling tasks under two conditions: (1) using the arms only, and (2) using both the arms and legs simultaneously.
- Extract muscle synergies by applying non-negative matrix factorization (NNMF) on the electromyographic (EMG) data.
- Structure the extracted synergy weights and activation coefficients (control signals) and perform quantitative comparisons to evaluate differences or similarities across conditions.

Question 2,

How do the ground reaction forces during walking change in case of incomplete spinal cord injured participants who, in addition to the conventional rehabilitation therapies, participated in simultaneous voluntary arm cranking and functional electrical stimulation-assisted leg cycling (hybrid FES cycling) training?

Objective 2,

- Perform gait assessments on participants with incomplete spinal cord injury at three time points: prior to, midway through, and following the hybrid FES cycling training program.
- Collect Ground Reaction Force (GRF) data and their derived measures, center of pressure (CoP) trajectories, from individuals with incomplete spinal cord injury.
- Acquire gait specific reference kinematic and EMG measurements from individuals with incomplete spinal cord injury.
- Extract and compute relevant biomechanical parameters from the force plate measurements and corresponding reference data.
- Quantitatively compare the extracted biomechanical and reference parameters before and after the hybrid FES cycling training.

4 Methods

In the following parts, I am going to display and illustrate the applied methods and calculations used to address the Objectives. These are the following topics: 1. neural network-based prediction of lower limb muscle activities from arm muscle activities of arm cycling; 2. synergy calculation on upper limb muscles during only arm cycling and simultaneous arm and leg cycling; 3. gait assessments and analysis of iSCI patients who received hybrid FES cycling.

The structure of this chapter follows the same order as the listed topics. Each topic is discussed in a dedicated sub-chapter, building up systematically from participant selection and data collection technique to the computational methods and analytical procedures.

4.1 Arm & leg cycling - neural network

4.1.1 Participants

In this exploratory study, four adults (24-30 years old, 2 women, 2 men) were enrolled. Before the measurements, participants gave their written informed consent to take part in this study, which was approved by The Ethical Committee of the National Institute of Medical Rehabilitation, Budapest.

4.1.2 Instrumentation

I measured simultaneous arm and leg cycling exercises with MotoMed Viva2 arm & leg cycle ergometers (Reck GMBH, Betzenweiler, Germany).

I used synchronized wireless EMG and 3D motion analyzer systems for the measurements. The specifications of the EMG, kinematic recording devices are the following:

Cometa MiniWave (Cometa, Italy, Bareggio) wireless EMG system was used for the muscle activity recordings, using a sampling frequency of 1200 Hz. Electrode placement and the skin surface preparation were carried out following SENIAM recommendations [80]. We used Kendall H124SG (30 - 24 mm)-type foam, hydrogel electrodes.

To capture the kinematics of the movements, an infrared (IR) six-camera motion analyzer system (Vicon Nexus, England, Oxford) was used. IR reflective markers were placed on relevant anatomical points of the body regarding the tasks. The 3D coordinates of these markers were recorded with a sampling frequency of 120 Hz.

4.1.3 Recorded Muscles

The list of the recorded muscles is the following:

right gluteus maximus (GM), right rectus femoris (RF), right vastus medialis (VM), right vastus lateralis (VL), right biceps femoris (BF), right tibialis anterior (TA), right gastrocnemius medialis (GM), right gastrocnemius lateralis (GL), right anterior deltoid (AD), right posterior deltoid (PD), right biceps brachii (BB), right triceps brachii (TB), right flexor carpi radialis (FCR), and right (BR)

4.1.4 Used kinematic templates

The Vicon motion analyser camera system records the human movements by specific, predefined points of the body. These points are defined by templates.

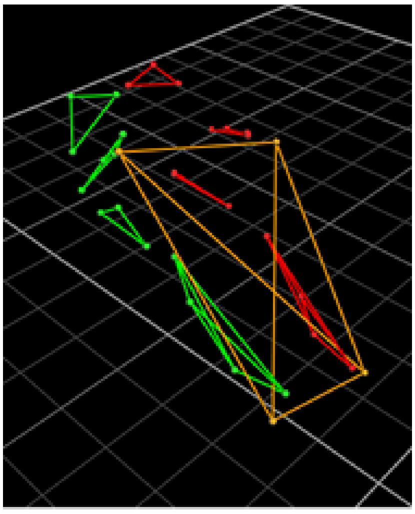

Figure 4.1: The 3D model off the human body and its motion during the arm & leg cycling exercise.

The arm & leg cycling template is custom specific template which was created by our research group. It was designed to record the four limb motion of the participant during arm & leg cycling exercise. The model is symmetrical, which means that the template has the same organization and same number of marker point on both sides of the participant. See Figure 1. The red and green colors represent the markers of left and the right sides of the participants, meanwhile the orange color denotes the Motomed Viva2 device, more specifically the endings of the upper and lower crank' levers. For each side the model has four body segments plus the orange structure of the ergometer. The segments denotes specific body segments. These segments are the following: segment 1. – lower arm and hand, segment 2. – upper arm and shoulder, segment 3. shank and foot. segment 4. – thigh and hip.

4.1.5 Exercise and Measurement protocol

The participant was seated comfortably on a backrest chair at the front of the Motomed Viva2 hybrid arm and leg cycle ergometer. The distance between the chair and the ergometer was set in such a manner that when the pedal of the ergometer's lower crank was at the most distant position with respect to the participant, the external angle of the knee (the angle of the shank with respect to the thigh) was approximately 10°–15°. This corresponded approximately to the most extended knee position. The ergometer upper pedals' spindle was set at the level of chest center.

The participant was asked to perform arm and leg cycling in asynchronous mode (with the ipsilateral lower crank and upper crank angles out-of-phase 180°) and in synchronous mode (ipsilateral crank angles in-phase). Cycling in each condition lasted in the range of 30–60 s. Between conditions, the participants had a short resting time, with a similar amount of time provided to each participant. At the beginning of the measurements, we independently measured the arms and the legs cycling while the participants had to keep a pedaling speed of 60 rpm (revolutions per minute). To give the participants feedback about the proper cycling speed, audio signals were provided with the required frequency in every case. After that, the user had to cycle synchronously with his upper and lower limbs at the same speed of 60 rpm. When it was finished, the protocol continued with similar exercises, where the only difference was that the task had to be performed asynchronously.

4.1.6 Eletromyogram signal processing

The EMG signals were filtered by a fourth-order Butterworth filter (bandpass 20–500 Hz) and a notch filter (50 Hz) and then smoothed by root mean square (RMS) with a window length of 80 samples (66.6 ms). The selection of the Butterworth method, among the several others, was based on the consideration that the Butterworth filtering utilizes only the past values of the records. Therefore, it can also be suitable for future real time applications. In the last preprocessing step, we concatenated 30-s EMG records from each participant for synchronous and asynchronous cycling separately. Thus, we had two time series, each with a length of 4×30 s. Then, these time series were amplitude normalized to the range [0–1]. For normalization, we applied the rescale() MATLAB function. This was beneficial because the activation functions of the neural network have a similar range. This method restricts the neural network weights, which helps the learning method. For the previously introduced preprocessing task, the MATLAB2020b software environment was applied.

Although we measured 14 muscles, eight of them were used for the neural network training. We used all six EMG channels of the right arm as an input for the neural network, and two muscles, the right rectus femoris (R. Rect. Fem.) and right biceps femoris (R. Bic. Fem.), were used as targets for the output prediction. The reduction of the lower limb channels is based on the following consideration. The aim was to use only the EMG signals of the arm muscles for the prediction of lower limb muscle activities. Hence, we cannot apply the lower limb EMG as a direct input of the transformation.

The construction of a transformation with more output is theoretically possible, but the increasing complexity of the task demands a rapidly increasing training dataset (in both the number of participants and the record length [81]). Therefore, in this exploratory study, we attempted to predict only two EMG channels for the FES control signal calculation. The FES cycling movement task can be carried out with flexor-extensor muscle group pairs

(Quadriceps and Hamstrings). For this reason, we selected one muscle from each muscle group for the prediction. The illustration of the mapping is found in Figure 4.2.

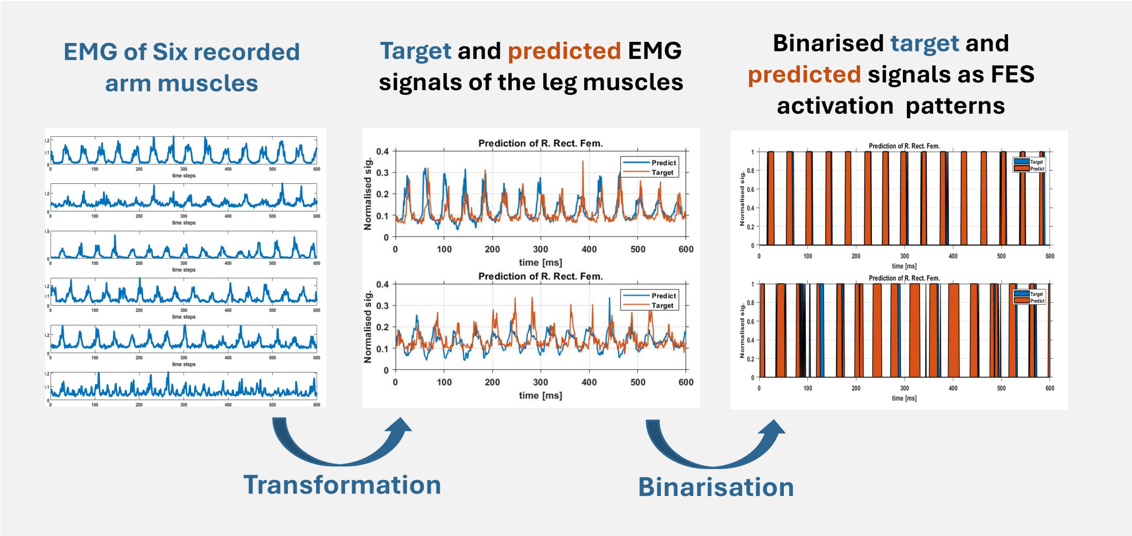

Figure 4.2: Calculation steps for FES onset-offset timings. The neural network predicts knee flexor and extensor EMG activity from EMG signals of six arm muscles, which are then binarized into FES activation patterns.

We also reduced the record size by under sampling the filtered and smoothed time series. During the under sampling, we selected every 30^{th} sample for the network training, which was necessary to perform reasonable computation times in our resources. In addition to the computational speed increase, it could also be beneficial for the learning capability of the system. This method highlights the evolution of the main features over time.

4.1.7 Kinematic signal processing

The vertical coordinates of the marker on the right handle of the ergometer were used for cycle segmentation. One cycle was defined as an interval between two consecutive 12 o'clock positions of the right crank. These positions were applied for both arms, for the right and left too.

4.1.8 Neural network model

For the arm & leg cycling – neural network training tasks, we used nonlinear auto-regressive exogenous (NARX) neural networks. This neural network is a subtype of the recurrent neural networks. This means that the output of the network is fed back to the system as an input. Another important expression is "exogen," which refers to the type of inputs. The terminology is used because this network — in every step — has one or more external inputs beside the feedback. Our model uses the actual and the last 14 recorded values of the six arm muscle activities (EMG channels) for external input. For internal input, it uses the feedback of the actual and the last 24 recorded output values for the two output channels.

These output values represent the predictions of the R. Rect. Fem. and R. Bic. Fem. EMG signals. The internal and external input order selections are based on a mathematical heuristic. This means that, for providing the value of the predicted signal at a given time, the system takes into account the approximate number of samples obtained during the last half cycle preceding the actual sample. One cycle is defined by 360 of rotation of the crank. Higher-order models were excluded to limit the complexity of the neural network and to avoid long computational latency, while empirical fine-tuning of the network showed that lower orders caused worse prediction outcomes.

The description of the system is mathematically formalized in Equation 4.1.8, where $u(t)$ and $y(t)$ represent the input and output of the network at time t. D_u and D_y are the input and output orders, respectively, and the function f is a nonlinear function [82].

$$y(t) = f[u(t - D_u), \ldots, u(t-1), u(t), y(t - D_y), \ldots, y(t-1)] \tag{4.1}$$

For the task, we used three hidden layers with the following number of neurons from the first to the third layer: 10, 7, and 5. In the hidden layers, we applied sigmoid activation functions. A hidden layer is fully connected with the previous and the next layers. The output layer contains two neurons with an identity transfer function where the predicted outputs are fed back to the first hidden layer. The neural network is illustrated in Figure 4.3. For the implementation of the neural network, the MATLAB2020b software environment was applied.

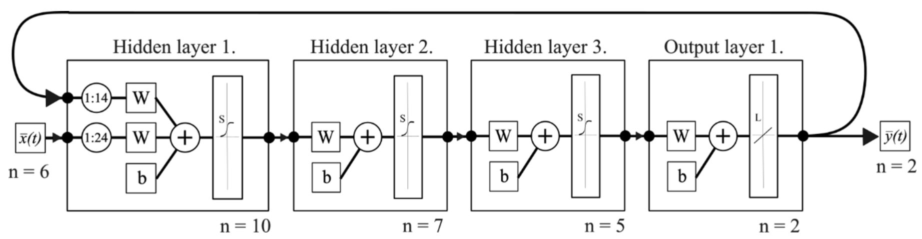

Figure 4.3: The applied neural network for the task. The neural network has three hidden layer with n = 10, 7, 5 number of neuron and one output layer with two neurons. The layers were fully connected. The W letters denote the weight matrices and the b letters are the bias values. The direction of the information flow is denoted by the arrows.

4.1.9 Training of the network model

For neural network learning, we only used the EMG records of synchronous and asynchronous cycling exercises.Although, it is a reasonable idea to use the kinematic data as well, since it contains inherent information of the actual phase of the cycles, in this work we focused on the EMG data, since our goal was to use more direct information of the motor control to investigate common

For each condition, equal size recordings of four participants were concatenated, and using these time series, we trained the neural network for each condition separately. The network training used the Levenberg-Marquard built-in method for optimization for 80 epochs. The training error was measured by a mean square error (MSE) calculation. For the program testing, 8×10 cross-validation was applied. This means that the data sequences that contain the records of four participants are divided into eight subgroups. From these eight subgroups, we constructed eight different training and testing groups in the following way: the test set contains only one subgroup, while the training set includes all the remaining seven subgroups.

With this kind of arrangement, eight different training and test sets can be constructed. After the construction of these learning sets, the learning algorithm was applied 10 times. In each round, the program calculated its prediction accuracy for the thresholded signals. Because learning is not a deterministic process, it produces different outcomes for 10 different attempts, which is why we can obtain 8×10 quantitative results at the end. Finally, these results were aggregated by the arithmetic mean for each quantity and learning set. "We evaluated the generalization performance of the learning process with this method.

4.1.10 Thresholding for binary control signal construction

In this section, I show a simple construction of binary control signals derived from the predicted EMG of the target muscles. This method is the following: We calculated the normalized histogram of the selected EMG signal. For the normalization, we applied the total number of points in the EMG time series. The histogram is constructed with 200 bins. This means that we divided the overall scale of the signal to its 0.05% long intervals, which provided a good resolution on the signal, according to our empirical experiences. Then, we determined the threshold as a value that can divide the samples of the signal into a predefined ratio among the area of the upper bounded values and the total area. This ratio was approximately 2/3.

To measure the accuracy of the binary activation patterns (predicted and target patterns), we calculated the average total phase difference in one 360°circle. We used the assumption that the crank movement in one circle had constant angular velocity in one period. It is formalized mathematically in the following way:

$$\text{Angle accuracy} = 360 - \frac{1}{N_{\text{cycle}}} \sum_{i=1}^{n} |\vec{y}_i - \vec{p}_i| \, \alpha_{\text{res}}, \tag{4.2}$$

$$\text{where } \vec{y}, \vec{p} \in \{0,1\}^n \text{ and } \alpha_{\text{res}} \in \mathbb{R}$$

where $\vec{y}$ is the thresholded target signal, $\vec{p}$ is the thresholded prediction, n is the length of the two time series, i is the actual coordinate, N_{cycle} is the number of cycles and α_{res} is the angular resolution of the method. This value can be obtained as 360°/(number of EMG points used in one circle).

4.2 Arm & leg cycling – muscle synergy analysis

4.2.1 Participants

Ten healthy women (age 22.2 ± 3.7 years, height 1.64 ± 0.06 m, weight 59.6 ± 5.3 kg) without any known orthopedic or neurological problems participated in this study and provided informed consent. All of them were right-handed and right-footed. The experiments were conducted in accordance with the Declaration of Helsinki. The Ethics Committee of the National Medical Institute for Rehabilitation, Budapest, Hungary (presently Semmelweis University, Rehabilitation Clinic) provided approval for this research (protocol number: 20/2017/10/04) and all participants provided informed consent.

4.2.2 Instrumentation

Our research group used the same instrumentation as it was used in the neural network project. See in subsection 4.1.2.

4.2.3 Recorded Muscles

The list of the recorded muscles is the following:

left and right anterior deltoid (AD), left and right posterior deltoid (PD), left and right biceps brachii (BB), left and right triceps brachii (TB), left and right extensor carpi radialis (ECR), left and right flexor carpi radialis (FCR)

4.2.4 Used kinematic templates

Our research group used the same kinematic template as it was used in the neural network project. See in subsection 4.1.4.

4.2.5 Exercise and Measurement protocol

Each participant performed several cycling tasks on a MotoMed Viva2 (Reck GMBH, Betzenweiler, Germany) arm and leg cycle ergometer (Figure. 4.4). Each participant cycled with her arms against 2 different levels of arm crank resistance: low (9W power output) and moderate (19W power output). The motor of the lower cranks was switched off, and so we used the passive resistance of the lower crank. Moreover, cycling was performed in 2 different modes: cycling only with the arms ("only-arm" mode) and cycling with both arms and legs ("arm & leg" mode). Therefore, each participant performed 4 different combinations of cycling: 2 cycling modes with 2 levels of resistance.

In the arm & leg cycling mode, each participant was asked to cycle with both arms and legs simultaneously, with the right arm cycling at the same cycling frequency and same phase of the left leg and to try to keep it synchronized during performing the armleg cycling task. For both the arm and the leg, the left crank and the right crank were mechanically

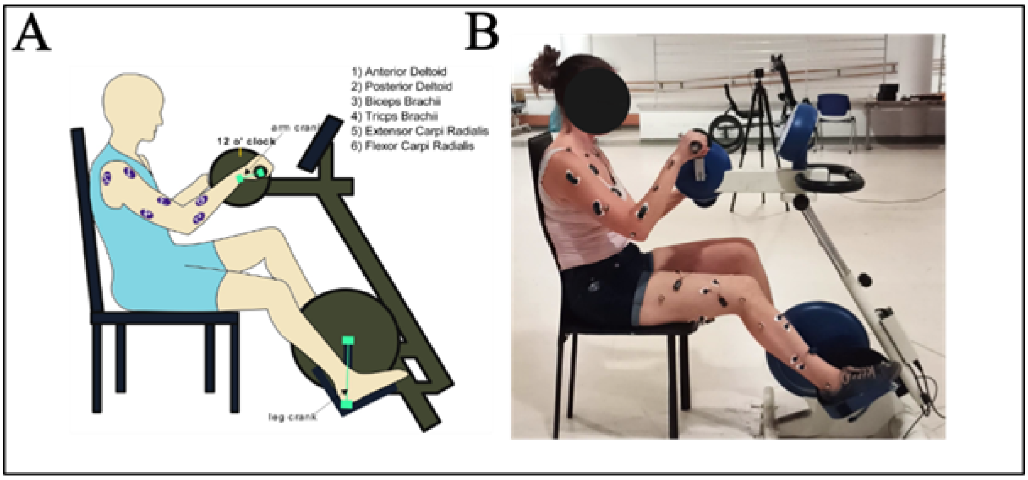

Figure 4.4: The schematic figure of the arm & leg cycling exercises. During the exercises six arm muscles were measured by electromyography. These muscles are highlighted in Panel A. The muscle activity of the left and right sides were recorded independently. Panel B: A real example of a participant sitting in front of the ergometer while performing an arm and leg cycling task.

coupled and were set 180 degrees out of phase, but the arm cranks were not coupled with the leg cranks. The arm cranks' spindle was set at the chest center level. Each participant was positioned as far as possible from the ergometer, guaranteeing that they were able to stretch their legs almost fully, similar to our previous work [J2].

For each combination of cycling, surface signals were recorded for each side independently. First each participant performed each combination of cycling recorded from one side, and after a break, each combination was repeated, while data were recorded from the other side.

Electrode placement and skin surface preparation were carried out following SENIAM recommendations [80].

At the beginning of the assessment, the order of the only-arm and arm & leg cycling modes and the order of the measured sides (left and right) were randomly selected.

Moreover, the order of the resistance levels was as follows: low, moderate. This restriction was applied because, in arm & leg cycling, it was rather challenging for participants to adapt to different randomly selected resistance levels. In total, 8 setups were produced: 4 combinations from 2 sides.

In each setup the participants had opportunity to try out the cycling modes before each recording. They got the instruction to start to execute the actual cycling task, and we gave them the opportunity to practice several dozens of cycles before we started the recording. A predefined time or cycle limit was not set; the recording started when the participant confirmed that a stable rhythm was achieved and the examiner also confirmed it by visual observation.

The cycling frequency was predefined as 60 revolutions per minute (rpm). A 60-rpm audio feedback was provided by a metronome, which helped the participants to maintain the target cadence. For each setup, the participants cycled in total for three minutes (recorded in two or three intervals to reduce the possible measurement errors). Short breaks (60 s) were taken between these 3-minute cycling trials to avoid muscle fatigue. A longer break (20 min) was also taken when the EMG recorders were placed from one side to the other (with new gel electrodes).

4.2.6 Kinematic signal processing

The vertical coordinates of the marker on the right handle of the ergometer were used for cycle segmentation. One cycle was defined as an interval between two consecutive 12 o'clock positions of the right crank. To determine these events, the findpeaks() MATLAB The MathWorks, Natick, MA, USA). function was applied to the time series. These positions were then used to segment the movement of both the right and left arms.

4.2.7 Electromyogram signal processing

All recorded EMG signals from each setup were band-pass filtered (25-300 Hz, 3^{rd} order Butterworth). We then applied a 2^{nd} order IIR Notch filter at 50 Hz on these filtered data to remove power-line noise. Then, the mean signal value was subtracted from the EMG signals. Finally, the EMG signals were rectified and low-pass filtered at 5 Hz (3^{rd}-order Butterworth) to obtain the EMG envelopes [30], [83]. EMG envelopes were then time-normalized by resampling the data at each percentage of the cycle (101 points: 0-100).

EMG envelopes were analyzed on a cycle-by-cycle basis to identify outliers that needed to be removed. Outliers were identified as cases where the amplitude of the EMG signal was either very small or very large, or the EMG shape was very different than the mean of the other cycles. To decide whether a cycle was an outlier or not, we started by calculating the mean cycle and defined two thresholds. First, we assessed if the mean cycle and each individual cycle was statistically correlated (correlation coefficient was higher than 0.3, $p > 0.05$, based on Student table).

Second, we assessed if the range of the amplitude (difference between maximum and minimum) of each cycle was within the range 50%-150% of the mean cycle. Another criterion was also added, the retained data had to be at least 40000 samples (for one setup, approximately 33 cycles were taken totally) long. This criterion was used to retain cycles, that were less spoiled by artifacts but still reached a statistically interpretable cycle count. If this criterion was not met, the threshold of amplitude range was increased by 5%-5%. When all criteria were met, the cycle was saved for further analysis. Otherwise, it would be disregarded. At the end, EMG envelopes corresponding to the selected cycles were concatenated for each subject, cycling mode and resistance.

On average, more than 60 cycles were retained for further analysis (across participants) for each setup. This number of cycles is considered adequate, based on the recommendation of Turpin et al. [84].

For each participant (10), the maximum of EMG envelopes of all cycles for each setup

(8) and muscle (6) were found. Then for each muscle, the largest one of these 8 EMG maximum values was used to normalize all EMG time series for that muscle.

4.2.8 Synergy calculations

For each setup, concatenated EMG envelopes were combined into $m \times t$ (EMG_o) matrices, where m is the number of muscles (six, in this case) and t is the time base (number of concatenated cycles $\times 100$). Muscle synergies components were calculated applying a non-negative matrix factorization (NNMF) method [28] with MATLAB (The MathWorks, Natick, MA, USA). Mathematically, the algorithm is described as

$$EMG_o = WH + e = EMG_r + e \tag{4.3}$$

Where W is the $m \times n$ matrix specifying the weight of each muscle in each synergy, n is the number of muscle synergies, and H is the $n \times t$ matrix specifying the time-varying activation coefficients representing the recruitment of each synergy throughout the cycle. EMG_r is the matrix $m \times t$ resulting from the multiplication of W and H (reconstructed EMG envelopes), and e is the residual error. See Figure 4.5. We considered 3 and 4 synergies ($n = 3, 4$) as input to the NNMF algorithm. For each n, NNMF was run 40 times, and the repetition with the smallest reconstruction error was selected. The minimum number of synergies required to guarantee an adequate reconstruction of the EMG signals was determined as the minimum number necessary to obtain a variability accounted for (VAF) greater than or equal to 90%, as done in other studies [30], [56], [62].

4.2.9 Synergy vector ordering

We applied max-normalization on the W synergy weight matrix [85]. We normalized each column of the W synergy matrix by the maximal value of the column. Synergy vectors (columns of W matrices) were then ordered for each participant and setup, based on their similarity to each other. We used the cosine similarity of the synergy weights as a metric of similarity [30], [62]. For each setup, we ordered the synergy vectors of each participant compared to a reference participant. Next, for each setup, corresponding synergy vectors were averaged across participants. Finally, we also ordered the averaged synergy vectors with respect to the reference condition (only arm cycling mode, low resistance, left side). The activation coefficients (H matrices) followed the order corresponding to the synergy vectors.

4.2.10 Statistical analysis

Our main goal was to explore the effects of different cycling combinations (mode or resistance) on muscle synergies. First, the normality of the synergy vectors was checked with Shapiro-Wilk test. Given that the data did not show a normal distribution, non-parametric statistical methods were used. The elements of the synergy vectors, i.e., the

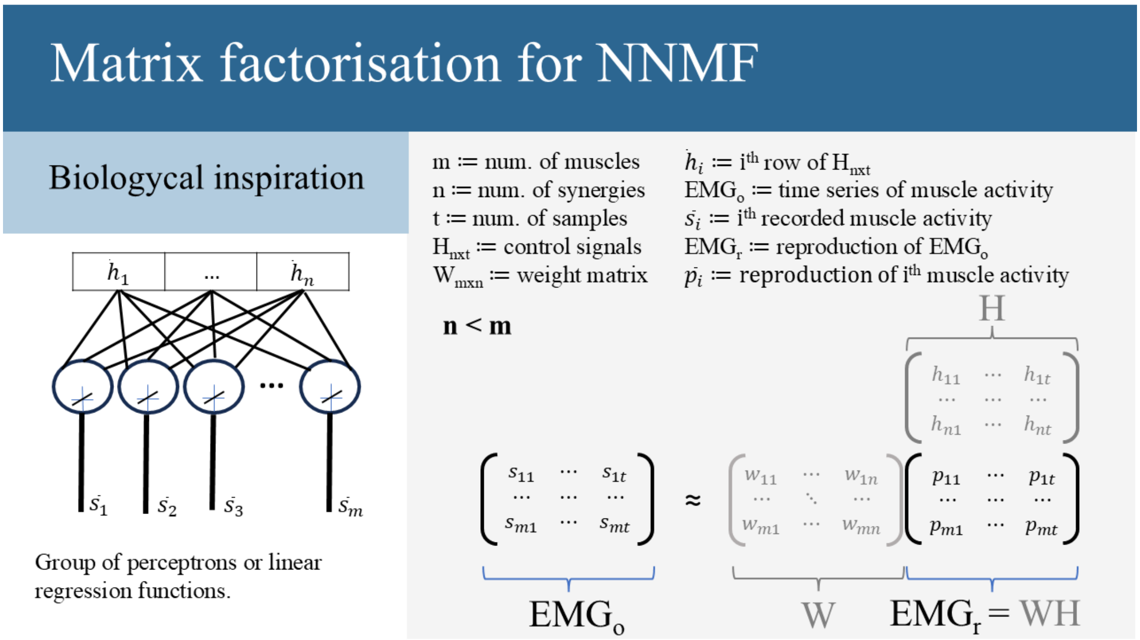

Figure 4.5: Biological inspiration, visual interpretation, and mathematical detail of NNMF The Left Panel illustrates the biological and network inspiration for the NNMF algorithm (as defined in Eq. 4.3.), which can be interpreted as the weighted graph. In this graph, the nodes represent a group of perceptrons or linear regression functions. The Right Panel details the mathematical operations of the matrix factorization, specifically showing the dimensions and multiplication formula for matrices.

activation coefficients and the synergy weights, were analyzed with several different methods to strengthen our findings.

The activation coefficients were averaged across cycles for each participant and time normalized to 101 samples (0-100). The averaged activation coefficient array for each cycling setup was created as follows: number of participants x number of synergies x length of averaged cycle (10x4x101).

To examine the similarity between the different cycling combinations, Spearman rank test was applied on the averaged cycle of activation coefficients in participants, separately the four coefficients. To calculate the significancy (p-values) of the correlation and the effect size (Cohen's d), we applied Fisher-z transformation.

Moreover, we investigated also the differences between the cycling combinations on the mean activation coefficients. Statistical Parametric Mapping (SPM) vector-field analysis is an established method for quantitative correlation of biological time series (28).

This method is applicable to the statistical association of continuous biomechanical datasets, while numerous statistical tests (parametric and non-parametric) can be used within SPM. For pairwise comparisons of the activation coefficients, non-parametric paired T-test was applied within the SPM with Bonferroni correction. We used the open sorce SPM library for MATLAB.

The synergy weights were also compared between the different cycling combinations. To analyze the similarity of the different cycling combinations in terms of synergy weights, cosine similarity was calculated between the averaged (across participants) synergy weights (29)

We also investigated the differences between the synergy weights in cycling combinations, applying Friedman test for the synergy weights of each muscle in the JASP statistical software (30). Conover post-hoc test was used (31), which is recommended after the Friedman test for pairwise comparisons (32). The significance level was set at a p value of 0.05, with the application of the Holm-Bonferroni correction.

4.3 Hybrid FES cycling training - walking assessment

4.3.1 Participants

Five male participants with subacute iSCI, who provided written consent prior to participate, are included in this study in accordance with the Declaration of Helsinki. The National Public Health Center, Budapest, Hungary, gave authorization, the Scientific and Research Ethics Committee of the Health Scientific Council approved the authorization for this research (File number: 18609-6/2023/EUIG). The participants were involved in the study between January 2022 and February 2024. The prior state of the participants, before the hybrid FES cycling training, are summarized in the following table:

Table 4.1: The prior state of the iSCI participants before hybrid FES cycling training.

ID	Age (Year)	Level of Injury	Cause of injury	Initial supplementary devices	Time since injury	AIS score
p01	52	T3	Traumatic	none	3 months	C
p02	70	L1	Surgery	rollator	2 months	C
p03	63	C2, T11-L3	Traumatic	walker, 1 (left) knee brace	3 months	C
p06	49	T9	Surgery	2 crutches	4 months	D
p07	46	C4-C8	Surgery	none	8 months	D

4.3.2 The Organization of the training

The participants had 2×30 minutes long hybrid FES cycling training sessions per week for 12 weeks. In each training session, they had to perform simultaneous FES-assisted lower limb cycling and voluntary arm cycling. Besides the training, the participants got conventional rehabilitation therapy. During the training, three walking ability assessments and three clinical assessments were taken: before the training program started, six weeks later, and when the training was completed. See Figure 4.6.

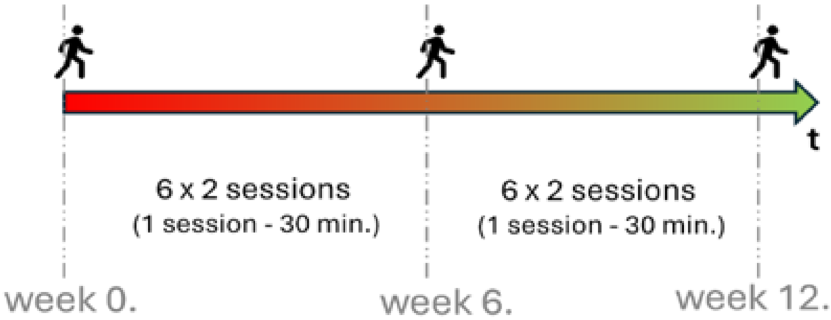

Figure 4.6: It illustrates the number of cycling training sessions and the distributions of the gait assessments of the participants. The human pictograms represent the biomechanical gait and clinical assessments.

4.3.3 The training sessions

All of the training sessions had the following specification: The physiotherapist assisted the participants in positioning themselves to the ergometer. Then, bipolar surface electrodes (PG473W TENS ELEC 45×80 mm) were placed on the quadriceps and hamstrings muscle groups on both legs. The exercises are illustrated at Figure 4.7. The stimulation frequency (30 Hz), and the pulse width (300 µs) were constant in each training session. The current amplitude was set and changed by the physiotherapist.

Figure 4.7: Clinical application of hybrid FES cycling training.

At the beginning of the session, five minutes of passive leg cycling was applied without electrical stimulation, when the ergometer's motor rotated the lower cranks. This was a warm-up period. Then, the participant performed 20 minutes of hybrid FES cycling.

There were no restrictions for the cadence or mode of the upper limb cycling and only the natural friction of the upper crank gave resistance. However, the resistance of the lower crank was adjusted to the actual condition of the participant. The session was finished with 5 minutes of passive leg cycling to relax the leg muscles.

4.3.4 Clinical assessments

The following tests were taken to evaluate the walking abilities of the participants: Walking Index for Spinal Cord Injury (WISCI) [86], Functional Independence Measure (FIM) and Motor FIM [70], Spinal Cord Independence Measure III (SCIM III) [87] and Modified Ashworth Scale (MAS) [88]. We also documented the used assistive devices.

4.3.5 Instrumentation

For the gait assessments, Vicon motion capture system and Cometa EMG recording systems were used with similar sampling frequencies as in the case of simultaneous arm and leg cycling exercises, which is described in Chapter 4.1.2. Besides these modalities, additionally to quantify the dynamic characteristics of the participants' walking patterns, we applied three AMTI BMS400600-2K (AMTI, Boston, USA) force plates for the Center of Pressure (CoP) and Ground Reaction Force (GRF) measurements. The force plates are built in the path of the walking area and leveled with its surface. The three platforms (size 40×60 cm, each) are placed and attached along their shorter sides, which produces a 40 cm wide and 180 cm long measurement surface. The sampling frequency of the force plates was set at 600 Hz.

4.3.6 Recorded Muscles

The list of the recorded muscles is the following:

left and right rectus femoris (RF), left and right vastus lateralis (VL), left and right vastus medialis (VM), left and right semitendinosus (Smt), left and right biceps femoris (BF).

4.3.7 Used kinematic templates

The extended Vicon full-boady plug-in template is built-in template which is widely used in the motion analysis. It was designed to record the whole body motion and most of the cases it is used to monitor walking related tasks. Our group extended this model with additional markers on the hip, elbow, knee and on the floor. We added this points to make the system more precise to the measurements of the hip, elbow and knee joint angle changes and to place reference points on the floor. The red and green colors represent the left and the right limbs of the participants, meanwhile the orange color denotes the floor around the force plates. The three blue segments are the head and the parts of the torso. See Figure 4.8.

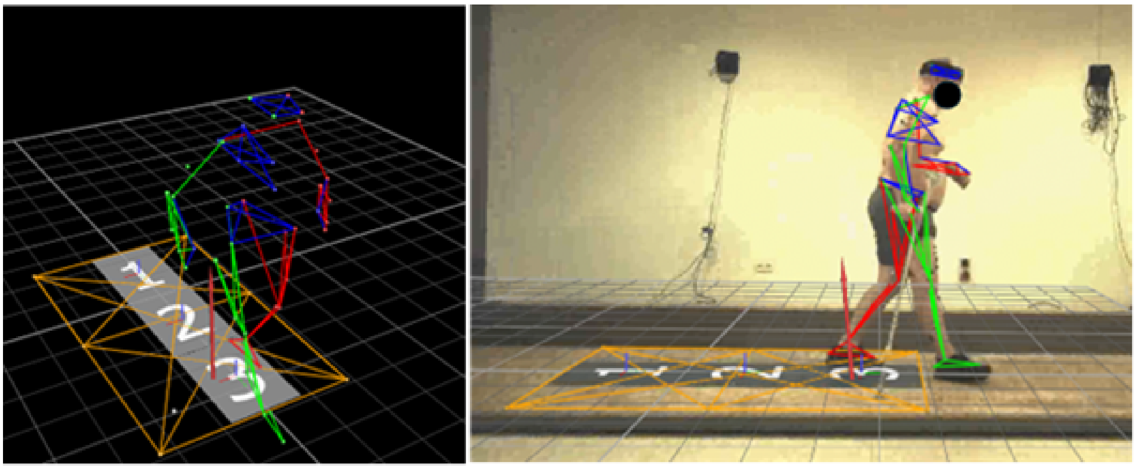

Figure 4.8: The 3D kinematic model of the human body is illustrated on the left panel. The right panel shows a merged video frame with the 3D model of the participant. The numbered tiles on the floor represent the force plates. The red arrow shows the actual Ground Reaction Force.

The segments of the template are the following: segment 1. – head, segment 2. – back and chest, segment 3. hip, segment 4. – left upper arm, segment 5. – left lower arm, segment 6. – left hand. segment 7. – right upper arm, segment 8. – right lower arm, segment 9. – right hand, segment 10. –left thigh, segment 11. – left shin, segment 12. – left foot. segment 13. –right thigh, segment 14. – right shin, segment 15. – right foot. segment 16. – floor.

4.3.8 Gait assessment

Walking was performed at the preferred speed along a straight path over 3D force plates. It is illustrated in Figure 4.8. In each assessment, we observed four walking trials. The estimation of the number of trials is based on the work of Gao et al. [89] who used three valid CoP paths each for the left and right side of all participants.

The following parameters were analyzed: step length, step time, walking speed, and maxima of absolute values of 3 orthogonal components of ground reaction forces (medi-olateral -x, posteroanterior -y, and vertical -z components of GRF), for each component separately. Euclidean lengths and total jerk of the CoP progression curves were computed. After each assessment GRFs and CoPs were averaged across the stance phases of several steps for each side (from 4 walking trials, above the 3 force plates).

Beside the biomechanical parameter assessments, I wanted to quantify the repeatability and regularity of the EMG activity of the leg muscles during the walking since it gives us additional information of the neuro-muscular control of the patients.

Our considerations was to find a quite simple and well interpretable feature or measure for clinical application. We found that the extended definitions of Shannon entropy on the EMG time series are good choices because it is a scalar quantity and despite that, it describes the general regularity of the time series. To quantify this property I calculated the Sample Entropy (SampEn) which was defined by Richman et al. [90], The preliminary results of the application of SampEn in our work have already been published [C1].

4.3.9 Electromyogram signal processing

During the SampEn analysis of the knee extensor and flexor muscles, the following preprocessing steps were applied to the recorded signals. First, the raw EMG signals were band-pass filtered between 25 - 350 Hz using a third-order Butterworth filter. The filtering was performed in both forward and reverse directions to eliminate phase distortion, implemented via MATLAB's built-in filtfilt()function.

Subsequently, the 50 Hz power line interference was attenuated using a third-order Butterworth notch filter with [49–51] Hz range. Again, I applied bidirectionally filtering function filtfilt().

Finally, the signals were full-wave rectified and smoothed using the Root Mean Square (RMS) smoothing technique. A moving window of 61 samples was used, corresponding to an approximate time window of 51 ms, in accordance with recommendations found in the relevant literature [91]. The filtered and smoothed EMG signals were segmented into gait cycles, each defined as the interval between two consecutive left heel strikes. The EMG data corresponding to each gait cycle were linearly interpolated to a uniform length of 500 samples.

SampEn values were computed from each uniform length gait cycles for each muscle separately. Then, the mean and standard deviation of the gained SampEn values were aggregated across the gait cycles. For the entropy calculation, the open-source sampen() MATLAB function developed by Richman et al. [92] was used. The parameters for the function were set to $m = 4$ and $r = 0.2$. The parameters were set according to our previous work [C1] which follows the best practices of the literature.

4.3.10 Kinematic signal processing

One step was defined as the event during two consecutive heel strikes of the legs. For the heel strike event detection, we used the left and right heel markers (placed on the heel bone). The local minima of the time courses of the vertical (z-axis) coordinates of these markers correspond to the heel strikes. The step time is defined as the time difference between the two local maxima. The step length is calculated as the Euclidean distance of two heel strikes with respect to the forward-backward (y-axis) direction. The walking speed is calculated as the mean ratio of the step length and step time.

4.3.11 Dynamic signal processing

Ground Reaction Force components

The time courses of the absolute values of (x,y,z) components of 3D GRFs were investigated for each step. The maximum of each of these time series was selected in each step. Then the mean (μ_{cord}) and the standard deviation (SD_{cord}) of these values across steps and trials were calculated using Eq. 4.4 and 4.5. The illustration of this calculations is found in Figure 4.9.

$$\mu_{\text{cord}} = \text{mean}\left(\max_{1\leq t\leq N}(|\text{GRF}_{\text{cord},t}|)\right) \tag{4.4}$$

$$SD_{\text{cord}} = \text{std}\left(\max_{1\leq t\leq N}(|\text{GRF}_{\text{cord},t}|)\right) \tag{4.5}$$

Where $GRF_{cord} \in \mathbb{R}$ and $N, t \in \mathbb{N}$; N is the length of the time series in the actual step and t is the actual timestamp . Meanwhile cord $\in x, y, z$ are orthonormal directions.

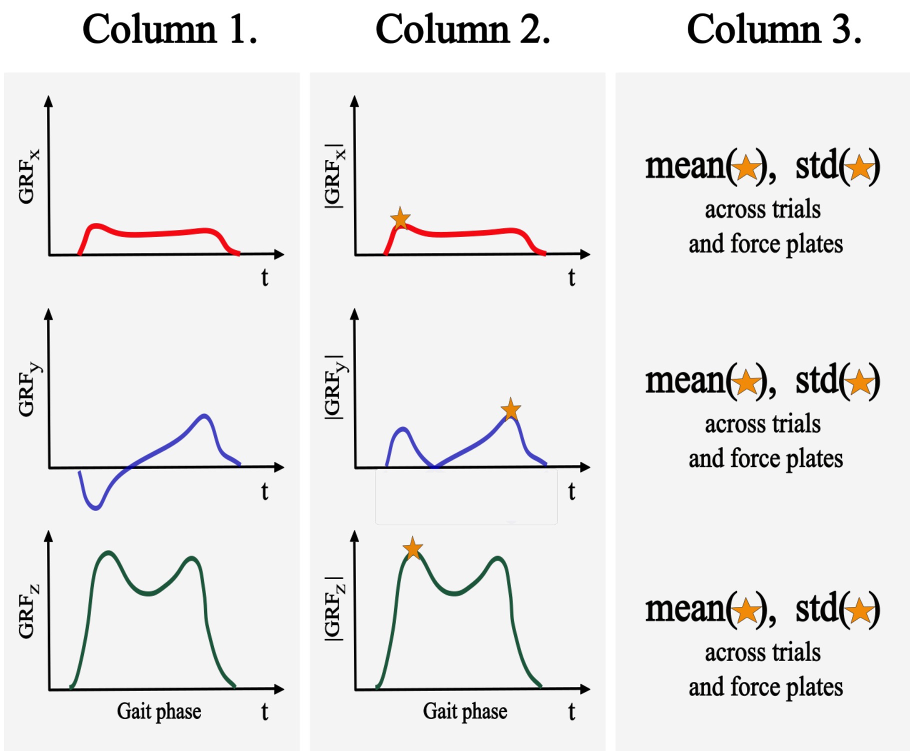

Figure 4.9: This figure is the visual representation of the Eq. 4.4 and 4.5. First column represents the components of the Ground Reaction Force (GRF): GRF_x - mediolateral, GRF_y - posterio-anterior, GRF_z - horizontal components. Second column represents the absolute values of the GRF components and the selection of maxima denoted by asterisks. The third column denotes the aggregation of the maxima of each force plates and measurement trials.

Center of Pressure progression

The length of the CoP curve for each step is calculated as follows: the starting and the end time points of the CoP curve are determined as the time points of the two greatest local maxima of the vertical GRF (z-axis) component during the actual step. See Figure 4.10. These time points are associated with the events of loading and push-off. In these time intervals, we calculated the summed Euclidean distances between the recorded CoP points. Then the curve lengths were averaged across the steps.

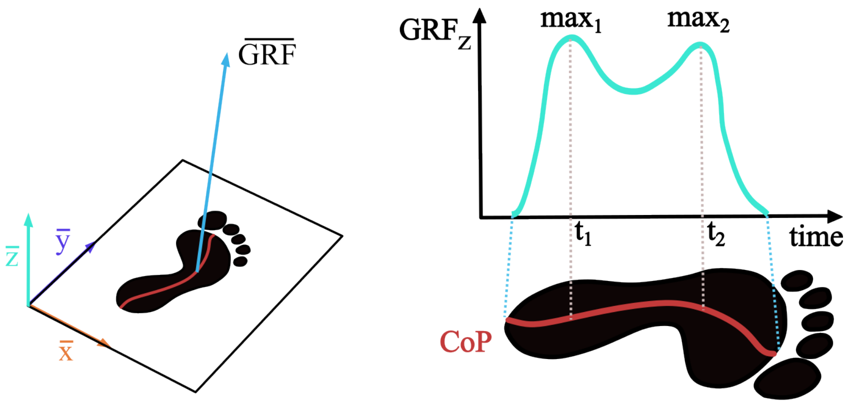

Figure 4.10: The connection between the Ground Reaction Forces (GRF) and the Center of Pressure (CoP). The CoP progression curve is created by the set of origin points of the GRF vector on force plate during stance phase of the walking.

Jerk computation

Time courses of CoP coordinates $[CoP_x(t), CoP_y(t)]$ and their derivatives with respect to time were computed, up to the third order. After each differentiation data were filtered by second order Butterworth filter with 10 Hz cut-off frequency. The total jerk of the CoP path trajectory was computed as follows:

$$J_{\text{total}} = \int_{t_1}^{t_2} (CoP_x'''(t))^2 + (CoP_y'''(t))^2 dt \tag{4.6}$$

Where $[t_1, t_2]$ is the studied time interval of the CoP progression, illustrated in Figure 4.10. $CoP_x(t)$, $CoP_y(t)$ represent mediolateral and posteroanterior components of the CoP displacement as function of time, $<, >$ denotes scalar product.

4.3.12 Statistical comparison of biomechanical parameters between the three assessments

For all gait parameters presented in this study, the following analytical procedure was applied. To ensure statistical comparability, the distribution of the data was first assessed to determine whether it followed a normal or non-normal distribution. This was evaluated using the Shapiro–Wilk hypothesis test, with a standard significance level set at $p = 0.05$. The test was implemented using the open-source swtest() function available on the MathWorks website of MATLAB.

During the execution of the Shapiro–Wilk test, I found that nearly all examined parameters had non-normal distributions, regardless of whether the parameters were analyzed collectively or separately for the left and right legs, for different gait assessments. In cases where the data did not follow a normal distribution, a log-normalization was applied, followed by a repeated Shapiro–Wilk test. However, log-normalization did not result normal distributions in these cases. Consequently, to ensure consistency in the statistical analysis across parameters, sides (left and right), and gait assessments, all subsequent analyses were conducted using non-parametric statistical methods.

To compare the results obtained at week 0., 6., and 12., a non-parametric Friedman test was applied. This analysis was conducted using MATLAB's built-in friedman() function. To reduce the risk of Type I errors (false positives), the results of the Friedman test were followed by Bonferroni post hoc test. For this purpose, MATLAB's multicompare() function was utilized.

5 Results

5.1 Outcomes of arm & leg cycling - neural network

5.1.1 Predicted EMG Signal Profiles and Binarization Outcomes

In this section, I present the predicted EMG signal profiles obtained from the experimental setup. These results, which have been previously published in [J2], include prediction outcomes for synchronous and asynchronous hybrid cycling tasks. See Figure 5.1. In both experimental conditions, the cycling cadence was asked from the participants to maintain 60 revolutions per minute (rpm).

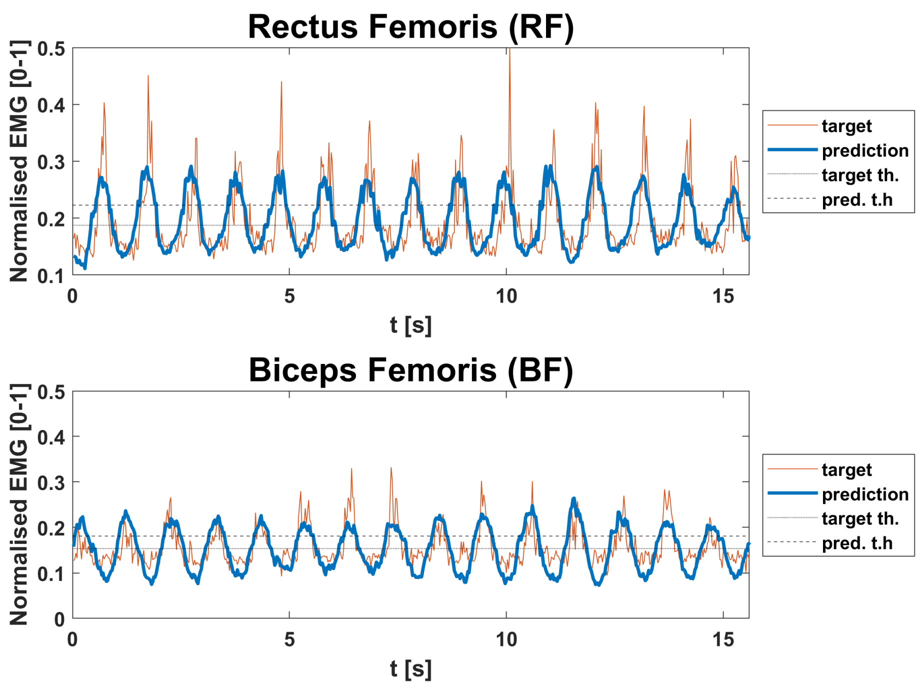

Figure 5.1: The normalized original (orange) and the predicted (blue) EMG signals of one participant. The predicted signal was obtained by the NARX neural network during 15 periods of asynchronous cycling. The model was applied for the prediction of the EMG signals of the R. Rectus Femoris (upper graph) and the R. Biceps Femoris (lower graph) from the six EMG signals of the right arm. Four participants' records were used for the learning. Dotted lines represent thresholds.

Subsequently, we illustrate the outcomes of the binarization process. Specifically, we provide two representative examples of averaged binary matching values under the two distinct learning conditions, see Figure 5.2.

The performance of the employed learning algorithm is quantitatively assessed by comparing the predicted binary signals to the corresponding target signals. These accuracy metrics are summarized in Table 5.1., and were computed in accordance with Equation 4.2.

An additional noteworthy result of this study refers how accurately the participants can keep the same cycling frequencies of the upper and lower limbs. The accuracy of this synchronization is quantified and presented in Table 5.2.

Table 5.1: The table summarizes the mean performance and standard deviation of the binarized activation patterns for two selected muscles during both synchronous and asynchronous cycling. These metrics were calculated across 80 learning attempts. Note: Performance in this context means the average degree of the total number of samples where the predicted and the target binary signals are the same. The capital letter "P" means participant.

Task	Muscle	P1	P2	P3	P4
Synchronous	r. rectus fem.	228° ± 26°	225° ± 31°	212° ± 19°	174° ± 43°
	r. biceps fem.	201° ± 15°	181° ± 24°	195° ± 20°	186° ± 30°
Asynchronous	r. rectus fem.	272° ± 36°	208° ± 31°	190° ± 27°	208° ± 41°
	r. biceps fem.	200° ± 29°	205° ± 14°	227° ± 17°	237° ± 35°

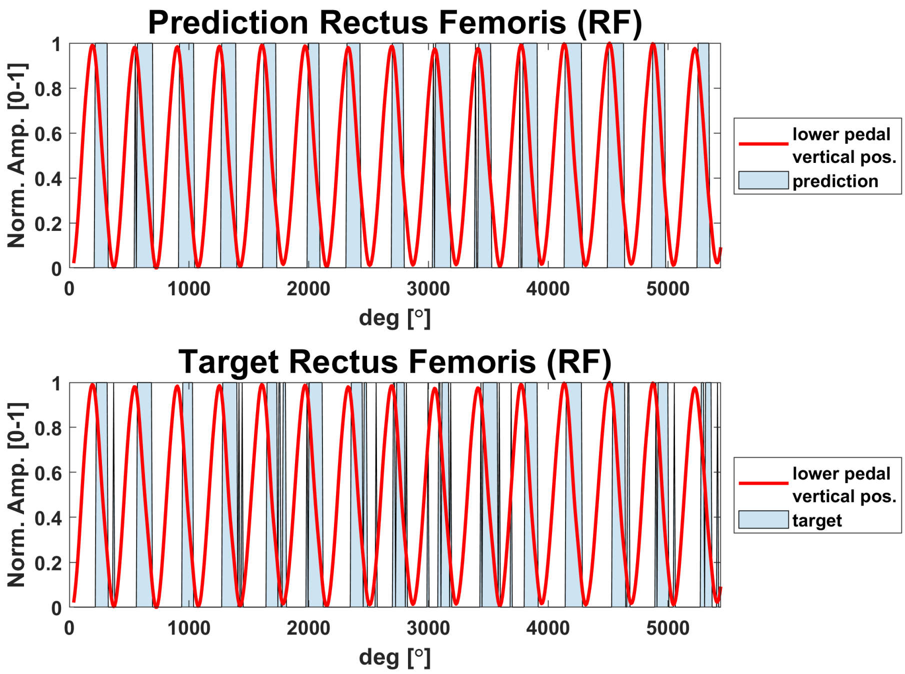

Figure 5.2: The measured (lower panel) and the predicted (upper panel) binarized R. Rectus Femoris (RF) muscle activity pattern for asynchronous cycling as a function of crank angle during 15 consecutive cycles. The 360°degree relates to the top dead center position of the pedal. The binary signal (blue) is 1 if the analog signal is above the threshold value; otherwise, it is zero. The red curve represents the vertical position of the pedal that is driven by the leg; it is 1 when the pedal is at the top dead center and 0 when it is in the bottom dead center.

Table 5.2: The average cycling frequency and standard deviation of the upper and lower crank during the hybrid FES cycling.

Cycling frequencies [Hz]	Mode	P1	P2	P3	P4
Right upper crank	Asynchron	1.01 ± 0.09	0.66 ± 0.08	0.94 ± 0.13	0.93 ± 0.08
	Synchron	1.16 ± 0.06	1.00 ± 0.06	0.88 ± 0.04	0.95 ± 0.11
Right lower crank	Asynchron	0.98 ± 0.11	0.66 ± 0.04	1.05 ± 0.07	1.00 ± 0.02
	Synchron	1.13 ± 0.13	1.00 ± 0.05	0.88 ± 0.02	1.19 ± 0.03
Δ cycling frequency	Asynchron	0.03 ± 0.02	0.00 ± 0.04	-0.09 ± 0.05	-0.07 ± 0.06
	Synchron	0.03 ± 0.07	0.00 ± 0.01	0.00 ± 0.02	-0.21 ± 0.07

5.2 Outcomes of arm & leg cycling - muscle synergy analysis

We compared the average EMG envelopes of the only-arm and arm & leg cycling exercises across participants. The VAF values obtained in the two types of exercises were also compared, and the resulting synergy weights (W) and coefficients (H) were investigated. These results have been accepted for publication by *Journal of NeuroEngineering and Rehabilitation* [J3].

5.2.1 Comparison of muscle activities

The average and standard deviations of time-normalized EMG envelopes (across participants) of the recorded arm muscle activities from the two cycling modes (only-arm and arm & leg) are presented in Figure 5.3. For all the recorded muscles, the EMG envelopes from both cycling modes (only-arm and arm & leg) were very similar, both on the left and right sides. Only minor differences can be observed in the graphs comparing the two cases. The EMGs from PD, TB, ECR and FCR presented considerable standard deviations, and the EMG envelopes obtained from the two cycling modes overlapped. Notably, the EMGs from the other two muscles with small standard deviations (anterior deltoid (AD) and biceps brachii (BB)) also overlapped when comparing only-arm and arm&leg curves. These observations are supported by the high correlation coefficients (higher than 0.85) obtained when comparing the EMG envelopes from the different cycling modes (Table 5.3).

Table 5.3: Correlation coefficients of averaged (across participants) EMG envelopes for each muscle with respect to the cycling mode (only-arm and arm & leg) based on the Spearman rank test.

Cycling mode	AD	PD	BB	TB	ECR	FCR
left, low	0.97	0.95	0.89	0.94	0.98	0.90
left, mod.	0.96	0.92	0.99	0.95	0.99	0.96
right, low	0.94	0.86	0.96	0.89	0.96	0.91
right, mod.	0.96	0.94	0.99	0.94	0.97	0.97

5.2.2 Evaluation of VAF values

The total VAF values were calculated for each cycling setups. Using three synergies, total VAF values were below 90% for most settings (minimum of total VAF was 84% and maximum was 94%). Using four synergies, total VAF values ranged from 92% to 97%. None of the participants required five synergies to achieve the acceptance criteria. Since four synergies accounted for more than 90% of the variance in muscle activation in all settings, for all participants, four synergy vectors were applied for further analysis. The distribution (among the participants) of total VAF values were presented in boxplot diagrams for the different cycling setups for 3 and 4 Synergies (Figure 5.4).

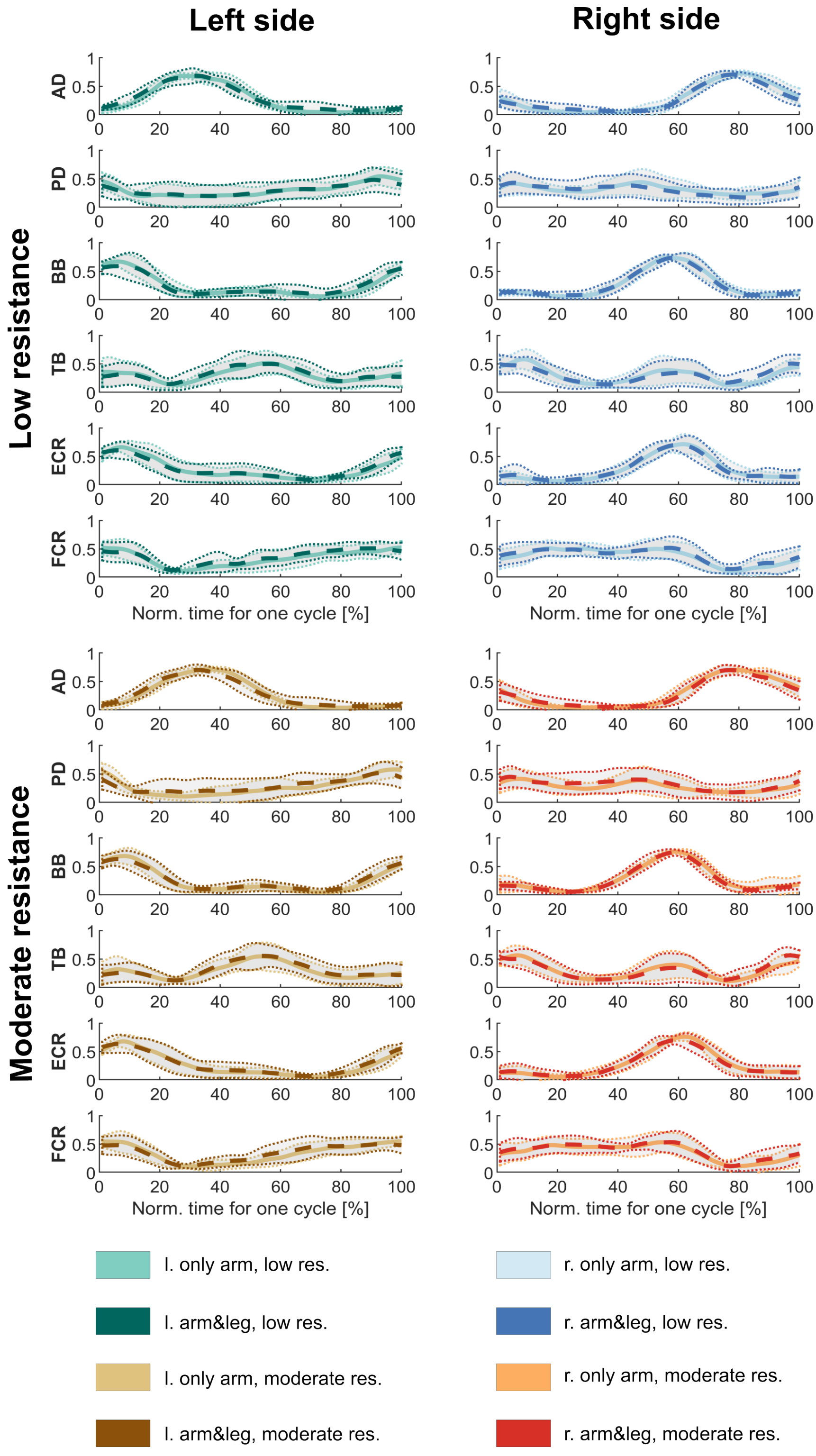

Figure 5.3: Mean muscle activities (across cycles and across participants) recorded from six arm muscles for each setup. EMG signals (with standard deviations) were compared between arm & leg (dashed curves) and only-arm cycling (continuous curves) modes [J3].

The median of total VAF values was higher for 4 Synergies in all setups. Considering four synergies, VAF values did not differ meaningfully comparing cycling modes or resistances.

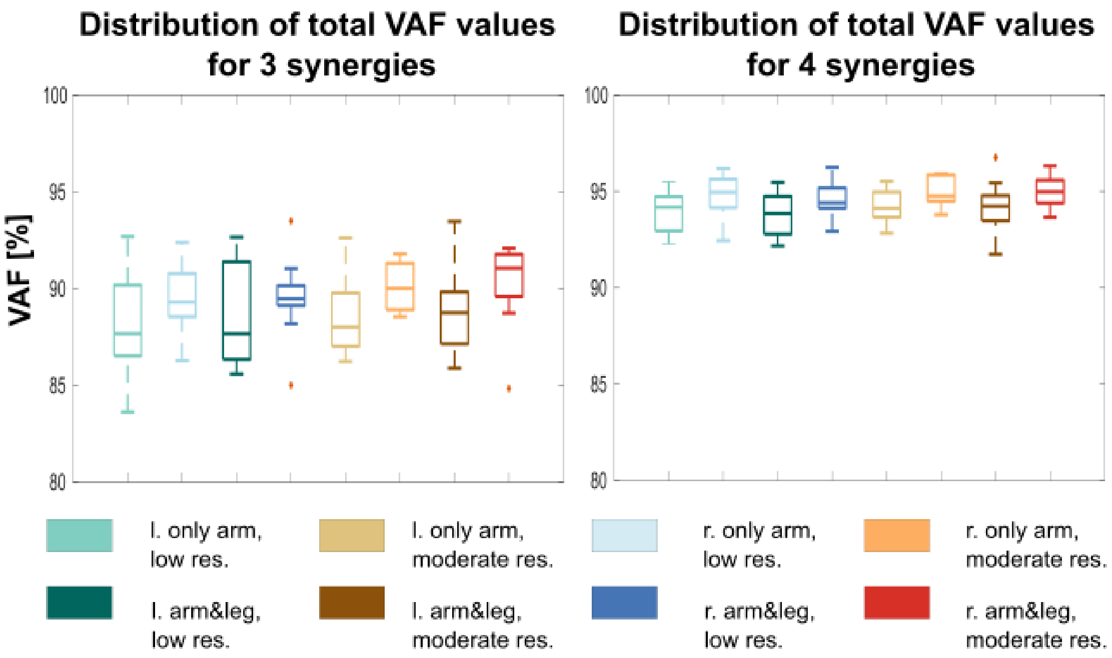

Figure 5.4: The distribution (among participants) of total VAF values were presented for different cycling setups for three and four synergies. The VAF by four synergies explained more than 90% of the variance of the EMG envelopes. The setups were as follows: 1) only arm with low resistance, left side; 2) only arm with low resistance, right side; 3) arm and leg cycling with low resistance, left side; 4) arm and leg cycling with low resistance, right side; 5) only arm with moderate resistance, left side; 6) only arm with moderate resistance, right side; 7) arm and leg cycling with moderate resistance, left side; 8) arm and leg cycling with moderate resistance, right side.

5.2.3 Comparison of muscle synergies components

The results of the synergy calculations are shown in Figure 5.5. The average and standard error of the synergy weights (W) and coefficients (H) across the participants are illustrated.

We compared the synergy vectors in pairs according to the following: we compared the cycling setups between low and moderate resistance and between the "only arm" and "arm & leg" cycling modes in level of activation coefficients and in synergy weights.

With respect to the activation coefficients, the results of similarity analysis the ϱ values based on Spearman rank test was presented with p-values and Cohen's d effect size in the Table 5.4. There was statistically significant high correlation between the cycling modes and resistance levels ($p < 0.05$, $d > 0.8$). Only in one case, in arm & leg cycling mode, the left arm was not significantly high in the correlation ($\varrho = 0.46$, $p = 0.09$, $d = 0.6$) between the two resistances.

The comparison of the activation coefficients using the SPM method did not reveal statistically significant differences between the setups. There was no significant difference between the resistances nor between the cycling modes (See Figure 5.6.).

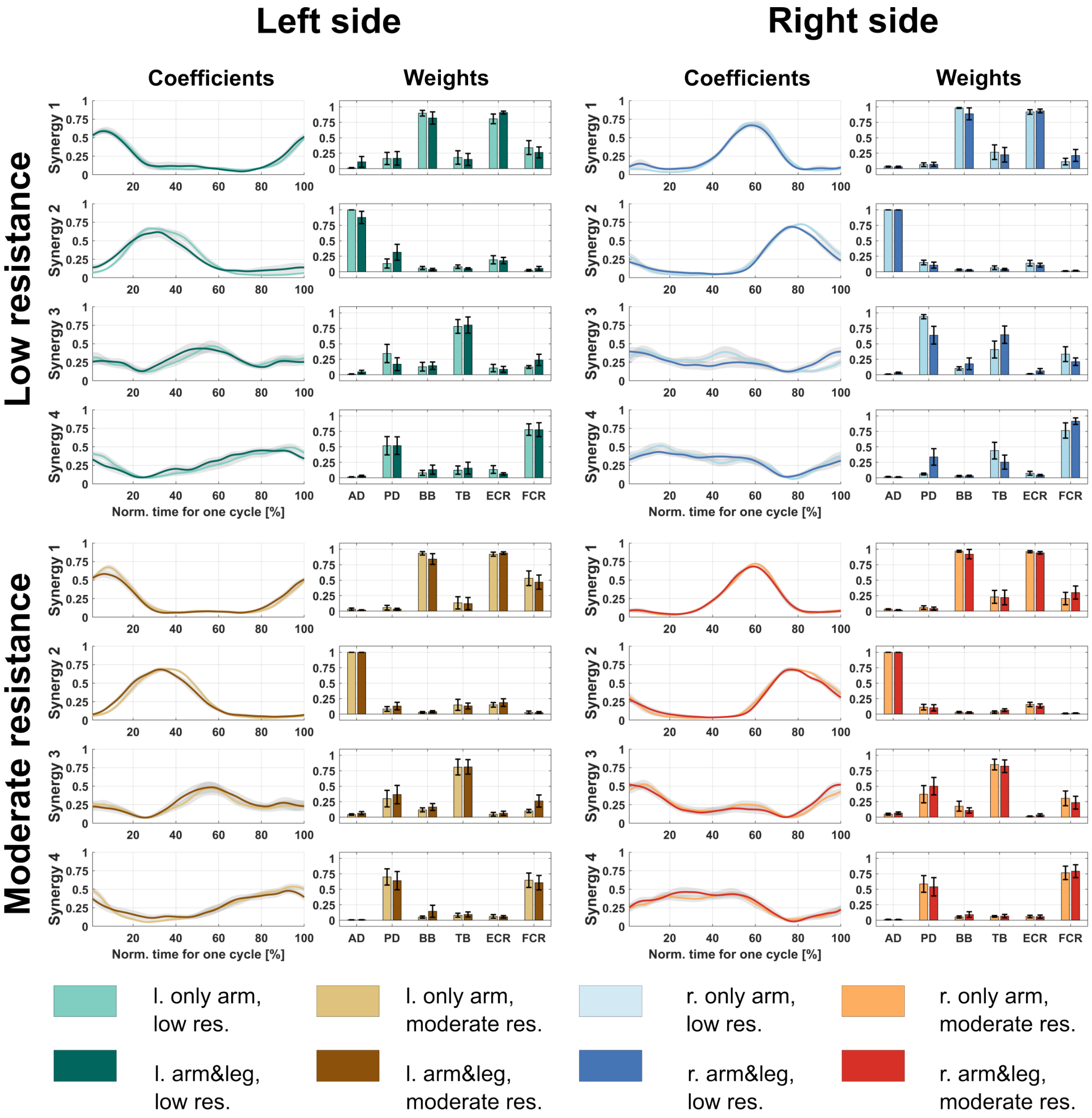

Figure 5.5: Averaged activation coefficients and synergy vectors obtained in eight setups. The activation coefficients are presented as a function of normalized time. The shaded area represent the standard errors. The bar diagrams show the average and standard errors (across participants, n = 10) of muscle weights in each synergy vector.

Table 5.4: Detailed correlation analysis of activation coefficients. The ϱ value means the results of Spearman rank correlation, the p is significance level (calculated by the Fisher-z transformation), and the is the Cohen's d effect size

Synergy		**Resistance**				**Cycling mode**			
		left, only arm	left, arm &leg	right, only arm	right, arm &leg	left, low	left, mod	right, low	right, mod
S1	ϱ	0.84	0.82	0.51	0.78	0.76	0.90	0.59	0.81
	p	0.00	0.00	0.02	0.00	0.00	0.00	0.03	0.00
	d	2.29	2.10	0.91	1.38	2.14	2.29	0.83	2.66
S2	ϱ	0.89	0.74	0.63	0.79	0.80	0.79	0.58	0.71
	p	0.00	0.03	0.01	0.00	0.02	0.01	0.00	0.00
	d	1.42	0.81	1.15	1.43	0.90	0.96	1.50	1.20
S3	ϱ	0.75	0.70	0.93	0.92	0.68	0.74	0.83	0.90
	p	0.00	0.01	0.00	0.00	0.01	0.00	0.00	0.00
	d	1.24	1.00	2.58	2.66	1.08	1.31	2.02	2.86
S4	ϱ	0.79	**0.46**	0.97	0.95	0.65	0.71	0.91	0.94
	p	0.00	0.09	0.00	0.00	0.00	0.02	0.00	0.00
	d	1.35	0.60	4.71	5.01	1.36	0.90	3.71	3.16

Regarding synergy weights, the cosine similarity was presented between the cycling combinations, in the Table 5.5. The synergy weights between the low and moderate level of resistance were similar for left side, in two cycling modes, and for the right side for arm & leg cycling mode (cosine similarity was higher than 0.83). Only for third Synergy weights, in the right side, only arm cycling mode was the cosine similarity below 0.8 (0.76), which was the similarity threshold in other studies [93], [94].

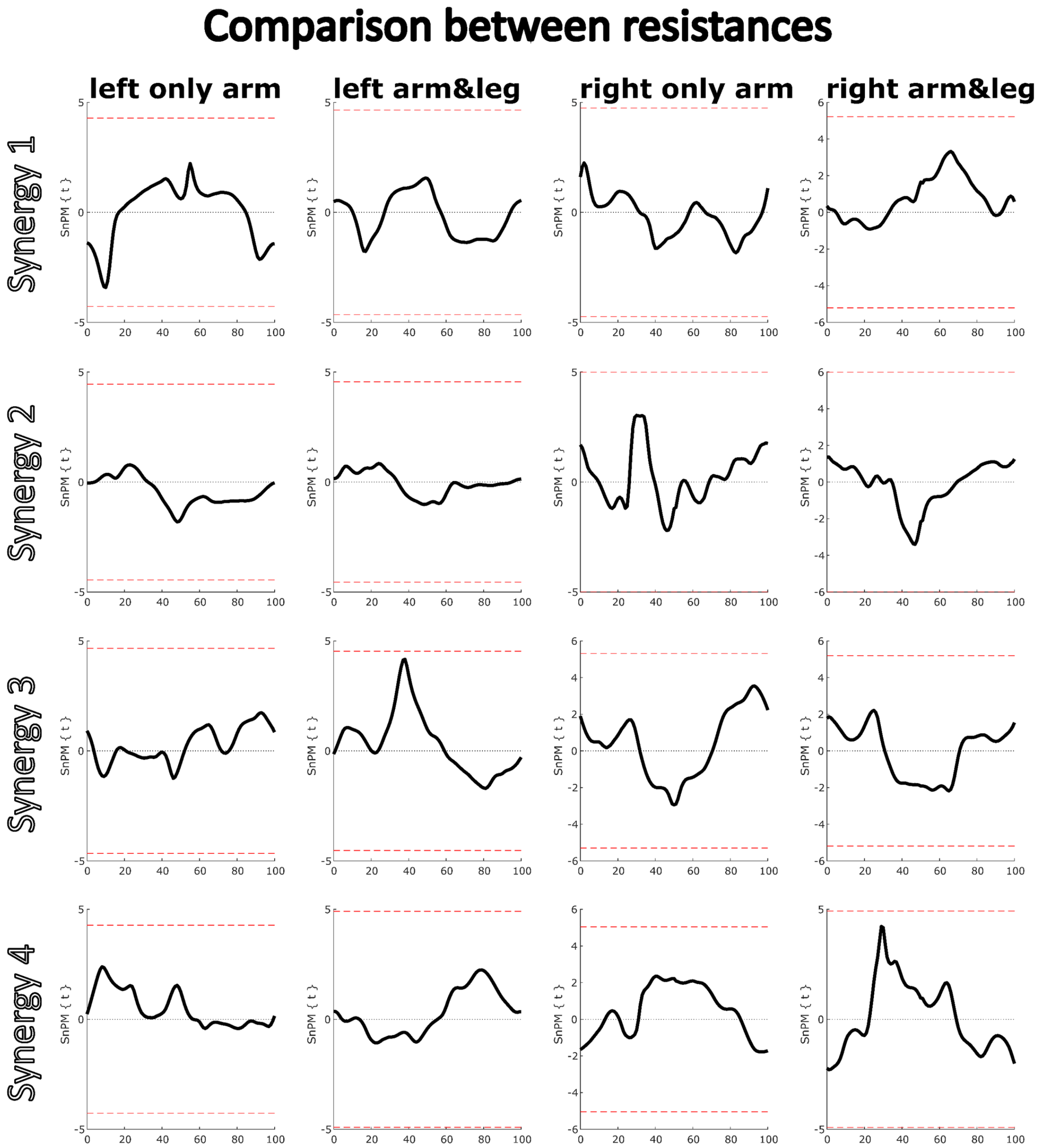

Figure 5.6: Statistical comparison between low and moderate resistances is based on Statistical Parametric Mapping (SPM). This method calculates the differences between the activation coefficients (black line). Points where the SPM curve exceeds the significant differences threshold (indicated by the red dashed line) are interpreted as statistically significant differences. In the present analysis, no significant differences were observed between the activation coefficients with respect to the resistances.

Complementary with these findings, the comparison of synergy weights, using Friedman test, is presented in the Table 5.6. Since we performed multiple comparisons (we examined the four cycling combinations in pairs, separately on the right and left sides), the corrected significance level due to the Holm-Bonferroni correction is $\alpha = 0.006$. Based on the correction, the Conover post-hoc test also did not show significant differences between the cycling combinations.

Table 5.5: Cosine similarity of synergy weights. The setups were as follows: resistance – low (low) or moderate (mod), cycling mode – only-arm or arm&leg, and side – left or right side.

	Resistance				**Cycling mode**			
	left, only arm	left, arm &leg	right, only arm	right, arm &leg	left, low	left, mod	right, low	right, mod
S1	1.00	0.96	0.99	1.00	0.99	0.99	0.99	0.99
S2	0.99	0.97	1.00	1.00	0.96	0.98	1.00	1.00
S3	0.97	0.89	**0.76**	0.97	0.93	0.95	0.92	0.99
S4	0.98	0.92	0.83	0.95	0.97	0.95	0.93	0.99

Table 5.6: Comparison of the differences between cycling combinations in level of synergy weights. The setups were as follows: resistance – low (low) or moderate (mod), cycling mode – only-arm or arm & leg, and side – left or right side. Friedman test was used with Conover post-hoc test for the comparison of the weights of each muscle in each synergy vector, with a p<0.006 Holmes-Bonferroni corrected significance level.

Muscle		**Resistance**				**Cycling mode**			
		left		right		left		right	
		only arm	arm &leg	only arm	arm &leg	low	mod	low	mod
S1	**AD**	0.26	0.15	0.85	0.24	0.40	0.61	0.78	0.21
	PD	0.59	0.62	0.40	0.59	0.10	0.53	0.76	1.00
	BB	0.53	0.85	0.85	0.53	0.70	0.67	0.89	0.34
	TB	0.93	0.11	0.61	0.71	0.38	0.40	0.75	0.85
	ECR	0.49	0.49	1.00	0.64	0.93	0.93	0.58	0.93
	FCR	0.29	**0.02**	0.50	0.63	0.27	0.89	0.29	0.39
S2	**AD**	0.83	0.83	1.00	1.00	0.51	0.51	1.00	1.00
	PD	0.53	0.59	0.53	0.47	0.24	1.00	0.65	0.59
	BB	0.18	0.62	0.89	0.86	0.75	0.13	0.53	0.56
	TB	0.31	0.27	0.36	0.85	0.20	0.41	0.96	0.29
	ECR	0.93	0.89	0.11	0.44	0.42	0.56	0.93	0.34
	FCR	0.47	0.82	0.45	0.47	0.96	0.59	0.12	0.93
S3	**AD**	0.05	0.96	0.06	0.11	0.07	0.92	0.18	0.29
	PD	0.12	**0.03**	**0.01**	0.54	0.09	**0.04**	0.32	0.20
	BB	0.54	0.86	1.00	0.79	0.86	0.54	0.93	0.73
	TB	0.87	0.12	**0.02**	0.74	0.27	0.51	0.35	0.30
	ECR	0.19	0.82	0.58	0.12	0.17	0.86	0.44	0.82
	FCR	0.12	0.45	0.69	0.96	0.86	0.33	0.79	0.47
S4	**AD**	0.59	0.86	0.45	0.31	0.50	0.76	0.37	0.37
	PD	0.57	**0.08**	**0.02**	0.02	0.68	0.06	0.72	0.61
	BB	0.59	0.26	0.42	0.20	0.20	0.72	0.96	0.65
	TB	0.78	0.38	**0.16**	0.03	0.85	0.34	0.96	0.41
	ECR	0.06	0.32	0.93	0.79	0.86	0.47	0.59	0.72
	FCR	0.48	**0.02**	0.67	0.48	0.48	0.33	0.45	0.63

5.3 Outcomes of hybrid FES cycling training - walking assessment

The biomechanical results of the five participants, who had successfully completed the 12 week-long training without any complication, are displayed in this section. From the kinematic data, the following parameters were calculated: *average step length, step time, step speed, average length and jerk of CoP progression and average max. abs GRF components.*

5.3.1 Step length, time, speed

Step length

The average step length of the participants, except p06, are increased after the training and these changes were significant ($p = 0.05$) in case of p01 and p02 participants between the first and the other two assessments. See Figure 5.7. Interestingly, the week 6th (middle) assessments compared to the first and the last measurements had person specific changes. If we look at the standard deviations on the data, the same results have been found. There is a decrease between the before and after state in the magnitude of the standard deviations, which potentially reflect an improvement in the motor control. In contrast, the comparison of the 6th week state to the other states has not got a general trend.

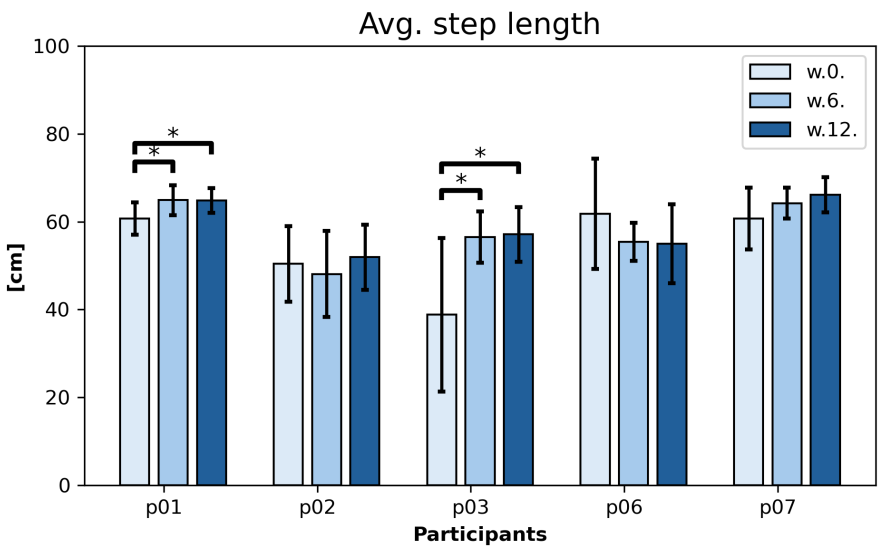

Figure 5.7: Average (across steps) step length and standard deviation of the data prior, at the middle and after the training for the left and the right legs together. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$).

If we look at the step lengths separately for the left and the right legs, then p01, p03, p07 participants had similar changes along the training. On the other hand, p02 and p06 participants had asymmetry between the left and the right legs. See Figure 5.8. Significant differences were found only at the before-after comparison of the p01 left and p03 right sides.

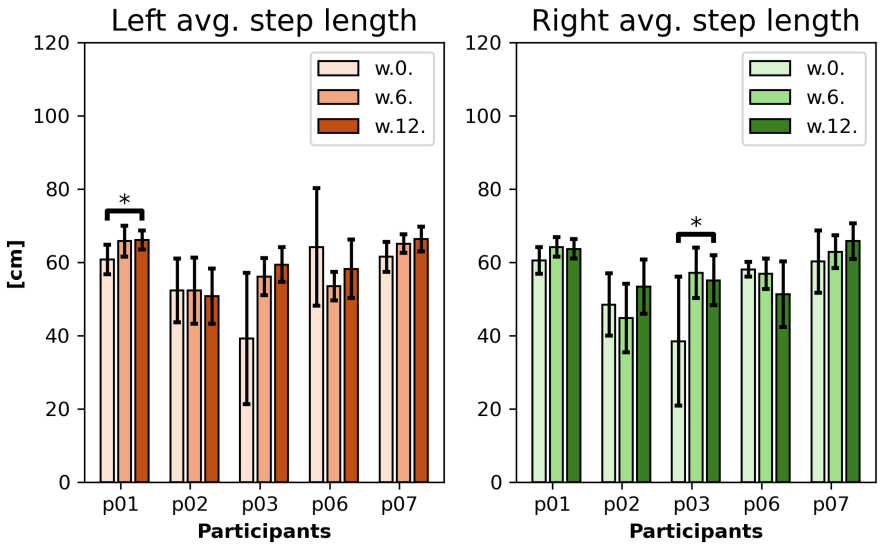

Figure 5.8: Average (across steps) step length and standard deviation of the data prior, at the middle and after the training for the left and the right legs separately. The black lines and asterisks denote statistically significant changes between assessments ($p = 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

In case of p02 the left leg was stable but the standard deviation decreased at the end of the training, meanwhile the right leg had a decreased and later, an increased step length at the end of the training. In case of p06, for both sides the step lengths decreased but with different magnitude. The standard deviation decreased for the left and increased for the right side. This may reflect some weight shift from the left to the right side.

Step time

The average step time for all the participants decreased or stayed stable. The changes between the start and the middle state was person specific. Significant changes were before-after the training in case of p01, p03 and p06 and significant changes were between the before-middle states for p01, p02, p03 and p06 patients. See Figure 5.9.

The bar diagrams of the left and right average step times (Figure 5.10.) show similar changes to the cumulated results (Figure 5.9.). Significant ($p = 0.05$) differences between the assessments were observed in p01, p03 and p06 participants.

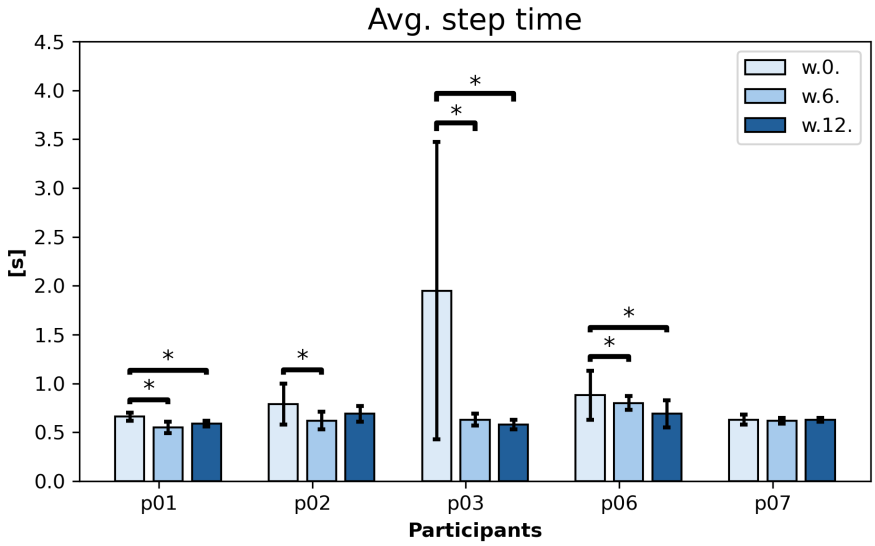

Figure 5.9: Average (across steps) step time and standard deviation of the data prior, at the middle and after the training for the left and the right legs together. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

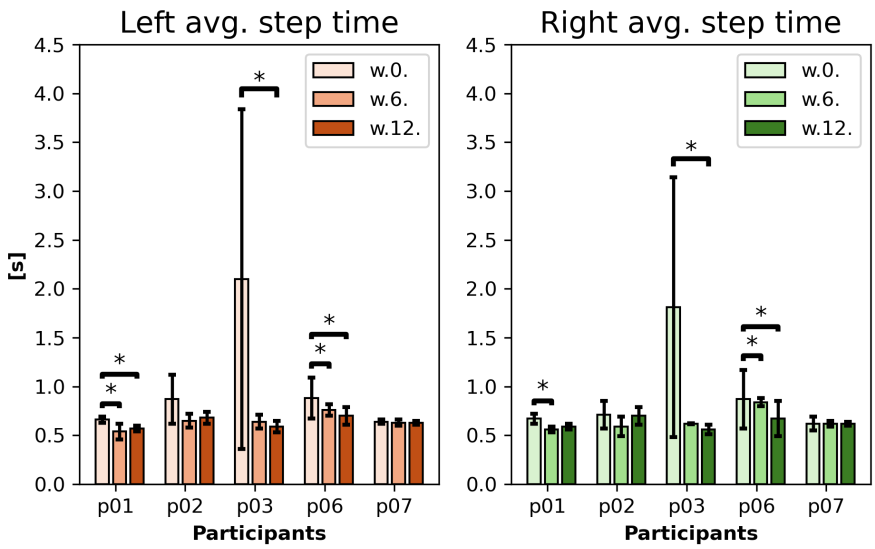

Figure 5.10: Average (across steps) step time and standard deviation of the data prior, at the middle and after the training for the left and the right legs separately. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

Step speed

Based on our measurements, the average step speed for all participants improved and four out of five had significant improvements at least before-after the training. See Figure 5.11.

The following participants had improvement between the prior and middle states: p01, p03, and p06. In case of p03 there was improvement between the middle and after states as well.

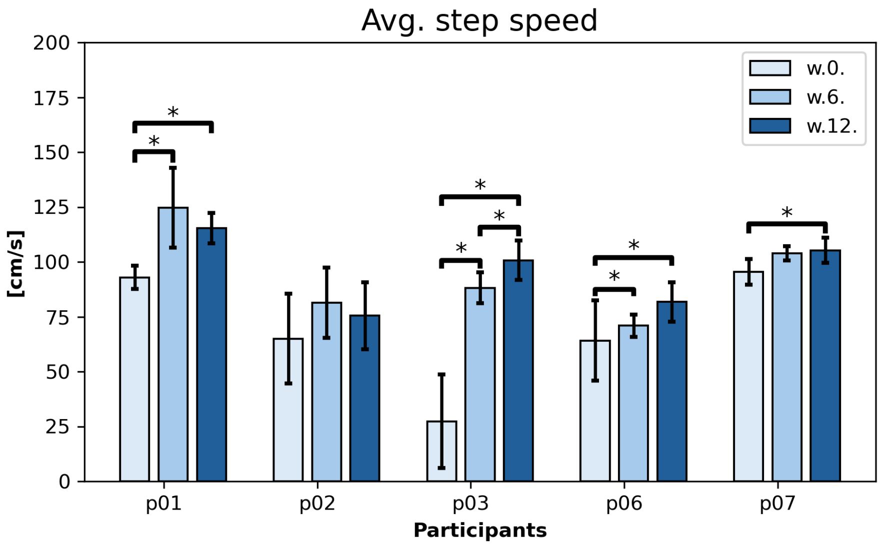

Figure 5.11: Average (across steps) step speed and standard deviation of the data prior, at the middle and after the training for the left and the right legs together. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

Interestingly, the left and right sides had similar improvement trend for each participant but there are more significant changes at the left side compared to the right. See Figure 5.12.

5.3.2 CoP progression length and jerk

CoP progression length

A statistically significant decreasing in the length of center of pressure (CoP) progression was observed in participants p01, p02, p03, and p07. Participant p06 also exhibited a decrease, but this change did not reach statistical significance. Notably, for participant p03, a significant difference was detected between week 0 and week 6. These results are illustrated in Figure 5.13.

The CoP lengths decreased or kept stable regarding the left and right legs separately, except p06. There was significant decrease of the left CoP length in case of p02 before – after, and p03 before – middle states. See Figure 5.14. The lack of significant differences, especially for the right side may be caused by the small number ($n = 4$) of data points.

The standard deviations of the CoP lengths decreased or remained the same between the before and after the training, except p06 participant.

Between weeks 0 and 6, participant p06 showed a moderate CoP length increase on the

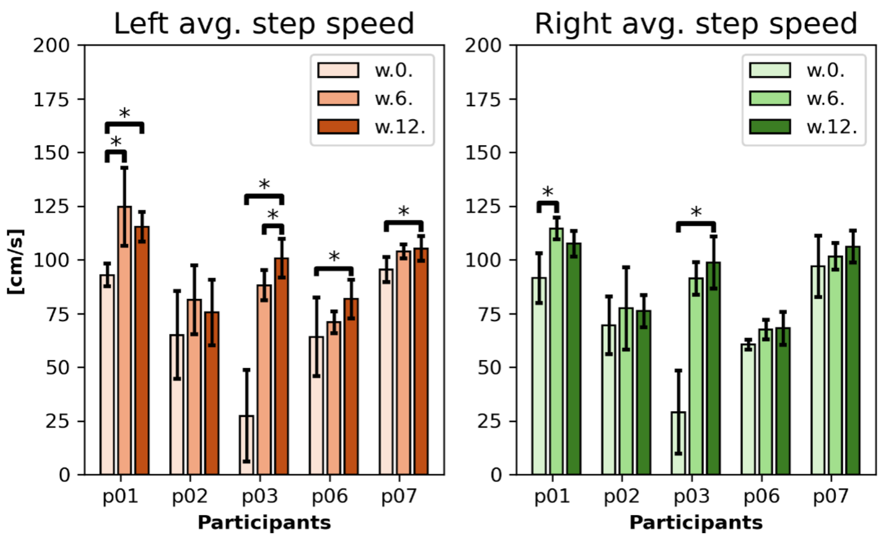

Figure 5.12: Average (across steps) step speed and standard deviation of the data prior, at the middle and after the training for the left and the right legs separately. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

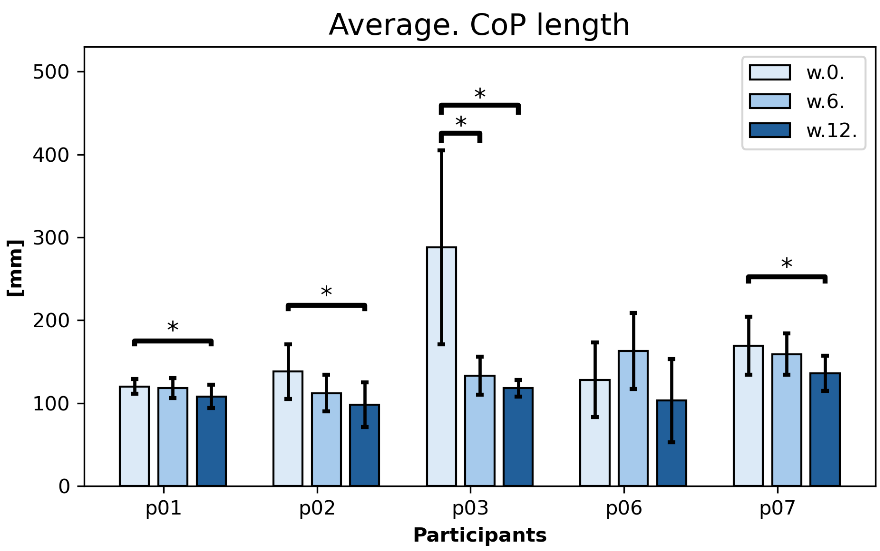

Figure 5.13: Average (across steps) center of pressure (CoP) progression length and its standard deviation of the data prior, at the middle and after the training for the left and the right legs together. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

left and a strong increase on the right sides. While left-side standard deviation decreased, it rose on the right. By week 12, left-side CoP length returned near baseline (despite elevated standard deviation), meanwhile the right side showed marked reductions in both CoP

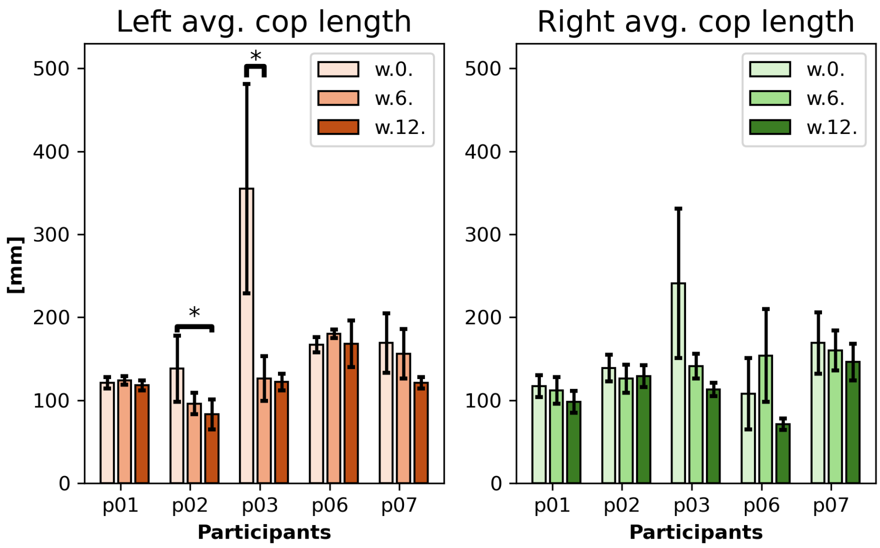

Figure 5.14: Average (across steps) step speed and standard deviation of the data prior, at the middle and after the training for the left and the right legs separately. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

length and standard deviation. This shift likely reflects the transition from dual crutches to a single walking stick on the right side.

CoP progression jerk

The average (across steps) total CoP jerk is decreased for all participants. Four out of five had significantly decreasing total jerk from the first to the last assessments and two participant (p01, p03) had significantly decreasing values between the 0th and 6th week measurements. See Figure 5.15.

The separately illustrated average total jerk values are shown in Figure 5.16. Left and right side magnitude changes of p01, p02, p06 participants are different between the two sides. Significant changes were found for the left side between the before – middle assessments in case of p01 and p03. Significant changes of the left side were only observed between the before – after states at p07 participant. At the right side, significant changes were only found at p01 and p03 before – after the training.

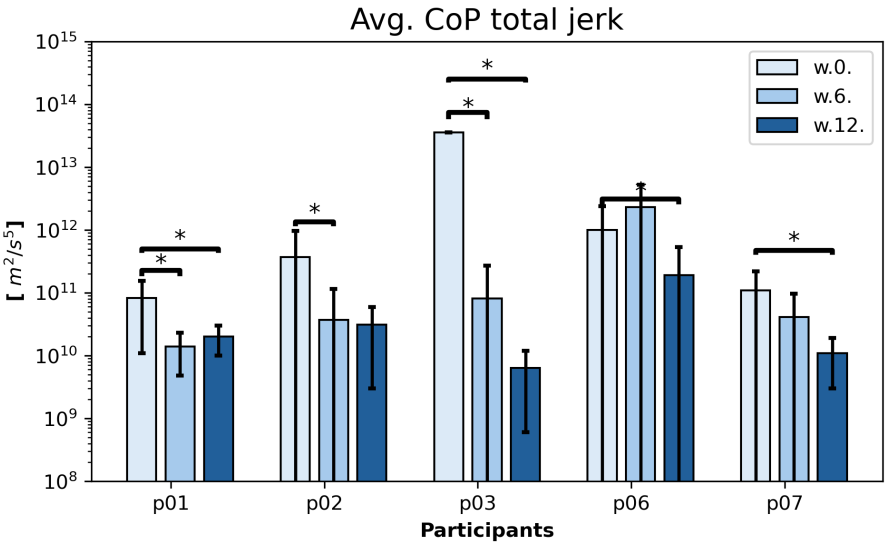

Figure 5.15: Average center of pressure (CoP) total jerk and its standard deviation of the data prior, at the middle and after the training for the left and the right legs together. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

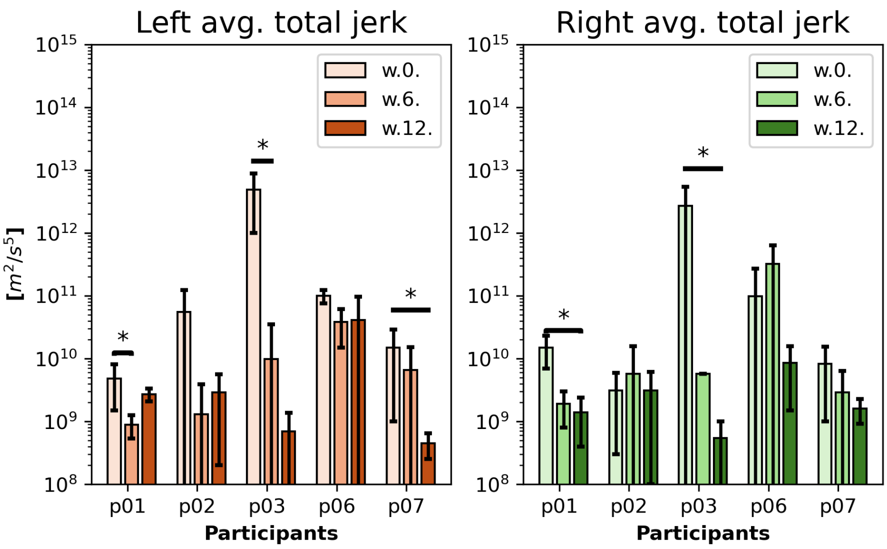

Figure 5.16: Average (avg.) total jerk and standard deviation of the data prior, at the middle and after the training for the left and the right legs separately. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

5.3.3 Ground Reaction Forces

The average maximum of absolute values of ground reaction forces (max. abs. GRF) express the upper boundaries of possible force exertion. In the following section, this parameter changes regarding the week 0th, 6th and 12th gait assessments will be displayed. The results are illustrated separately for the three (x, y, z) components of the GRF and for the two legs.

For the **x** (medial-lateral) component of the max. abs. GRF, the changes were personal specific. Significant differences between the measurements were only found in case of p03, at before - middle and before – after states. Difference between the trend of the two sides were observed at p02 and p06. See Figure 5.17.

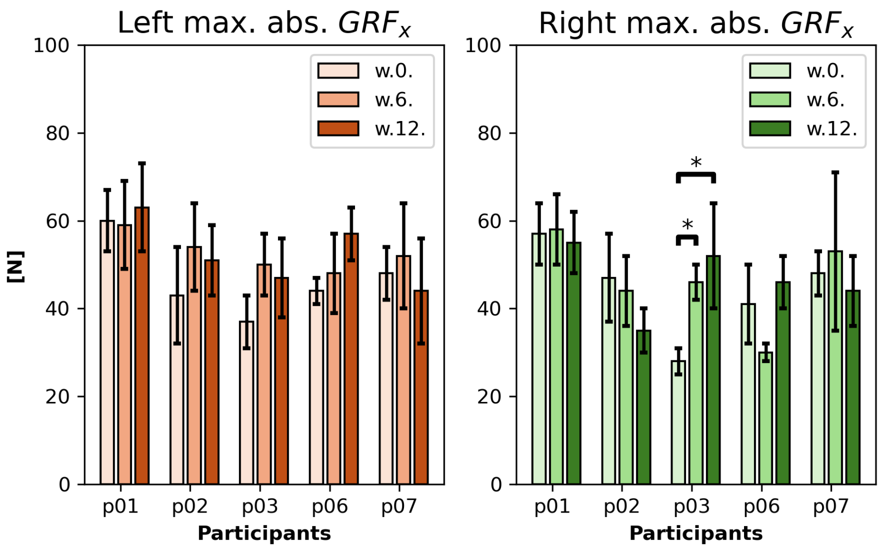

Figure 5.17: The average maximum absolute values of the ground reaction force (max. abs. GRF) in the x-component, along with the corresponding standard deviations, were evaluated separately for the left and right legs at three time points: prior to training, mid-training, and post-training. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

The **y** (anterior posterior) component of the max. abs. GRF were stable or increasing between the week 0. and week 6. Significant changes were found in the before – middle values of p02 for the left side and between the before – after values of p03. See Figure 5.18.

The **z** (vertical) component of the maximum absolute GRF increased significantly for participants p02, p03, and p06 on both sides between the first and last assessments. For p01, a significant increase was observed in the left vertical component, while the right remained stable. Only in the case of p07 were there no significant changes in the z component. See Figure 5.19.

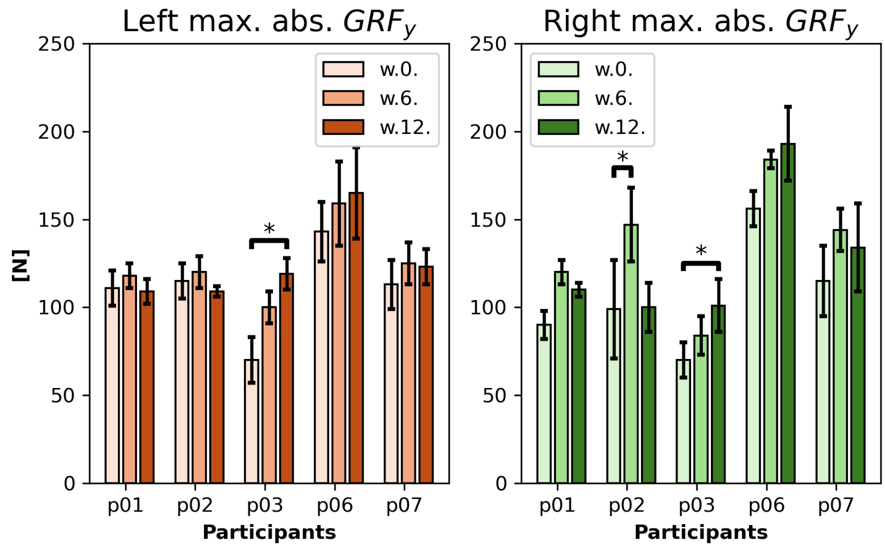

Figure 5.18: The average maximum absolute values of the ground reaction force (max. abs. GRF) in the y-component, along with the corresponding standard deviations, were evaluated separately for the left and right legs at three time points: prior to training, mid-training, and post-training. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

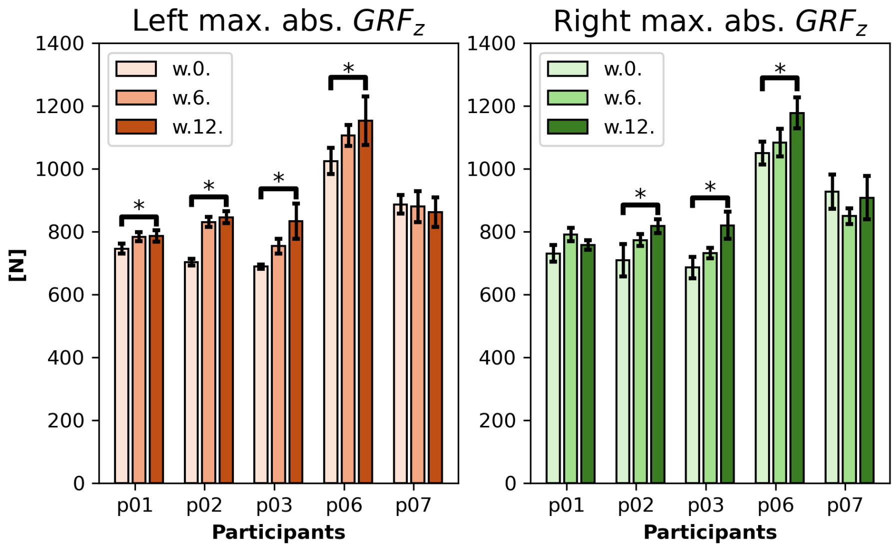

Figure 5.19: The average maximum absolute values of the ground reaction force (max. abs. GRF) in the z-component, along with the corresponding standard deviations, were evaluated separately for the left and right legs at three time points: prior to training, mid-training , and post-training. The black lines and asterisks denote statistically significant changes between assessments ($p < 0.05$). The three assessments were taken at week 0. (w.0.), week 6. (w.6.) and week 12. (w. 12.).

5.3.4 Sample Entropy results

The Sample Entropy (SampEn) is a metric of complexity of a dynamical system. It can describe the periodicity of a timeseries. In our case these time series are the average and standard deviation of step cycle EMG envelopes of the knee flexor and extensor muscles. In the following section, the SamEn values of the 0th (before) and 12th (after) weeks of the training are presented. The results of the five participants are shown in Figure 5.20.

Although there are individual changes of the SampEn, there is a similar trend across the participants. Some preliminary results of this work had been already published [C1] at the *IEEE International Conference of Engineering in Medicine and Biology Society (EMBC)*.

p01 participant has decreased entropy values for all cases, except the left Rectus Femoris (RF). The standard deviation also decreased almost all cases (except Right Semitendinosus). The change of the entropy values were higher at the right side.

In case of p02, the mean values are decreased or stayed stable, except the right Biceps Femoris (BF). The standard deviation of the Vastus Lateralis (VL) and Biceps Femoris (BF) are increased after the 12 weeks. The magnitude of the changes of the two sides are similar.

p03 has the strongest decrease of the SampEn values among all the participants. For both sides, the mean and standard deviation of the SampEn are decreased strongly.

p06 has a strong difference between the knee fexor and extensor muscles at the left side. This difference suggest that, the knee flexor muscles had less regulated muscle activity compared to the extensors. On the left side, the entropy of the Rectus Femoris (FR) decreased strongly, for the Vastus Lateralis (VL) was stable and for the Vastus Medialis (VM) had a small increase in the value although it is still a small value compared to the other muscles of participants. In case if the left knee flexors, the Semitendinosus (Smt) has decreased but still high values after the 12 weeks compared to the other participants. The Biceps Femioris (BF) has a slightly increased SampEn and its prior end after values are both high compared to the other participants. The changes of the standard deviations do not show any pattern.

At the right side of p06, there are more preferabele changes. All the mean values are decreased except the Vastus Lateralis (VL) where a small increase happened. The same changes are observable for the standard deviations on this side.

p07 has increased SampEn after the training for both Rectus Femoris (RF) muscles, and for the left Vastus Medialis (VM) and right Semitendinosus (Smt) muscles. For the left side, the standard deviation increased almost every cases (except the Vastus Lateralis). In contrast, at the right side, the standard deviations decreased except the Rectus Femoris (RF).

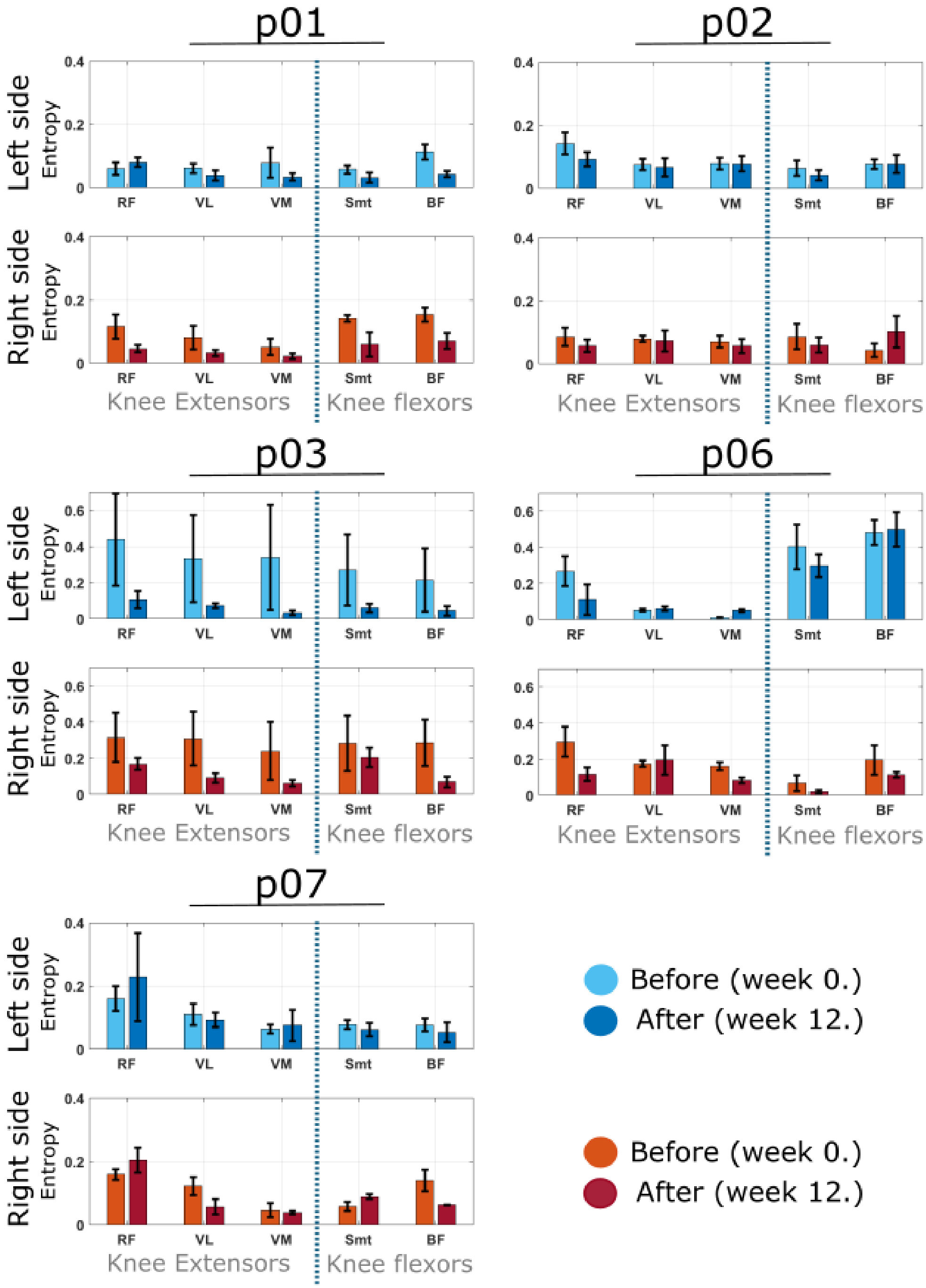

Figure 5.20: Comparison of mean and standard deviation values for Sample Entropy (SampEn) in participant EMG envelopes: Pre- vs. post-hybrid FES cycling training intervention.

5.3.5 Clinical metrics

To make the outcomes of biomechanical and EMG data more comparable, I also present the clinical metrics in Table 5.7 that were assessed and provided by clinicians after each measurement of walking ability. Unfortunately, from p01, we had missing clinical test and in case of p02, the week 0. assessment is also incomplete.

Participant p02

He had strong improvement in his walking ability, moving from using a rollator to walking independently. He left the usage of rollator. ASIA score also progressed from B to D, which indicates a strong improvement in motor functionality of muscles which were under the level if SCI.

According to the Modified Ashworth Scale (MAS), no spasticity was observed in the lower limbs of p02 at either Week 6 or Week 12.

The other metrics, did not show any changes between week 6. and 12.

Participant p03

Participant had a strong improvement which is reflected in all clinical metrics. He started the training with multiple assistive devises such as walker, left peroneal elevator and left knee brace, and at the end of the training he was able to walk independently.

Only the MAS values remained stable, as the muscle tone was already normal.

Participant p06

Participant p06 had moderate improvements, he replaced two forearm crutches to one right side walking cane. A slight improvement was recorded at the SCIM III. Mobility score as well.

He had suffered from mild (quadriceps and hamstrins) and moderate (tibialis anterior and soleus) spasticity of his muscles. After the 12-week training, he had decreased mild spasticity only at the left tibialis anterior and soleus muscles.

The other clinical metric did not show any change in his status.

Participant p07

He had one of the best baseline conditions among the participants. He was able to walk independently from the beginning of the training. He showed a slight improvement according to the Mobility score.

He also had mild level spasticity in his tibialis antrior and soleus muscles, which were recovered after 12 weeks. The other clinical scores remained stable.

Table 5.7: Summary of clinical metrics for participants (p02–p07) at weeks 0, 6, and 12. MAS: Modified Ashworth Scale; SCIM III: Spinal Cord Independence Measure; ASIA: American Spinal Injury Association; WISCI: Walking Index for Spinal Cord Injury; FIM: Functional Independence Measure. Unfortunately, data for p01 and the initial assessment (w. 0) of p02 were not or partially recorded. Missing values for assistive devices indicate that the participant no longer required any assistive device. * denotes that p03 participant had additionally a left knee peroneal elevator and a left knee brace beside beside the walker.

Participants			**p02**			**p03**			**p06**			**p07**		
Assessments time			**w. 0.**	**w. 6.**	**w. 12.**	**w. 0.**	**w. 6.**	**w. 12.**	**w. 0.**	**w. 6.**	**w. 12.**	**w. 0.**	**w. 6.**	**w. 12.**
Used assistive device			rollator	–	–	walker*	–	–	2 crutch	2 crutch	1 cane	–	–	–
MAS	Quadriceps	left	–	0	0	0	0	0	1	1	0	0	0	0
	Quadriceps	right	–	0	0	0	0	0	1	1	0	0	0	0
	Hamstrings	left	–	0	0	0	0	0	1	1	0	0	0	0
	Hamstrings	right	–	0	0	0	0	0	1	1	0	0	0	0
	Tib. Ant.	left	–	0	0	0	0	0	2	2	1	1	1	0
	Tib. Ant.	right	–	0	0	0	0	0	2	0	0	1	1	0
	Soleus	left	–	0	0	0	0	0	2	2	1	1	1	0
	Soleus	right	–	0	0	0	0	0	2	0	0	1	1	0
SCIM III.	**Self Care**		–	20	20	11	16	16	20	20	20	20	20	20
	Mobility		–	35	35	25	39	39	30	30	31	39	39	40
ASIA Impairment Scale			B	B	D	C	D	D	D	D	D	D	D	D
WISCI			–	20	20	9	20	20	16	16	16	20	20	20
FIM Total			–	124	124	104	119	119	124	124	124	124	124	124
Motor FIM			–	89	89	69	84	84	89	89	89	89	89	89

6 Discussion

6.1 Arm & leg cycling - neural network

6.1.1 Comparison of the predicted and test EMG signals.

The resulting graphs were obtained by our approximation method for an example for asynchronous arm and leg cycling. The applied neural network was trained with data recorded from four participants. The neural network was partially able to estimate the high-amplitude, spike-like elements of the target EMG signals. These spiking and stochastic phenomena are typical hardly determinable features of EMG activity, which should also be taken into account in the evaluation [95]. In consequence, the introduced prediction examples are smoother than their target signals in Figure 5.1.

This phenomena is known in the literature as "spectral bias",as neural networks tend to learn the low-frequency components of signals more easily. Distinction between noise and relevant high frequency features is often difficult. Therefore the networks prefer models with smoother patterns.

Additionally, the use of mean square error (MSE) as a loss function, during the optimization of the network, This metric encourages the network to try to get the expected values of the stochastic process.

The neural network behaves like a low pass filter, which eliminates stochastic and noise-like effects . This may mean that the neural network tries to highlight the general features and patterns of the target signals, which can be beneficial to the construction of a deterministic engineering solution for control.

6.1.2 Comparison of FES activation patterns

For quantitative evaluation, we applied the previously introduced accuracy measure in Eq. 4.2 for the derived control signals for both asynchronous and synchronous cycling. The prediction accuracy shows the average performance with standard deviation and is summarized in Table 5.1. Based on the results, the average predictive performance of the system is weak, although there are some better individual results.

The system's performance was similar during both synchronous and asynchronous cycling. A slight trend toward improved performance was observed only for the asynchronous r. biceps femoris compared to the same muscle in synchronous mode.

6.1.3 Limitations

We suppose that the reasons for the low performance are as follows. Across participants, the EMG variability of the measured muscles is high, which is a commonly appearing problem with this data type. This may suggest different strategies for the implementation of particular cycling tasks. For example, the cycling movement may be maintained by the rhythmic impulse of the quadriceps; therefore, the hamstrings activity could be minimal or where the leg pulls the crank by the hamstrings and pushes it by the quadriceps.

To overcome this issue, the involvement of further participants and the increase of model complexity by additional layers or architectural elements would be required. Maybe even the investigation and construction of subsets of training sets would be beneficial to distinguish the main motor control strategies.

Another reason for the performance limitation is assumed to be that the participants were not able to cycle with exactly the same frequency using their upper and lower limbs, as summarized in Table 5.2. A slight frequency difference almost always exists between the upper and lower cranks. Consequently, continuous phase shifting occurred and accumulated across multiple periods. This shifting corrupted the mapping between the upper and lower limb EMG activity. To avoid this effect, further signal processing techniques should be tested to align the upper and lower cycles.

For example, a reasonable adjustment of the method would be to add the kinematic data such as the actual phase of the upper and lower crank to the input of the neural network. This extra information would help to compensate the phase shift effects and imply a less complex learning problem, where the actual phase is not computed by the neural network itself. We focused only on the EMG data, since our goal was to examine as direct as possible the motor control of participants and investigate whether the information content of the arm muscle's activations can be utilized for the leg cycling as well.

6.1.4 Independent citations

Henrique et al. [96] investigated linear and nonlinear control models for FES cycling, focusing on the relationship between pedal angles and FES activation patterns. They cited our study as prior work that implements a nonlinear control model. Their findings indicate that nonlinear models outperform linear ones, suggesting that FES activation pattern generation is a non-trivial task and that the system behavior is inherently nonlinear.

Rashid et al. also mention our publication as an application of NARX neural network [97].

The following two article highlights the idea to control the FES cycling by the arm cycling of the participants [98], [99].

6.2 Arm & leg cycling – muscle synergy analysis

In this investigation, simultaneous arm & leg cycling and only-arm cycling exercises were performed by able bodied persons. Arm muscle synergies were computed using nonnegative matrix factorization, and the synergies obtained in simultaneous arm & leg cycling and in only-arm cycling were investigated.

6.2.1 Effect of leg cycling on arm muscle coordination

The main aim of this study was to investigate whether leg cycling, added simultaneously to arm cycling, affects arm muscle synergies in able-bodied people. Our results show that there were no significant differences in the muscle synergy vectors or in the activation coefficients between the 2 cycling modes (only-arm cycling and arm & leg cycling). This suggests that the arm muscle coordination is invariant to leg cycling, and the central nervous system employs the same arm muscle coordination strategy, when lower limb activity is added to the examined arm cycling movement. The neural coordination of only-arm cycling is not necessarily influenced by the movement of the body parts, such as the lower limbs, whose main role is locomotion.

This investigation of arm muscle coordination helps to discern how upper-limb motor control is influenced by lower-limb activity and provides insights into sensorimotor integration and has implications in neurorehabilitation. Understanding how leg cycling affects arm coordination is important for designing rehabilitation protocols, including hybrid exercises (e.g. for people with spinal cord injury (SCI) or for stroke survivors).

The literature on the effects of lower limb cycling on upper limb movements and muscle activation is relatively limited compared with that on the effects of arm cycling on leg muscle activation. One study [26] investigated synergies both for arm cycling and leg cycling but not for simultaneous cycling. Biomechanical and electrophysiological methods have been used to investigate the effects of lower limb cycling on upper limb kinematics and muscle activation, leading to various results [74], [100], [101]. Sakamoto investigated the effect of leg cycling cadence on arm cycling cadence and reported that, during simultaneous arm and leg cycling, arm cycling cadence significantly decreased during an instant change in leg cycling cadence. This suggests a neural interaction of the central pattern generator systems that control arm cycling and leg movements.

These studies, which investigated the effect of lower limb cycling on arm muscle activation, considered either kinematic or electrophysiological properties of the studied systems and motor tasks. A novelty of our study is that we applied the muscle synergy approach to investigate whether lower limb cycling influences upper limb muscle coordination. Our results support the assumption that lower limb movement does not significantly influence upper limb muscle coordination during arm cycling.

6.2.2 Effect of crank resistance on muscle coordination

One particular aim of our study was to investigate whether different arm crank resistances require different muscle coordination in terms of muscle synergies. The results revealed that synergies were not affected by crank resistance in either cycling mode or in either the dominant or non-dominant arm. A previous study showed that variance profiles of muscle activation in arm cranking was not affected by crank resistance [31]. The amplitude of muscle activation (assessed by EMG) increases with higher loads, but the activation profile does not necessarily alter.

The EMG signal consists of a combination of activation coefficients and synergy weights, so the magnitude of the activation coefficient is not directly depend on the EMG amplitude. Thus, it is possible that there is a slight difference between the two resistances in both the weights and the activation coefficients, but it is not significant.

The cycling task in our study used low loads which may not provide sufficient stimulus to alter synergies, but higher loads might have caused changes in synergies. Chaytor et al. [102] studied the effect of workload on EMG amplitudes during arm cycling and showed a linear relationship between EMG amplitude of the examined muscles and the power output. Only the slope of the linear relation differed among muscles. However, muscle coordination was not investigated. Esmaeili et al. [103] found high degrees of similarity among muscle synergies in leg cycling across various load conditions, and demonstrated that different mechanical conditions use the same motor control strategies for cycling. If muscle synergies are shared across load conditions in lower-limb cycling, it is reasonable to assume that similar properties may apply to upper-limb cycling.

6.2.3 Effects of cycling mode and crank resistance on VAF values

We assumed that cycling with four limbs is more challenging than cycling only with the arms, and this is reflected in the number of arm muscle synergies that dominantly account for the arm muscle activation variance (VAF). In a recent study, it was shown that for walking tasks, a greater number of synergies are used if the task is more difficult. In particular, leg muscle synergies were assessed and compared during walking on a taped line on the floor and on a 6-cm wide, 2-cm high beam [104]. A greater number of muscle synergies were recruited during beam walking, which was more challenging than tape walking for both young and older participants.

In our study if adding leg cycling to arm cycling leads to a more difficult motor task, that might be associated with a larger number of arm muscle synergies. However, we found that the same number of synergies are able to generate muscle activities with VAF higher than 90% (Figure 3). Arm cycling performed simultaneously with leg cycling may require more attention [74], but from an arm muscle coordination point of view, it does not seem to be more demanding than arm cycling alone.

6.2.4 Implications for rehabilitation

The common neural control of lower limb and upper limb movements has implications for the rehabilitation of patients with SCI. Dietz [105] posited consequences for rehabilitation of task-dependent neuronal linkage of cervical and thoracic–lumbar propriospinal circuits controlling leg and arm movements. Simultaneous arm and leg cycling is an excellent candidate for rehabilitation therapy for patients with incomplete spinal cord injury [105]. The combination of arm and leg cycling in rehabilitation training protocols may result in higher oxygen uptake than cycling by only two limbs. This is a desired goal of cycling exercises [106], [107]. From the aspect of motor control, our present study suggests that arm muscle coordination is preserved while the CNS controls the cyclist's leg movements in addition to arm movement. Arm cycling control can be maintained when training setups are changing. A previous study revealed that arm configuration variance during arm cranking was not affected by changes in crank resistance [31]. Our study suggests that arm muscle coordination in terms of muscle synergies is not affected by crank resistance either. Furthermore, muscle coordination in arm cycling does not depend on additional training setups, such as simultaneous leg cycling.

Here, we provide insights into the relationship between leg cycling and arm cycling control in able-bodied, healthy individuals. In other studies, arm cycling exercises have been used in combination with functional electrical stimulation-assisted leg cycling training (hybrid cycling) in individuals with SCI [60]. Further studies are needed to investigate arm cycling control during hybrid cycling in people with neurological disorders.

6.2.5 Limitations

The gender body structure may differ [108], [109], [110], but for reasons of homogeneity, only female participants' movements were investigated. Although the number of participants is small, this group is homogeneous in terms of age and gender, therefore we assume that our analysis is relevant.

The designed protocol considered that the performance of the arm & leg cycling exercise demanded focused attention from the participants. Therefore, they had a short familiarization time to practice the exercise. Our experience indicated that a randomized ordering of the crank resistance levels would have required significantly longer practicing time, which we aimed to limit in order to avoid the long-term skill acquisition and overlearning of the motor task. In this sense, we had to find a practical compromise to execute our measurement protocol while minimizing the risk of overlearning.

To discard measurement artifacts, cycle selection criteria were applied. The cycle selection process might hide some differences in motor control between conditions. At the same time, high standard deviations resulting from artifacts can also obscure characteristic parameters. We attempted to set the criterion in such a way as to filter out deviant signals while retaining the characteristics of the given cycling setup. The remaining amount of data (on average more than 60 cycles per condition) is still enough for our study based on the recommendations of Turpin et al. [84].

In this study, one flexor–extensor muscle pair was selected for the shoulder, elbow and wrist joints, the most important and strongest flexors and extensors of these joints. Extracting four synergies when recording six muscles seems to be a limited dimension reduction.

Our results show similar synergies of the arm muscles regardless of leg cycling, and support that the findings of arm-only cycling studies are relevant sources for comparison with our work. In this context, interestingly, Cartier et al. [26] identified the same number of muscle synergies from eleven EMG channels.

We believe that comparing synergies and VAF values for movement tasks performed under different setups provides useful information about the possible effects of these setups on the central control of the movement. Even if the considered number of muscles is small and the number of muscles is a limitation of the study, it gives insights into important characteristics of arm cycling coordination during only arm cycling and simultaneous arm and leg cycling motor tasks.

Future studies might focus on the effect of arm cycling on leg muscle synergies as well.

6.3 Hybrid FES cycling training - walking assessment

6.3.1 Effect of Hybrid FES cycling on step length time and speed

Step length

Regarding the average step lengths (Figure 5.7.), a significant increase was found in two out of the five subjects. However, when examining only the average values, an improving trend was observed in four out of five patients. The positive trend is particularly true when investigating the changes in the standard deviation values associated with the average steps. The standard deviation values decreased for all patients, which indicates a positive development from a motor control perspective [111], [112].

Based on these findings, it can be hypothesized that positive development in step lengths occurred in more than two subjects, despite the limited amount of data is available for a statistically significant demonstration of this trend.

This hypothesis is further supported by the fact that when the average step lengths are separated for the left and right legs (Figure 5.8.), the number of statistically demonstrable differences further decreases. A statistically significant difference is only observed in the left leg of patient p01 and the right leg of patient p03. This might suggest a different progression between the legs. However, the data for these two specific subjects do not support this strong dissimilarity.

The hypothesis is also supported by a comparison with the average step time and step velocity parameters, which will be discussed in the following subsections.

Step time

Regarding the average step time, a statistically significant improvement was demonstrable in four out of the five patients (Figure 5.9.). It should be noted that patient p02 exhibited a significant difference only during the initial six-week treatment period. Furthermore, participant p07 showed no significant change in this parameter.

The Figure 5.10 shows the separated step time for the left and right legs.

Less significant differences were detected for the separated legs. p02 and p07 did not have any significant changes for the left and the right legs.

An intriguing finding is that the average step time for all subjects converged to very similar values by the end of the training. Biomechanical considerations may explain this, assuming that, subjects have nearly identical leg lengths and that the step's swing phase can be approximated by a simple pendulum. Therefore, the oscillation time should be similar [113].

Based on this premise, the stability of subject p07's condition suggests that the individual's step time was already relatively optimal at the start of the training, so the potential for significant improvement was small.

The standard deviations decreased for all patients by the end of the training, including patient p07. This leads to the conclusion that the step times became more regulated, and the gait of all individuals showed improvement based on this parameter as well.

Step speed

The average step speed significantly improved for four out of five subjects by the end of the training (Figure 5.11.). For patient p02, a positive change in the average value was observed, but this was not statistically demonstrable.

Due to the limited data quantity, fewer significant changes were observed when the data was separated by side (Figure 5.11.).

It should, be noted that patient p06 exhibited an asymmetry in step velocities between the two sides; while the left-sided steps were faster and showed a demonstrable significant difference, this was not apparent on the right side. Consequently, the aggregated significant improvement at Figure 5.11. can be primarily attributed to the enhancement of the left leg's performance.

No clear trend was evident in the changes of the standard deviations during the training, although the premise that smaller standard deviations indicate better motor control holds true here as well. This aggregated positive change was observed between the first and last measurement occasions for patients p02, p03, and p06.

Patient p06 demonstrated a negative, increasing change in standard deviation of the right leg, which suggests an asymmetry resulting from the change in assistive device (from crutch to walking stick).

For subjects p01 and p07, a favorable decrease in standard deviation was observed between the first and last assessments for the right leg.

The relationship of step time, length and speed

Based on the aggregated left and right leg figures, the highest number of statistically significant changes was observed for the average step speed, followed by the average step time, and finally the average step length. Among the three parameters, the average step time exhibited a convergence across all patients by the end of the training. Furthermore, in terms of aggregated significant differences, the step time lagged only slightly behind the step velocity, and in the separated left-right leg breakdown, more significant differences were observed for step time.

This observation leads to the hypothesis that during rehabilitation, human motor control tends to prioritize achieving a relatively fixed step time over step lengths, which shows a much larger variance.

Regarding the aggregated step speed, patient p07 showed a significant increase in velocity, even though the changes in the total average step lengths and step times were not significant. This outcome may be caused by the noise reduction from the division operation ($velocity = length/time$), which was primarily able to reveal an improvement originating from the increase in step time. This result further supports the assumption that there were positive, although statistically non-significant, changes in the average step lengths as well.

6.3.2 Effect of Hybrid FES cycling on Cop length and jerk

CoP progression length

The average length of the Center of Pressure (CoP) curves decreased for all subjects, with a statistically significant reduction observed in four out of five subjects by the end of the training (Figure 5.13.). Individual variations were observed in the magnitude of the standard deviations. Figure 5.14 presents the CoP curve length separated for the left and right legs. It only shows a significant change for subjects p02 and p03.

The average values for both the left and right legs decreased for all subjects except for the left side of p06. The standard deviation of CoP length remained stable for p01, while it decreased for p02, p03, and p07 after 12 weeks. Notably, P06 displayed asymmetry between the left and right legs in both mean and standard deviation, which is likely attributable to a change in the assistive device used.

The length of the CoP curves is generally inversely proportional to increased stability during static tasks [114]. Similarly, in case of gait, increased walking speed can also lead to a decrease in curve length.

An interesting analog result was published by Chiu et al. [115]. They found that the percentage of COP progression time decreased in mid-stance, which begins with the contralateral toe off and ends when the CoP is directly over the reference foot.

In our cases, the reduction of CoP lengths align with the changes observed in step time, length and speed parameters discussed previously.

However, not just the CoP length but the smoothness of the CoP progression can also indicate the walking stability and control. It is true especially in case of patients.

Jerk of CoP progression

A statistically significant reduction in total CoP jerk was observed across all participants. Only p02 has not got statistically significant improvement before and after the training.

Due to the limited data quantity, fewer significant differences were observed between the left and right sides. Based on these and the total jerk outcomes, it can be concluded that the smoothness of the subjects' CoP curves increased.

Furthermore, it is noteworthy that this metric revealed strong asymmetries in nearly all subjects.

Discussion the CoP length and jerk in context

In general, the length of the patients' CoP curves decreased, and their smoothness increased, alongside an increase in average step speed. Therefore, it can be assumed that the point of application of the ground reaction forces during stepping changed more smoothly, resulting in a more consistent change in the direction of the forces acting on the body. Based on these findings, we hypothesize that the balance of the individuals improved.

6.3.3 Effect of Hybrid FES cycling on Ground Reaction Forces

Regarding the Maximum Absolute Ground Reaction Force (GRF), a statistically significant increase between the first and last measurements was observed only in patient p03 for the X (mediolateral) and Y (anterior-posterior) components. Conversely, an increase in the vertical components was observed in all subjects except patient p07. These changes align with the observation that patient p02, p03, and p06 either ceased using (p02, p03) or switched (p06) assistive devices, implying that weight support was primarily or entirely managed by their own musculature.

Based on this, the magnitude interval of the forces exerted in the X and Y directions does not necessarily change during gait rehabilitation. However, strong improvement can occur in the vertical direction, demonstrating that the skeletal muscles are increasingly capable of counteracting the body's mass with greater forces against the ground.

A further interesting observation is that although the mediolateral and anterior-posterior ground reaction forces did not increase, the subjects' average step velocity improved in almost every case. This implies the assumption that either the subjects' body mass decreased or their gait efficiency must have increased. Based on the positive changes observed in the other metrics, it can be hypothesized that the subjects' gait efficiency improved.

6.3.4 Changes of EMG activity during the Hybrid FES cycling

The regularity of the EMG signals were investigated by the application of the Sample Entropy (SampEn) for each gait cycle. The aggregated mean and standard deviation of the SampEn values were calculated.

The clinical interpretation of SampEn depends heavily on the type of injury. For instance, following a stroke, an increase in SampEn is beneficial after successful motor rehabilitation [116], [117]. In this context, signal regularity is associated with the rigidity and lack of responsiveness in the patient's motor control to the environmental changes; therefore, an increasing entropy reflects a higher complexity of the underlying neural control. This reasoning is based on the fact that most strokes affect the motor cortex, therefore fine motor commands become more stereotypical and less complex compared to able-bodied participants.

In the case of an incomplete spinal cord injury, the damage mostly affects the transmission of motor commands rather than their generation, resulting in noisier signals. Therefore, a decrease in entropy indicates an increased quality of signal transmission. The work of Li et al. support this idea although they do not find significant mean entropy difference between the iSCI and healthy groups [118]. It must be noted that, they focused on micro level characteristics of the EMG signals, which means that they recorded with 2000 Hz sampling frequency and did not apply any rectification or smoothing on their data.

In this thesis, the assessment focused on the macro-level functional changes of the signals and filtering and smoothing were applied. Therefore, in the case of highly automated cyclic motions such as human gait, a decrease in mean SampEn values at the end of the rehabilitation training compared to the baseline is considered a beneficial development, the regularity of the timeseries is reciprocal by the SampEn values.

Additionally, the decrease of the standard deviation of the SampEn values denotes the increased repeatability of muscle activity between gait cycles. Therefore it could indicate consistent muscle activity and walking ability during the gait.

Participants p01 and p03 had decreased mean and standard deviation values for almost all observed muscles. Only the left rectus femoris (RF) muscle of p01 had a small increase in the mean value. Despite this, both participants had improved regularity of the EMG activity in the knee extensor and flexor muscles.

In the case of participant p02, the mean values decreased or stabilized, except for the right biceps femoris (BF). Interestingly, the other knee flexor muscle, the semitendinosus (Smt), showed improvement. This may indicate a functional shift in knee flexion control toward the Smt.

Beside that, there are muscles, which had increasing standard deviation. This increased variability may be caused by the absence of the use of rollator or increased walking speed. The evaluation of these changes require the involvement of biomechanical data as well.

For participant p06, a notable reciprocal asymmetry is observable between the two sides regarding the knee flexor and extensor muscles. The knee flexor muscles showed a marked difference in SampEn values, the left flexors exhibiting higher entropy compared to the right side. In contrast, in two out of three knee extensor muscles, the SampEn values were smaller on the left side compared to the right.

The asymmetry of gait parameters commonly reflect the asymmetrical weight-bearing, in everyday terms "limping" of the participant. This gait abnormality, is usually caused by muscle weakness or pain [119]. Usually, the stance phase of the gait cycle is shortening. During the stance phase the knee extensor muscles have an important role. Based on the SampEn outcomes of p06, he used more stable and reliably his left leg which gave opportunity to the right leg's knee felxors to operate smoothly during the anti-phase of the gait cycle.

Overall, the regularity of the muscle activity is improved for p06, although there are muscles (e.g. left biceps femoris (BF) and right vastus lateralis (VL)) which had a small increase in irregularity.

For participant p07, the SampEn values mostly improved or remained stable; however, it is difficult to identify a general pattern in these changes. On both sides, the mean and standard deviation values of the rectus femoris (RF) muscles increased, particularly in the left leg. This clearly indicates a decline in the regularity of muscle activity. Similar to the case of p02, this may indicate the shift of primacy in the control of the knee felxor muscles, which means that the vastus lateralis (VL) and vastus medialis (VM) muscles are more involved in the control of the knee extension. This assumption is supported by the fact that his general walking ability is strongly improved based on the biomechanical outcomes.

6.3.5 Comparison of changes in biomechanical and EMG parameters

In the evaluation of patients' walking ability, the combined interpretation of biomechanical and electrophysiological data can be valuable. It makes it possible to study the connection between motor control and executed movements. In this work I interpret together the previously introduced biomechanical and the SampEn of the EMG data.

In most cases, the average SampEn values decreased or stabilized. The most pronounced improvement was observed in participant p03. In his case, all biomechanical and SampEn values showed outstanding positive changes, reflecting a clear improvement in walking ability.

A similar but less marked trend was observed in participants p01, p02, and p06. Generally, their biomechanical parameters also improved, with negative changes in SampEn values found in only a few isolated cases. Specifically, increased entropy was observed in the left rectus femoris (RF) for p01, the right biceps femoris (BF) for p02, and the left vastus medialis (VM) for p06. These increased entropy values have individual causes (See Figure 5.20).

In the case of p01, a slightly increased asymmetry of SampEn but a more stable gait was found after twelve weeks. This is supported by the decreased standard deviation of the SampEn values at the 12th week and the non-significant, mild asymmetry of the mediolateral (x-axis) ground reaction forces and total jerk values.

Participant p02 had a clear negative change in their right BF SampEn value. This requires further clinical and gait analysis. Since it affects only one side of the participant, it is not a systematic weakening of the control system, but most probably the effect of a compensatory mechanism or an injured proprioceptive pathway. This assumption is supported by the slight asymmetry of the CoP length and the mediolateral (x-axis) and anterioposterior (y-axis) components of the GRF.

In the case of p06, the vastus medialis (VM) muscle had a small increase in the SampEn. This increase was probably caused by the change in walking aids which is reflected in the asymmetry of CoP parameters and mediolateral (x-axis) ground reaction forces.

Participant p07 had an interesting phenomena. His biomechnaical parameters improved, while both of his rectus femoris (RF) and his right semitendinosus (Smt) muscles had worsening entropy values. In his case as well, further clinical and gait assessments would be required to get clear answer and resolve this contradiction.

Most probably, his walking ability improved but did not develop into autonomous motor control. So the walking requires active attention and voluntary control of the legs which is mentally demanding and slows the creation of a fine tuned neural control.

Note that the RF muscle participates not only in knee extension but also in hip stabilization. Therefore, increased instability in trunk control can influence the activation of the RF muscle. Another or additional reason could be the decreased proprioception of the participant, which is highly common in patients with iSCI. This can lead to reduced control over the body even in case of the Smt muscle.

6.3.6 Overall walking ability changes of the participants

The summary of gait parameters for all five patients reveals that step length and step time changed in such a way that step velocity increased in every case. Moreover, this increase was statistically significant for four of the five patients.

For this three parameters (step length, step time, and step speed), the values either remained stable or changed in a positive direction, with the single exception of subject p06. In subject p06, step length decreased. However, a more rapid decrease in step time resulted a significant improvement in step speed.

Comparing these results with the length and jerk of the CoP progression curves, it can be observed that the CoP parameters demonstrate a positive development for all patients, with a significant change noted in nearly every instance. These findings suggest that all subjects have improved walking ability, in both step velocity and dynamic.

The change in the maximum absolute values of the Ground Reaction Forces (GRFs) in the x (lateral-medial) and y (anterior-posterior) directions was not statistically significant for any patient, with the exception of subject p03.

However, given the simultaneous increase in step speed, the participants were able to achieve a higher step speed using the same average magnitude of muscular force in the x and y directions. Therefore, the movement became more efficient in these directions.

The vertical (z-direction) Ground Reaction Forces exhibited a significant increase in four out of five cases. It is hypothesized that this increase is attributable to enhanced body support capability.

The changes in SampEn values are in line with the biomechanical parameter changes of participants p01, p02, p03, and p06. Participant p02 showed low SampEn values with mild improvements; similarly, this participant had mild, statistically non-significant improvements in other biomechanical parameters as well. In the case of p07, the biomechanical parameters showed improvement, which was not confirmed by the SampEn results.

Excluding the MAS scores and comparing our findings with other clinical assessments, it becomes evident that most clinical tests had lower resolution for describing walking ability than biomechanical measurements.

The only exception was p03, who showed improvement in every clinical parameter and showed the most significant improvements in the measured biomechanical parameters as well. For all other participants, clinical scores remained almost entirely unchanged.

In case of Modified Asworth Scale (MAS), those patients who had spasticity, the chances of spastic muscle tone can be tracked throughout the 12-week training. These improvements aligned with the positive trends observed in the biomechanical parameters.

At the same time, it remains an open question how the MAS, which describes muscle tone, relates to the SampEn, which measures the regularity of muscle activity.

The SampEn is even measurable even in cases, when MAS score indicates healthy thone (score 0). For example, p03 who had strong SampEn changes. In other cases, such as participants p06 and p07, both metrics changed over the 12-week period, yet their outcomes did not follow the same trend. The interpretation of these features may require further investigation. A few relatively recent but methodologically different work have already begun to address these topics [120], [121].

In summary, the collective analysis of the dynamic and kinematic parameters indicates an improvement in the patients' condition, with individual parameters either remaining stable or showing positive change. These data are inline with the results of clinical test but provide a more detailed resolution of the patients rehabilitation progress.

6.3.7 Comparison with other studies of FES cycling training

The study by Yasar et al. [71] involved non-acute individuals with iSCI ($n = 15$). The participants underwent FES cycling training three times a week for one hour per session. The parameters measured in their work included average gait speed (v), step length (l), and stepping cadence (steps/minute), are comparable to the results discussed in the present work. Based on a comparison with the data we collected, the conventional FES leg cycling training demonstrated a slight improvement, showing a 10–15% gain ($\alpha < 0.05$). However, It did not show a statistically significant improvement at the group level. Unfortunately, no detailed information regarding the magnitude of individual progression rates was provided

In the five individuals we followed up, two out of the five subjects showed a significant improvement in both average step length and average gait speed. However, a significant increase in gait speed was observed in four out of five cases.

It is important to note, that the patients I studied were in the subacute phase of injury, which means they were within the one year post-injury time interval, which constitutes a significant physiological difference.

Also important to note that, our participants had received only the hybrid FES cycling training twice weekly for half an hour per session .

Table 6.1: Data from the work of Yasar et al. [71]. The mean (μ) and standard deviation (SD) of the parameters across participants. * Note that step time is a derived quantity from the originally published cadence values.

Parameters	**week 0.** ($\mu \pm SD$)	**week 12.** ($\mu \pm SD$)
Gait speed $[m/s]$	0.38 ± 0.24	0.44 ± 0.25
Step length $[m]$	0.36 ± 0.12	0.40 ± 0.13
Step time* $[s]$	1.02 ± 0.33	0.94 ± 0.29

Another important study that investigated the effect of FES cycling on the change in condition of individuals with partial spinal cord injury was the work of Duffell et al. [122]. This study included both acute and non-acute spinal cord injured subjects. The paper demonstrated improvement in certain clinical and performance parameters; however, since biomechanical parameters were not examined, the results cannot be compared.

The work most closely related to the one presented here is the article by Zhou et al., which provides detailed changes in clinical, biomechanical, and EMG parameters during the comparison of conventional and hybrid FES cycling training. This study involved seven non-acute individuals with iSCI (incomplete spinal cord injury) who received hybrid FES cycling therapy.

The results obtained by the authors pre- and post-training are as follows: the average step length of the stronger leg increased from 0.41 m to 0.47 m; the average step time significantly decreased from 1.47 to 1.13 seconds. Furthermore, the average gait velocity significantly increased from 0.27 m/s to 0.44 m/s.

Comparing these results with the findings presented in this thesis, it can be stated that the patients investigated by Zhou et al. started and finished the program with poorer walking ability compared with our participants. It is noteworthy that the patients' average gait velocity increased by 50% based on the 10-meter walk tests, and by 62% based on the biomechanical measurements.

The patients investigated by our group, demonstrated a significant 35% step speed improvement. While this rate of improvement is lower than that reported by Zhou et al., several significant differences are observable between the two cohorts. Our protocol used hybrid FES cycling for 30 minutes, twice a week, while Zhou et al. employed a much more intensive protocol of one hour, five times a week. Our patients also started the training in a better baseline condition, which likely accounts for the smaller rate of improvement observed. On the other hand, it should be noted that our patients were acute individuals.

The article by Zhou et al. did not report any information on the participants' dynamic gait parameters (GRF and CoP). To the best of our knowledge, the inclusion of these data in the present thesis provides entirely novel findings.The clinical Berg Balance Scale [123] assessed by Zhou et al. may serve as a reference point. Based on this, a significant increase can be demonstrated in patients who participated in hybrid FES cycling therapy. This finding is in line with the improvements we observed in the dynamic gait parameters.

6.3.8 Limitations

A limitation of this section is the current lack of a control group to validate our results. Our research group is actively working on the recruitment and data processing for such a group. However, as a reference, Zhou et al. [60] also investigated the effects of hybrid FES cycling and reported data from a reference group. Based on this information, the positive improvements found in our participants are comparable to the outcomes of their participants who received hybrid FES cycling.

Furthermore, comparative data obtained from able-bodied individuals would provide an interesting basis for comparison as well. I am also aware that the number of step cycles are small obtained from the gait assessments; however, there are examples in the literature of gait analysis performed on small datasets [89], [124]. A limiting factor in collecting a higher number of step cycles is the physical condition and fatigue of the patients. To ensure patient safety and avoid falls or accidents, our research group limited the assessments to only a limited number of measurement trials.

I am also aware of the fact that the CoP jerk parameter inherently and reciprocally depends on the walking speed of the participants. Therefore, it is hard to distinguish between the stabilizing effect of a higher walking speed and the improved motor control of the participants. Nevertheless, the normalization of the jerk parameter is not straightforward, as multiple methods of normalization are known from the literature for this problem [125], [126], [127]. Investigating the best normalization method for this parameter is a subject for future work. Despite this limitation, it is reasonable to assume that in the context of the other biomechanical and clinical parameters, My results show relevant improvements in the participants' walking ability.

6.4 Comprehensive aspects of neurorehabilitation

The results of my thesis explore the potential of hybrid FES cycling training in the gait rehabilitation of patients with spinal cord injury by integrating three complementary approaches: technological, neuro-mechanical, and clinical.

The first approach involves predicting lower limb muscle activity based on information gained from upper limb EMG signals. This method introduces a novel control idea of the FES assisted leg cycling. The advantage of this method compared to classical mechatronic solutions—such as encoder-based crank position control—is that the synchronized timing between upper-limb motor control and lower-limb FES cycling control signals can be utilized to develop Hebbian-learning-based motor rehabilitation paradigms for spinal cord-injured and potentially stroke-surviving participants.

These preliminary results provide a good reference to work out a real word clinical application as well.

The second approach investigated whether muscle synergies of arm cycling are influenced by simultaneous leg cycling. Our results showed no effect on arm muscle synergies during leg cycling. These findings support the hypothesis that information flow is directed from the arms (proximal limbs) toward the legs (distal limbs), or that bidirectional interaction only occurs during changes in phase or frequency between the upper and lower limbs. These findings can inform the design of physiotherapy training for iSCI patients. For example, in the case of participants with paraplegia, the muscle coordination during arm cycling is stable and probably similar to the motor control of able-bodied participants. Therefore, the idea of using arm cycling data from participants with unimpaired upper-limb mobility to control the disabled lower limbs—as in the case of my neural network-based first approach—is valid.

Furthermore, it is feasible to combine the knowledge gained from the first and second approaches. It is possible to reduce the dimensionality and the noise of the six recorded EMG channels into four dimensions by applying the NNMF algorithm. Then, the time series of the four synergy coefficients should be used for the training of the neural network.

The third approach examines the non-time-intensive clinical application of hybrid FES cycling by assessing the walking ability of iSCI patients who received this supplementary training. The results indicate that while the improvement in walking ability was smaller in absolute terms than in the reference study by Zhou et al. [60], it remained within a similar order of magnitude. Notably, considering the proportionally lower time intensity, the relative improvement was higher. This time efficiency makes it possible to incorporate this training into standard rehabilitation procedures, making it accessible to broader patient groups. In the USA and Canada, around 14000 new spinal cord injuries (SCI) are registered annually; approximately two-thirds of these patients have incomplete injuries [58], [59], who could benefit from hybrid FES cycling. Moreover, the optimization of the method, based on the proper timing of upper and lower limb cycling by the introduced neural network FES control, could potentially further improve training efficiency.

7 Conclusion

7.1 New scientific results

Thesis 1.

Question 1, Is there a detectable neural interlimb coordination between the arms and legs during simultaneous arm cranking and leg cycling motor tasks?

Response to Question 1,

The neural network-based approach indirectly indicates that arm muscle activities contain information relevant to the regulation of leg muscles and could be transferred to control leg muscle activities. Conversely, the muscle synergy-based approach detected no significant effect propagating from the legs toward the arms during constant frequency arm and leg cycling. [J2], [J3].

These results are in line with the following interpretation of the common motor control of the upper and lower limbs:

- Beyond reflex-level connections, modulatory influences act primarily from the arms toward the legs during stationary rhythmic arm and leg movements.

Thesis point based on Objective 1a,

I have developed a neural network which was capable of learning and estimating the activity of specific knee extensor and flexor muscles based on the EMG activity of the arm muscles. Although the prediction accuracy was insufficient to generate a unipolar FES (Functional Electrical Stimulation) stimulation pattern, further refinement remains highly relevant for the automation of muscle stimulation during FES assisted leg cycling.

The accuracy of the model's learning capabilities was primarily limited by the inconsistent frequency and phase synchronization between the arms and legs, caused by natural movement variability and fluctuations in the subjects' attention. Despite these factors, the neural network demonstrated partial learning, suggesting that EMG data collected from the arms can be utilized—at least partially—to control leg muscles during simultaneous arm and leg cycling tasks. Given that this study utilized a relatively small and limited dataset across multiple subjects, it can be assumed that the significantly more complex architecture of a nervous system may also be capable of co-controlling the arm and leg muscles [J2].

Thesis point based on Objective 1b,

I have found no statistically significant differences in upper-limb muscle synergies between arm cranking alone and simultaneous arm and leg cycling at a steady-state cadence, using Non-Negative Matrix Factorization (NNMF) for the analysis. However, these findings do not exclude the reflex-level modulation or modulation of upper-limb motor control induced by the variable-frequency movement of the lower extremities [J3].

Thesis 2.

Question 2, How do the ground reaction forces during walking change in case of incomplete spinal cord injured participants who, in addition to the conventional rehabilitation therapies, participated in simultaneous voluntary arm cranking and functional electrical stimulation-assisted leg cycling (hybrid FES cycling) training?

Response to Question 2,

I have designed a measurement protocol to discern gait characteristics and I have presented the changes of ground reaction force related dynamic parameters in particular the length and smoothness of center of pressure (CoP) progression in cases of iSCI participants who received hybrid FES cycling training. After twelve weeks, the GRF was acting more consistently on a shorter and smoother paths for all participants compared to the initial values. These results also support that the walking ability of the participants become more stable and controlled [C1], [C2], [C3], [C4].

Thesis point based on Objective 2,

I have pointed out that the lengths of CoP progression curves decreased for all participants and the changes were significant for four out of five participants at the end of the training based on the combined data from both sides. Similarly, CoP total jerk decreased for all patients, with the reduction being significant in four out of five cases according to the combined data from both sides.

My analysis indicates that the medio-lateral (x-axis) components of the GRF show individual-specific variations in the changes of maximum absolute values. For the anterio-posterior (y-axis) components, results showed either stagnation or a slight increase between the beginning and the end of the training. Regarding the vertical (z-axis) components, three out of five subjects showed a clear significant increase, while one subject exhibited a significant increase specifically in the left leg. One subject showed stagnation or a slight decrease in this parameter.

Based on these results, the increase in force production is primarily characteristic of the vertical component. This suggests an enhanced capacity for weight-bearing during gait. Meanwhile, the time course of the application point of the GRF became smoother. When interpreted alongside classical biomechanical parameters and clinical scores, my findings indicate that patients' walking ability became more stable while their gait speed increased.

7.2 Future plan

Regarding the neural network-based mapping between the EMG of upper and lower limbs, I will further refine the data curation and preprocessing steps with the application of NNMF to reduce the noise and dimensionality of the data before to the neural network training. I also plan to align the segmented EMG periods of upper and lower limb cycling according to their phase to achieve a more consistent mapping between the time series. As one version of the neural network, I will test the application to add the upper and lower crank position of the ergometer to the input of the neural network.

I am aware of the limited number of participant of this method, therefore I intend to incorporate data from additional participants into the training process. This extended dataset will be utilized to enhance the generalization and learning performance of the neural network.

Finally, I plan to investigate the mapping between the legs to the arms in the opposite direction as well to gain a symmetrical knowledge with these approaches.

Non-negative Matrix Factorization (NMF)-based muscle synergy analysis is one of the most common and standardized approaches for the mathematical modeling of muscle co-activations during motor tasks. However, a significant limitation of this method is its limited ability to detect and represent transitions between different cycling tasks. NMF tends to mask or suppress short-term temporal changes and slow, gradual trends. To overcome these limitations, I plan to apply an alternative dimensionality reduction method known as Tensor Factorization. Unlike NMF, this method factorizes the data into at least three matrices instead of two. In the context of my research, the third matrix will describe the temporal variations of the muscle synergies and relationships of between them. This additional information will be really valuable for extending our knowledge, particularly when the cycling frequency or phase of the upper or lower limbs changes. Building on our recent results, my goal is to further investigate the reciprocal influence of upper and lower limb cycling across varying cycling modes.

I intend to continue the investigation and assessment of hybrid FES cycling effects on the walking ability of individuals with iSCI. I plan to recruit additional participants to increase the sample size and establish a control group. Furthermore, I aim to compare the calculated parameters between our iSCI patient cohort and a new group of stroke patients. For this purpose, I will utilize the OpenGait database, which contains EMG and biomechanical data from chronic stroke survivors. It is interesting to compare these groups because these two patient groups represent different hierarchical levels of injury. Consequently, it will be possible to investigate whether these distinct types of neurological impairments are reflected in injury-specific features.

List of Publications

List of journal publications

[J1] M. Mravcsik, A. Fodor, **B. Radeleczki**, M. Feher, P. Cserhati, A. Klauber, J. Laczko, and L. Botzheim, “Retrospective analysis of cardiovascular effects of fes cycling in people with complete and incomplete spinal cord injury”, *Journal of Clinical Medicine*, vol. 15, no. 5, p. 1967, 2026. DOI: 10.3390/jcm15051967.

[J2] **B. Radeleczki**, M. Mravcsik, L. Bozheim, and J. Laczko, “Prediction of leg muscle activities from arm muscle activities in arm and leg cycling”, *The Anatomical Record*, vol. 306, no. 4, pp. 710–719, 2023. DOI: 10.1002/ar.25004.

[J3] L. Botzheim, **B. Radeleczki**, M. Mravcsik, J. L. Pons, F. O. Barroso, and J. Laczko, “Assessment of the influence of lower limb cycling on arm muscle coordination during upper limb cycling: A pilot study”, *Journal of NeuroEngineering and Rehabilitation*, vol. 23, p. 151, 2026, ISSN: 1743-0003. DOI: 10.1186/s12984-026-01959-y.

[J4] **B. Radeleczki**, N. Nagy, M. Mravcsik, P. Szemeredi, M. Futo, L. Ware, M. Faher, A. Klauber, P. Cserhati, J. Laczko, and L. Botzheim, “A hibrid fes-kerékpározó terápia szerepe részleges gerincvelősérültek rehabilitációjában – esettanulmány”, *A Magyar Rehabilitációs Társaság Folyóirata*, vol. 34, no. 1, pp. 10–17, 2024.

List of conference publications

[C1] L. Botzheim, **B. Radeleczki**, M. Feher, P. Cserhati, and J. Laczko, “Computational methods to support clinical assessment in examination of walking ability”, in *2025 47th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, IEEE, 2025, pp. 1–6.

[C2] **B. Radeleczki**, M. Feher, M. Mravcsik, J. Laczko, J. L. Pons, and L. Botzheim, “Kinesiological gait parameter changes in two incomplete spinal cord injured patients due to hybrid arm and leg cycling therapy–pilot study”, in *International Conference on NeuroRehabilitation*, Springer, 2024, pp. 15–19.

[C3] **B. Radeleczki**, L. Botzheim, N. Nagy, J. Laczko, and M. Mravcsik, “Change of ground reaction force and center of pressure in walking of spinal cord injured patients after fes cycling training”, in *Progress in Clinical Motor Control II.*, Shirley Ryan AbilityLab, 2023, p. 120.

[C4] L. Botzheim, **B. Radeleczki**, A. Fodor, M. Feher, and J. Laczko, “Jerk analysis of gait in persons with incomplete spinal cord injury: A study about the effect of hybrid arm and leg cycling”, in *International Scientific Conference Motor Control 2024: From Theory To Applications*, The International Society of Motor Control, 2024, p. 16.

[C5] L. Botzheim, **B. Radeleczki**, M. Mravcsik, F. O. BArosso, and J. Laczko, “Investigation of muscle synergies during simultaneous arm-leg cycling – case study”, in *Progress in Motor Control XIV*, The International Society of Motor Control, 2023, p. 75.

[C6] P. Mayer, N. Zentai, M. Mravcsik, H. Bartok, **B. Radeleczki**, and J. Laczko, “The effect of body position on the spasticity of quadriceps muscle after spinal cord injury. program no. 303.15 neuroscience meeting planner. san diego”, *CA: Society for Neuroscience*, 2022.

List of other publications

[O1] **B. Radeleczki** and J. Laczko, “Cycling frequencies in simultaneous arm and leg cycling”, in *Summer School on Neurorehabilitation*, Springer, 2022, pp. 137–141.

[O2] **B. Radeleczki**, “Biomechanical changes in gait of incomplete spinal cord injured patients after fes cycling therapy”, in *Phd Proceedings Annual Issues of The Doctoral School Faculty Of Information Technology and Bionics*, Pazmany Peter Catholic University, 2024, p. 1.

[O3] **B. Radeleczki**, “Theoretical and applied studies on the cyclic movements of human limbs”, in *Phd Proceedings Annual Issues of The Doctoral School Faculty Of Information Technology and Bionics*, Pazmany Peter Catholic University, 2023, p. 1.

[O4] **B. Radeleczki**, “Human movement analysis to improve control algorithms”, in *Phd Proceedings Annual Issues of The Doctoral School Faculty Of Information Technology and Bionics*, Pazmany Peter Catholic University, 2022, p. 1.

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