The organisation of the neuromuscular responses to the presence of perturbations during the execution of balance training exercises

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Abstract

Though moving over diverse terrain conditions has been an integral part of human evolution, falls are today the second leading cause of unintentional injury and death worldwide. Moreover, some fall-related injuries can significantly impair mobility, independence and quality of life, and the financial consequences of falls for any healthcare system represent a massive burden. The causes of falls are manifold. Yet, most fall result from a failed response to unexpected perturbations such as a trip or slip. Thus, populations with a diminished response capacity exhibit an increased risk of falling and getting injured. As the ongoing demographic change leads to a global population's ageing, there is a consensus about the need for effective strategies to reduce the number of falls. Amid many existing intervention paradigms targeting the causes and risk of falls, exercise-based interventions are the most cost-effective. However, different training approaches yield different outcomes. As most training approaches have a limited transfer of the improved balance skills to untrained situations, elements like retention rate and dose-response relationship are yet to be determined. Furthermore, the underlying mechanisms of effective training interventions are still not fully understood.

Nonetheless, training the execution of the fundamental balance recovery mechanism (i.e., counterrotating body segments and increasing the base of support) in the presence of perturbations has been reported to improve balance recovery performance in both trained and non-trained situations. Moreover, it also increases the force-generating capacities of the lower limb muscles, further promoting the execution of balance recovery reactions. Based on these promising results, this thesis endeavours to provide insight into the fundamental elements promoting the neuromechanical adaptations underpinning the reported advantages of training the balance recovery mechanism in the presence of perturbations.

The modular organisation of the neuromotor responses, assessed through the analysis of muscle synergies, revealed different strategies to cope with perturbations and increase robustness when performing exercises promoting the execution of the balance-recovery mechanism on unstable surfaces. The selection of the strategy is likely governed by elements such as the characteristics and the timing of the perturbation as well as the characteristics of the task, its constraints and the perceived challenge to balance. Moreover, performing exercises promoting the execution of the balance-recovery mechanism on unstable surfaces showed no indication of an increased mechanical demand on the lower limb muscles. Therefore, robustness can emerge as a consequence of different modulations of muscle synergies that depends on several factors such as the characteristics of the task and the individual capacities. Moreover, training on unstable surfaces does not increase the mechanical demands upon the leg muscles per-se. Thus the gains in muscle force observed after training the fundamental mechanism of balance recovery onto unstable surfaces are likely a consequence of neural adaptations.

Keywords: Muscle synergies, Motor Control, Fall-prevention, Perturbations, Balance training

Zusammenfassung

Obwohl die Fortbewegung auf unterschiedlichem Terrain ein wesentlicher Bestandteil der menschlichen Evolution war, sind Stürze heute weltweit die zweithäufigste Ursache für Verletzungen und Todesfälle. Darüber hinaus können sturzbedingte Verletzungen die Mobilität, Unabhängigkeit und Lebensqualität erheblich beeinträchtigen, und stellen durch ihre finanziellen Folgen eine massive Belastung für jedes Gesundheitssystem dar.

Die Ursachen für Stürze sind vielfältig. Die meisten resultieren aus einer fehlgeschlagenen Reaktion auf unerwartete Störungen der Fortbewegung, wie z. B. Stolpern oder Ausrutschen. Personen mit eingeschränkter Reaktionsfähigkeit weisen daher ein erhöhtes Sturz- und Verletzungsrisiko auf. Da der fortschreitende demografische Wandel zu einem zunehmenden Anstieg der weltweiten Lebenserwartung führt, besteht ein Konsens darüber, dass wirksame Maßnahmen zur Sturzprophylaxe zwingend erforderlich sind, um die Zahl an Stürzen zu verringern. Unter den vielen bestehenden Interventionsmodellen, die auf die Ursachen und das Risiko von Stürzen abzielen, sind bewegungsbasierte Interventionen die kosteneffektivsten. Verschiedene Trainingsansätze führen jedoch zu unterschiedlichen Ergebnissen. Da bei den meisten Trainingsansätzen die verbesserte Gleichgewichtsfähigkeit nur begrenzt auf untrainierte Situationen übertragen werden kann, müssen Faktoren, wie die Retention und die Dosis-Wirkungs-Beziehung noch ermittelt werden. Des Weiteren sind die Mechanismen, welche den wirksamen Trainingsmaßnahmen zugrunde liegen, noch nicht vollständig erforscht. Nichtsdestotrotz wurde berichtet, dass ein Training der grundlegenden Mechanismen zur Wiederherstellung des Gleichgewichts (d. h. die Gegenrotation von Körpersegmenten und die Modulation der Unterstützungsfläche) unter instabilen Bedingungen, sowohl unter den trainierten Bedingungen als auch unter unbekannten Bedingungen, verbessert. Darüber hinaus erhöhte dieses Training die kraftgenerierende Kapazität der Muskeln der unteren Extremitäten, was die Ausführung von Gleichgewichtswiederherstellungsreaktionen weiter fördert. Auf der Grundlage dieser vielversprechenden Ergebnisse versucht diese Arbeit, Kenntnisse über die zugrundeliegenden neuromechanischen Anpassungen dieses vorteilhaften Trainingsansatzes, zu liefern.

Die modulare Organisation der neuromotorischen Reaktionen, die durch die Analyse der Muskelsynergien bewertet wurde, ergab verschiedene Strategien zur Bewältigung von Störungen und zur Erhöhung der Robustheit bei der Durchführung von Übungen, die die Ausführung des Gleichgewichtsausgleichmechanismus auf instabilen Oberflächen fördern. Die Ergebnisse der Dissertation legen nahe, dass die Wahl der Strategie von Faktoren wie der Ausprägung und dem Zeitpunkt der Störung, sowie der Ausprägung der Bewegungsaufgabe, ihren Beschränkungen und der wahrgenommenen Herausforderung für das Gleichgewicht bestimmt wird. Darüber hinaus ergaben sich bei der Durchführung von Übungen, welche die Ausführung des Gleichgewichts-ausgleichsmechanismus auf instabilem Untergrund fördern, keine Hinweise auf eine erhöhte mechanische Beanspruchung der Muskulatur der unteren Extremitäten. Robustheit kann also als Folge verschiedener Modulationen von Muskelsynergien entstehen. Außerdem erhöht das Training auf instabilen Oberflächen nicht per se die mechanischen Anforderungen an die Beinmuskulatur. Die Zunahme der Muskelkraft, die nach dem Training des grundlegenden Mechanismus zur Wiederherstellung des Gleichgewichts auf instabilem Untergrund beobachtet wurde, scheint daher eine Folge neuronaler Anpassungen zu sein.

Stichworte: Muskelsynergien, Motorische Kontrolle, Sturzprophylaxe, Perturbationen, Gleichgewichtstraining

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A mi familia.

1. Introduction

1.1. Perturbations

1.1.1. Perturbations in daily life motion

In the XVII century, Sir Isaac Newton observed: "*An object at rest or moving in a straight line will remain in such state unless it is acted upon an unbalanced force*"[1]. This general principle of physics withstands true until today and provides us with a fundamental explanation of what we observe when a person trips with an object whilst walking, altering the walking pattern by modifying the trajectory of the leg and maybe the entire body from its original course. Observing people tripping, sliding, stumbling or bumping into another person is part of everyday living. Each of these events induces a mechanical disturbance to the actual posture or movement of the person, thus deviating her/him from hers/his regular state. These mechanical disturbances are, among the scientific literature, referred to as perturbations and although the definition of the term fluctuates amid different fields of study, within the field of biology perturbations are commonly defined as *"… an alteration of the function of a biological system, induced by external or internal mechanisms"*[2]. Hence, modern life presents us with multiple sources of perturbations, like disturbances resulting from uneven surfaces or different ground configurations. Furthermore, the daily routine includes a substantial element of unpredictability, like a dog barking whilst walking next to him or colliding with somebody else when turning a corner.

Since bipedalism is a crucial evolutionary behaviour that provided the genus *Homo* with many physiological advantages and cultural adaptations that contributed to modern human diversity[3,4], it might seem appropriate to state that moving over diverse terrain conditions has been an integral part of human evolution. Thus, controlling perturbations should be trivial to the neuromotor system. Yet, the bipedal position places a large portion of the body mass (i.e., the upper body, represented by the centre of mass - CoM) over a relatively small base of support (roughly the area between the two feet - BoS) making bipedalism inherently unstable[5,6]. Furthermore, in dynamic conditions like walking the height and inertial load of the upper body needs to be controlled with regard to a BoS that is changing size over time[5–7]. Therefore, even in relatively simple conditions, the postural system is greatly challenged to balance the centre of gravity over the base of support during both stationary postures and dynamic activities. So, the control of posture and balance is a condition *sine qua non* for human locomotion. Concordantly, compensating perturbations provide a fundamental basis for the execution of

movements and failing to do so might result in serious consequences like falling. The latter is particularly relevant considering that falls, defined as "... an event which results in a person coming to rest inadvertently on the ground or floor or other lower level", have been described as a major public health problem by the world health organisation[8].

Environmental conditions affect the amount and nature of perturbations faced by a person. Accordingly, factors like the slipperiness or grip between the underfoot surface and the feet and the presence of obstacles are considered primary sources of perturbations and fall-risk factors[9,10]. Hence, indoor and outdoor environments present different sources of perturbations. For example, outdoor surfaces might vary, among many others, from cobblestones to asphalt, concrete, gravel, grass, or soil, all of which present different degrees of regularity and friction. Moreover, the slipperiness of these surfaces is affected by seasonal elements like the presence of ice or water on the ground. In addition, outdoor terrains are likely uneven, making outdoor walking a constant challenge for the dynamic stability of gait due to the multiple and variable sources of perturbations[11–14]. Conversely, indoor floors tend to be more regular. However, they also present surfaces with different slipperiness as wooden, ceramic or carpeted floors. Furthermore, indoor environments often present multiple hazardous obstacles like steps, stairs, chair legs or loose carpets on the floor. Thus, dealing with visible obstacles is a frequent task in daily life. However, albeit its apparent simplicity and high frequency, around 2% of the steps taken over a visible stationary object result in a trip[15].

Real-world perturbations are particularly challenging to identify and record. Hence, epidemiological data such as the number and context in which perturbations occur is scarce. Moreover, perturbations can be so common that they might be routinely ignored[16]. Therefore, the true incidence of perturbation is likely underestimated in the reported epidemiological data[17,18]. Nonetheless, the self-reported losses of balance that did not result in a fall are recognized to be more frequent than falls[19–21] occurring up to 15 times per day in a healthy and active young population[16]. The level of physical activity influences, among others factors, the number of perturbations experienced by a person. Hence, those with higher levels of physical activity will likely be more exposed to perturbations than a person spending most of her/his day sitting. Assuming that young are physically more active and keener to engage in vigorous activities than older adults, it is not surprising that the number of reported perturbations is higher in younger than in older adults, albeit the aforementioned methodological limitation of epidemiological data. Thus, whilst older adults living in the community reported at least one perturbation over three weeks[19,22], healthy young reports range from 15 perturbations per day[16] to a minimum of one per week[23]. Active population also reported a frequency of one

perturbation per week in their working environments[24]. Physically impaired individuals might also be more prone to perturbations. Concordantly, 80% of older adults with hip osteoarthritis recalled facing a disturbance frequently (i.e., at least once per week) or occasionally (i.e., <1 per week but more than a couple of times) over one year[20].

1.1.2. Consequences of perturbations

In any biological system, a perturbation induces a corrective response that aims to restore its balance (i.e., homeostasis)[25]. Maintaining functionality despite being perturbed is a ubiquitous property of biological systems known as robustness and it is fundamental to evolve and function properly in unpredictable environments[26]. The neuromuscular system is not an exception to this principle. Thus, humans[14,27–29] and other animals[30–35] show compensatory responses to minimize the disturbance evoked by any given perturbation and maintain the ongoing movement. These compensatory responses are typically scaled to the magnitude of the perturbation, providing an adequate response to the context of the task while keeping a postural balance[36–40]. Considering the inherent mechanical instability of the bipedal position, failing to compensate for the mechanical disturbance induced by a perturbation might lead to a fall. Concordantly, unexpected environmental perturbations while walking such as trips or slips are reported as the principal cause of falls in all ages, genders and environments[41–45] except for young men, who are commonly engaged in vigorous activity when falling[23,42]. Not surprisingly, physically active individuals are also more likely to fall outdoors[42,46]. Since falls are a predominant health problem arising from a perturbation, the following section briefly addresses the incidence of falls and their consequences.

By the end of the 1950s, falls were already recognized as a health risk[47,48] and tripping, slipping and stair walking as the most common causes of falling[47]. Since then, numerous reports on the incidence of falls are available in the literature. An overview of the fall incidence reported for young and older adults resulting from a semi-structured literature search based on a snowball search using the reference list from articles known to the author and the results from a search in PubMed with the following criteria:

(falls [Title] OR fall [Title])) AND (older adults [Title/Abstract] OR elderly [Title/Abstract] OR aged [Title/Abstract]) OR (adults [Title/Abstract] OR young [Title/Abstract] OR young adults [Title/Abstract]) AND incidence [Title/Abstract]
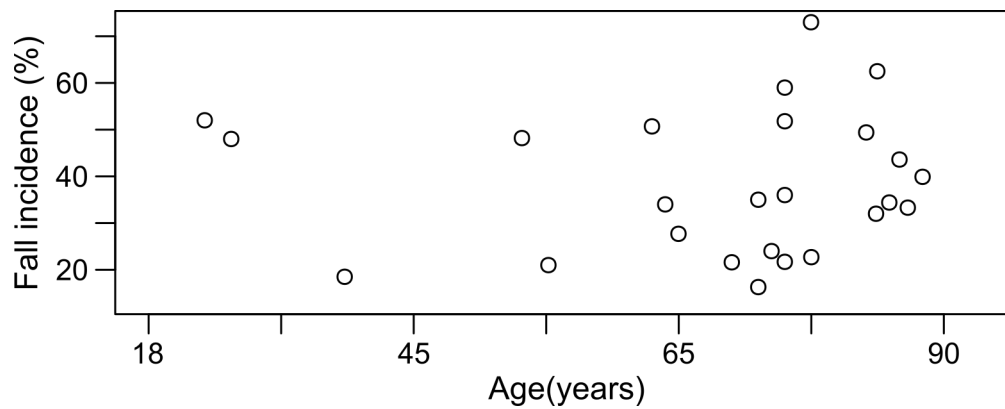
is presented in Figure 1.1.

Figure 1.1 *Summary of the reported fall incidence for different age populations. Age is presented as the average age of the reported population in each study.*

Fall incidence showed large variability across reports, ranging from 13% to 62.%. Some of this variability might be accounted for by methodological differences in assessing falls, such as using a retrospective or prospective approach[17,18]. Cultural differences might also influence the number of falls since East Asian countries presented lower fall incidences (below 20%) than the rest of the world population (~ 25 – 40%). Furthermore, a clear focus on the elderly population is observed as only a few studies examined fall rates in the age group below 45 years. Despite any differences across populations and methodological approaches, the reported fall incidence is sufficiently high to represent a scientific interest and a public health problem. So, approximately 37.3 million falls are severe enough to require medical attention every year[8]. Along superficial wounds, the most common fall-related injuries are hip or upper limb fractures and traumatic brain injuries[49–51]. These injuries can significantly impair mobility and the quality of life for long periods, and some of them can result in chronic pain, disability and loss of independence[42,51,52]. Moreover, fall-related injuries are also associated with a risk of mortality during the hospital stay[53] or within the first year of recovery[53,54], and the number of reported fall-related injuries and deaths has increased over the years in several countries[55,56]. Consequently, falls are today the second leading cause of unintentional injury and death worldwide[8].

Whilst every fall represents a risk of injury, the age, gender and general health condition of a person are important risk factors for fall-related injuries. Whereas females are more prone to falls and fall-related injuries from the second decade of their lifespan[23,43,57], age itself is one of the leading risk factors for fall-related injuries[8]. The latter, probably explains the extensive description of fall circumstances in older adults. The necessity of hospital admission due to fall-related injuries also increases with age, reaching 44% of falls in the elderly requiring in-hospital care[57]. Moreover, older adults significantly show higher injury severity scores and

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spend more time hospitalized[58]. Poor baseline health characteristics also relate to elevated rates of falls and fall-related injuries. Hence, special populations with medical conditions that affect posture, balance or gait, like those surviving a stroke[59] or Parkinson's[59–61] fall more. A higher fall incidence is also reported in people with a history of falls[44,62,63], and particularly in the frail[64,65] and the institutionalized elderly[44,63,66]. In the aforementioned special populations, falls are not only related to tripping and slipping but also often related to incorrect bodyweight shifting[67,68]. The latter exposes the importance of the ability to respond to a perturbation and not only the magnitude of the perturbation itself.

Fall-related injuries also place a humongous financial burden on the healthcare systems due to hospital admissions, rehabilitation and related care costs[69–71]. For example, caring for fall-related injuries amounted in the United Kingdom $1.6 billion and $23.3 billion in the USA[71,72]. Concordantly, the estimated cost per fall requiring medical attention is between £1,720 and £8,600 in Scotland[53] and between $3,476 and $10,749 in the USA[72]. This cost might rise to £21,960 for injuries requiring hospital admission in Scotland[53] or £39,490 in case of hip fractures and, on average, to $26,483 in the USA[72]. As the demographic change leads to the ageing of the global population, these costs are likely to keep increasing. Consequently, in the Netherlands, the estimated total annual cost of fall-related injuries between 2007 and 2009 reached $675.4 million, a ~42% increase from the previous period[52,55]. Similarly, the cost of hip fractures in Germany was 2.77 billion and is projected to reach 3.85 billion in 2030[73]. Thus, the overall cost of fall-related injuries may represent 1.5% of the total national healthcare expenditure or 0.20% of the gross domestic product[74].

1.1.3. Biological responses to perturbations

Coping perturbations and successfully avoiding falls depends on the ability to control the mechanical disturbance induced by the perturbation. As most falls occur due to a disturbance while walking, the following section uses a walking example to briefly outline the responses of the neuromotor system to cope with perturbations. Nonetheless, the underlying mechanisms governing the responses might apply to any movement (for an overview see Patla 2003[75] or Sousa et al. 2012[76]).

Imagine a person walking in a park on a path among the trees, a quick gasp reveals an uneven terrain and several trip threads like stones and tree roots. Bruijn et al.[77] proposed a simplified vision of the requirements for walking and avoiding falls despite the presence of such perturbations: " ...(i) the system has to be able to recover from or limit the small perturbations

that occur during every stride (e.g. owing to small differences in floor height and noise), (ii) the system has to be able to recover from large perturbations, which require a change in behaviour, and (iii) the largest recoverable perturbation specified by the limits of the system needs to be larger than the perturbations encountered.".

Achieving the first criterion allows the person to walk despite the small perturbations induced by the uneven ground, and involves responsive behaviours that are not too large but have meaningful effects on the gait pattern. The person uses visual information and his/her experience to identify threads (i.e., a stone that might cause a trip or a change in the ground level), and then the tread is evaluated according to the ongoing movement creating an estimation of the magnitude of the perturbation. Based on this estimation, a proactive control strategy modifies the motor pattern to best cope with the perturbation (i.e., increasing foot clearance to step over the stone or preparing the reaction for uneven foot placement)[78–80]. The adapted motor pattern will likely involve some steps before[81] and the compensatory responses after the expected perturbation[75,76,82]. Hence, although proactive control strategies rely on estimating the perturbation, it is subsequently influenced and updated by sensory feedback[75,79,83]. Updating the motor pattern allows, in most cases, the person to safely cope with the uneven ground. The latter is supported by previous observations of foot placement being critical for achieving a stable and safe gait[75,84,85].

The second and third criterion from Bruijn and colleagues relates, in our example, to larger disturbances arising from a failed estimation or an unexpected perturbation that resulted in a trip or slip. In contrast to the above-mentioned proactive strategy, the response to this unexpected perturbation is triggered by the perception of the perturbation itself. Therefore, it relies on integrating inputs from all major sensory systems (i.e., proprioceptive, vestibular and visual) to elicit both, fast balance-supporting reflexes and more complex, functionally appropriate motor responses[75,76,86,87]. Figure 1.2 presents an overview of the temporal relationship between proactive and reactive strategies. From a biomechanical point of view, the reactive responses to this larger perturbation are organized to control the relationship between the position and velocity of the centre of mass and the base of support[6,77,84,88,89]. Maki and McIlroy[90] presented a description of the balance recovery mechanisms based on the nature of the support. Distinguished by the absence or presence of limb movement to modify the base of support (i.e., taking a step or reaching for support with the upper limb increases the BoS resulting in a change of support strategy), they classified balance reactions in "fixed" or "change in support" strategies. Later, based on an inverted pendulum model[6], Hof[91] described three mechanisms of balance control, namely, i) moving the centre of pressure (the point of

application of the ground reaction force, CoP) under the feet with respect to the centre of mass, ii) counter-rotating the body segments around the centre of mass and iii) applying an external force other than ground reaction forces (e.g. grasping a handrail). Despite the didactic advantages of both approaches, the aforementioned categories overlap in the context of large mechanical perturbations. Following our example of a trip while walking in the park, reaching and holding to a surface like a handrail is a preferred option for rapid control of the CoM[90,92]. Holding a handrail corresponds to a change in support strategy according to the classification proposed by Maki and McIlroy, is also the third mechanism described by Hof (i.e., applying an external force). However using this strategy is limited by the environmental availability of external support and the constraints of the ongoing movement[93,94]. Therefore, in the tripping example, a rapid corrective step is probably the elicited response. This stepping reaction moves the CoP to control the accelerations of the centre of mass and increases the base of support[6,37,91]. Nonetheless, some degree of counter-rotating movement is likely included during and immediately after the reactive step. Hence, the reactive strategy exploits every available mechanism to compensate for the mechanical disturbance induced by the tripping, albeit its classification. Thus, if the corrective step fails to achieve its goal within a single step, further corrective steps might be taken[90,95–97]. Moreover, each perturbed step during the walk incremented the person's awareness of the characteristics of the perturbation induced by this particular path, reinforcing hers/his knowledge of dealing with uneven paths from previous experiences. Hence, although unexpected perturbations are inevitably related to reactive control, any of the aforementioned reactive mechanisms or strategies can be subsequently modulated by both predictive and reactive control[88,98–100].

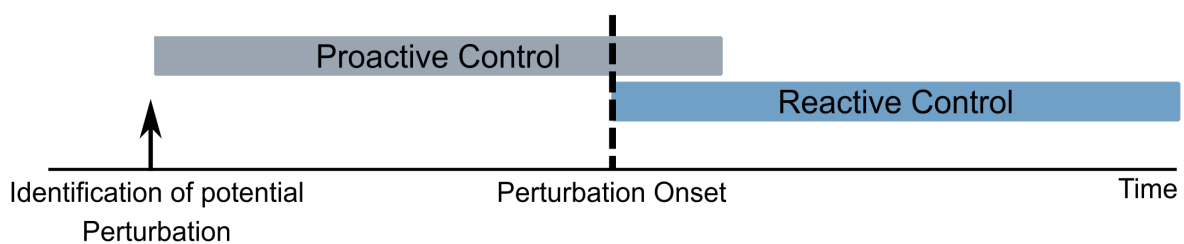*Figure 1.2. Schematic diagram outlining the temporal relationship of the proactive and reactive control strategies for cooping with perturbations.*

In consequence, the overall success of responding to a perturbation depends on the accurate perception of a threat. Therefore, integrating sensory information is crucial for balance recovery performance[93,101,102]. Yet, different components of the sensorimotor system deteriorate

with age affecting sensory perception and integration[103–105], as well as the motor capacities[106–108]. This decline in motor performance relates to a reduced physical activity along with neuropathic, hormonal, immunological and nutritional factors[109–111]. As the functionality of the sensorimotor system declines with ageing, the ability to respond to perturbations declines and the risk of falling increases[112–114]. Concordantly, ageing is a prominent factor leading to fall-related injuries[43,62,63]. Due to the close relationship between ageing and fall-related injuries along with their detrimental physical, psychological and financial consequences, most fall-preventing interventions focus on the elderly. The following chapter of this dissertation explores the rationale and main characteristics of such interventions.

1.2. Interventions to reduce fall risk

1.2.1. Ageing challenges the ability to respond to perturbations

As mentioned above, the deterioration in the functionality of most of the components of the sensorimotor system impairs the ability of the elderly to respond to perturbations. Thus, older adults commonly show an occurrence of peripheral neuropathy, along with decreased muscle spindle activity and sensitivity of joint and skin receptors[105,115–119]. These sensory deteriorations affect proprioception and hinder the ability of the elderly to integrate the limb position relative to other body parts[118,120]. Vestibular and visual functions are also affected, resulting in reduced head-stabilising reflex activity[121,122] and a diminished perception of depth and visual acuity[119,123]. This impaired ability of the elderly to perceive and integrate sensory information increases the risk of falling[119].

The motor capacity of the effectors also declines with age as a consequence of architectural and functional changes in the muscle and tendon[108,124–126]. As these architectural changes come along with a selective atrophy of fast-twitching fibres, the capacity of the elderly to generate force at fast speeds is particularly hindered[110,124,127,128]. Generating fast movements is crucial for the success of a corrective response[129]. Thus, muscle power (i.e., the product of muscle force and muscle shortening velocity) is a fundamental limiting factor for successfully recovering balance after a slip[130], a trip[114,131,132] or a lean-and-release test[133–136]. Consequently, the deterioration of the muscular capacities of the lower limb in terms of muscle power, strength and muscle mass are considered intrinsic factors and reliable predictors for risk and rate of falls in the elderly[114,137–139].

The deterioration of the sensorimotor components also hinders the integration and transformation of sensory information commands[140]. As older adults show more neuromuscular noise, their force production fluctuates more than in young adults affecting their performance

in repetitive tasks like standing or walking[141,142]. The neural drive of the agonist and antagonist muscles is also modified in the elderly, resulting in increased co-contraction[143]. Increasing co-contraction is a typical response to improve balance control in challenging environments[144–146]. Yet, older adults show higher levels of co-contraction than young adults for a similar task[147,148] and are less able to modulate the level of co-contraction according to the difficulty of the task[148]. Furthermore, a high level of co-contraction might decrease the total muscle force output[149,150], further hindering the ability to react to unexpected perturbations of high intensity. Thus, despite the positive effect of co-contraction on stabilizing joints and posture, the decreased muscle power and increased co-contraction observed in the elderly have been proposed to increase the risk of falling[131,151].

Responding to a balance disturbance timely and appropriately depends on: i) acquiring accurate sensory information, ii) integrating and processing it to create a motor command that will activate the adequate muscles and iii) on the capacity of the motor system to execute the motor command[105]. As the above-mentioned age-related changes affect the capacity of the elderly to control balance, older adults are recognised as being less able to successfully recover balance after an unexpected trip compared with younger adults[114,152–154]. As a consequence, the high fall incidence reported in the elderly is proposed to arise from the deterioration of their performance on the execution of balance recovery actions[97,114,131,133].

Nevertheless, as we age the balance control system can adapt to the deterioration of its components, allowing the elderly to control their balance in most daily life situations. Consequently, older adults modify the influence of the available sensory information for controlling balance, relying primarily upon visual over proprioceptive or vestibular information[155–157]. Planning and controlling posture and other motor tasks also differ in the elderly[140,158,159] as a consequence of a different way to integrate sensory information into motor commands[160]. Hence, balance-correcting strategies in the elderly differ from those observed in younger adults, with older adults relying more on the counter-rotation mechanism (i.e., the so-called "hip strategy") to counteract perturbations whilst standing[39,161]. Stepping reactions are also modified in older adults, as they are elicited by smaller perturbations when standing[162,163] and produce longer steps in response to disturbances whilst walking[164].

The perception of the difficulty of the task and the self-capacities play a fundamental role in the decision-making process, control and performance of a motor task[165,166]. Thus, despite earlier assumptions, the cerebral cortex contributes substantially to postural control and to elicit effective balance recovery responses in challenging environments[102,167]. Henceforth, supraspinal control is essential for integrating sensory information and motor planning even in the most

simple balance task[168–170]. Consequently, as the challenge imposed by the task increases, so does the role of supraspinal structures[93,169,171]. Yet, either because of being effectively more challenged or for having the perception of being more challenged for the same task, older adults rely more on supraspinal control[172–174] and are less able to modulate spinal control to the environmental demands[148,175] than younger adults. Given the above, the accommodations of the sensorimotor system to its age-related changes do not appear to be flawless, as balance control in the elderly might not be robust or responsive enough to adapt to balance challenging environments. Such less-than-optimal adaptations are revealed by the aforementioned decrease in balance control performance and the high risk of falling reported in older adults. Thus, the necessity for effective interventions to decelerate or even reverse the retrogression in the balance and gait control systems has become increasingly explicit in the last few years[176,177].

1.2.2. Fall preventing interventions

Reducing the number of people falling (i.e., fall incidence), fall rate (i.e., number of falls per person) and fall risk (i.e., the proportion of people having one or more falls) are the main objectives of any fall prevention programme. Reducing a potential injury should a fall occur by addressing the above-mentioned age-related deteriorations of the sensorimotor function is also an objective. Yet, as shown by different Cochrane systematic reviews, not every intervention fulfils these goals equally[178–180]. Thus, while treating vision impairments decreased the rate of falls compared to those not undergoing visual surgery, an increased risk of falling is recognized while adjusting to new spectacles or major changes in the prescription[178]. Similarly, tailoring medication and other multifactorial interventions reduces the fall rate but not the risk of falling[178,180]. On the other hand, modifying environmental hazards by improving home safety effectively reduces both fall risk and fall rate[178]. Nonetheless, such multifactorial interventions require assessing, identifying and working on the identified risk factors at an individual level affecting the efficiency and applicability of such interventions at a population level. Conversely and most important a strong body of evidence concluded that exercise-based interventions effectively reduce fall rate and fall risk in the elderly[178,179,181,182] regardless of their supervision strategy[179]. In addition, exercise-based interventions reduce fall rate and fall risk when delivered in a group or individual setting[179] and, delivered as a single intervention, exercise has a fall prevention effect similar to multifaceted interventions[178,183]. Therefore, implementing exercise-based programmes is an effective strategy for fall prevention at a population level[184] and is promoted as a cost-efficient prevention tool by international guidelines and several national health services[179,185,186].

Many of the outlined impairments that lead to an increased risk of falls can be improved with structured exercise interventions[63] and so, conventional training programmes aim to improve individual components of motor function such as muscle strength, balance and mobility[187,188]. Increasing self-efficacy, safe negotiation of the environment, awareness of risk factors as well as reducing the fear of falling and improving functioning in activities of daily living are further goals of such interventions[63,189–191]. Training intervention programmes are capable of achieving most of these goals as confirmed with a high level of evidence by subsequent systematic reviews and meta-analyses concluding an effective reduction of fall rate up to a 23% after undergoing training[178,182]. Exercise-based interventions also reduced fall risk by 15% and the risk of fall-related injuries by 27%[179,182]. Fear of falling is also effectively reduced after training[189].

In all the aforementioned reviews, exercise is defined as "...*a subset of physical activity that is planned, structured and repetitive and has as a final or intermediate objective the improvement of physical fitness"[192]*, thus a wide range of exercise types are included. The Prevention of Falls Network Europe (ProFANE) project developed a taxonomy that classifies the type of exercise based on the characteristics of the exercise as i) gait, balance, and functional task training; ii) strength/resistance (including power); iii) flexibility; iv) three dimensional (3D) exercise (e.g. Tai Chi, dance, yoga); v) general physical activity; vi) endurance; and vii) other kinds of exercises[193]. Since exercise programmes often include one or more types of exercise, the taxonomy allows the delivery of more than one class of exercise within a programme. Yet, a Cochrane systematic review concluded that the fall-preventing effect differed among interventions depending on the predominant class of exercise delivered in the training[179]. For instance, neither general physical activity, flexibility nor resistance/strength are effective stand-alone interventions to reduce falls in older adults[179]. Alternatively, three-dimensional exercises have been found to have dissimilar results whereas dance is an ineffective intervention for reducing falls, Tai-Chi effectively reduces fall rate by 19%[179]. Yet, the positive outcomes of Tai-Chi in reducing fall rate are likely to arise from its ability to increase muscle strength, mobility and balance control rather than its three-dimensionality[194,195].

Within the frame of the PROFANE taxonomy, walking should not be confused with training gait. Instead walking is considered either a general physical activity or endurance training if it is performed for longer periods. In this scope, walking was found ineffective in preventing falls[196] and even increase fall risk in the elderly when performed briskly[197]. Nonetheless, walking promotes several health benefits and is a very popular activity among older adults[198]. Hence, due to its general health benefits and its inclusion in some successful multi-component

intervention programmes like the Otago Home Exercise Programme[199], walking is suggested to be carefully prescribed in addition to other fall-preventing exercise programmes[179,182]. On the contrary, in the PROFANE taxonomy, gait interventions share classification with balance training and differ from walking by specifically targeting walking technique (e.g., focussing on posture, stride length and cadence) and challenging balance control while walking by inducing changes of pace, level and direction. Examples of these gait interventions include heel or toe raises, walking on the toes/ heels, walking backwards, sideways and turning. As such, balance, gait and functional exercises have been shown to induce the greater fall prevention effects among the PROFANE taxonomy categories, reducing fall rate by 24% and fall incidence by 13%[179,182]. The rationale for effective training interventions is further addressed in the following section.

1.2.3. The rationale for effective interventions

Given the aforementioned age-related deterioration of the sensorimotor functionality, an effective training intervention is expected to improve reactive balance control by addressing at least one of the following alternatives: (a) increasing the acuity of the sensory information, (b) inducing adaptations to the sensorimotor transformations, or (c) improving the capacities of the motor system such as muscle strength[200].

Improving the capacities of the motor system is a traditional and very straightforward strategy, and increasing muscle strength is a common objective of training interventions and guidelines aiming to reduce fall rate and falling risk in the elderly[178,182,201,202]. The rationale for promoting this approach is based on the recognised capacity of strength and resistance training to attenuate and even reverse the age-related loss in muscle strength and improve the physical functionality of older adults[188,203,204]. Additionally, increasing muscle strength has been reported to improve balance recovery performance[114,205,206] and elicit positive effects on daily life activities and the incidence of falls[199,207]. However, increasing muscle strength does not improve balance control[131,208,209] nor reflective balance responses after a sudden perturbation[114]. Further, strength training did not yield any effect on the reflex excitability of plantar flexors, nor on the recovering performance after a trip, despite improving the voluntary activation, maximum force and the rate of force development of the lower limb muscles[131,210]. As a consequence, strength training is recognised to have a limited ability to improve reactive balance performance[211,212] and reduce fall risk[213–215] and thus, it is not advised as an effective stand-alone intervention for reducing the rate of falls nor fall risk [179]. Yet, the ability to produce

muscle work with the lower extremities in a short period is recognized as a limiting factor for recovering balance[114,132,135,153] which is significantly lower in older compared to young adults, and most especially in the elderly with a history of falls[216,217]. Hence, increasing muscle power instead of muscle force appears as a better alternative for enhancing successful balance recovery actions[216,218] and has been classified as a very effective intervention to improve reactive balance by a recent meta-analysis[177]. Yet, not every training intervention targeting the increase of muscle power has been able to overcome the effects of strength training on balance performance[218–220]. A plausible explanation for contradictory results might be related to the large battery of tests normally used to assess balance and the reduced capacity of the elderly to control the CoP limiting the transfer between dynamic and static responses[221,222]. Consequently, it has been proposed that muscle power and strength should be trained in a complementary manner with postural control[223] and such intervention programmes including functional balance challenging exercises and resistance training increased the reduction of fall rate from 24 to 39%[178,179,182]. However, training individual components of physical fitness has been shown to require long and intensive training periods to avoid a deterioration of their positive effects[191,213,224] and thus, the necessity of developing effective fall prevention interventions that are easy to implement is still acknowledged[63,179].

Considering the above-mentioned shortcoming it follows that improving the capacities of the motor system individually is not the best alternative to improve balance control. Moreover, the reported higher effectiveness of training interventions focussing on balance and gait for reducing falls[63,179] indicates that the larger benefits for fall avoidance are promoted by improving the capacity of integrating and transforming sensory information into motor commands or, in other words, by improving the capacity of the trainees to perceive and react to a fall-leading event.

Perceiving and integrating sensory information is recognised as of paramount importance for both motor control and learning[225,226]. Consequently, the integration of sensory information with the efferent motor commands is ensured by several convergence points in different levels of the neuroanatomy of the sensorimotor system[227]. This redundancy of convergence points occurs mainly at the spinal level and allows the modulation of the ongoing motor command based on comparing the sensed motor outcome against the desired output[87,228,229]. Thus, these convergent points allow the spatial and temporal coordination of the voluntary movement with any anticipatory or reactive postural adjustments needed to provide balance control along with the intended action[87,229]. Online movement control and motor learning are largely driven by sensory feedback and the discrepancies between the ongoing sensory feedback and the predicted

consequences of a motor command, commonly defined as sensory prediction errors[226]. Correcting or modulating an ongoing motor output in response to a sensory prediction error is commonly known as motor adaptation[230] and, depending on the result of such motor adaptations related to the desired goal, they can be retained based on both a reward- or error-based learning processes[230–232]. This process guides the nervous system to learn how to predict and minimize the impacts of a novel environment by minimizing the prediction error and thus, motor adaptation maximizes the motor performance in that environment[233]. Consequently, it is established that both motor adaptation and learning are promoted by repeated exposure to an environment[177,234,235], despite some uncertainties on how motor adaptation is affected by the goal of the task[230,236]. Furthermore, it has been shown that the older adult preserves most of his motor adaptation and learning capacities, as well as neuromuscular plasticity[98,237–239]. Henceforth, balance and gait training interventions are normally based on exposing trainees to repeated challenges of gait or balance control that aim to maximize motor performance by promoting error-based learning.

Due to the paramount importance of adequate stepping responses for reactive balance control and fall avoidance, gait training interventions have focussed on improving the execution and speed of both volitional and reactive steps to reduce fall risk[240–243]. Consequently, step execution and the decision-making process of stepping have been successfully improved by target stepping[244,245], stepping choice reaction time, an indicator of cognitive and physical fall risk is also improved by step training[246]. Moreover, a meta-analysis including both reactive and volitional stepping interventions reported an impressive 50% reduction in falls among the elderly[242]. Yet, training voluntary stepping onto a target has been criticised for lacking the specificity to train fast reactive compensatory stepping, where the possibility of using anticipatory postural adjustments is scarce[247,248].

Alternatively, balance training has traditionally focused on improving static and dynamic balance by challenging the ability of the trainee to maintain the centre of mass within the base of support[249–252]. Although exercises such as tandem stance, single-leg stance, reaching and walking sideways are commonly included in balance training programmes[182,249,250,253], being challenged is of paramount importance to any effective balance training and thus, the intensity of the challenge needs to be tailored to the functional capacities of the trainees[179,254,255]. Correspondingly, whilst reducing the reliance on the upper limbs for standing is already a challenge for the frailer or balance-impaired individuals[182], in the regular population balance can be further challenged by reducing the base of support or by increasing the distance or the velocity of a bodyweight shift[248,256,257]. Diminishing or altering the sensory information

processing by closing the eyes or using compliant/unstable surfaces are also alternatives to increase the challenge to the balance control system[248,257–259].

Unstable surfaces made out of foam or inflated devices are frequently employed for balance training in athletic and rehabilitation environments to mimic the demands of coping with varying settings[260–262]. Such unstable devices promote postural perturbations or imbalances by making the postural sway project the centre of mass beyond the device's area of support, by altering the association of changes in the centre of pressure in response to the reaction forces due to the surface distortions[263] and by increasing the velocity of the centre of mass[148]. Hence, balance training presents manifold alternatives yet, performing static and dynamic exercises on stable and unstable surfaces during double or single-leg stances with eyes open or closed represents the core of traditional balance training[248].

Conventional balance training is reported to enhance balance control and other functional capacities in a large amount[264–267] and training on unstable surfaces resulted in an improved balance performance on young and older adults[248,251,259,264,268]. Moreover, such improvements in balance performance are larger[269,270] and elicited faster[249] than those elicited by training on stable surfaces. As a consequence, several guidelines promote the use of unstable surfaces as part of balance training in the elderly[248,256]. Yet, improving static balance does not necessarily improve the balance recovery performance after a sudden perturbation leading to a simulated fall[271,272], and the capacity of transferring the gains in static balance control to balance recovery actions and fall avoidance is limited[222,273]. Hence, due to the necessity of improving the ability of the elderly to cope with unexpected balance disturbances and their manifold presentations, it has been proposed that balance training should not only aim at the ability to control a steady state under static or dynamic conditions (i.e., maintaining a steady position in sitting, standing or a steady walking) but also target proactive and reactive control strategies[257,274].

Concordantly, challenging balance control by presenting sensory conflicts has been proposed as an attractive alternative to promote motor adaptation and learning of effective balance reactions. For example, immersing trainees in virtual environments or having them perform motor tasks on unstable surfaces elicited sensory inputs recalibration and motor adaptation in the CNS resulting in an improved balance performance[158,275]. Although reactive control strategies evoked by postural perturbations are not under direct volitional control[90], the cerebral cortex is of paramount importance to facilitate and acquire balance recovery skills[102,276,277] particularly, like for any other motor skill, during the early phase of the acquisition[278–280]. Concordantly, cortical excitability, cortico-muscular coherence and muscular activity are increased in the early stages of skill training, denoting a relevant contribution of cortical

modulation over spinal circuits for motor learning[281,282]. When facing a challenge to balance control the sensorimotor transformations are adjusted to modulate the organisation of the active muscles and secure balance[283–285]. Then, by being repeatedly exposed to postural or sensory perturbations, the sensorimotor system learns new internal models that predict the sensory consequences of a perturbation to a motor command. This internal model is used to explore a movement plan that minimizes the cost and maximizes the success of the motor outcome[233,284]. Thus, the internal models of stability are modified and updated, improving both predictive and reactive control strategies to deal with similar perturbations[286,287]. As a consequence, the cortical structure is modified after undergoing balance challenging training[288] and the level of cortico-spinal excitability when facing perturbations is decreased[276,277]. On the contrary, the levels of spinal excitability are not modified with training[148,276] and thus, balance challenging training interventions are proposed to reduce the requirements of supraspinal control for controlling balance making the recovery responses even more automatic[276].

Moreover, presenting low-intensity sensory fluctuations (i.e., like those induced by the deformations of a compliant surface) during the sensorimotor transformation process facilitates the sensitivity of the nervous system to weak sensory signals[289,290], and promotes neural networks that are more robust and more efficient to cope with environmental changes[291]. Further, such low-level fluctuations (i.e., sensory noise) have been proposed to improve the performance of the sensorimotor system[291,292]. Concordantly, unstable surfaces are reported to increase the sensorimotor demands to perceive sensory information and integrate motor commands, resulting in increased activation of the muscles when performing different motor tasks on them[293–295]. These increments in muscle strength and functional outcomes are proposed to relate mainly to enhancing muscle coordination and sensory-motor integration[293,296]. Furthermore, balance performance has been also reported to improve when facing low-intensity mechanical fluctuations[290,297].

Specificity is a fundamental principle of successful exercise prescription[234] and concordantly, eliciting balance recovery responses by using perturbations to train reactive balance has been proposed as a more task-specific approach than general balance exercises or strength training for preventing falls after a loss of balance[248,298]. Hence, being exposed to repeated external perturbations while performing a motor task is widely reported to effectively enhance balance reactions[181,242,299–303]. This perturbation-based paradigm is presented as a novel alternative to filling the gap of specificity observed with conventional approaches to training reactive balance control[304] and has received increasing attention in fall prevention programmes[247,305]. More importantly, these training interventions including a reactive balance component show the most

improvements in reactive balance performance and fall avoidance[177,179]. Given these promissory results of perturbation-based interventions as an effective means to reduce fall incidence[181,303], the following section explores the most common alternatives of such balance challenging interventions and their effects.

1.2.4. Perturbation-based training interventions

As above-mentioned, improving reactive balance is proposed as a more specific approach to reducing falls[177,298]. Thus, training reactive balance control by applying repeated unpredictable mechanical perturbations is a common practice in prevention and rehabilitation settings[181,200]. These perturbation-based training interventions aim at improving reactive balance responses to postural disturbances as well as other contributing factors to successful balance maintenance such as the response reaction time, perception of losses of balance and speed of sensory information processing[181]. Under this paradigm, unexpected mechanical perturbations have been repeatedly induced while standing and walking[181,248,301,304,306] and such approach is reported to effectively induce sensorimotor adaptations and improve balance recovery responses to perturbations through repetition in the elderly[181,237,240,307].

As most falls occur during walking due to mechanical perturbations such as slips or trips[44,45,67], eliciting slip- or trip-like compensatory responses has been proposed as an ecologically valid and highly specific training strategy to target fall prevention. Hence, gait has been unexpectedly perturbed using overground walkways and treadmill settings. In treadmill-based interventions, reactive balance responses are elicited by modifying the acceleration of the belt to induce trips and/or slips[308,309]. While in overground settings the alternatives to induce perturbations include fitting the walkway with loose or pop-up tiles[154,310], moving platforms[99,311,312] or cable trip systems[238,240,272,313]. Despite several other gait-perturbing methods been also described in the literature such as waist pushing and pulling mechanisms[314–316] and suddenly changing the ground's height[317,318] or compliance[88,100], these perturbations mechanisms have mainly been used to investigate gait stability and adaptability rather than for training purposes. Compared to a walkway setting, treadmill-based interventions present some practical advantages such as the reduced need for space making them more feasible for clinical settings[319]. Moreover, the timing and magnitude of the perturbation can be easily adjusted further increasing the difficulty of predicting the perturbation. A comprehensive review of the alternatives for perturbing gait has been performed by McCrum et al.[181].

Gait has not been the only task unexpectedly perturbed in training interventions, as postural trials have also been conducted to train the ability to maintain balance despite the presence of perturbations. Concordantly, multidirectional balance disturbances have been induced while standing onto translating[311,320,321], or on rotating platforms[200,322] and by waist pulls[251,323].

Perturbation-based training is proposed to challenge anticipatory and reactive balance control under the same rationale of effective balance training addressed in section 2.3. Concordantly, after facing the first perturbation, trainees explore alternatives to best tune their anticipatory strategies (i.e., anticipatory postural adjustments) and the reactive balance responses that might increase the success of a balance-recovery action. As a consequence, acute modifications in the characteristics of the following step responses such as altering the step length, position of the centre of mass and margin of stability have been described[88,100,148,273]. Neural plasticity and adaptation are also effectively and quickly promoted resulting in modulating sensorimotor integration at the spinal and cortical level[148,273,324,325]. Sensory perception, integration and central processing are also improved with perturbation-base training leading to significant reductions in the reaction time and an increase in the velocity of movement execution, both major components of a successful balance recovery[114,133]. Thus, improving sensorimotor processing is proposed to elicit the larger benefits for fall reduction and prevention by improving the speed and efficacy of reactive control strategies after facing unexpected perturbations[42,43].

Consequently, perturbation-based interventions using a gait paradigm improved reactive recovery responses to disturbances regardless of the perturbation induction mechanism[320,321,326]. In addition, perturbation-based gait interventions also improved balance and gait performance along with self-confidence and fear of falling[99,311,321,326,327]. As gait and balance are improved, older adults can successfully negotiate higher perturbation magnitudes[309,319]. Moreover, training gait reactive balance reduced fall incidence up to a remarkable 50%[312,320,327].

Training interventions using disturbances in a standing setting have also been successful in improving balance. For example, perturbation-based training using a standing paradigm has been reported to increase the control of the centre of mass[90] and improve the performance in both, the "fixed-support" and "change-in-support" strategies[322,328]. Hence, after undergoing training, trainees are capable of withstanding larger perturbations before modifying the base of support while standing[273,329,330]. Moreover, the speed of grasping[200] and stepping compensatory responses is improved[322]. Also, training responses to surface displacements led to a reduction in the excursion of the centre of mass[239,322] and the number of steps and foot collisions during the responses[239]. Thus, perturbation-based training is reported to induce a significant reduction in the incidence of falls in older adults independent of using a gait or standing paradigm[239,322] and

training reactive stepping is proposed to induce large fall-protecting adaptations even after brief periods of training[311,312,321]. As a consequence, the efficiency of perturbation-based training in reducing the risk of falling and falls is widely reported[181,242,301,304]. Furthermore, some perturbation-based training interventions reported improving muscle strength and other functional capacities besides balance recovery actions after a few weeks[302,331]. Though these additional gains further increase the ability of the elderly to cope with challenging balance condition[98,242], the fast onset of the early improvements in functional capacities are recognized to rely primarily on neural plasticity rather than on changes in muscle structure[332–336].

The characteristics of the perturbation determine the sensory integration, processing and the succeeding muscular and joint coordination of a reactive response[298,337]. Hence, the intensity of the perturbation delivered during the training session appears to relate to the gains in motor performance as larger perturbations led to greater training effects[308,338,339]. The degree of retention and transfer of the learning effects seems to also depend on the intensity of the experienced perturbation, with greater effects seen with greater postural threats[301,340]. Concordantly, experiencing near-fall situations during training is reported to improve motor recovery responses and promote strong learning effects after short exposures due to its task-specificity[181,326]. Hence, improvements in reactive control and gait stability have been reported after a single[88,309,320,326] or just a couple of sessions[239,287,324] and perturbation-base training has been reported to induce fast adaptations even in neurologically impaired people[341,342].

The predictability of the perturbation also plays a role and thus, dual-task exercises or sensory challenges have been added to reduce it and enhance the reactive component of the responses. Although issues with the predictability of the perturbation have been explicitly reported in overground walkway settings[343], it is also true that by agreeing to undergo training trainees are at least to some degree aware of the perturbations. A truly unexpected perturbation, where young participants were under the impression that they were taking part in a normal gait analysis and were subsequently perturbed, has been shown to elicit remarkably greater effects than the subsequent "less unpredictable" perturbations[344]. Nonetheless, most of the neural adaptations elicited by perturbation-based training are retained shortly after the initial exposure to the perturbations and maintained for over one year[240,311,320,321,345–349].

Yet, the reorganisation of the motor maps and synaptic changes in the cerebral cortex[277], as well as the observed improvements in the reactive balance strategies[298] are recognised to be specific for a task with similar characteristics. For example, while pulls at the waist induce changes in the speed of a grasping reaction[200], moving surfaces elicit improved stepping responses[322,326]. Hence, albeit this high specificity has been proposed to account for the larger improvements in

reactive responses elicited by perturbation base training[177], it also complicates the transference of the gains. Thus, a specific type of reactive balance exercise has no, or at most a limited transfer effect on non-trained reactive balance tasks[242,304]. Concordantly, improving standing balance control and stepping reaction speed did not induce changes in stepping corrections while perturbed walking[305,350].

The direction of the perturbation is also relevant as most of the perturbed gait interventions delivered anterior or posterior perturbations, and the benefits in stability control do not necessarily transfer to other planes of motion[200,239,315]. It follows that training interventions should include different patterns of perturbations to maximize the unpredictability and prepare older adults for real-world environments[350]. Combining gait and standing perturbations paradigms has also been proposed[326]. Yet, this will probably result in long and complex training interventions.

Since daily life presents manifold perturbations, training specifically for every type of perturbation is impossible. Hence, Arampatzis and colleagues proposed that the fundamental mechanisms of balance recovery (i.e., modifying the CoP by increasing the base of support and counter-rotating segments around the centre of mass[91]) should be the base of a more generic and effective alternative of a training intervention for reducing the incidence of falls[205,351]. Although this training approach does not qualifies as a perturbation-based intervention according to a recent classification[352], it is supported by the strong dependence on the ability to perform the aforementioned general mechanisms of balance recovery to successfully respond to sudden perturbations and consequently avoid a fall[88,135]. Under this view, exercising multidirectional stepping and movements promoting counter-rotation of body segments rather than focusing on specific perturbations facilitates effective use of the balance recovery mechanism when facing different perturbations leading to an improved ability to regain balance and avoidance of falls[205,351,353]. This training approach successfully improved balance performance and the gains exceeded those observed after a mixed paradigm that included balance and strength training[351]. In addition, training the fundamental mechanism of balance recovery induced an increase in plantar flexors strength when performed on a mini trampoline[353], but not when performed on regular ground[205,351]. Considering that muscle strength and tendon stiffness are limiting factors for the performance of balance recovery mechanisms[133] and thus, increasing muscle strength is a common objective in fall-prevention programmes[178,179], Arampatzis and colleagues included in subsequent studies, the use of compliant and unstable surfaces to induce perturbations while exercising the balance recovery mechanism[354]. The rationale for including unstable surfaces is based on the reported capacity of

unstable surfaces to increase muscle activity and enhanced motor performance[293,294] and the subsequent reports of increased muscle strength after training on unstable surfaces[355,356], particularly in the older adult[357]. Thus, exercising multidirectional stepping and counter-rotating mechanisms on unstable surfaces successfully improved stability performance and muscle strength[302,354] even after short periods of training (i.e., 3 weeks)[302]. Furthermore, although the effects of such type of intervention on daily life fall incidence have not been assessed, training the balance recovery mechanism has been shown to successfully transfer the improvements in stability and balance recovery performance to a non-trained balance test[205,302,351,353,354]. Therefore, such training approach has been proposed to be a very effective way to reduce fall risk by counteracting the age-related impairments related to balance recovery performance when facing daily life unexpected perturbations[302,303,354]. Further and despite the lack of a cost analysis of this training approach, it seems logical to presume that the relatively low cost of unstable devices compared to instrumented treadmills and robotic platforms makes it a very feasible and attractive alternative to target fall prevention even in developing countries.

As addressed in section 2.3, the reported improving balance and motor capacities relies heavily upon the capacity of a training intervention to induce sensorimotor adaptation for which presenting trainees with balance-challenging conditions is crucial. Concordantly, unstable surfaces are proposed to enhance sensorimotor integration and muscle coordination[293,296] and thus, understanding the acute sensorimotor modulations while performing a task on unstable surfaces might provide insights into the relevant factors promoting fall avoidance. The following section addresses the fundamental background of an experimental approach to assess acute changes in the neuromuscular organisation of the sensorimotor system to be used in this dissertation.

1.3. Organization of neuromotor responses

"You probably do not know that God has a cousin who has never been very famous. So, the cousin asked God to help him achieve fame and glory in science. To please the cousin, God gave him the ability to get any information about physical systems in no time and to travel anywhere within a microsecond. First, the cousin decided to check whether there was life on other planets. No problems; he travelled to all the planets simultaneously and got an answer. Then he decided to find out what the foundation of matter was. Again, this was easy: He became extremely small, crawled inside the elementary particles, looked around, and got an answer. Then, he decided to learn how the human brain controls movements. He acquired the information about all the neurons and their connections, sat at his desk and looked at the blueprint. If the story has it right, he is still sitting there and staring at the map of neuronal connections."

Story usually recounted by N.A. Bernstein. Recollected by his former mentee Prof. V.M Zatsiorsky and published by M. Latash in the book "Synergies" (p. 50)

1.3.1. Motor redundancy and the organisation of muscle synergies

If we touch our nose with the tip of our right index finger, we can move the arm without losing contact between the fingertip and the nose. This simple task reflects that we could have touched our nose through many combinations of joint angles of the arm. Nevertheless, when the task was presented, we did it with a particular joint combination. How did the brain select it? This elegant observation was presented by one of the greatest minds of the twentieth century, Nikolai Alexandrovich Bernstein (1896 – 1966), whose major work appeared to most of the scientific community in a volume translating his work into English in 1967[358]. In his work, Bernstein recognised the large number of degrees of freedom (i.e., the possible combination of joint angles in the example) as one of the main challenges for the central nervous system, in his words: *"the basic difficulties for co-ordination consist precisely in the extreme abundance of degrees of freedom, with which the central nervous system is not at first in a position to deal."*[358]. Following Bernstein's example, and excluding the joints of the hand and fingers for the sake of simplicity, the human arm has at least seven degrees of freedom which are easily increased to over 10 if the contribution of the shoulder blade and portions of the upper body to natural movement are considered[359,360]. These degrees of freedom are

provided by the axes of rotation at the shoulder (i.e., three axes of rotation at the shoulder allowing flexion-extension, abduction-adduction, and internal-external rotation, respectively), the elbow (one axis for flexion-extension) and the wrist rotation (two axes for flexion-extension and ulnar-radial deviation plus one axis shared between the wrist and the elbow allowing pronation and supination) and impose the challenge to the sensorimotor system of determining a minimum of seven angles to reach a three-dimensional point in space (i.e., the location of the tip of the nose in our example). From a mathematical perspective, this is equivalent to solving a set of simultaneous equations with many more unknowns (i.e., the seven angles) than equations (i.e., the three space coordinates), leading to an infinite number of solutions. The challenge of coordinating several degrees of freedom is, consequently, also known as Bernstein's Problem[361] and it can be observed in most of the descriptive levels of the sensorimotor system. For example, when trying to deduce how much torque should each elbow muscle deliver to produce an exact total joint moment provided that the joint is crossed by three flexors and three extensors or when considering that there are some 5,000,000 descending fibres to control over 150.000 motor neurons, 750 muscles and 100-150 biomechanical degrees of freedom of movement[358,362]. As aforementioned, Bernstein considered motor redundancy a challenge to coordination. Yet, he was far from being the first to recognise coordination as an essential function of the central nervous system. For example, in the middle of the XIX century, the French Neurophysiologist Marie J Flourens worked on the role of the cerebellum in motor coordination[363]. Later on, Roger Sperry eloquently argued in a scientific communication: *".. the principal function of the nervous system (is the coordinated innervation of the musculature). . .[and] the sole product of brain function is motor coordination"*[364]. Yet, understanding a neural mechanism capable of coordinating tractably and robustly the high number of degrees of freedom and simultaneously generating diverse motor behaviours relevant to survival has remained, to date, a central open question in neuroscience[365,366].

One of Bernstein's most iconic propositions arises from his definition of coordination, which states: *"… The co-ordination of a movement is the process of mastering the very many degrees of freedom involved in a particular movement, in other words its conversion to a controllable system - of reducing the number of independent variables to be controlled… More briefly, co-ordination is the organization of the control of the motor apparatus."*[358,361]. In his work Bernstein not only made the problem of redundancy explicit but partially solved it by suggesting that the CNS unites elements into groups, synergistically organising them to decrease the number of variables to be controlled. Hence, his work became a milestone in the

study of motor control and has motivated copious research into muscle synergies as a solution for motor redundancy.

Like most cases in science, Bernstein's proposals were based on previous research. For example, the notion of muscle synergies, a Greek-derived word that means working together (συνεργός), was developed by the French neurologist Joseph Babinski, who linked impaired muscle coordination to a pathology in the cerebellum and called such discoordinated movements "*cerebellar asynergies*"[367]. Furthermore, in the descriptions of his three-level representation of movement in the CNS theory, the great J. Hughlings Jackson wrote: *"...the central nervous system knows nothing about muscles, it only knows movements" (p.358),* and continued on the same page: *"In the highest motor centres (prae-frontal lobes) . . . the same muscles are represented (re-re-represented) in innumerable different combinations, as most complex and most special movements."*[368]. In the same direction, the observations of a German scientist on the wiping reflex in decapitated frogs provided the notion of some level of movement organisation in the spine. In his experiments, Eduard Pflüger placed a small piece of paper soaked in a weak acid solution on the back of a headless frog suspended from a frame. After a short delay, the frog wiped the piece of paper off its back with a coordinated motion of the hindlimb, leading him to conclude that the spinal cord can control targeted movements and that spinal reflexes could switch and lead to the activation of different muscle groups[369].

Later on, the school of the Russian physiologist Ivan Sechenov introduced the concept of inhibition, a remarkable development in the understanding of the neural control of locomotion[370]. An insight further developed later by whom is considered by many as the father of contemporary neurophysiology and Nobel Prize in Physiology or Medicine in 1932, Sir Charles Sherrington and his school. Along with incorporating the notion of synapse into neurophysiology and introducing the idea of active inhibition within the CNS as a method of coordination of movements (for a review of his contributions, see Stuart et al. 2001[371] and Callister et al. 2020[372]), Sherrington was the first to view muscle reflexes not as stereotypical responses but rather as tunable mechanisms that formed the basis of motor behaviour. Based on his experiments, he proposed that the excitation of a population of spinal neurons that connect multiple spinal cord segments (i.e., what we call today interneurons and which mere existence was also first described by him) evoked complex or "long" motor reflexes. Moreover, he also proposed that complex motor patterns like stepping or standing resulted from modulating reflex loops originating from sensory receptors[373,374]. One of his trainees reached, however a different opinion. After continuing working on one idea that Sherrington had previously abandoned, Thomas Graham Brown concluded that the spinal cord contained neural structures able to

produce rhythmic patterns without sensory input. In this proposal, an independent spinal neuronal network called "half-centres" were capable of producing flexion and extension of the limbs independently of descending and/or sensory inputs. Then, some interneuronal spinal connections created a mutual inhibition between the flexion and the extension "half centres" to create locomotion[375]. This seminal work was subsequently supported by several decades of evidence from the 1960s onwards with the development of intracellular recordings. Consequently, a group led by the Swedish Anders Lundberg recorded the location and functional organisation of interneurons in the lumbosacral spinal cord coordinating the ipsi- and contralateral long latency effects of the withdrawal reflex, also known as the flexion reflex afferent[376,377]. Furthermore, given their corresponding rhythmic activity, Lundberg and colleagues proposed that a reciprocal inhibition between the withdrawal and stretch reflexes could participate in the production of a locomotor pattern[376,377]. Since then, the neuronal networks providing the connectivity for these reflexes and their reciprocal inhibitions have been generally referred to as central pattern generators (CPG) and a variety of conceptual designs regarding its organization were proposed[378–381]. Beyond any conceptual differences, the existence of a neuronal network in the spinal cord that controls rhythmic and stereotyped motor behaviours like walking, flying, and swimming is nowadays well established across species and is generally referred to as the CPG for locomotion[382,383]. Furthermore, other functions have been also shown to be coordinated by different central pattern generators[384].

Along with the experiments supporting the existence of the CPG, several behavioural and neurophysiological experiments support the long-standing idea that intrinsic neurally-based motor units with a relatively stereotyped output, such as reflexes or postural responses, are the foundations of coordinated purposeful motor actions [379,385–388]. Yet, these experiments lacked a testable hypothesis about how intentional movement could be generated. Aiming to solve this deficiency, Wynne Lee wrote an essay presenting his "neuromotor synergy hypothesis"[389]. In his essay, Lee developed fundamental concepts to describe and compare the phenomena of synergies under the hypothesis that: *"...low-level, neurally based patterns significantly constrain intentional actions. The hypothesis implies that a wide range of coordinated intentional actions can be generated by recruiting, suppressing, and/or modulating sets of neuromotor synergies, or networks subserving synergies. Neuromotor synergies are hypothesized to differ from biomechanical, task, or cognitive constraints; although in many cases, these constraints doubtless overlap in both effect and mechanism."*. Moreover, he drifted away from the goal-oriented definition of synergy (i.e., a set of muscles which act together to produce a desired effect[386]) and defined neuromotor synergies in a structural approach as

"neurally based units of action", implying a substantial difference with other neural entities like a reflex- or a CPG-generated response, in his words: *"… as used here, the neuromotor synergy concept is extended to include other types of neurally based patterns and processes… Some examples of what I mean by neuromotor synergies are: (a) coherent patterns of electromyographic (EMG) activity in sets of muscles (or, patterns of torques or movements around sets of joints) which can be elicited by electrical stimulation of localized supraspinal neural structures; (b) action patterns generated by spinal circuitry; (c) multi-muscle postural reactions; and (d) classically defined responses such as stretch, vestibular, cervical, and flexor-withdrawal reflexes. Such patterns all can be generated by automatic, non-intentional processes. The problem for this essay is to develop ways to decide whether such automatic synergies are also involved in generating intentional actions.".* Lastly, Lee also build empirically testable models for how synergies might be combined to generate intentional actions and proposed that neuromotor synergies should be characterised statistically to be recognised and compared in automatic and intentional actions. However, due to the lack of available data, he failed to provide conclusive support for or against his hypothesis[389].

A few years later Emilio Bizzi and colleagues began publishing a series of papers providing experimental evidence of the existence of neuromuscular synergies in the spinal cord. In the first one, they identified a discrete map of a few spinal locations that, when stimulated, imposed a specific pattern of muscle activation that generated a specific motor output[390]. This motor output was characterised by the endpoint of the corresponding hindlimb generating a collection of forces that varied according to the biomechanical constraints of the limb and converged towards a specific direction. Consequently, they proposed that these evoked "force fields" represented the mechanism whereby the CNS performed the sensorimotor transformation from movement planning to execution[390]. Later on, Bizzi and colleagues established that stimulating two individual force fields resulted in a pattern equal to the vectorial addition of both fields[391,392]. These experimental observations led them to hypothesise that the linear combination of a few basic modules may account for the production of movement and posture. Under this paradigm, a module was defined as *"a functional unit in the spinal cord that generates a specific motor output by imposing a specific pattern of muscle activation"[393]* and, in subsequent reports, they provided further evidence of a modular organisation in the spinal circuitry of the frog that reduced the number of variables to be controlled for the production of movement[393,394]. This series of work represented an extraordinary step in the field, as it proposed a feasible solution for the CNS to achieve both control and behavioural diversity via the combination of such pre-organised low-level units

(i.e., motor modules) to compute motor commands. Furthermore, in 1999 Bizzi and colleagues were able to bring the numerical ideas of Lee into practice y using a computational approach. After obtaining a range of electromyographic recordings generated by numerous cutaneous stimulation of frogs' hindlimbs, they extracted a small set of modules from the EMG recordings based on a factorisation method. Further, they provided evidence that the flexible combination of these modules accounted for a large number of different motor patterns produced by different animals. Thus, they concluded that it is possible to identify a set of motor modules by factorising EMG recording during behavioural actions and inspired by the work of Lee, they called these modules "muscle synergies"[395]. Moreover, based on the similarities of these results with their previous observation of direct spinal recordings, they also proposed these synergies to represent the basic elements or "building blocks" of coordination for the production of complex movement and posture[395,396].

Following these experiments, in the last two decades, the idea that spinal neural circuitries are organized into modules, each of which activates a set of muscles together as a "muscle synergy" has been supported by a substantial body of experimental evidence in the frog[397,398], rat[399], cat[400] and monkeys[401]. These neural modules have been proposed to be underpinned by interneurons in the spinal grey matter[402–404] and good experimental evidence supporting such proposal has been provided by spinal focal stimulation[397,405] and spinal spike recordings[406–408]. Similarly, several reports confirmed that combining these neural modules' output can account for reproducing functional movements[398,401,409,410]. Furthermore, a recent optogenetic study provided strong evidence supporting the topographic representation of spinal modules and the linearity in their combination for producing movement[411]. The results from this optogenetic study are strongly related to a specific class of interneurons previously identified by Levine and colleagues which are molecularly linked with organising spinal modules and they called "*motor synergy encoder*"[412]. These synergy encoders receive inputs from both the motor cortex and sensory pathways and drive motoneuronal activations to multiple muscles at different spinal levels[412]. Thus, their circuitry provides support to the idea that motor modules are driven by descending motor commands from the cortex and the brain stem[413] and that sensory afferents modulate them[414]. Moreover, based on the excitatory characteristics of these synergy encoders and some previous observations of activating glutaminergic neurons being sufficient to initiate and maintain locomotor rhythm[392], it has been proposed that the spinal interneuronal networks shaping motor modules are likely excitatory, though they can be modulated by other neurons expressing other neurotransmitters[411,412,415]. Yet and despite these tremendous advances, the structural principle within the neural circuitries that allows the CNS to represent and

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execute motor commands in a simplified manner is still a motivating open question in neuroscience[416,417].

In the last decades, along with the aforementioned experiments assessing the neural circuitry structure of muscle synergies, several publications have used a factorisation method to retrieve the structures of muscle synergies from behavioural EMG of various species and across different motor behaviours[396,418–420]. In all these experiments embracing the muscle synergies concept, synergies are proposed to reflect a neural strategy to simplify the coordination and control of functional motor behaviours. Taken together, the results of all these experiments indicate that for a single task, it is possible to reduce the number of muscle activation into a discrete number of units (i.e., the muscle synergies). Concordantly, muscle synergies have been used successfully retrieved to describe muscle coordination during manifold motor behaviours including balance control[418,421], reaching[422,423], grasping[420], cycling[424–426] and walking[427–429].

1.3.2. The numerical approach to muscle synergies

As mentioned above, the modular organisation of natural behaviour can be observed using a decomposition technique on the muscle activation patterns during a motor task in animals and humans. A typical decomposition algorithm retrieves the structure of the muscle synergies from the variability of the activation EMG patterns of the acting muscles[395]. Thus, when decomposing the recorded EMG signals, the resultant synergies are composed of two elements derived from the following model:

$$m_j^{obs} = \sum_{i=1}^{N} C_{ij} W_i ; C_{ij} W_i \geq 0 \quad \text{(eq. 1.1)}$$

where m^{obs}_j is the recorded EMG signals, C is the positive weighted coefficient of the ith muscle synergy for the jth response W_i is the ith muscle synergy and N is the number of synergies[395]. Note that the authors restricted both elements of the synergies (i.e., C and W) to positive values due to the undeniable non-negative nature of the muscle activation[395]. Since then, several other methods for reducing the dimensionality of the data and represent the structure of the synergies by extracting the statistical regularities from the EMG variability have been used. Although these algorithms differ in their assumptions and implementations, all of their formulations match the original muscle synergy model and enforce linearity in the combination of the synergies as a constraint[417,430]. Thus, a typical synergies analysis collects the recorded EMG signals in a matrix M and decomposes them through an algorithm into two matrices C and W so that:

$$M = CW^T + R = \Sigma C_i W_i^t + R \quad \textit{(eq. 1.2)}$$

where M is the matrix containing the recorded EMG signals, matrix C contains the temporal coefficients of the synergies, matrix W contains the weighted components of the muscle synergies, and R is the residual explained by the model[395,430]. The best linear combination of the synergies is obtained through an iterative rule that minimises the error of the EMG reconstruction[395,430]. The above formulation presupposes each synergy as a time-independent vector, despite a muscle belonging to multiple synergies. Other models of muscle synergies, such as those based on time-varying bases, have been proposed[396,431], yet most of the experimental evidence supports the concept of movement arising from the combination of time-independent synergies via temporal recruitment[228,432,433]. Thus, methods such as factor analysis, principal components analysis, independent component analysis and non-negative matrix factorisation have been used to extract muscle synergies[430,434]. However, applying any of these factorisation methods will produce very similar results on a simulated and experimental dataset[430,435].

Among the factorisation methods for extracting muscle synergies, the non-negative matrix factorisation algorithm (NMF) is recognised as the best alternative[436]. Proposed in 1999 by Lee and Seung, NMF is an alternative machine learning algorithm that distinguishes itself from other methods by constraining its elements to be non-negative. These constraints allow only additive, not subtractive combinations leading to a part-based representation (i.e., learning) of the original data. Thus, when the NMF is implemented as a neural network, such part-based representation emerges, "… *by virtue of two properties: the firing rates of neurons are never negative and synaptic strength do not change sing*"[435]. As also acknowledged in the original model[395], imposing a non-negative restriction relates to the non-negative nature of firing neurons and muscle activation, facilitating the interpretation of the extracted synergies to a physiological meaning[434]. Concordantly, NMF is proposed as the best factorisation method for identifying muscle synergies in dynamic tasks with different levels of muscle contraction[436].

Although alternative algorithms have been developed to improve the performance of the reconstruction capability and speed of the NMF[437–440], the classical approach is still the most used for extracting synergies from EMG data[429,441,442]. Since this approach is the method of choice for extracting muscle synergies and the synergies concept will be used further in this dissertation, the following paragraphs endeavour to provide a comprehensive description of the classical NMF approach.

First EMG signals are assessed from a large number of muscles during a motor behaviour. Secondly, NMF is used to extract muscle synergies from the EMG, using the historical notation, the classical NMF algorithm can be written as:

$$V(t) \approx V_R(t) = WH(t) \quad \text{(eq. 1.3)}$$

where V represent the original EMG data organised in a m x n matrix and V_R represents the reconstructed matrix approximation of the original matrix V[435]. If m is the number of muscles measured and n the number of recorded time points, then W is a matrix with dimensions m × r containing the time-invariant muscle weightings, which will be called motor modules and H has dimensions r × n and contains the time-dependent coefficients of the factorisation, which in this dissertation will be referred to as motor primitives[437]. Thus, the NMF aims to reconstruct the original data V starting from completely random values of H and W through several iterations until a good quality of reconstruction (i.e., a low residual R in equation 1.2) is obtained assuming that the error follows a Gaussian distribution[443]. Then, the similarity between original and reconstructed data is calculated for each iteration of the algorithm and the limit of convergence is set to a change smaller than 0.01% in the last 20 iterations[414,437]. This is done for a number of synergies successively increased from 1 to a number smaller than the dimension m of V, satisfying (n + m)r < nm. The solution with the highest similarity is selected for each value of r. Then, the dimensionality reduction is achieved by selecting the minimum rank of factorisation r (i.e., the number of synergies) that yields only small changes in the reconstruction quality[435,437].

Lastly, the extracted synergies from all subjects are classified based on their similarities and each cluster is related to a relevant variable for the task. A typical result of a synergies extraction and identification process is presented in Figure 1.3.
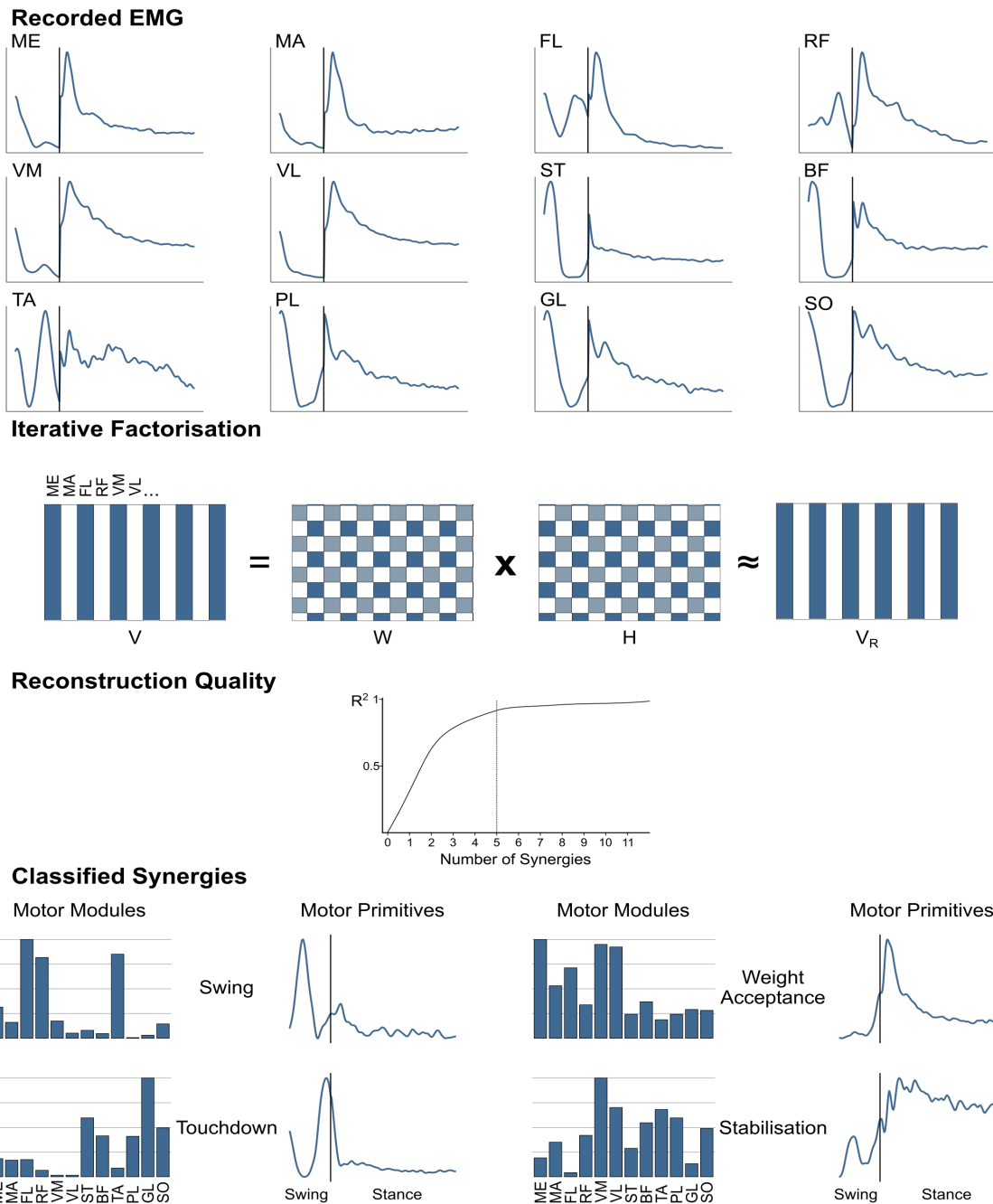
Recorded EMG

Iterative Factorisation

Reconstruction Quality

Classified Synergies

Figure 1.3*. Schematic representation of the muscle synergies extraction process. Twelve behavioural EMG are grouped in a matrix V and factorised via non-negative matrix factorisation into two matrices W containing the time-independent coefficient and H containing the time-dependent coefficients. The matrices W and H are iterated until their multiplication provides the best approximation (V_R) of the original data V. A reduction of dimensionality is obtained by determining by finding the point where the use of an extra synergy yields small changes in the reconstruction quality. The synergies are sorted by the position of the main activity in the motor primitive (i.e., the time-dependent coefficient) and related to a functional goal.*

1.3.3. Neurophysiological basis for the existence of muscle synergies

Despite the vast use of the muscle synergies concept among the scientific community, it is still unclear whether a muscle synergy identified by an extraction algorithm corresponds to an entity of neural origin. For example, a mathematical approach similar to the one above-mentioned has also described "building blocks" at the kinematic level[444,445] and thus, the general idea of modularity in the generation of motor actions can be defined at different levels of the sensorimotor system[404]. Concordantly, one of the main critiques to the muscle synergies hypothesis (i.e., the experimental approach of extracting synergies from EMG data) is that they might reflect constraints imposed by the task rather than reflect a strategy of neural control[446–449]. In this direction, Kutch and Valero-Cuevas showed, through cadaveric experiments and computational models, that the selected task and the anatomy or limb's biomechanics imposed constraints that resulted in an apparent muscle coupling. This coupling was similar to the reported extracted synergies for reaching despite forcing each muscle to be independently controlled in the computational mode Thus, they concluded that muscle coupling arises from a feedback-control (e.g., the stretch reflex) related to the changes in the muscle length rather than a neurally-based synergy[446]. However, a conciliatory alternative proposes that the observations from Valero-Cuevas et al. are not inconsistent with the muscle synergies hypothesis as synergies might be tailored to the biomechanics of the individual[450]. Based on the reported existence of muscle synergies at birth and the subsequent enhancement of the synergies' repertoire through our development into maturity[451–453], this alternative view states that sensory feedback plays a role in learning and tuning the synergies within the spinal circuitry. Then, these neural adaptations incorporate the changes in the sensorimotor system through our entire lifespan tailoring the motor command to the biomechanical output and integrating it into every level of the CNS[450]. Thus, this proposal is compatible with the reported subject-specificity of some synergieies[421] as they would be a consequence of individual biomechanical differences. Furthermore, it allows the precise structure of synergies to incorporate knowledge of musculoskeletal dynamics[454] whilst acknowledging the observations of Kutch and Valero-Cuevas emphasizing the contribution of non-neural constraints in the dimensionality reduction of muscle activations[455].

Further proof against the notion of muscle synergies was provided by the observations that the production and control of finger force are facilitated by controlling muscles individually[448]. Moreover, the variability observed in the finger's force control supports the idea of minimal intervention or uncontrolled manifold rather than a synergies approach[447]. Nonetheless, the same authors criticising the synergies model acknowledged that their observations are not

completely against the existence of synergies as their analyses were based on intra-trial variability and, in this context, synergies might be useful for planning the task[447] and proposed experimental direction that might disambiguate synergies of neural origin from the potential confounds[446]. Furthermore, the uncontrolled manifold hypothesis relates to structures which are identical to muscle synergies (i.e., referred to as 'muscle-modes' or 'm-modes' in that work) with the sole difference that they are not the main element of motor control but a subsystem of it[456–458]. Concordantly, it is well accepted that proving the muscle synergies hypothesis wrong is very difficult, though there is no consensus as to how much muscle synergies extracted from EMG represent neural constraints on movement[455,459,460]. Nonetheless, as the muscle synergies concept provides the possibility of accessing their spatial and temporal components separately (i.e., the motor modules and motor primitives respectively) they can be validated through different experimental techniques of neuroscience[417]. As a consequence, several publications and comprehensive reviews have attempted to further establish the connection between synergies identified from behavioural EMG signals and their neurophysiological foundations[402,404,407,417,450,461–464]. Hence, despite it remains challenging to pinpoint the exact anatomical and physiological properties of a synergy, these observations suggest that the spatial (i.e., the motor module) and temporal (i.e., the motor primitive) coefficients of a synergy may originate from different anatomical neuronal networks. Thus, whilst the existence of neural synergies in the spinal cord organised by interneurons in the intermediate zone of the spine is strongly supported by experimental evidence[393,397,398,407,411], the relationship of the extracted motor modules with these spinal structures is supported by direct measurements of the muscle field of some pre-motor interneurons (i.e., the pattern of projection of a pre-motor neuron to the motoneuronal pool of multiple muscles) resulting in a distribution which correlates directly with the synergies extracted from EMG recordings by an NMF algorithm[406–408] and the observations of motor modules remaining unaltered after spinal transection across different locomotion speeds and even several left-right speed differences[465,466].

There is also experimental support evidencing that the temporal activations of muscle synergies identified by computational algorithms (i.e., the motor primitive) are an expression of neural activity[450,467]. The existence of multiple sensorimotor loops involving the cortex, other brain regions, the spinal cord and the periphery converging upon the primary and pre-motor cortex and including descending paths from the cortex is well established[463,468,469]. Thus, as the temporal coefficient of a synergy represents the temporal coordinating patterns that generate goal-oriented movements, motor primitives should largely involve neuronal activity from other supra-spinal areas in the CNS organizing and driving the muscle synergies. Concordantly, there

is supporting evidence demonstrating the existence of representations of synergies in the motor cortex[470,471] and such representations have been proposed to have a direct neural connection with the corresponding muscle synergy via a neural loop[471]. Moreover, stimulating such specific cortical areas evoked an action that correlated with the activation of specific motor modules that were previously extracted from behavioural EMG recordings[472,473]. In addition, a synchronic neural activity between the motor cortex and muscle synergies was revealed by a specific cortico-synergy coherence encoding information for controlling movement and balance in humans[470,474].

In consequence, although it is hard to prove a direct relationship between synergies extracted from EMG and their neural basis, it seems that the neuroscience community is converging around a consensus regarding the existence of some kind of synergies. Yet, up to date we still lack a mechanistic understanding as to how supra-spinal networks, possibly in conjunction with midbrain circuits, generate a series of commands selecting spinal synergies with their different timing and scaling factors. Nonetheless, assessing motor modularity based on the muscle synergies approach remains recognised as an advantageous alternative for studying a simplified representation of motor coordination.

1.3.4. Synergies in the presence of perturbations

Since the activity of each muscle synergy extracted from EMG is hypothesised to accomplish a biomechanical task[409,419,475], the recruitment of a synergy during a motor behaviour depends on the spatiotemporal requirements of the task's goals[228,433]. Hence, whilst muscle synergies related to standing balance produce vectors of ground reaction force with different functions for controlling the centre of mass[419,476], muscle synergies extracted during walking are associated with biomechanical sub-task such as weight acceptance, propulsion and swinging the leg[427,428,477]. Thus, muscle synergies are proposed to represent a translation of the sensorimotor transformations needed to produce a task-level goal with the required execution commands for coordinating a multi-joint movement[285,478,479]. As these task goals might be shared by several motor behaviours, common muscle synergies have been reported across different motor behaviours in different species[419,455,480]. Concordantly, scaling and temporally tuning the muscle synergies have been reported to account for changes in the locomotion speed[429,481], walking under different load conditions[427,482] or when performing a concurrent voluntary task[483]. Considering the individual characteristics of the modules, modulating muscle synergies has been proposed to underlie the variability of a motor task[465,477,484]. Moreover, common muscle

synergies were observed when reaching under different dynamic and postural conditions[423] and variations of standing postures and reactive balance strategies[421,476]. Shared synergies were also reported between stepping and non-stepping balance responses[476] and between walking and stepping reactions[485]. Thus, muscle synergies are proposed to allow a generalisation of coordinative patterns that is exploited by the CNS to simplify control, allowing a rapid adaptation to different dynamic conditions[461,486,487]. Consequently, muscle synergies can also promote motor adaptation to a novel task, facilitating learning[404,488]. Under this view, they facilitate motor learning by permitting the execution of new motor behaviours based on existing modules that can be shaped throughout training to improve performance or create new synergies[489].

A remarkable support for muscle synergies being capable of reflecting motor adaptation and learning was provided by studies showing a progressive addition of new muscle synergies to those observed at birth and that these synergies are fine-tuned during motor development[451,490]. Further support for evidencing differences in the structure of muscle synergies across levels of motor ability comes from the reported larger number of synergies in highly skilled or trained individuals[491] and studies on motor-impaired populations. In the latter, both the spatial and temporal structure of the synergies are related to motor impairment as the number of synergies is altered due to merging or fractionation[484,492,493], the number of co-active muscles in the motor modules is also increased[484,493] and the motor primitives (i.e., the temporal recruitment) becomes broader and more variable[494,495].

The widening of the motor primitives is strongly related to the diminished capacity of the neurologically impaired for integrating sensory information, as evidenced by a study assessing the effects of impairing proprioceptive integration on the modular organisation of murine locomotor patterns. Genetically modified mice lacking muscle spindles also modified the muscle synergies mainly by widening their temporal structure[496].

Indubitably sensory information also plays a fundamental role in acutely modulating muscle synergies and the muscle synergies have also been proven to account for such acute modulations as a consequence of mechanical or sensory perturbations during a postural task[476,497] or locomotion[12,441,498,499]. For example, locomotor muscle synergies exhibited a variation in their temporal recruitment that could account for cycle-by-cycle variations in muscle activity and accounted for both anticipatory and reactive responses to perturbations while walking[499]. Among these responses, it is noteworthy that perturbing locomotion with slippery, narrow or uneven surfaces also induced a widening of the motor primitives[12,498]. Since the wider primitives created an overlap of temporal adjacent synergies, this overlap was

proposed to provide a buffer of muscular activity that increases the ability of the system to cope with perturbations[12]. Thus, robust locomotion is promoted by producing control signals that are less wider, less complex and more stable over time[441].

Maintaining functionality despite internal and external perturbations is commonly referred to as robustness and it is considered a fundamental feature of complex biological systems[26]. Thus, this property is widely observed across many species as an organisational principle from the level of gene transcription to system homeostasis. Moreover, traits that enhance the robustness of a system or organism are often selected by evolution[26,500]. Though robustness is often misunderstood to represent an unvarying state regardless of stimuli or mutations, robustness often requires the system to change its mode of operation in a flexible way to maintain functionality[26,501]. Thus, from a dynamic system theory standing, a robust system presented to perturbing stimuli, will either return to its current state (i.e., its attractor) or it can transition to a new state where the system behaves consistently against such perturbations (i.e., a new attractor). Attractors can represent coordination tendencies among different components of a system[502] and robust adaptations have been proposed to reflect training effects[503,504]. Considering the association between the ability to withstand perturbations and decreasing the rate of falls, the reported widening of the motor primitives appears to be a potentially relevant adaptation that calls for further research, particularly since the mechanisms underpinning the adaptations to perturbations are largely unknown.

1.4. Purpose of the thesis

Falls are a major and increasing public health problem. They represent a significant threat to the health, mobility and well-being of people which may result in substantive financial costs[72]. As most falls result from unexpected perturbations, fall avoidance largely relies upon the capacity to generate appropriate responses to such perturbations[43]. However, the ability to perceive a perturbation and promptly generate an adequate motor response declines with age along most sensorimotor capacities leading to an increased risk of falling in the elderly[119]. Consequently, several intervention modalities have been carried out to reduce the risk of falling. Yet, due to the multifactorial nature of falls, the effectiveness of these interventions has shown manifold[214]. Nonetheless, the sensorimotor capacity can be enhanced by training exercise and thus, exercise is extensively recommended as a valid intervention for reducing the number of falls and fall risk[179]. However, not every training yields a reduction in the number of falls and a closer examination of the effectiveness of the training interventions has also shown

manifold[179,182]. Our current understanding indicates that targeting reactive balance is of paramount importance for effective training interventions and, concordantly several perturbation-based paradigms have been developed[181]. Yet, most of the gains are specific to the characteristics of the perturbation and thus, these interventions have failed in transferring the improved balance recovery skills to untrained situations[240,346,352]. On the other hand, a promising capability to improve balance performance and transfer the gains to untrained task have been consistently reported over a training approach focussing on eliciting the fundamental balance recovery mechanisms (i.e., counter-rotating body segments around the centre of mass and increasing the base of support) onto unstable surfaces to induce perturbations[205,351]. Moreover, such training approach also induced an increment in muscle strength[302,354]. However, we still lack a mechanistic understanding of the factors underpinning these promising results and, consequently promote an effective training intervention for reducing falls.

This dissertation aims to further our understanding of the fundamental neuromotor elements promoting the functional benefits of the above-mentioned effective training intervention, with the perspective that this knowledge could improve tailoring the design of effective training interventions for reducing falls in both healthy elderly and clinical populations. For investigating what are the factors underpinning the reported improvements, comparing the execution of exercises that resembles those included in a typical training session with and without the presence of perturbations in healthy young individuals is an interesting choice. Firstly, because this design might highlight the different demands of performing a task in the presence of perturbations that underpin the sensorimotor adaptations promoting the desired functional benefits. Secondly, because any difference in the assessed variables should be explained by the demands of the task and not the functional capacities of the participants and thirdly because a single training session should be enough to identify the variable(s) that acts as training stimulus which will promote a sensorimotor adaptation with repeated exposure. Furthermore, the muscle synergies approach is a useful tool as it provides a compact representation of the sensorimotor transformations undergone to perform a task and also insights into the neuromuscular organisation of motor control. Moreover, as some of the reported gains can be also explained by a muscular adaptation, assessing an indicator of the mechanical demands arising from performing the task is also necessary.

These issues were addressed in four working steps:

1. Training and development of generic and specific research skills, particularly to the study and development of the experimental and computational tools for assessing and analysing EMG activities, the extraction of muscle synergies from EMG signals, capturing and analysing kinematic and kinetic data.

2. Understanding the rationale for effective fall reduction training interventions and designing the experimental protocols.

3. Investigate the neuromuscular responses to the presence of perturbations when performing exercises that promote the use of the fundamental balance recovery mechanism on unstable surfaces.

4. Analyse the acute changes of the neuromuscular organisation in the sensorimotor system and the selected mechanical variables of the motor output induced by the unstable surfaces with respect to the unperturbed condition.

Based on the reported ability of training the fundamental balance recovery mechanism onto unstable surfaces to improve balance performance and increase the muscle strenght[302,354], the working hypotheses underlying the body of this thesis were the following:

1. The presence of perturbations will result in a challenge to balance inducing changes in the integration of sensory information into motor commands to create adequate responses

2. The different sensorimotor transformations will be reflected in the modular organisation of movement control

3. The responses to the perturbation will be characterised by a widening of the motor primitives which promotes increased robustness of the movement control

4. The instability induced by the unstable surfaces will also induce an increased activation of the muscles

5. The increased muscular activity act as training stimuli that promote the reported gains in muscle force

The topics were addressed in three different published studies presented in the body of this thesis. Each study is reported here with a reference style that matches the one of the whole thesis to improve readability. References, figures, tables and equations are numbered consecutively for the same reason.

2. First study: Neuromuscular organisation and robustness of postural control in the presence of perturbations

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2.1. Abstract

Perturbation-based exercise interventions challenge balance and improve reactive motor control. Our purpose was to investigate the modular organisation during a standing balance task in both stable and unstable conditions to provide new insights into the neuromuscular control mechanisms needed to cope with perturbations. Fifteen participants performed 54 cycles of a specific task (i.e. pass from a double- to a single-leg standing) on stable ground and an unstable oscillating platform (Posturomed). Muscle synergies were extracted from the electromyographic activity of thirteen lower limb muscles. The maximum Lyapunov exponents of different body segments were calculated using kinematic data. We found two synergies functionally associated with the single- and double-leg stance in both stable and unstable conditions. Nonetheless, in the unstable condition participants needed an extra muscle synergy also functionally related to the single stance. Although a simple organisation of the neuromuscular system was sufficient to maintain the postural control in both conditions, the increased challenge in the oscillating platform was solved by adding one extra synergy. The addition of a new synergy with complementary function highlighted an increased motor output's robustness (i.e. ability to cope with errors) in the presence of perturbations.

2.2. Introduction

For humans, maintaining balance is a necessary requirement not only during locomotion[505] but in many other motor tasks as well[5,314,506,507]. Daily-life activities involve perturbations which challenge the neuromuscular system to modify its control strategies[12,508,509]. Challenging balance conditions and perturbations have been proposed as an effective exercise intervention to reduce fall risk in older adults[242,303,510]. Training programmes using unexpected or continuous

perturbations to exercise the mechanisms of dynamic stability have the potential to enhance muscle strength as well as sensory information processing within the motor system[354]. Furthermore, perturbation-based interventions improve reactive balance control in post-stroke[254,511] and Parkinson's disease patients[241]. The reaction to a perturbation is related to the type of perturbation, whilst a large perturbation may require a recovery movement a small perturbation will not necessarily modify the motor behaviour[504]. Both abilities, cooping with large and small perturbations are key components for a stable motor output[512]. The sensitivity of any system to small perturbations is normally referred as "local stability"[513] and is crucial for the execution of a task uninterruptedly in dynamic conditions[75,237]. The maximum Lyapunov exponent (MLE) is a measure of the local dynamic stability and is considered to reflect the ability of dynamical systems -such as humans during gait- to withstand perturbations[512–515]. The theoretical concept of the MLE suggests that although the entire dynamic of the system can be approximated by measuring only one site[516,517], assessing different components of the system may also provide specific information about the sub-system being evaluated[514].

There is little information about how muscle activations are organized to control the body in the presence of perturbations. Nonetheless, challenging motor control strategies through perturbations is an effective way to investigate the neuromuscular responses to unstable conditions[12] and could highlight possible neuromuscular mechanisms responsible for the positive effects of perturbation-based interventions.

A generally accepted idea is that the central nervous system (CNS) might simplify the production of movement by activating muscles in common patterns called synergies[358,391,402]. Instead of activating each muscle individually, the CNS might create a motor output by combining small sets of time-dependent commands (motor primitives) and time-independent weights (motor modules) that create patterns in muscles[391,402,450]. It has been proposed that synergies may be specific to each task[421]. This task-related control could allow for fast reconfigurations when the task demands change[518,519]. During walking and running, although the general modular organisation remains unaltered in the presence of perturbations, a modification of the temporal components of the muscle synergies, characterized by a widening of the motor primitives, has been reported[12,498]. This widening increases the overlap of chronologically adjacent synergies and has been interpreted as a motor control strategy that is used to increase the robustness of the neuromuscular system's output while performing a task[12,496,504]. Kitano proposed that a biological system is evolutionarily robust when its characteristics can withstand perturbations or uncertainty[26]. In a similar manner, robustness can be defined as the ability of the CNS to cope with perturbations or with errors of execution[12].

Therefore, using perturbations offers advantages to study the neuromuscular responses that might be providing robustness to the neuromuscular system's output, and be, consequently, related to the effectiveness of fall prevention programs. Hence, the purpose of the current study was to investigate the modular organisation in healthy young adults during a standing balance task on a stable and an unstable platform in order to improve our understanding of the neuromuscular control mechanisms in the presence of external perturbations. We hypothesized an increased robustness of the motor output in the unstable compared to the stable condition, achieved through a reorganisation of the time-dependent activation coefficients (motor primitives) of muscle synergies.

2.3. Methods

2.3.1. Experimental protocol

We recruited 15 healthy adults (11 males, 4 females, height 1.75 ± 0.10 m, body mass 67 ± 11 kg, age 28 ± 5 years). The sample size was a priori calculated based on the aforementioned motor primitive's modification in the presence of perturbation during locomotion[12]. All participants were regularly active and had no history of neuromuscular or musculoskeletal impairments, nor any injury at the time of the measurements or in the previous six months. The Ethics Committee of the Humboldt-Universität zu Berlin reviewed and approved the study design (HU-KSBF-EK_2018_0013). All the participants gave written informed consent for the experimental procedure, in accordance with the Declaration of Helsinki. Kinematics data were recorded through a ten infrared-camera motion capture system (Vicon, Oxford, U.K.) operating at 250 Hz. The activity of 13 ipsilateral muscles was recorded using a 16-channel wireless electromyography (EMG) system (Myon m320, Myon AG, Schwarzenberg, Switzerland), with a sampling frequency of 1 kHz.

The participants were asked to pass from an initial double- to a single-leg standing on the right foot (DLS and SLS, respectively), maintain the SLS position for 3 s and return to the DLS. The whole cycle, defined as the time between two consecutive foot lift-offs, lasted for 6 s and the task was then immediately repeated (Figure 2.1). A metronome aided with timing the task. The participants performed 54 cycles, on two different surfaces: hard uniform stable ground (SG) and damped oscillating unstable platform (Unstable Ground – UG, Posturomed Haider GmbH, Germany). The platform consisted of a 60 * 60 cm plate suspended by a double swinging mechanism that responded to any force application with a maximum damped displacement of

50 mm to the sides and 80 mm in the anteroposterior direction with an oscillation frequency between 1.0 and 3.2 Hz. (Figure 2.2). The order of conditions was randomized.
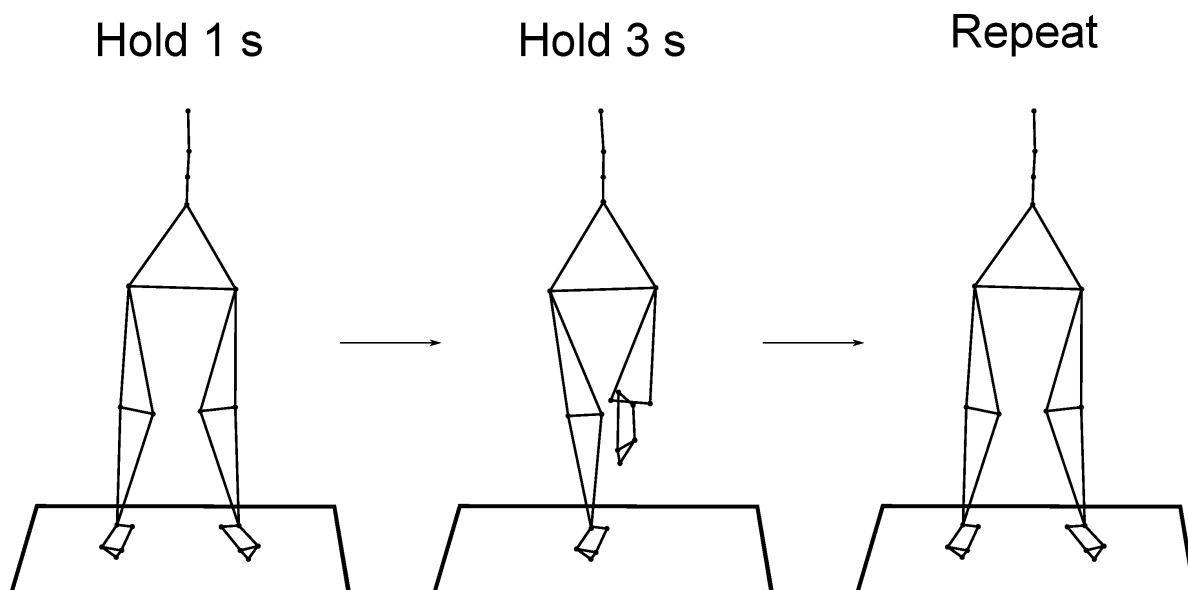

Figure 2.1. *Description of the performed task. Participants were asked to pass from a double- to a single-leg stance, maintain the position for 3 s, return to the bipedal position and after 1 s repeat the task*

2.3.2. Cycle assessment

Sixteen reflective markers were placed bilaterally on the following anatomic landmarks: greater trochanter, lateral and medial epicondyle of the femur, Achilles tendon insertion on the calcaneus, lateral malleolus, tip of the first toe, dorsal margin of the fifth and first metatarsal heads. The second, seventh and tenth thoracic and the second lumbar *vertebrae* were marked as well. The cycle breakdown was obtained from the kinematics of the foot (calcaneus, toe tip, fifth and first metatarsal). This data was low-pass filtered using a 4th order IIR Butterworth zero-phase filter with cut-off frequency of 50 Hz[520]. Touchdown was estimated using the modified foot contact algorithm developed by Maiwald *et al.*[12,520]. For assessing lift-off, we used the foot acceleration and jerk algorithm[12]. The algorithm searches for the vertical acceleration's global maximum of the fifth metatarsal between two consecutive touchdown events to estimate the lift-off (LOe, where the "e" stays for "estimated"). To get closer to the "real" lift-off timing, a characteristic minimum in the vertical acceleration (i.e. when the jerk equals zero) of the fifth metatarsal marker is identified in a reasonably small neighbourhood of the LOe. We found [LOe – 50 ms, LOe + 200 ms] to be the sufficiently narrow intervals

needed to make the initial lift-off estimation. Since all participants, in the SG condition, stepped with the left foot onto a force plate (AMTI BP600, Advanced Mechanical Technology, Inc., Watertown, MA, USA) we assessed the performance of both approaches in this condition against true values assessed from kinetic data. True errors were of 9 ± 6 ms for the estimation of touchdown and 13 ± 9 ms for the estimation of lift-off. To avoid inaccuracies, the first and last two cycles were removed from each data set and the central 50 cycles were kept for further analysis.
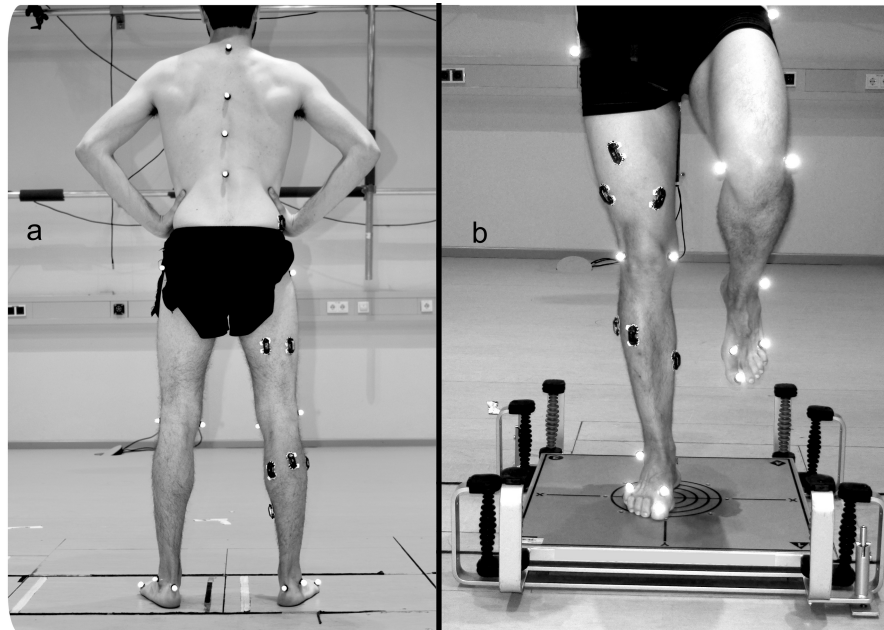

Figure 2.2. Reflective markers and EMG sensors position. Panel "a" shows the hard ground condition and panel "b" shows the damped oscillating platform used as unstable ground condition.

2.3.3. EMG recording and processing

The activity of the following 13 ipsilateral (right side) muscles was recorded: *gluteus medius (ME), gluteus maximus (MA), tensor fasciae latae (FL), rectus femoris (RF), vastus medialis (VM), vastus lateralis (VL), semitendinosus (ST), biceps femoris (long head, BF), tibialis anterior (TA), peroneus longus (PL), gastrocnemius medialis (GM), gastrocnemius lateralis (GL)* and *soleus (SO)*. The EMG signals were high-pass filtered and then full-wave rectified and low-pass filtered using a 4th order IIR Butterworth zero-phase filter with cut-off frequencies of 50 Hz (high-pass) and 20 Hz (low-pass), respectively[12,437] using R v3.4.4 (R Found. for Stat. Comp.). After subtracting the minimum, the amplitude was normalised to the maximum activation recorded in each trial[418]. Each cycle was time-normalised to a length of

1200 points through resampling the data. To approximately maintain the ratio between the SLS and DLS timing, we assigned 800 points to the SLS and 400 points to the DLS.

2.3.4. Muscle synergies assessment

The classical Gaussian non-negative matrix factorisation (NMF) algorithm[12,435] was used for the extraction of muscle synergies from EMG data through a custom script (R v3.4.4, R Found. for Stat. Comp.). The time-dependent muscle activity vectors were grouped in an $m \times n$ matrix V, where $m = 13$ (number of muscles) and n = number of normalised time points. This matrix was factorised such that $V \approx V_R = WH$. The new reconstructed matrix V_R approximates the original matrix V. H represents the motor primitives matrix[437,451] containing the time-dependent coefficients of the factorisation with dimensions $r \times n$, where r represents the number of synergies necessary to sufficiently reconstruct the EMG signals. The $m \times r$ motor modules matrix $W^{437,493}$, contained the time-invariant muscle weightings. H and W described the synergies necessary to accomplish a movement. The update rules for H and W are presented in Equation 2.1 and Equation 2.2.

$$H_{i+1} = H_i \frac{W_i^T V}{W_i^T W_i H_i} \quad \text{(eq. 2.1)}$$

$$W_{i+1} = W_i \frac{V(H_{i+1})^T}{W_i H_{i+1}(H_{i+1})^T} \quad \text{(eq. 2.2)}$$

The limit of convergence was reached when a change in the calculated R^2 between V and V_R was smaller than the 0.01% in the last 20 iterations[12,437,521], meaning that, with that amount of synergies, the signal could not be reconstructed any better. This operation was first completed by setting the number of synergies to 1. Then, it was repeated by increasing the number of synergies each time, until a maximum of 10 synergies. The number 10 was chosen to be lower than the number of muscles, since extracting a number of synergies equal to the number of measured EMG activities would not reduce the dimensionality of the data. Specifically, 10 is the rounded 75% of 13, which is the number of considered muscles. The computation was repeated 10 times for each synergy, each time creating new randomised initial matrices H and W, in order to avoid local minima[12,480]. The solution with the highest R^2 was then selected for each of the 10 synergies.

The minimum number of synergies required to represent the original signals was chosen fitting the curve of R^2 values versus synergies using a simple linear regression model for all the synergies. The mean squared error was then repeatedly calculated, each time removing the lower synergy point, until only two points were left or until the mean squared error fell below 10^{-5} [12,437]. The extracted synergies were classified based on the timing of motor primitives' global maxima. Following previous definitions [12,437] only fundamental primitives (i.e. showing a single activation peak) were considered. When two or more fundamental synergies are blended into one, a combined synergy appears. Combined synergies usually constitute, in our data, 10 to 20% of the total extracted synergies. Due to the lack of consent in the literature on how to interpret them, we excluded the combined synergies from the analysis.

2.3.5. Metrics for comparison of curves

In order to compare the motor primitives of both conditions, we evaluated the centre of activity (*CoA*) and full width at half maximum (FWHM). The *CoA* was defined as the angle of the vector (in polar coordinates) that points to the centre of mass of that circular distribution [12,522]. The polar direction represented the cycle's phase, with angle $0 \leq \theta_t \leq 2\pi$. The following equations define the *CoA*:

$$A = \sum_{t=1}^{p} \left(\cos \Theta_t \times P_t \right) \quad \text{(eq. 2.3)}$$

$$B = \sum_{t=1}^{p} \left(\sin \Theta_t \times P_t \right) \quad \text{(eq. 2.4)}$$

$$CoA = \arctan \left(B / A \right) \quad \text{(eq. 2.5)}$$

where p is the number of points of each cycle ($p = 1200$) and P is the activation vector. The FWHM was calculated as the number of points exceeding each cycle's half maximum, after subtracting the cycle's minimum [12,522].

2.3.6. Local dynamic stability assessment

We calculated the point-by-point Euclidean norm of the vectors containing the 3D-coordinates of the reflective markers, thus converting the three components (xi, yi, zi) to a single value $n_2 = \sqrt{x_i^2 \, y_i^2 \, z_i^2}$. The resulting data was filtered with a 4th order IIR Butterworth zero-phase filter with a low-pass cut-off frequency of 20 Hz. The anatomical regions of interest were then represented by the respective markers: spine (the 2nd, 7th, 10th thoracic and 2nd lumbar

vertebrae), pelvis (greater trochanter), knee joint (lateral and medial epicondyle of the femur) and foot (lateral malleolus). When two or more markers were related to a region (i.e. spine and knee joint), a point-by-point average was calculated for each marker group after filtering. The resulting single-vector time series for each right lower limb's region and spine were used for further analysis and calculation of the Maximum Lyapunov Exponent. To avoid dependencies, we used the maximum number of shared cycles (50) for all trials and participants[514,523], and excluded the first and last cycle (analysing a total of 48 cycles per participant), one participant was excluded from the analysis due to missing data. The coordinates of the data segments corresponding to the exact number of cycles were then extracted and normalised to a uniform length. The high number of analysed cycles ensured the reliability of the measurements based on our previous studies on locomotion[514,524]. Moreover during our pilot tests we noticed that after the designated number of repetitions fatigue began to set in.

State space reconstruction was achieved through delay coordinate embedding[525,526] for each point of the time series and its time-delayed copies as follows:

$$S(t) = [z(t), z(t+\tau), ..., z(t+(m-1)\tau)]$$

with *S(t)* being the *m*-dimensional reconstructed state vector, *z(t)* the input 1D coordinate series, τ the time delay and *m* the embedding dimension. Time delays were calculated for each time series from the first minimum of the mutual-information curve, based on the Average Mutual Information function[527].

Different values of τ and *m* can yield very different state-space reconstructions[528–530]. It is therefore suggested that optimised values of τ and *m* are necessary to best represent a dynamical system[514,531]. In the current study dimension of 3 was sufficient[514,532] and time delays were individually chosen for each participant and each analysed segment[531]. Time delays were approximately 0.33 of the cycle length which is common in human movement stuides[514,532]. Following the reconstruction of the times series, the Rosenstein algorithm was used to compute the average exponential rate of divergence of the trajectories in the state space, by calculating the linear distance of each point's trajectory divergence to its closest trajectory[513,517]. The MLE were then calculated from the slope of the linear fit in the resulting divergence curves from 0 to 0.25 of a whole cycle. Analysis of the data was performed on MATLAB 2014b (Mathworks Inc., Natick, United States). Higher values in MLE indicate increased instability of the system.

2.3.7. Statistics

To compare *CoA* and FWHM, we used a two-way analysis of variance (ANOVA) with repeated measures, using synergy (SLS, DLS) and condition (SG, UG) as within-subjects factor followed by a Tukey *post-hoc* analysis with false discovery rate *p-value* adjustment. To compare modules between conditions we adopted the same procedure using muscle (number of muscles) and condition as within-subjects factor. A two-way ANOVA for repeated measures was performed with anatomical segment (spine, pelvis, knee joint, foot) and condition (SG and UG) as within-subjects factor on the MLE. A Bonferroni-corrected *post-hoc* analysis was conducted in the case of a significant time effect or interaction of the factors anatomical segment and condition. All the significance levels were set to $\alpha = 0.05$ and analyses were conducted on R v3.4.4.

2.4. Results

2.4.1. Cycle parameters

The duration of the cycles (lift-off to lift-off) did not differ when switching from SG to UG (6.035 ± 0.109 s and 6.013 ± 0.073 s for SG and UG, respectively, p=0.522). The average duration of the SLS did not show differences between conditions either (stable = 3.684 ± 0.509 s, unstable = 3.512 ± 0.534 s, p=0.374). Nonetheless, participants in the unstable condition showed an increased variability expressed in a significant larger variance (stable = 0.137 ± 0.069 s, unstable = 0.307 ± 0.270 s, paired t-test p=0.012).

2.4.2. Local dynamic stability

The MLE was significantly higher at the ankle compared to proximal segments ($F_{(3,39)} = 15.909$, p= 0.001, $\eta^2 = 0.550$) regardless the ground condition. Furthermore, there was an interaction between anatomical segment and condition group ($F_{(3,39)} = 6.866$, p=0.02, $\eta^2 = 0.346$). The MLE was significantly lower at the spine on the unstable ground (p = 0.006, 95% C.I = 86.7:97.7 for the SG and 75.7:86.6 for UG, Table. 2.1). There were no differences for the pelvis (p=0.444) nor the knee joint (p=0.754) or ankle among conditions (Table. 2.1).

Table 2.1. *Maximum Lyapunov exponent between conditions for every segment. The values are presented in mean ± standard deviation, positive differences (Δ>0) denote higher values in the unstable condition. Asterisks denote statistically significant (p<0.05) differences. Post hoc analysis are Bonferroni corrected.*

Maximum Lyapunov Exponent					
Segments	F (3,13) = 15.909, p=0.001, η^2 = 0.550				
Post hoc		Mean ± sd	Δ	p. value	Effect size
Ankle compared to	Knee joint	86.7 ± 1.8	61.7 ± 13.3	0.003*	0.96
	Pelvis	88.7 ± 4.4	62.5 ± 16.0	0.011*	0.98
	Spine	86.7 ± 1.8	63.7 ± 16.4	0.011*	0.99
Condition	F(1,13) = 0.018 , p = 0.895 , η2 = 0.001				
Segment/Condition	F(3,39) = 6.866 , p = 0.002 , η2 = 0.346				
Post-hoc	Stable	Unstable	Δ	*p. value*	Effect size
Foot	142.7 ± 54.0	158.4 ± 70.7	11.0%	0.030*	0.65
Knee joint	89.3 ± 18.6	88.2 ± 17.4	-1.3%	0.754	-0.08
Pelvis	89.2 ± 11.2	86.8 ± 13.5	-2.7%	0.444	-0.21
Spine	81.2 ± 9.4	81.2 ± 9.4	-11.9%	0.006*	0.86

2.4.3. Modular organisation

For all the trials, a minimum of two synergies and a maximum of four were sufficient to satisfactorily reconstruct the measured EMG activity (median = 2 and 3 for SG and UG respectively). More synergies were needed to reconstruct the trials of the unstable (mean= 3.2 ± 0.5) compared to the stable condition (mean 2.5 ± 0.7, paired t-test p = 0.029, Figure 2.3). In both conditions, the fundamental activation patterns were associated with temporally different phases of the task (Figure 2.4). The first synergy was shared between conditions and functionally referred to the SLS (peak at ~9% and ~16% of the cycle for stable and unstable, respectively) and showed a major involvement of hip abductors, hip extensors and plantar flexors. The second synergy, which was also shared among conditions, described the DLS (peak at ~90% and ~89% of the cycle for stable and unstable, respectively) and showed a main contribution of knee extensors and flexors and *hip extensors.* The extra synergy for the unstable ground condition was functionally related to the SLS (peak at ~21%) and was mainly characterized by the involvement of mediolateral stabilizers of the lower leg. For this reason, from now on it will be referred to as SLS mediolateral synergy. Since this synergy was only present in the UG condition, comparisons between SG and UG conditions were performed for the SLS and DLS synergies exclusively.

There were no differences for the shared motor primitives of the SLS and DLS in either the FWHM or the CoA between SG and UG (F (1,14) = 8.16, p = 0.201, Table 2.2). Similarly, the motor modules in any of the shared synergies (SLS and DLS) did not differ between conditions (F (12, 364) = 0.28, p = 0.972 for the SLS and p = 0.267 for the DLS).
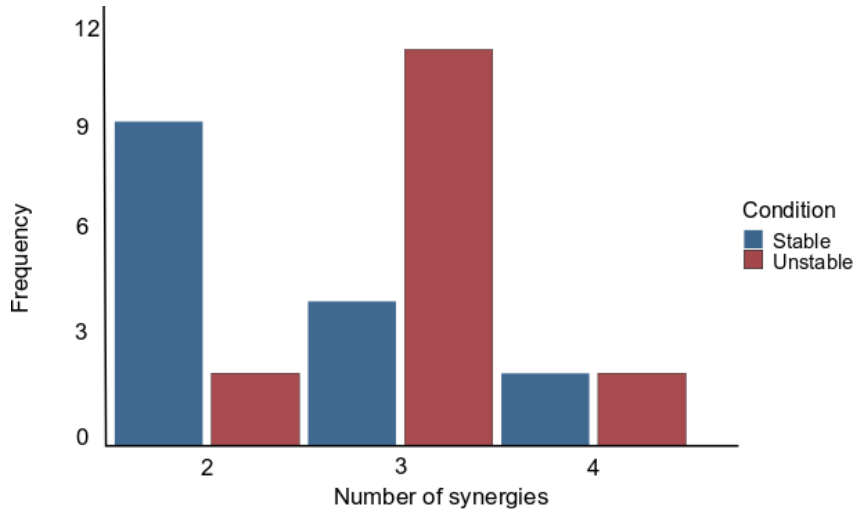
Figure 2.3. Frequency distribution of the minimum number of synergies necessary to sufficiently reconstruct the EMG signals recorded from all participants on stable and unstable ground. Significant differences were observed for the mean (2.5 ± 0.7 for the stable and 3.2 ± 0.5 for the unstable condition, p = 0.029) and median values ((2 for the stable and 3 for the unstable condition, p = 0.035).
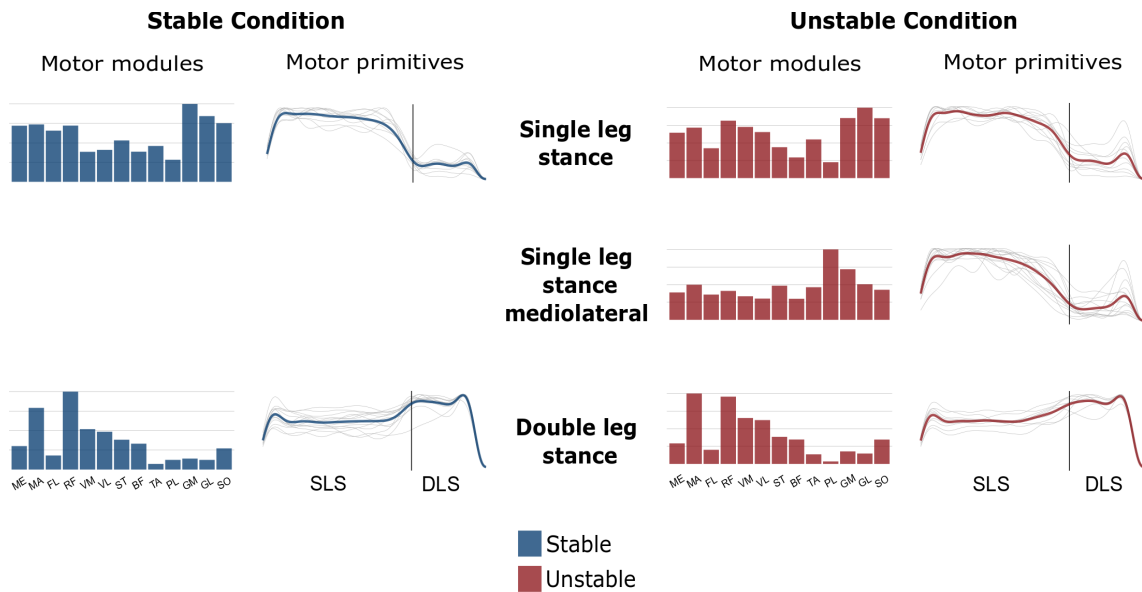

Figure 2.4. Average motor modules and motor primitives of the fundamental synergies needed to perform the postural task on stable and unstable ground. The motor modules are presented on a normalised y-axis base. For the motor primitives, the x-axis full scale represents one cycle (lift-off to lift-off, time-normalised to the same amount of points, the vertical line indicates the touchdown, i.e. the beginning of the double leg stance) and the y-axis the normalised amplitude. SLS = single leg stance, DSL = double leg stance, ME = gluteus medius, MA = gluteus maximus, FL = tensor fasciae latae, RF = rectus femoris, VM = vastus medialis, VL = vastus lateralis, ST = semitendinosus, BF = biceps femoris (long head), TA = tibialis anterior, PL = peroneus longus, GM = gastrocnemius medialis, GL = gastrocnemius lateralis and SO = soleus.

Table 2.2. *Differences for motor modules and primitives between ground conditions. Motor primitives are compared by means of full width at half maximum (FWHM) and centre of activity (CoA). Standing (SLS) and double leg standing (DLS) synergies were shared by both the stable and unstable ground condition, while a new synergy (SLS mediolateral) was found only in the unstable trials. For this reason, we only presented the comparison between stable and unstable, where positive differences (Δ>0) denote bigger values in the unstable condition, whereas negative differences imply lower values.*

	FWHM			CoA		
Motor Primitives	Δ	p-value	Effect size	Δ	p-value	Effect size
SLS stable vs. SLS unstable	-0.4%	0.977	-0.10	+2.3%	0.344	0.32
DLS stable vs. DLS unstable	- 6.2%	0.440	-0.22	-2.1%	0.577	0.14
Motor Modules	p-value					
SLS stable vs. SLS unstable	0.972					0.15
DLS stable vs. DLS unstable	0.267					0.22

2.5. Discussion

In the present study, we investigated the modular organisation of a standing balance task on stable and unstable ground in order to improve our understanding of the neuromuscular control mechanisms adopted by the CNS to maintain motor task functionality during external perturbations. Our results show that a very simple organisation of the neuromuscular system is sufficient to maintain the postural control in DLS and SLS on both SG and UG. In the SG condition, two synergies were sufficient to describe the modular organisation of the task, one for each stance, and achieve the functional goal of keeping the upright posture. In the UG condition, the increased challenge of postural stability was solved by adding one extra synergy during the SLS.

Stability increased (lower MLE) from the distal (ankle joint) to the proximal (spine) segments in both SG and UG. Remarkably, this phenomenon was more pronounced in the unstable condition. The lower MLE from the spine in UG compared to SG suggest that the neuromuscular system increased the stability of the trunk in relation to the ankle joint to a higher extent in presence of distal perturbations. Previous studies reported a stability prioritization of proximal over distal segments during balancing and walking[533–536]. Our results show that this phenomenon (i.e. priority of proximal segment stability) is facilitated in the perturbed condition. It has been shown that stability of the head is critical to obtain visual and vestibular references that are crucial for dynamic postural control[537–539]. In balance-challenging conditions, the integration of visual and vestibular information for effective postural control may be more relevant than in less challenging tasks, thus requiring higher trunk-head stability.

Furthermore, our data indicate that the preservation of the task functionality in the presence of perturbations was achieved at the expense of accuracy: the variability of the cycle duration was twice as high (p=0.012) in UG compared to SG.

It is well known that muscle activity is organized to control the displacement of the centre of mass by controlling the centre of pressure during upright posture[37,533,540]. The SLS synergy modules showed a main contribution of ankle (PL, GM, GL and SO) and hip muscles (MA, FL, ME), whilst in the DLS synergy, the main contribution was provided from *rectus femoris* and *gluteus maximus*. These two synergies remained unaffected by the change of ground condition (stable or unstable) in their spatial (i.e. motor modules) and their temporal (i.e. motor primitives) structure. In the UG condition, the displacement of the base of support amplified the need to compromise between keeping balance and maintaining the upright posture[506]. For this reason, any attempt to control the centre of mass necessarily results in a displacement of the base of support. From a mechanical point of view, these reciprocal constraints change the behaviour of the body from an inverted pendulum to a balancing pole[541,542].As stated above, the incremented postural stability challenge was solved by adding one extra synergy during the SLS. This new synergy was present in most of the participants (73.3%) and was characterised by a dominant contribution of the shank muscles, especially the *peroneus longus*. It has been reported that distal muscles are more sensitive to perturbations than proximal muscles[543]. This could be due to specific morphological and anatomical properties (i.e. short fascicles, long tendons, and large pennation angles) that allow these muscles to be particularly sensitive to perturbations happening at low levels of force[544].

Based on previous results from our group, we expected a conservation of the modular organisation of the system (i.e. same number of synergies) with a modification of its time coefficients (widening of motor primitives) leading to an increased motor output's robustness[12]. A "robust adaptation" in response to perturbations is observed when (a) the state of the system is modified and the system is able to return to its original attractor or (b) the system moves to a new attractor that is able to respond adequately to perturbations maintaining its functionality[26]. The ability to maintain specific functionalities by changing the modes of operation in a flexible way is a characteristic of robust adaptation[26]. Considering the observed addition in the number of synergies as a modification of the state of the system and that all participants managed to perform the task in face of perturbations, we can assume that functionality was maintained, despite an alteration of the modular organisation when comparing SG and UG tasks. Modularity is often presented as a biological design principle that allows robust responses[26,545]. Muscles synergies represent neural sets of task-specific modules that can be selected and

combined for the production of different movement patterns[396,419]. The performed task was partially mechanically constrained by maintaining the upright standing position on one and two legs and on stable and unstable ground. Considering that a task-specific mechanical goal is likely to be reflected in a task-specific muscle synergy[283,480], our results support the idea that for the induced perturbations, the control system increased its robustness by adding a new synergy with different muscle organisation, but complementary target function. In other words, while the shared SLS synergy is likely responsible for keeping the upright posture, the added synergy might be responsible for controlling the perturbations imposed by the displacement of the base of support. During the DLS, despite the presence of the same kind of perturbations (i.e moving ground), there was no necessity for an extra synergy. This might be due to the bigger base of support that provided larger boundaries of stability[89,133,537].

Recent studies reported that perturbation-based training programmes using continuously variable and partly unpredictable disturbances can improve the neuromuscular control of the motor system and increase its stability during sudden balance recovering tasks[354,546]. Furthermore, it has been proposed that exercise including small continuous and unpredictable perturbations may introduce a more robust response to large perturbations by improving the modular organisation of the control system[504]. In highly challenging conditions, humans increase the fuzziness of the temporal boundaries in the modular organisation of walking and running and create a "buffer" of motor control enhancing the robustness needed to cope with external perturbations[12]. In this notion and considering our results, we interpret the addition of a new independent synergy as a "safety buffer" created by the neuromuscular system to minimize the effects of perturbations on the motor output.

Feedback-based control is crucial for robust locomotion[547] and one of the main balance recovery mechanisms when perturbations are large or unexpected[82]. During bipedal balance tasks, in which distal segments are the first to move after a perturbation, proprioceptive pathways provide extremely fast feedback information[548]. However, large corrective responses undergo bigger time delays before being detectable[541,548]. These delays might be overcome by adaptive control strategies able to make up for the temporary lack of feedback[541,549]. Given the fundamental role of proprioception for feedback-based responses[496,548,550], we reasoned that the additional synergy, mainly involving lower leg muscles, could promote the adaptive control of posture. This might happen by allowing the control of the base of support after perturbation with the smallest possible latency[548].

Our results support the idea that the CNS takes advantage of sensorimotor integration to ensure robust control[285,541] and that a modular organisation facilitates robustness[12,26]. Furthermore, the

increased control's robustness in the presence of external perturbations might be one important neural mechanism contributing to stability performance and could be of special interest for training and rehabilitation designs. For the latter, the aforementioned sensitivity of lower leg muscles to perturbations might explain why perturbation-based training programmes promote strength increase in these muscles[354]. However, perturbations must be challenging enough to engage or trigger the additional response to having a training effect[354].

In conclusion, our results support the idea that the addition of a new synergy was a strategy to increase the robustness (i.e. ability to cope with errors) of the system's motor output to perturbations. The new synergy was characterised by a major contribution of the lower leg muscles and had a temporal profile that was similar to the one of the SLS synergy. Such temporally co-existing synergies are likely to have different but complementary goals, in this case keeping the upright posture and controlling the displacement of the base of support. Moreover, modularity in the neuromuscular system might be an important feature to ensure robustness by providing a source to adaptive control strategies depending on the task characteristics.

3. Second study: Neuromechanics of dynamic balance tasks in the presence of perturbations

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3.1. Abstract

Understanding the neuromechanical responses to perturbations in humans may help to explain the reported improvements in stability performance and muscle strength after perturbation-based training. In this study, we investigated the effects of perturbations, induced by unstable surfaces, on the mechanical loading and the modular organization of motor control in the lower limb muscles during lunging forward and backward. Fifteen healthy adults performed 50 forward and 50 backward lunges on stable and unstable ground. Ground reaction forces, joint kinematics, and the electromyogram (EMG) of 13 lower limb muscles were recorded. We calculated the resultant joint moments and extracted muscle synergies from the stepping limb. We found sparse alterations in the resultant joint moments and EMG activity, indicating a little if any effect of perturbations on muscle mechanical loading. The time-dependent structure of the muscle synergy responsible for the stabilization of the body was modified in the perturbed lunges by a shift in the centre of activity (later in the forward and earlier in the backward lunge) and a widening (in the backward lunge). Moreover, in the perturbed backward lunge, the synergy related to the body weight acceptance was not present. The found modulation of the modular organization of motor control in the unstable condition and related minor alteration in joint kinetics indicates increased control robustness that allowed the participants to maintain functionality in postural challenging settings. Triggering specific modulations in motor control to regulate robustness in the presence of perturbations may be associated with the reported benefits of perturbation-based training.

3.2. Introduction

During daily-life activities, humans are constantly required to maintain stable locomotion in different environmental conditions that present variable and often unpredictable locomotor

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disturbances. Challenging balance control by using perturbations has been described as an effective intervention for reducing fall risk in different populations[241,242,254,354]. Compliant or unstable surfaces represent a possibility to introduce external mechanical perturbations (i.e., an alteration of the function of a biological system induced by external mechanism) and challenge balance control. Increasing the base of support (i.e., a stepping response) and counter-rotating segments around the centre of mass are two of the main mechanism to recover a loss of balance[89]. Previous studies of our group have reported that training these mechanisms in the presence of perturbations improves muscle strength of the lower extremities and stability performance[205,302,303]. Nevertheless, despite the effectiveness of training in the presence of perturbations on balance performance has been generally accepted, the mechanisms explaining the improvement are still not fully understood.

Maintaining functionality despite the increased challenges induced by perturbations is a fundamental characteristic of biological systems defined as robustness[26]. In the presence of perturbations, the neuromuscular system overcomes challenges by modifying its control strategies in a highly coordinated and tuned manner, so that the motor task can be executed properly[418,421,551]. The idea that the neuromuscular system faces the redundancy of the available degrees of freedom by activating functionally related muscle groups rather than individual muscles is well accepted[358,390]. The coordinated patterns of muscle activity are commonly known as muscle synergies and are flexibly combined to produce robust motor output[12,402,551]. We have previously reported that a modulation of muscle synergies in challenging locomotion conditions allows the human system to increase the robustness of the motor control by widening the motor primitives, or time-dependent components of muscle synergies[12,441]. Further, we found that the motor system generates less unstable and less complex motor primitives in the presence of perturbations, making the motor execution less prone to the influence of disturbances[441]. In our opinion, understanding the modulations of motor control in the presence of perturbations is a key element to provide insight on the effects of external perturbations on postural control, yielding knowledge potentially useful for (a) explaining the positive effects of the perturbation-based interventions and (b) improving the design of effective exercise programs. In the presented study, we asked the participants to perform forward and backward lunges in both stable and unstable conditions to mimic one of the above mentioned balance-recovery mechanisms (i.e., increasing the base of support). The use of the muscle synergies approach might allow us to understand the organization of muscle coordination that underlies the adaptation of postural control in the presence of perturbations.

Therefore, the purpose of the current study was to investigate the effects of perturbations induced by unstable surfaces, on the mechanical loading and modular organization of motor control in the lower limb muscles during forward and backward lunges. Specifically, we investigated the spatiotemporal organization of muscle activation patterns using the muscle synergy concept and the resultant joint moments of the lower extremities during perturbed and unperturbed forward and backward lunges. We expected to find modulations of motor control in the presence of perturbations reflected in the spatiotemporal components of muscle synergies and the resultant joint moments. Specifically, we hypothesized that lunging on unstable surfaces would result in a reorganization of muscle synergies by modifying the time-dependent motor primitives and time-independent motor modules to increase the robustness of control. We also expected an increased mechanical loading of lower limb muscles.

3.3. Materials and Methods
3.3.1. Experimental protocol

Fifteen healthy, regularly active young adults volunteered for the study (11 males, 4 females, height 1.75 ± 0.10 m, body mass 67 ± 11 kg, age 28 ± 5 years). None of the participants had a history of neuromuscular or musculoskeletal impairments, nor any injury at the time of the measurements or in the previous six months. The study was reviewed and approved by the Ethics Committee of the Humboldt-Universität zu Berlin (HU-KSBF-EK_2018_0013). In accordance with the Declaration of Helsinki, all the participants gave written informed consent for the experimental procedure.

Participants were asked to stand in a comfortable position and lean as far as possible until they were forced to take a step reaction with their right leg onto a target marked in the middle of a force plate (sampling frequency 1 kHz, AMTI BP600, Advanced Mechanical Technology, Inc., Watertown, MA, USA), and hold the achieved lunge position until they felt stable, i.e., steady state. The same task was performed in two directions by leaning forwards or backward (Figure 3.1). The starting point was set at a distance from the target equal to 70% of each participant's lower limb length (measured from the Cresta Iliaca to the Lateral Malleolus of the recovery limb) for the forward and 60% for the backward lunge. Participants performed a series of lunges on two different surfaces: hard uniform stable ground (SG) and from a foam pad (2 x Airex® Balance Pad, 50 x 41 x 6 cm, Airex Switzerland) to a foam beam (Sport-Thieme Balance beam EVA foam, 95 x 16.5 x 5.8 cm, Sports-Thieme Germany) used as unstable ground (UG) to introduce external mechanical perturbations during the task. The foam beam was fixed to the force plate by double-sided tape and four five-kilogram weight discs aided to

prevent a possible sliding. If the participant was not able to maintain the achieved lunge position, moved the left foot or the beam flipped or slid out of position, the attempt was considered failed and repeated. In each trial, participants performed 52 valid lunges for each direction and ground condition at a self-managed pace. The order of the trials was randomized and a self-managed rest period (minimum 3 minutes, seating was allowed) was given in-between trials.

A ten-infrared-camera motion capture system (Vicon Motion Systems, Oxford, U.K.) operating at 250 Hz was used to collect kinematics from 20 spherical (diameter 14 mm) reflective markers placed over the following anatomical landmarks: spinal process of the second, seventh and tenth thoracic along with the second lumbar vertebrae, the greater trochanter, lateral and medial epicondyle of the femur, Achilles tendon insertion on the calcaneus, lateral malleolus, tip of the first toe, the dorsal margin of the first and fifth metatarsal heads. The lower limb markers were recorded bilaterally. Also, the muscle activity of the following 13 ipsilateral (right side) muscles was recorded using a 16-channel wireless electromyography (EMG) system (Myon m320, Myon AG, Schwarzenberg, Switzerland), with a sampling frequency of 1 kHz: Gluteus medius (ME), gluteus maximus (MA), tensor fasciae latae (FL), rectus femoris (RF), vastus medialis (VM), vastus lateralis (VL), semitendinosus (ST), biceps femoris (long head, BF), tibialis anterior (TA), peroneus longus (PL), gastrocnemius medialis (GM), gastrocnemius lateralis (GL) and soleus (SO). EMG and force plate analog data streams were collected together with the kinematics and then converted to digital information within the same A/D converter (Vicon MX Giganet). All further offline analysis was performed using R v3.6.1.
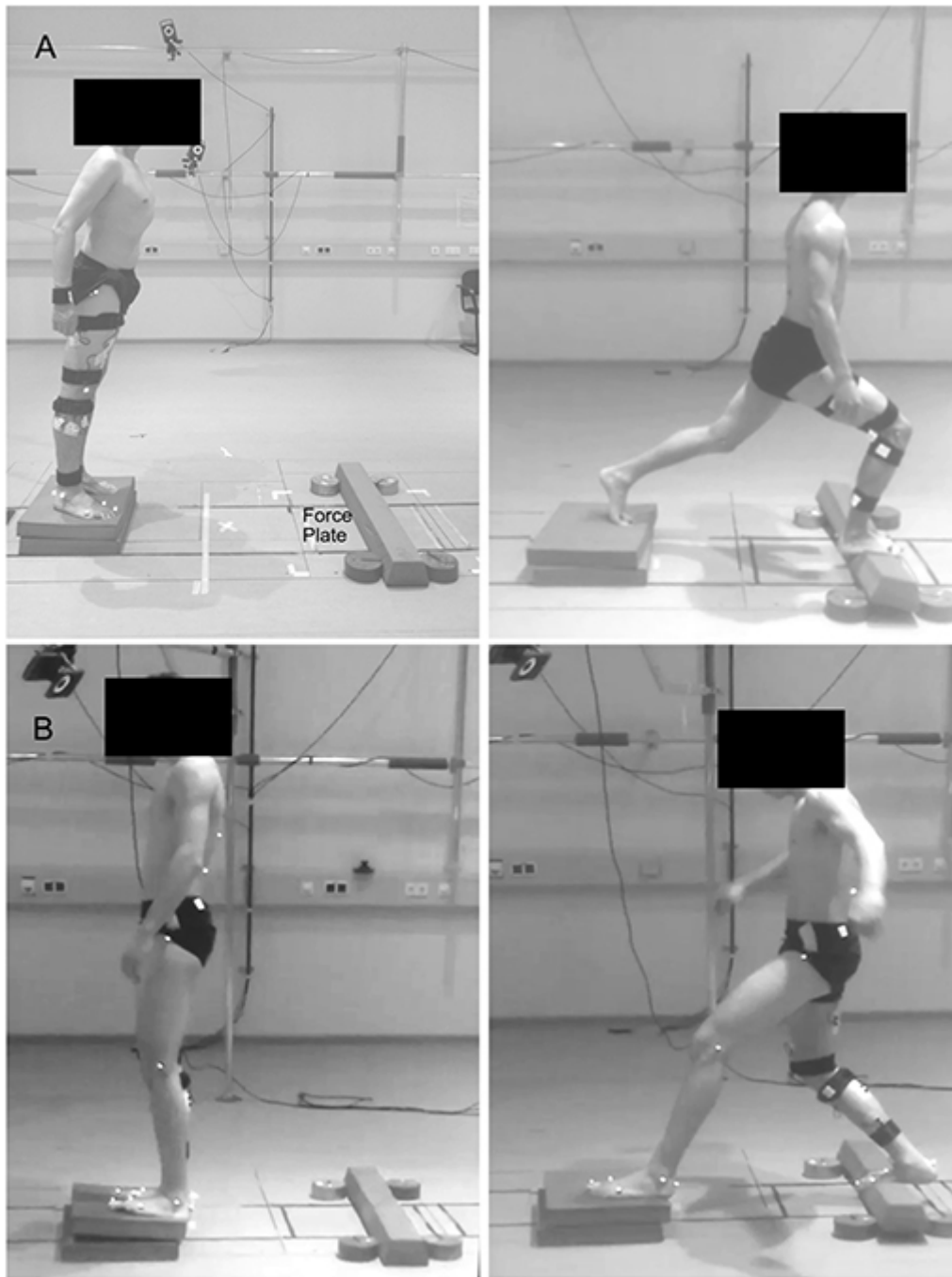
Figure 3.1. *Visual description of the performed task. Participants were asked to lean forward (a) or backward (b) as far as possible, take a step reaction and hold the achieved lunge position until steady state. Fifty trials were performed on solid stable ground and 50 on foam pads, used as unstable ground condition.*

3.3.2. Cycle segmentation

The interval of interest was defined as the time frame from the lift-off of the right foot until a steady-state after touchdown was achieved. The aforementioned lift-off defining the beginning of the lunge was assessed by the "foot acceleration and jerk" algorithm[12]. This approach has

been previously validated using force plate data with true errors being 12 ± 18 ms for walking, −16 ± 23 ms for running and 13 ± 9 ms for the estimation of a single leg standing lift-off (means ± s.d.). First, we identified touchdown as the first non-zero value observed in the ground reaction force (GRF) data. Then, the foot kinematic data was low-pass filtered using a 4th order IIR Butterworth zero-phase filter with a cut-off frequency of 50 Hz[520] and the second and third derivative of the fifth metatarsal marker's position (for obtaining the acceleration and jerk, respectively) were calculated. An estimation of the lift-off (LOe, where "e" stays for "estimated") was identified as the global maximum of the fifth metatarsal's vertical acceleration in a time window between the touchdown and 800 ms before it. Finally, the "true" lift-off was identified in a reasonably small neighborhood of the LOe (-50, 200 ms) as a characteristic minimum in the vertical acceleration (i.e., when the jerk equals zero).

The main stance phase of the recovery step ends around the maximum of knee joint flexion after touchdown. Therefore, we defined the end of the lunge as the time point with minimum fluctuation in the knee angle after maximum flexion. The minimum fluctuation was found using the technique of change point detection implemented in the function "e.divisive" from the R package ecp[552,553]. Briefly, the function performs nonparametric estimation of change points. A statistical significance is assigned to changes in the slope of the knee angle curve. When the slope stops to significantly depart from zero (i.e., when the knee joint is in a fixed, steady position), the beginning of the steady state is found and the cycle is trimmed at that time point.

The time window between the lift-off and the minimum fluctuation at the knee joint angle defined the duration of the cycle. Additionally, the time to achieve the minimum fluctuation from touch-down was also used to compare the performance between ground conditions. After removing the first and last cycles, all the following variables were calculated individually, cycle by cycle, and then the average of the central 50 cycles was used as a representative dataset for each participant in each direction and ground condition.

3.3.3. EMG assessments

The linear envelopes of the EMG signals were obtained by applying a 4th order IIR Butterworth zero-phase high-pass filter, full-wave rectification and low-pass filtered. Cut-off frequencies were 50 Hz (high-pass) and 20 Hz (low-pass)[12,437]. The amplitude was normalized to the maximum activity of each muscle for each direction. For the muscle synergies extraction, the amplitude was normalized to the maximum activation recorded for each muscle in each trial[418,551] followed by a subtraction of the minimum activity, thus each EMG signal

ranged between zero and unity. Also an EMG coactivation index was obtained by calculating the ratio between the averaged normalized EMG activities of the antagonist and the averaged agonist EMG activity for each related joint. Therefore, the corresponding ratios were calculated as follows:

$$\text{Hip:}$$
$$\frac{(FL+RF)/2}{(ME+MA)/2} \text{ (eq. 3.1)}$$
$$\text{Knee: :}$$
$$\frac{(BF+ST)/2}{(RF+VM+VL)/3} \text{ (eq. 3.2)}$$
$$\text{Ankle:}$$
$$\frac{TA}{(GM+GL+SO)/3} \text{ (eq. 3.3)}$$

Each interval of interest, from all above mentioned variables, was thereafter time-normalized to 200 points with 50 points assigned to the swing and 150 to the stance phase. The time-normalized intervals were then cut and pasted one after the other (i.e., concatenated).

3.3.4. Muscle synergies assessment

A custom R script (R v3.6.1 , R Core Team, 2020, R Foundation for Statistical Computing, Vienna, Austria) implementing the classical Gaussian NMF algorithm[12,435] was used for extraction of the muscle synergies. The concatenated EMG data vectors were grouped in an m × n matrix V, where m = 13 (number of muscles) and n = number of points. This matrix was factorized such that V ≈ V_R = WH. Where V_R represents a new reconstructed matrix that approximates the original matrix V and both H and W described the synergies necessary to accomplish a movement. H represents the r × n time-dependent coefficients (motor primitives) matrix[437,451] of the factorisation, where r represents the number of synergies necessary to reconstruct the signal and n the number of data points. W represents the m × r motor modules matrix[437,554], containing the time-invariant muscle weightings. The update rules for H and W are presented as follows (Equation 3.4 and Equation 3.5).

$$H_{i+1} = H_i \frac{W_i^T V}{W_i^T W_i H_i} \quad \text{(eq. 3.4)}$$

$$W_{i+1} = W_i \frac{V (H_{i+1})^T}{W_i H_{i+1} (H_{i+1})^T} \quad \text{(eq. 3.5)}$$

The limit of convergence was defined as the amount of synergies that did not improve the reconstruction of the signals with the addition of an extra module and it was reached when a

change in the calculated R^2 between V and V_R was smaller than 0.01% in the last 20 iterations[12,437,521]. This was done for a number of synergies successively increased from 1 to a maximum of the rounded 75% of the number of assessed muscles (i.e., 10 synergies)[496].The computation was repeated 10 times for each synergy, each time creating new randomized initial matrices H and W, in order to avoid local minima[480]. For each of the 10 synergies the solution with the highest R^2 was then selected.

The minimum number of synergies required to reconstruct the original EMG signals was chosen using a linear regression model fitting the curve of R^2 values versus synergies for all the synergies. The mean squared error was then repeatedly calculated, each time removing the lower synergy point, until only two points were left or until the mean squared error fell below 10^{-5} [12,437], assuming that at this point the addition of an extra synergy did not improve the quality of the reconstruction. In order to compare the extracted synergies and give them a functionally meaningful interpretation, we classified the extracted synergies using an unsupervised method, previously described in detail[555]. Unsupervised algorithms reduce possible operator-dependent bias in the classification. The algorithm clustered the primitives that showed similar shapes. Fundamental primitives, i.e. primitives that show one peak in their activation pattern[12,437], were then ordered based on their centre of activity (CoA, see equations 3.6, 3.7, 3.8). The primitives that were not clustered, were classified as combined (i.e., two or more fundamental synergies blended into one). In our data, combined synergies usually constitute 10 to 30% of the total extracted synergies. Due to the lack of consensus in the literature on how to interpret them, for the combined synergies we did not calculate the metrics reported in the following paragraphs.

3.3.5. Metrics for comparison of motor primitives

The motor primitives in both conditions were compared by means of the CoA and full width at half maximum (FWHM). The CoA was defined as the angle of the vector (in polar coordinates) that points to the centre of mass of that circular distribution[12,522]. The polar direction represented the cycle's phase, with angle $0 \leq \theta t \leq 2\pi$. The CoA is defined by the following equations:

$$A = \sum_{t=1}^{p} \left(\cos \Theta_t \times P_t \right) \quad \textit{(eq. 3.6)}$$

$$B = \sum_{t=1}^{p} \left(\sin \Theta_t \times P_t \right) \quad \textit{(eq. 3.7)}$$
$$CoA = \arctan \left(B / A \right) \quad \text{(eq. 3.8)}$$

The FWHM was calculated as the number of points exceeding each cycle's half maximum, after subtracting the cycle's minimum[12,522,551]. Moreover, for each lunge or cycle, we identified the time points when two or more motor primitives exceeded the half maximum simultaneously and defined this period as an overlap of primitives. The number of overlaps was calculated as the mean number of overlaps at a given time-point across all trials of a participant. The FWHM, CoA, and number of overlaps were calculated for each lunge and then averaged for the respective participant and ground condition.

3.3.6. Kinematics and resultant joint moments

The kinematics of the hip, knee and ankle joint were calculated from the 3D trajectories of the stepping limb using a custom R v3.6.1 algorithm. Subsequently, the resultant joint moments for the aforementioned joints were calculated using an inverse dynamics procedure[556] with segmental masses and inertial parameters derived from literature[7]. Similar to the EMG data, kinematics and resultant moments from each region of interest for each cycle were subsequently time-normalized to 200 points, with 50 points attributed to the swing phase and 150 points to the stance phase.

3.3.7. Statistical analysis

We performed a statistical parametric mapping (SPM) paired t-test[557,558] between conditions on the following time-dependent variables: sagittal plane kinematics and joint resultant moments, the Euclidean norm of the GRF, EMG activity of each muscle and coactivation ratios. A critical threshold t* was calculated based on the temporal smoothness of the input data through Random Field Theory and a test statistics SPM{t} was evaluated at each point in the time series. In the case that SPM{t} exceeded t*, a significant difference was detected. Significance level was set at 0.05 and Bonferroni corrected for multiple comparisons (N = 3 for joints, N = 13 for EMG of muscles.). All SPM calculations were performed in MATLAB using the open-source package spm1d (v 0.4.5).

To account for a possible effect of repetition on the neuromuscular organization, we split the CoA and FWHM datasets in two groups. Each group contained the first and last 25 repetitions ("early" and "late" cycles, respectively). We performed a two-way ANOVA for repeated measures on the CoA and FWHM with ground (stable, unstable) and repetition (early and late

cycles) as within subject factors. A Tukey post-hoc analysis with false discovery rate α-value adjustment was conducted in the case of a significant interaction between the factors. To investigate differences in the motor modules between conditions, the same statistical approach was performed using muscles and ground condition as independent variables. All the significance levels were set to $\alpha = 0.05$ and analyses were conducted in R v3.6.1.

3.4. Results

3.4.1. Temporal parameters

Participants needed a significantly longer time to reach a steady state after landing onto the unstable ground in the forward lunge compared to the stable condition (SG: 0.818 ± 0.210 s, UG: 1.055 ± 0.311 s, $t(14) = -5.04$; $p < 0.001$). This led to an increased duration of the task (SG: 1.117 ± 0.214 s, UG: 1.368 ± 0.319 s, $t(14) = -5.28$; $p < 0.001$). In the backward lunge, there were no statistically significant differences in the time to reach steady state between stable and unstable ground conditions (SG: 0.779 ± 0.226 s, UG: 0.863 ± 0.178 s, $t(14) = -1.49$; $p = 0.160$). Similarly, the duration of the task in the backward lunge did not show any statistically significant differences between the two conditions (SG: 1.082 ± 0.22 s, UG: 1.188 ± 0.18 s, $t(14) = -1.97$; $p = 0.07$).

3.4.2. Kinetics and kinematics

In the forward lunge onto the unstable ground, the hip was significantly less flexed ($t* = 3.989$, $p = 0.015$) closely after touchdown (~30% of the lunge duration) and during most of the stabilization phase (~40-100 % of the lunge duration, $t* = 3.989$, $p < 0.001$, Figure 3.2). Furthermore, the knee joint was also less flexed from briefly before touchdown and during the whole stance phase (~25-100% of the lunge duration, $t* = 4.177$, $p < 0.001$, Figure 3.2). The ankle joint angle showed no differences between stable and unstable ground conditions (Figure 3.2). In the backward lunge, a significantly higher flexion at the hip ($t* = 4.182$, $p = 0.010$) and knee ($t* = 4.181$, $p = 0.008$) joint was observed at the beginning of the swing phase (first 10% of the lunge) in the unstable ground. This condition induced a lower knee flexion around the touchdown (~20-30% of the task, $t* = 4.181$, $p = 0.009$) and ~70% of the stabilization phase ($t* = 4.181$, $p < 0.001$, Figure 3.2). A lower dorsiflexion was also observed in the middle of the swing phase (~15% of the lunge duration, $t* = 4.074$, $p = 0.015$) and towards the end of the stabilization (~85-100% of the task, $p < 0.001$) in the unstable ground.
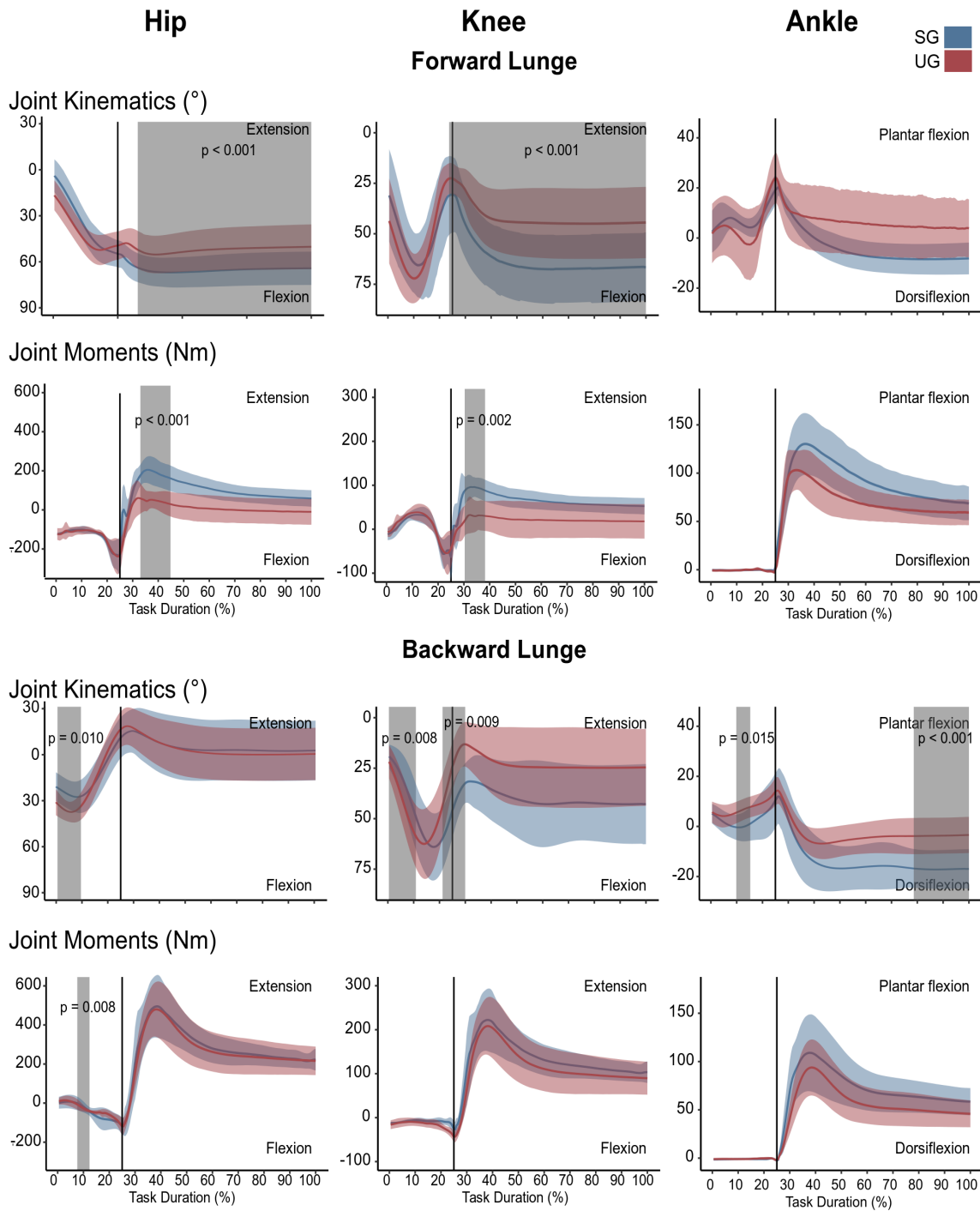
Figure 3.2. *Lower limb kinematics and resultant joint moments of the forward and backward lunges from lift-off until steady state. Each panel shows the mean values and standard deviation bands for the hip, knee and ankle joint angles and moments for the stable (SG - blue) and unstable ground (UG - red) condition. Panels are presented in a time normalized base, vertical lines represent touchdown. Grey bands denote periods of significant differences assessed with a statistical parametrical mapping difference estimator Bonferroni corrected.*

There were no differences in either of the lunge directions in the GRF (Figure 3.3). In the majority of the lunge duration, the resultant joint moments did not show statistically significant differences between the two ground conditions (Figure 3.2). A short decrease was found in the extensor moment at the beginning of the stabilization phase (~30-40% of the task duration) in both the hip ($t^* = 5.427$, $p < 0.001$) and knee joint ($t^* = 5.421$, $p = 0.002$) in the unstable ground during the forward lunge (Figure 3.2). Similarly, during the backward lunge, a brief decrease in the hip joint ($t^* = 4.661$, $p = 0.008$) was observed in the middle of the swing phase (~10 % of the task duration) in the unstable ground (Figure 3.2).
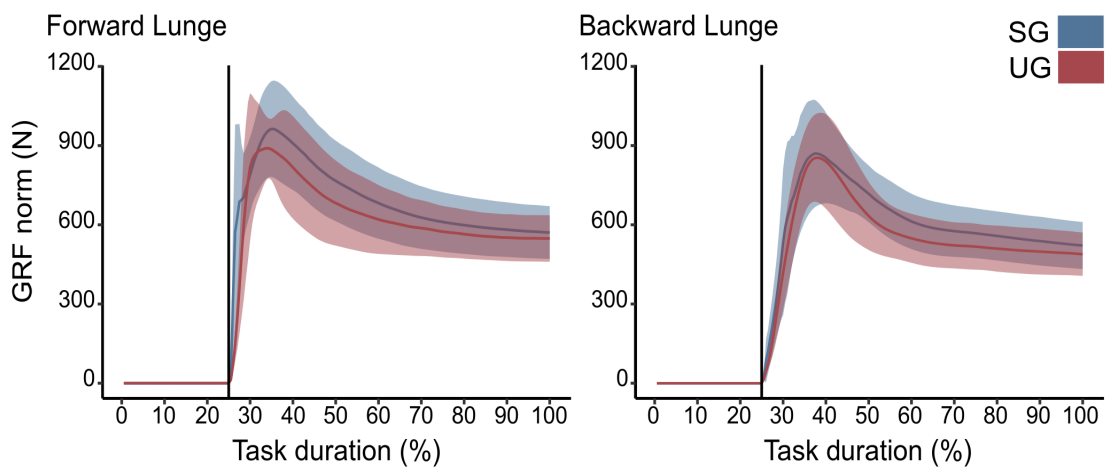

Figure 3.3. Euclidean norm of the ground reaction force (GRF) during forward and backward lunges from lift-off until steady state. Each panel show the mean values and standard deviation bands for the stable (SG - blue) and unstable ground conditions (UG -red). Both panels are presented in a time normalized base, vertical lines represent touchdown.

3.4.3. Electromyographic activity

Similar to the resultant joint moments, the observed significant differences in the EMG activity were short in time and not consistent (Figures 3.4). In the forward lunge, there was a decrease in the VM$_{EMG}$ activity after touchdown in the unstable ground (~30% of lunge duration, $t^* = 6.182$, $p = 0.003$). The ST$_{EMG}$ activity increased on the unstable ground around the 70% of the lunge duration ($t^* = 6.323$, $p < 0.001$) and close to the end of the stabilization phase (~90 % of the lunge duration, $p = 0.002$). Similarly, BF also showed a higher EMG activity around the touchdown in the unstable condition (~25% of the lunge duration, $t^* = 6.075$, $p = 0.004$, Figure 3.4). In the backward lunge, a decrease in ME ($t^* = 6.123$, $p < 0.001$) and BF EMG activity ($t^* = 5.994$, $p < 0.001$) during the swing phase (~10-20% of the lunge duration, Figure 3.4) was observed in the unstable ground. The coactivation ratios showed also brief differences between

the stable and unstable ground (Figure 3.5). In the forward lunge, the ratio in the unstable ground was higher briefly around the 80% of the task for the knee ($t^* = 5.371$, $p = 0.017$) and after touchdown for the ankle (~30% of the lunge duration, $t^* = 5.1818$, $p = 0.010$). In the backward lunge, the coactivation ratio in the unstable ground also increased in the ankle joint before touchdown (~25% of the lunge duration, $t^* = 5.058$, $p = 0.012$, Figure 3.5).
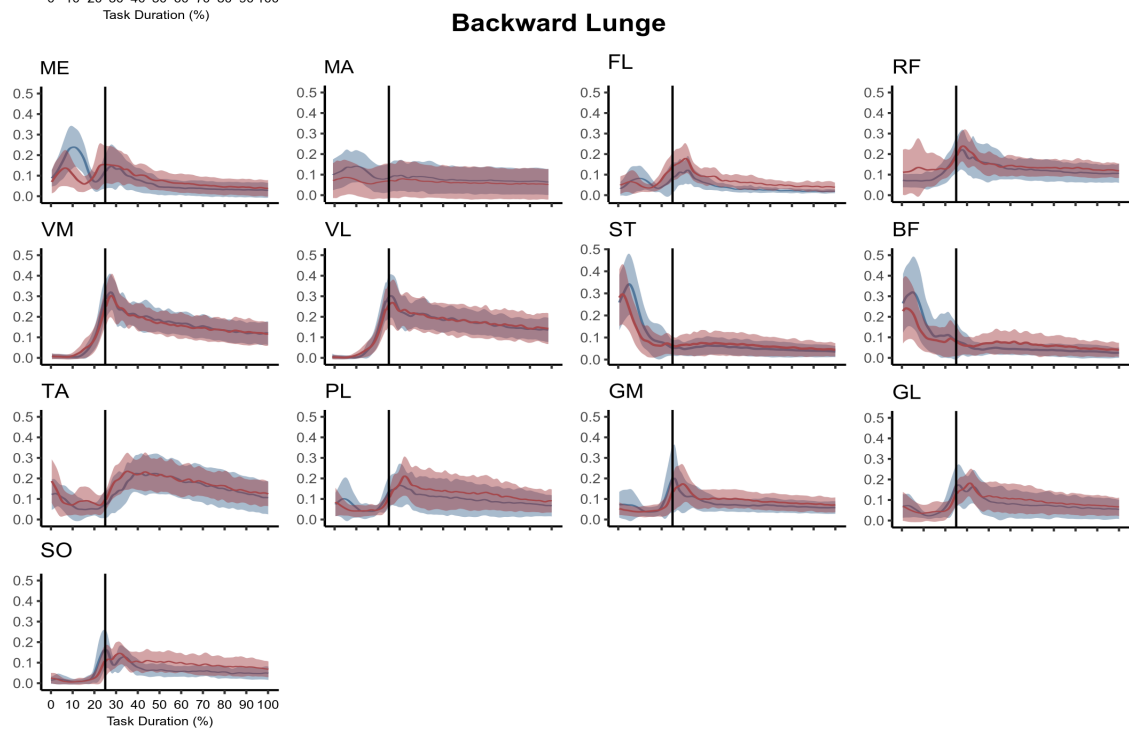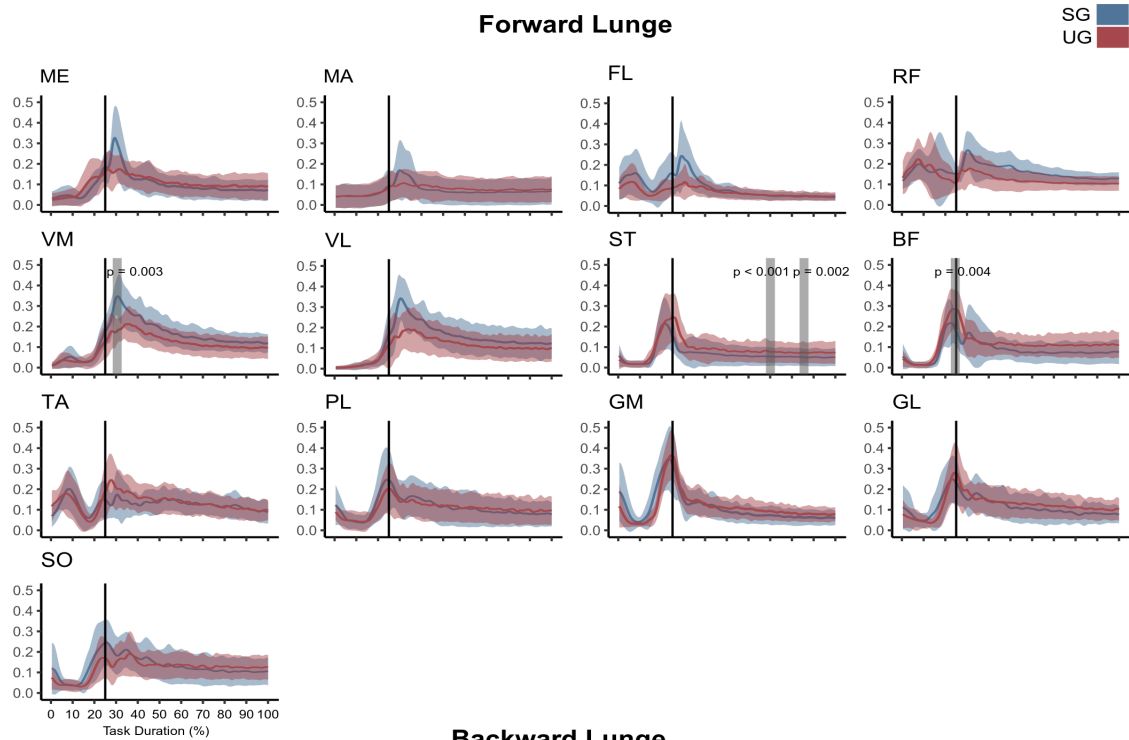
3.4. *Mean values and standard deviation bands for the EMG activities for a forward and backward lunge from lift-off until steady state on stable (SG –blue) and unstable ground condition (UG- red) normalized to the maximum activity between trials. Panels are presented in a time normalized base, vertical lines represent touchdown. Grey bands denote periods of significant difference estimated with a Bonferroni corrected statistical parametrical mapping difference estimator. Muscles: Gluteus Medius (ME), Gluteus Maximus (MA), Tensor Fascia Latae (FL), Rectus Femoris (RF), Vastus Medialis (VM), Vastus Lateralis (VL), Semitendinosus (ST), Biceps Femoris (long head, BF), Tibialis Anterior (TA), Peroneus Longus (PL), Gastrocnemius Medialis (GM), Gastrocnemius Lateralis (GL) and Soleus (SO).*
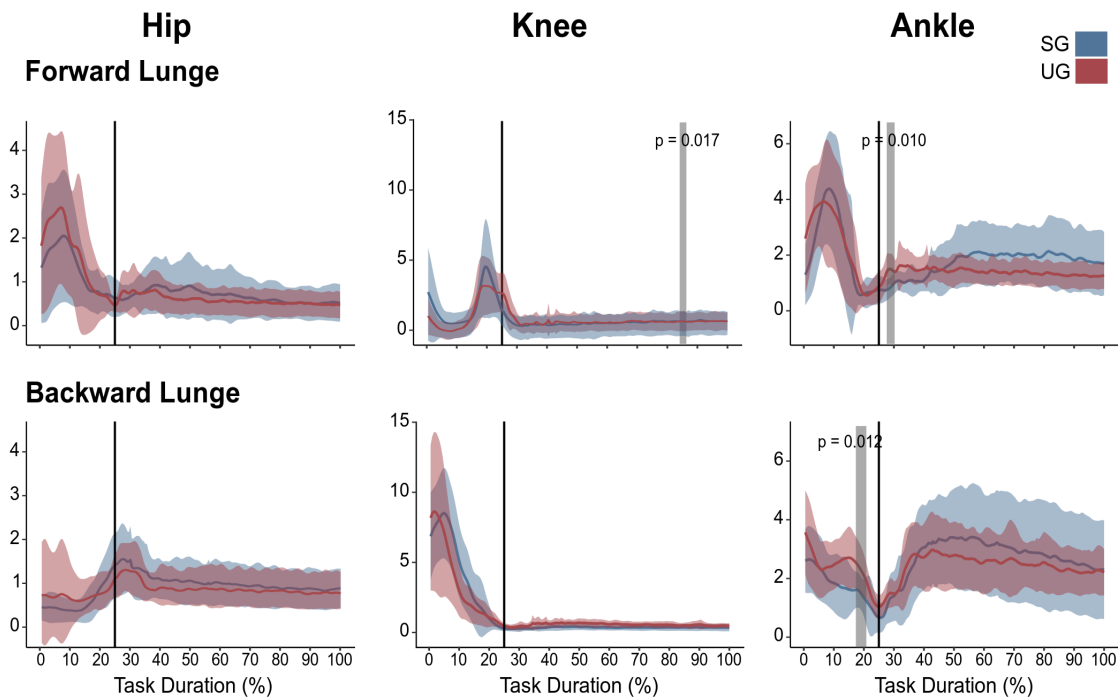
Figure 3.5. *Lower limb coactivation ratios (antagonist mean/agonist mean) of the forward and backward lunges from lift-off until steady state. Each panel show the mean values and standard deviation bands for the hip, knee and ankle joint coactivation index for the stable (SG - blue) and unstable ground condition (UG - red). Grey bands denote significant differences from the statistical parametrical mapping difference estimator. Both panels are presented in a time normalized base, vertical lines represent touchdown.*

3.4.4. Muscle synergies

The average number of synergies extracted to sufficiently reconstruct the original EMG activity was not significantly different between ground conditions in either the forward (SG = 5.0 ± 0.6, UG = 5.3 ± 0.6, p = 0.165) nor the backward lunges (SG = 4.7 ± 0.5, UG = 4.8 ± 0.6, p = 0.721). The classification identified a total of four fundamental synergies (i.e., a synergy whose motor primitive shows a single peak of activation[12] in the forward lunge (Figure 3.6) on both stable and unstable ground. In the backward lunge, the recognized fundamental synergies were four in the stable and three in the unstable condition (Figure 3.6).
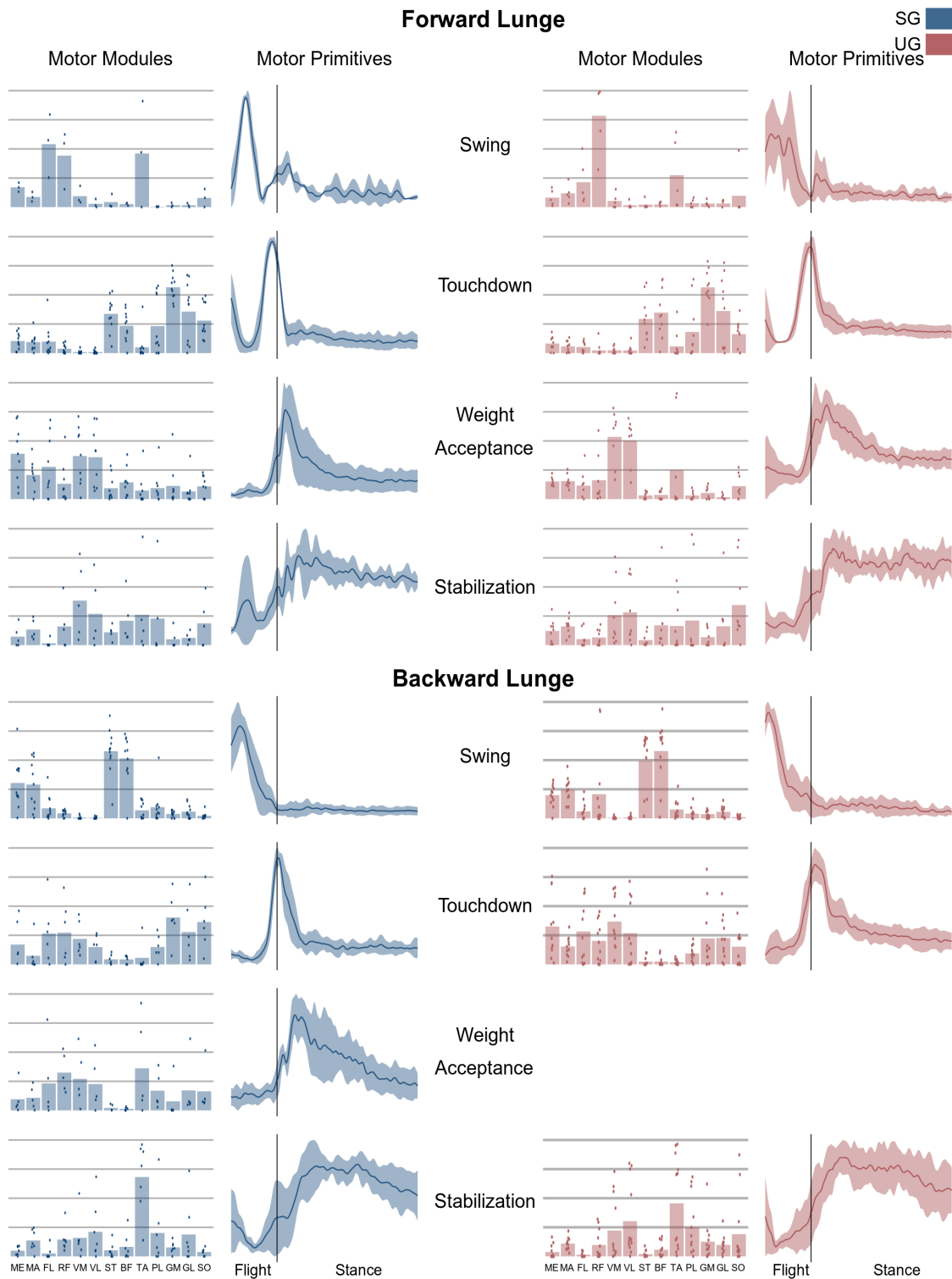
Figure 3.6. Average motor modules and motor primitives of the fundamental synergies needed to perform the forward and backward lunges on stable and unstable ground condition. The motor modules are presented on a normalized y-axis base: each muscle contribution within one synergy can range from 0 to 1 and each point represents an individual trial. Motor primitives mean and standard deviation bands are presented for one trial (from lift-off to steady-state), time-normalized to 200 points (x-axis), and amplitude normalized to maximum (y-axis). The vertical line in the primitive panels indicates the touchdown (i.e. the beginning of the double leg stance).

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In both the forward and backward lunges, the fundamental muscle synergies were associated with temporally different phases of the task. The first synergy was related to the swing phase and in the forward lunge showed a major involvement of the foot dorsiflexors, hip flexors, and hip abductors. In the backward lunge, the main contribution in the swing synergy resulted from the hamstrings and glutei. The second synergy identified the touchdown phase with a main contribution of the plantar flexors and hamstrings in the forward lunge, and plantar flexors, knee extensors, hip flexors and abductors in the backward lunge. The third synergy was functionally associated with the acceptance of the body weight and, in the forward lunge, was characterized by a main activity of knee and hip extensors. In the backward lunge, the third synergy was recognized only in the stable ground and showed a main contribution of knee extensors, dorsiflexors, and plantar flexors (Figure 3.6). The fourth synergy reflected the stabilization phase of the task and was, in the forward lunge, characterized by the involvement of dorsiflexors, knee extensors, lateral foot stabilizers, and plantar flexors, whilst in the backward lunge the dominant contribution of the stabilization synergy corresponded to dorsiflexors (Figure 3.6). In the forward lunges we observed a significant effect of the ground type (Table 3.1). The CoA was significantly shifted to a later moment in the touchdown ($F(1,20) = 13.43$, $p = 0.004$, Table 3.1) and stabilization ($F(1,12) = 15.31$, $p = 0.004$, Table 3.1) synergies in the unstable compared to stable condition. The motor module of the stabilization synergy showed also a statistically significant ground effect ($F(1,14) = 11.84$, $p = 0.001$, Table 3.1), the post-hoc analysis revealed a significant reduction in the contribution of VM ($p = 0.001$) and TA over unstable ground ($p = 0.020$, Figure 3.7). Moreover, we found a significant repetition effect, resulting in a significant shift towards an earlier CoA in the stabilization synergy ($F(1,20) = 5.21$, $p = 0.004$, Table 3.1) and FWHM in the swing synergy ($F(1,18) = 20.75$, $p = 0.010$, Table 3.1). An interaction of ground and repetition was observed in the CoA of the stabilization synergy ($F(1,12) = 7.425$, $p = 0.026$, Table 3.1). The post-hoc analysis revealed that the CoA shifted significantly later in time in the second half of the trial on SG ($p = 0.016$), and in both early and late cycles on UG ($p < 0.001$) compared to the early cycles on SG. Also, the post-hoc indicated that the CoA of the late cycles on SG was earlier than the CoA of the early cycles on UG ($p < 0.001$). Lunging backward on unstable ground resulted in a significant modification of the touchdown and stabilization synergies. The touchdown primitive shifted its CoA towards after the touchdown ($F(1,30) = 6.507$, $p = 0.016$, Table 3.1) and increased its FWHM ($F(1,30) = 4.974$, $p = 0.033$, Table 3.1). Furthermore, the motor module of the touchdown was also modified by the unstable ground ($F(1,14) = 4.11$, $p = 0.44$, Table 3.1) with a significant lower contribution of GM ($p = 0.009$) and SO ($p = 0.002$)

compared to the stable ground (Figure 3.7). In addition, the stabilization primitive was also wider (F(1,34) = 8.945, p = 0.005, Table 3.1) and shifted earlier in time (F(1,34) = 8.408, p = 0.007, Table 3.1) on UG. Lunging on UG resulted in an increased number of overlaps from shortly before the touchdown and through the entire stance phase of the lunge in both directions. In the forward lunge also an increased number of overlaps were observed at the beginning of the swing phase. These phenomenon resulted from a larger number of overlaps between the touchdown and weight acceptance as well as the weight acceptance with the stabilization motor primitives in the UG condition (Figure 3.8). Considering the absence of the weight acceptance primitive in the backward lunge in UG, the increased overlapping was observed between the touchdown and stabilization motor primitives (Figure 3.8).
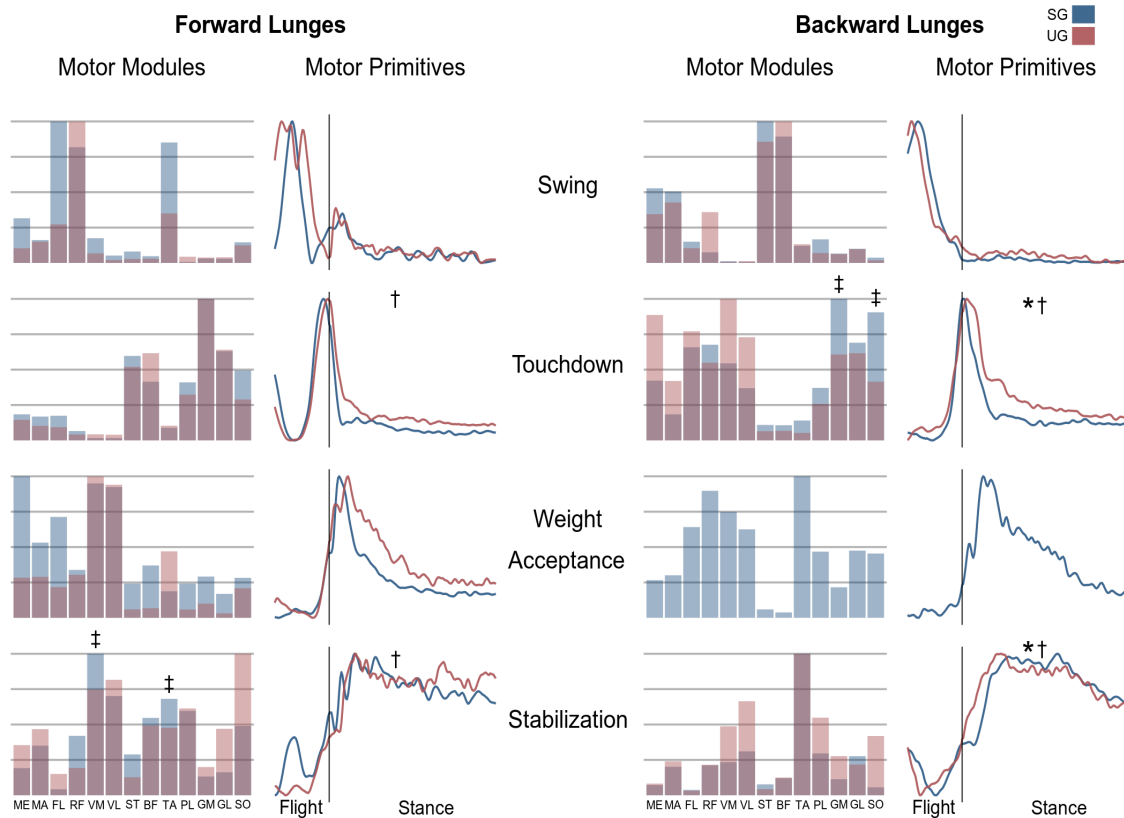
Figure 3.7. *Differences for motor modules and motor primitives for the recognized synergies in the forward and backward lunges. Significant differences in the full width at half maximum of the motor primitives are denoted by asterisks (*), differences in the motor primitives centre of activity by daggers (†). Double daggers (‡) denote post-hoc individual muscles differences in the motor modules.*
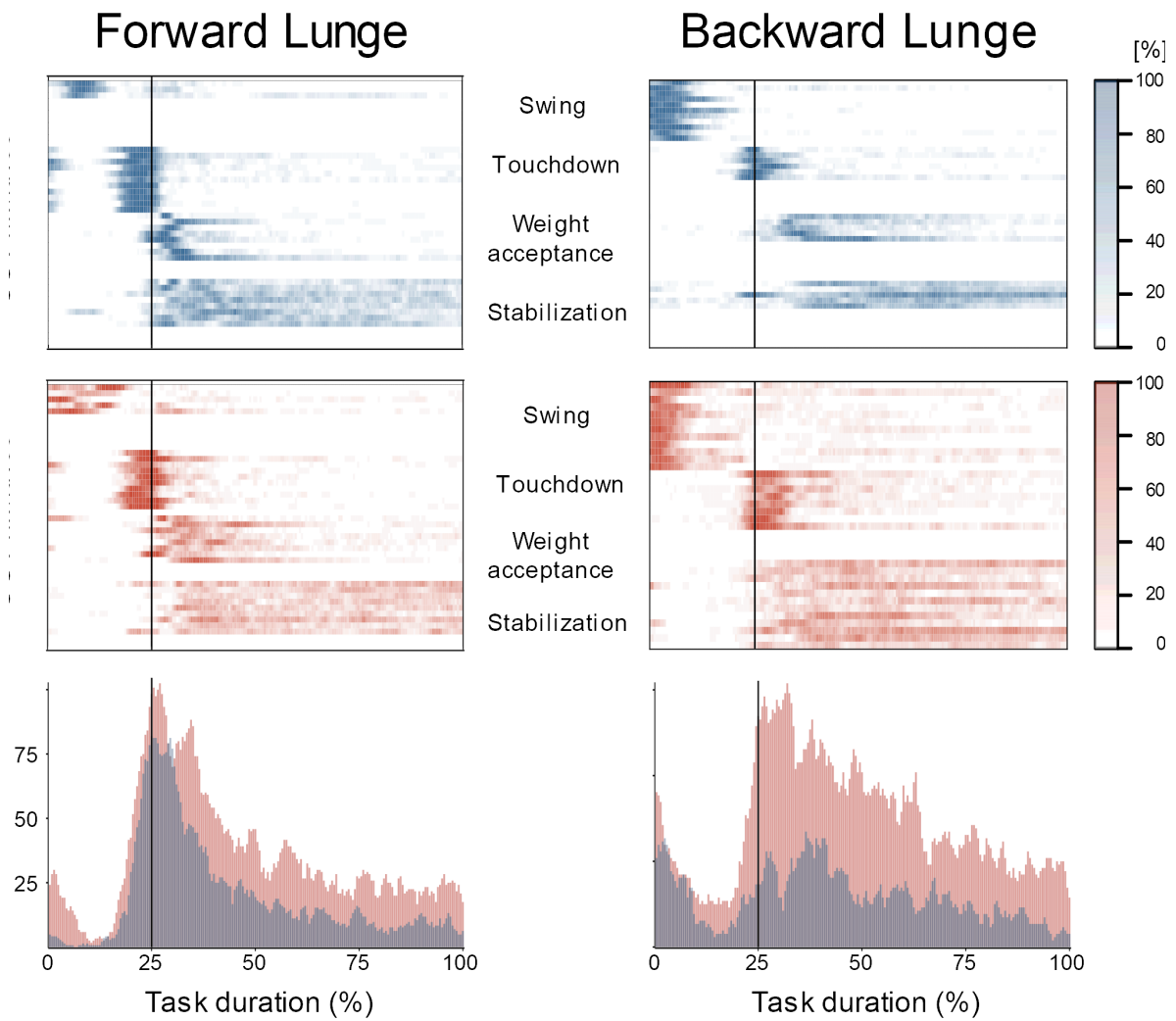
Figure 3.8. Overlapping time intervals of motor primitives for the forward (left) and backward (right) lunges on stable (SG, top-panel blue) and unstable ground (UG, middle panel red). Each row of the heat maps represents a single motor primitive. A colored time-point indicates the primitive is exceeding half maximum. Darker colors indicate higher number of occurrence across all cycles per participant. At the bottom panel the average number of overlaps across all trials and all participants per ground condition. For all graphs the x-axis full scale represents one trial (from lift-off to steady-state), time-normalized to 200 points. The vertical line indicates the touchdown i.e. the beginning of the double leg stance.

Table 3.1. *Differences for Full Width at Half Maximum (FWHM) and centre of Activity (CoA) for each extracted synergy between conditions (SG = stable ground, UG = unstable ground) and repetition (Early and Late cycles) for a forward and backward lunge. Values are presented in mean ± standard deviation for each ground condition and repetition group. Asterisks (*) denote significant differences.*

Synergy	SG		UG		p-values		
	Early	Late	Early	Late	Ground	Repetition	Interaction
Forward lunge							
FWHM							
Swing	33.3 ± 8.0	23.4 ± 5.9	29.8 ± 13.5	27.8 ± 12.6	0.935	0.010*	0.088
Touchdown	21.8 ± 3.1	20.5 ± 3.6	21.1 ± 5.1	22.9 ± 5.0	0.623	0.790	0.162
Weight Acceptance	21.8 ± 10.0	18.7 ± 11.0	23.2 ± 4.1	23.01 ± 5.4	0.410	0.282	0.242
Stabilization	50.9 ±10.6	49.2 ± 14.9	45.8 ± 20.0	43.0 ± 17.6	0.252	0.378	0.901
CoA							
Swing	63.5 ± 44.0	44.3 ± 24.9	55.5 ± 55.6	36.0 ± 21.0	0.523	0.337	0.98
Touchdown	51.6 ± 13.5	44.8 ± 6.7	60.6 ± 10.9	56.5 ± 8.9	0.004*	0.045*	0.551
Weight Acceptance	75.9 ± 12.1	75.5 ± 9.2	80.7 ± 13.1	77.4 ± 13.8	0.468	0.173	0.293
Stabilization	109.4 ± 10.6	117.1 ± 5.5	124.3 ± 6.2	120.8 ± 6.7	0.004*	0.25	0.026*
Backward lunge							
FWHM							
Swing	21.2 ± 5.2	20.3 ± 5.8	21.7 ± 5.8	21.1 ± 7.26	0.718	0.663	0.944
Touchdown	18.8 ±5.3	20.7 ± 5.0	29.0 ± 8.2	26.0 ± 13.4	0.033*	0.702	0.483
Weight Acceptance	36.0 ± 17.2	27.2 ± 13.4	n.a.	n.a.	n.a.	n.a.	n.a.
Stabilization	43.1 ± 22.9	46.7 ± 25.1	66.4 ± 15.6	64.8 ± 20.6	0.005*	0.807	0.714
CoA							
Swing	32.5 ± 21.5	29.1 ± 27.9	41.2 ± 18.6	50.9 ± 29.8	0.066	0.674	0.421
Touchdown	65.5 ± 6.2	60.3 ± 5.6	74.5 ± 11.8	69.9 ± 11.6	0.016*	0.178	0.930
Weight Acceptance	94.7 ± 14.6	94.6 ± 19.4	N.A	N.A	N.A	N.A	N.A
Stabilization	120.1 ± 11.3	133.2 ± 11.7	112.8 ± 14.4	112.2 ± 17.2	0.006*	0.352	0.166

3.5. Discussion

The purpose of the current study was to investigate the modular organization of the motor control system and the mechanical loading of the lower limb's muscles whilst lunging forward and backward in the presence of perturbations, induced by an unstable surface. We hypothesized that participants would modulate the spatiotemporal organization of their muscle synergies to cope with the unstable condition and maintain functionality by increasing their EMG activity and resultant joint moments. We found relevant modifications in the spatiotemporal structure of the muscle synergies, especially in the stabilization synergy, partly confirming our hypothesis. However, the EMG activities and resultant joint moments showed only small and inconsistent alterations.

An explicit modification in the kinematics of the lower limb was observed when lunging on unstable ground. During the forward lunge, both the hip and knee joints remained in a less flexed position compared to that achieved in the stable condition, indicating a lower range of flexion during the stance phase. Correspondingly to our findings, several studies have reported a reduced range of motion in the leg joints when interacting with soft surfaces during jumping[559], running[560], hopping[561] and landing[562]. These results have been proposed to reflect a mechanism for increasing the stiffness of the limb in order to compensate for the changes in the stiffness of the ground, allowing the system to move similarly on different surfaces[561,563].

We expected an increase in the EMG activity of the leg muscles as well as adjustments in the resultant joint moments to compensate for balance control in the presence of perturbations. However, despite some brief alterations in the resultant joint moments and the EMG activity on unstable ground, these parameters behaved quite similarly between the two ground conditions. Coactivation has the potential to increase the muscle mechanical loading without modifying the resultant joint moments. However, our results showed no differences in the coactivation ratios between ground conditions that could explain the increase in muscle force after perturbation-based training reported elsewhere[302,354]. Nonetheless, the resultant joint moments of both forward and backward lunges can be interpreted as high. We detected maximal joint moments between 100 and 500 Nm, which are substantially higher compared to the joint moments reported for postural swaying[211] and equivalent to running[556,564], jumping[565] and landing[566,567]. Recently, we found greater movement instability and higher EMG activity of the leg muscles in unstable ground conditions during postural tracking of an oscillating visual target[568]. The higher activation of the leg muscles was the consequence of the increased movement instability during postural swaying on unstable ground and was interpreted as a compensation mechanism to ensure balance in the presence of external perturbations[568]. Whilst postural tracking of an oscillating visual target is a periodic movement condition and required submaximal muscle force generation, forward and backward lunges are aperiodic, high-intensity tasks. Several studies examining EMG activity in aperiodic, high-intensity landing and jumping tasks reported no relevant alterations[562,569] or even a downregulation of muscle EMG activity[570,571] on unstable compared to stable surfaces.

Lunging relies mainly on predictive control until the first 30 – 90 ms after touchdown[75]. This is especially true for the present study, where participants performed several times the two lunges and, therefore were experienced about the task and characteristics of the surfaces. Furthermore, the task execution was performed with open eyes, thus based on the visual feedback information. Both, the available knowledge from experience about the intended movement and

the visual input guidance, influences the motor output through predictive motor control strategies[75,88,572]. However, the time from touchdown until steady state was on average >800 ms and therefore reactive feedback-based control components were included in the execution of the task, particularly because it was impossible to fully predict the behaviour of the surface and, thus the perturbation itself. Our findings and the additional literature reports indicate that the effects of unstable surfaces on muscle EMG activity are inconsistent, intensity- and task-specific. It follows that external perturbations do not necessarily increase muscle activation. The small and inconsistent differences in the resultant joint moments, muscle EMG activity, and muscle co-activation between stable and unstable surfaces indicate a more or less similar mechanical loading in leg muscles. Earlier randomized control studies[302,354] found improvements in muscle strength by exercising mechanisms of dynamic stability as forward and backward lunges in unstable conditions. In those studies, it was assumed that training on unstable surfaces that continuously introduce disturbances can increase muscle mechanical loading in the lower extremities and, thus, muscle strength[354]. Our current study evidenced that muscle mechanical loading is not affected by unstable conditions during forward and backward lunges and this finding may be of particular interest when planning perturbation-based balance training programs.

During the execution of the investigated task, the participants reached their individual "limit of stability" (i.e., lean as far as possible) to trigger a step reaction. The main goal of the task was to keep balance after the lunge reaction (i.e., regaining the extrapolated centre of mass within the base of support[135]). Four fundamental synergies were recognized for each lunge direction on stable ground, each of them associated to sub-functions of the lunge. The spatiotemporal structure of the synergies was modified in the unstable ground condition. In the forward lunge, the CoA of the touchdown and stabilization primitives were shifted later in time, towards the middle of the stance phase. In the backward lunge, the motor primitives of the touchdown and stabilization synergies became wider and, whilst the CoA of the touchdown primitive shifted to a later time, the CoA of the stabilization primitive shifted to an earlier time, resulting in an increased number of overlaps when lunging on UG. A temporal overlapping between chronologically-adjacent synergies might be a compensatory mechanism adopted by the CNS to cope with the postural instability resulting from disturbances[12,498,551,573]. Moreover, the increased overlap of the muscle synergies might create a "buffer" of motor control, enhancing the robustness of the motor system to cope with the perturbation[12,441,496,573]. The absence of the weight acceptance synergy during the backward lunges resulted in a reduction of the number of synergies by merging the weight acceptance and stabilization synergies in the unstable

condition. Merging of synergies has been reported in stroke patients and was found to be associated with the pathology related severity[484,492]. Although it is difficult, using the current methodology, to identify the concrete neurophysiological origin of this phenomenon, it has been suggested that the merging of synergies may be an alternative solution for stroke patients to compensate the pathology-related impairments when executing a motor task[461,492]. We found also differences in the motor modules indicating modifications in the contribution of individual muscles within the synergies. These findings characterize a modulation of motor control in the unstable condition to ensure functional movement execution, less prone to disturbances. All participants were able to perform both forward and backward lunges in the unstable condition, indicating retention of functionality despite external perturbations. Muscle synergies represent modules of spinal and supraspinal interactions coordinated to create a functional motor output[402,450,461] and modifications in their spatiotemporal activation patterns enhance the ability of the motor system to modulate effective robustness in challenging settings, ensuring functionality[12,441,551].

The FWHM was not affected by the ground condition whilst lunging forwards. However, whilst lunging backwards, where visual feedback is more limited, the touchdown and stabilization primitive increased the FWHM. Widening of motor primitives is associated with challenging locomotion and interpreted as a neuromotor mechanism robustly regulating motor output in the presence of external (e.g., mechanical)[12,441] or internal (e.g., pathology-related) perturbations[573,574]. Recently, we found similar modifications in muscle synergies in wild-type mice but not in genetically modified mice that lacked feedback from proprioceptors[496], evidencing a relevant contribution of sensory feedback in the modulation of motor control in the presence of perturbations. In the weight acceptance and stabilization synergies, sensory processing was likely involved in the motor control processes to increase the chance of reactive adjustments, based on proprioceptive information received during and after touchdown. The main alterations in the modular control occurred in the stabilization synergy. This synergy is characterized by a wide motor primitive which is extended during the whole stance phase when the participants deal with the perturbations. The observed alterations in the motor primitives of the stabilization synergy, and the shift of the touchdown CoA on both directions towards a later time after the touchdown, in the UG, indicate reactive adjustments in the modular organization as a consequence of the external perturbations. We cannot exclude any predictive or anticipatory motor control in this synergy because the participants expected mechanical disturbances after touchdown. The absence of the weight acceptance synergy in the backward lunge is likely the consequence of proactive adjustments. However, the effects of the unstable

condition on the temporal components of the synergies, strongly indicate that part of the resulting perturbations were unpredictable and initiated reactive modulation of motor control to perform the task successfully.

The temporal activation pattern of the swing synergy did not show any differences between the stable and unstable conditions in both tasks. The first synergy is functionally responsible for the increase of the base of support after stability is lost to recover the extrapolated centre of mass within the base of support and the second synergy functionally prepares for the contact of the leg with the ground. After the loss of balance, an increase in the base of support to regain the extrapolated centre of mass within its limits is a basic postural mechanism[135,351] independent of the landing surface. It can be argued, that relevant components of predictive and anticipatory control during the swing phase with minor reactive adjustments may explain the similar temporal organization of the first synergies. An effect of repetitions was observed only in the swing and touchdown synergies of the forward lunge (on FWHM and CoA respectively), in both cases in the direction of a reduction of the metric. This might indicate an acute adaptation to the repeated exposure to the perturbation, thus indicating the possibility of a "learning effect". We have to mention that in our analysis we did not consider the contralateral limb and trunk muscles that might be relevant for the stabilization process. During a step reaction, the supporting limb has been described for playing a role during the push-off phase, particularly providing time for correct positioning of the stepping leg[152,566]. The stepping limb, on the other hand, is of paramount importance for both, the swing phase[205,353] and decelerating the centre of mass after the touchdown[97,133,152,575].

In summary, our results evidenced that the neuromuscular system adjusts its modular organization in both forward and backward lunges in the presence of perturbations. Modifying the spatiotemporal structure of muscle synergies and kinematics allowed the participants to maintain functionality in challenging settings with minor alterations of movement kinetics. The observed alterations indicate that both proactive, as well as reactive control mechanisms, were involved in the modulation of muscle synergies to regulate motor control in unstable ground conditions. Such modifications in regulating motor function in challenging settings might affect the ability of the motor system to modulate effective control robustness in response to environmental changes and may contribute to the reported stability improvements after perturbation-based exercise[302,354].

4. Third study: Proactive modulation in the spatiotemporal structure of muscle synergies minimizes reactive responses in perturbed landings

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4.1. Abstract

Stability training in the presence of perturbations is an effective means of increasing muscle strength, improving reactive balance performance and reducing fall risk. We investigated the effects of perturbations induced by an unstable surface during single-leg landings on the mechanical loading and modular organization of the leg muscles. We hypothesized a modulation of neuromotor control when landing on the unstable surface, resulting in an increase of leg muscle loading. Fourteen healthy adults performed 50 single-leg landings from a 30 cm height onto two ground configurations: stable solid ground (SG) and unstable foam pads (UG). Ground reaction forces, joint kinematics and electromyographic activity of 13 muscles of the landing leg were measured. Resultant joint moments were calculated using inverse dynamics and muscle synergies with their time dependent (motor primitives) and time independent (motor modules) components were extracted via non-negative matrix factorisation. Three synergies related to the touchdown, weight acceptance and stabilization phase of landing were found for both SG and UG. When compared to SG, the motor primitive of the touchdown synergy was wider in UG ($p < 0.001$). Furthermore, in UG the contribution of gluteus medius increased ($p = 0.015$) and of gastrocnemius lateralis decreased ($p < 0.001$) in the touchdown synergy. Weight acceptance and stabilization did not show any statistically significant differences between the two landing conditions. The maximum ankle and hip joint moment as well as the rate of ankle, knee and hip joint moment development were significantly lower ($p < 0.05$) in the UG condition. The spatiotemporal modifications of the touchdown synergy in the UG condition highlight proactive adjustments in the neuromotor control of landings which preserve reactive adjustments during the weight acceptance and stabilization synergies. Furthermore, the performed proactive control in combination with the viscoelastic properties of the soft surface resulted in a reduction of the mechanical loading in the lower leg

muscles. We conclude that the use of unstable surfaces does not necessarily challenge reactive motor control, nor increase muscle loading per se. Thus, the characteristics of the unstable surface and the dynamics of the target task must be considered when designing perturbation-based interventions.

4.2. Introduction

Perturbation-based training interventions are an effective way to improve reactive balance performance and increase muscle strength[205,302,303]. Moreover, the effectiveness of perturbation-based interventions for successfully reducing fall risk in different populations has been previously reported[182,241,242,254,354]. Using compliant or unstable surfaces as well as specific treadmill-slips to challenge balance control by introducing external mechanical perturbations (i.e., an alteration of the function of a biological system induced by external mechanism) have been widely used in clinical and training settings[304,308,354,510]. Recently, it was found that exercising mechanisms of dynamic stability control (i.e., increasing the base of support and counter-rotating body segments around the centre of mass) in the presence of perturbations improved reactive balance recovery performance and muscle strength already after three weeks of exercise in older participants[302]. It was proposed that exercising specific balance tasks in the presence of perturbations could increase the demand for the neuromotor system to perceive sensory signals and to generate appropriate motor commands, thus facilitating the sensory-motor integration[302,354].

External mechanical perturbations increase movement instability[12,551,576] and challenge the neuromotor system during motion execution. In response, the neuromotor system modifies its strategies to increase control's robustness (i.e., the ability to cope with perturbations)[12,551]. In earlier studies adopting the muscle synergies approach, we found specific modulations (i.e., wider, less unstable and less complex basic activation patterns of muscle groups) of the temporal structure of muscle synergies in the presence of perturbations[12,441,577]. Such regulations of motor function in the presence of perturbations might be related to the efficacy of perturbation-based exercise interventions and its potential to enhance the ability of the motor system to respond and adapt to challenging conditions related to environmental changes during the daily life. Landing-related tasks on unstable surfaces have been widely used in perturbation-based training interventions in order to induce variable and partly unpredictable disturbances that promotes balance improvement and adaptation[205,302,354]. Compliant surfaces have the potential to modify foot kinematics and forefoot stability during landings[578,579], thus challenging the neuromotor control.

Fundamental basic building blocks defined as motor primitives are compositional elements for movement construction and have been established as kinematic, kinetic and neural drive entities which reflect an organizational principle of movement formation[390,406,409,580]. It is assumed that a complex movement task can be generated by rearranging and combining motor primitives and therefore motor primitives may provide an insight into underlying neurophysiological mechanisms for motor control[404]. The idea that the neuromotor system faces the redundancy of available degrees of freedom by activating functionally related muscle groups rather than individual muscles is well accepted[358,390]. The resultant coordinated patterns of muscle activity are commonly known as muscle synergies and are flexibly combined to produce robust locomotor drive[391,396,402]. Synergies - as low dimensional units - produce a complex electromyographic (EMG) pattern in muscles, involving a time dependent basic activation pattern (temporal structure of the synergy or motor primitives) with variable time independent weights of activity distribution to different muscles (spatial structure of the synergy or motor modules)[437,450,451].

Recently, investigating forward and backward lunges on stable and unstable surfaces and using the muscle synergies approach, we found alterations in the spatiotemporal structure of muscle synergies during the stance phase (i.e., weight acceptance and stabilization synergy), resulting in an increased overlap between chronologically-adjacent synergies in the unstable condition[577]. However, studies investigating the EMG activity in the lower leg muscles during landings on stable and unstable grounds reported marginal effects of landing surface on the EMG activity[562,569]. The biomechanical differences between lunges (movement of the centre of mass in both horizontal and vertical direction) and landings (mainly a vertical motion of the centre of mass) may affect the effectiveness of proactive neuromuscular adjustments (i.e., before touchdown), resulting in distinct modifications in the spatial and temporal components of the muscle synergies after touchdown in the two tasks. To the best of our knowledge, no study investigated the spatiotemporal activation structure of muscle synergies during landings on unstable surfaces yet. Investigating the spatiotemporal structure of muscle synergies might present an opportunity to better understand the neuromotor control of landings in the presence of perturbations and thus promoting the design of effective exercise programs.

Therefore, the purpose of the current study was to investigate the effects of perturbations induced by an unstable surface on the mechanical loading (i.e., each muscle's group mechanical demands) and modular organization of neuromotor control during single-leg drop landings. We hypothesized that landing on unstable surfaces would result in a modulation of motor control, reflected in the spatiotemporal components of muscle synergies and in an

increase of muscle loading reflected by an increased muscle activity and/or resultant joint moments, in response to the increased challenges in balance control.

4.3. Materials and Methods

4.3.1. Experimental protocol

We performed an a priori power analysis using the findings from our earlier study investigating forward and backward lunges in stable and unstable surfaces[577]. We found an effect size of 1.17 for the differences in the temporal structure of muscle synergies (i.e. width of the motor primitives) between stable and unstable condition and assuming a Type I and Type II errors of 0.05 we calculated that seven participants were sufficient for the designed study. Fourteen healthy adults volunteered for the study (10 males, 4 females, height 1.75 ± 0.10 m, body mass 67 ± 11 kg, age 28 ± 5 years). None of the participants had a history of acute lower limb injury or back pain in the six months preceding the recordings, nor did they suffer from any chronic neuromuscular or musculoskeletal impairments. In accordance with the Declaration of Helsinki, all participants provided written informed consent for the experimental procedure which was reviewed and approved by the Ethics Committee of the Humboldt-Universität zu Berlin (HU-KSBF-EK_2018_0013).

Participants were instructed to step off a platform, dropping into a single-leg landing (right leg) and maintain the achieved single-leg stance after the touchdown with a strategy of their choice until they felt completely stable (Figure 4.1). The height of the platform was adjusted to keep a drop height of 30 cm over two possible ground configurations: hard uniform stable ground or unstable ground built out of two 100 x 100 x 10 cm foam pads (one cold foam pad with density = 50 kg/m³ and compressive strength = 6.0 kPa; one polyurethane foam pad with density = 40 kg/m³ and compressive strength = 7.0 kPa). Landings happened over a force plate (40 x 60 cm, AMTI BP400600-200, Advanced Mechanical Technology, Inc., Watertown, MA, USA) sampling the ground reaction forces (GRF) at 1 kHz. A minimum of five landings in each condition were used as familiarization and warm up, after which the participants performed a series of 52 valid landings per condition at a self-managed pace. If the participant was not able to maintain the single-leg stance (e.g., touched the floor with any other part of the body or changed the position of the foot on the ground) the attempt was considered failed and repeated. The order of the series was randomized and a self-managed rest period (minimum 3 minutes, seating allowed) was given in-between series to avoid fatigue.
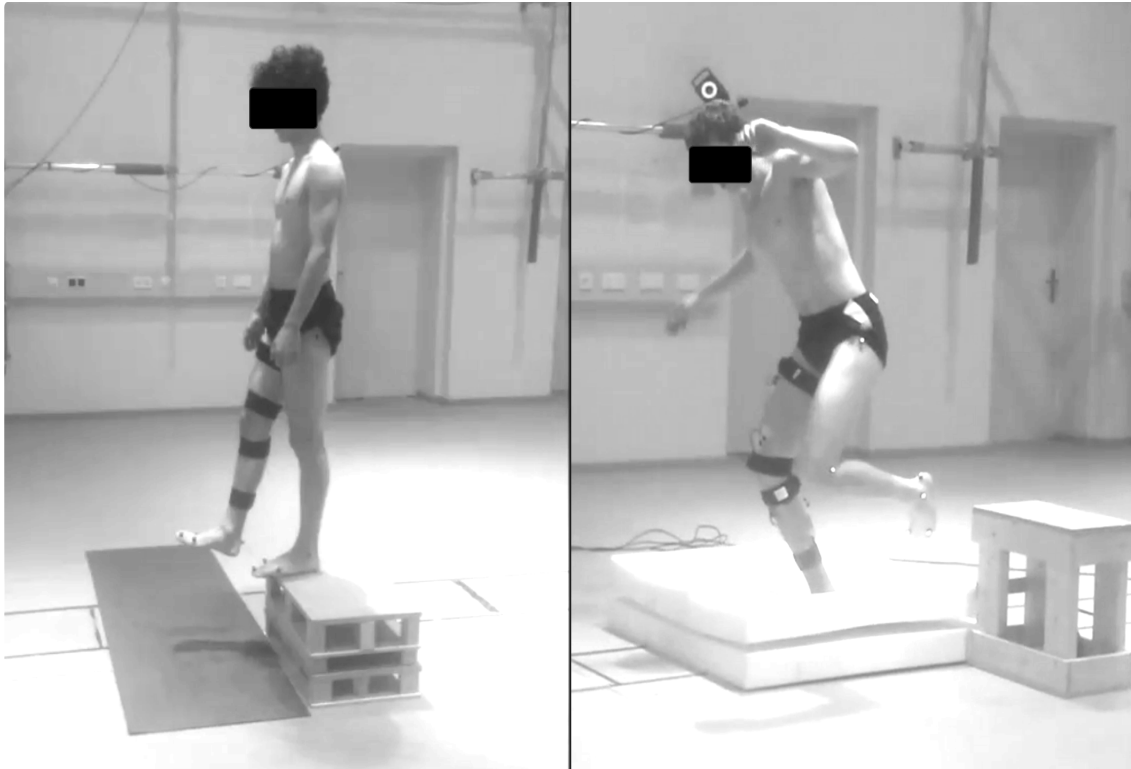
Figure 4.1. *Visual description of the performed task. Participants performed a single-leg landing by dropping onto two ground configurations: stable solid ground (left) and two foam pads used as unstable ground (right). Fifty repetitions were performed onto each ground condition and the height of the platform was adjusted to keep a 30 cm distance to the surface.*

A ten-infrared-camera motion capture system (Vicon Motion Systems, Oxford, U.K.) operating at 250 Hz was used to collect kinematic data from 20 spherical reflective markers (14 mm diameter) placed over the following anatomical landmarks: spinal process of the second, seventh and tenth thoracic along with the second lumbar vertebrae, and bilaterally over the greater trochanter, lateral and medial epicondyle of the femur, Achilles tendon insertion on the calcaneus, lateral malleolus, tip of the first toe, the dorsal margin of the first and fifth metatarsal heads. We also assessed the EMG activity of the following 13 right-leg muscles: gluteus medius, gluteus maximus, tensor fasciae latae, rectus femoris, vastus medialis, vastus lateralis, semitendinosus, biceps femoris (long head), tibialis anterior, peroneus longus, gastrocnemius medialis, gastrocnemius lateralis and soleus using a 16-channel wireless EMG system (Myon m320, Myon AG, Schwarzenberg, Switzerland), with a sampling frequency of 1 kHz. The electrodes were not replaced between series. EMG and force plate analog data streams were collected together with the kinematics and then converted to digital information within the same A/D converter (Vicon MX Giganet).

4.3.2. Kinetic analysis

Touchdown of each landing was defined as the first data point of the vertical GRF crossing a 20 N threshold[581]. An interval of interest was defined for each landing as the time window between 300 ms prior to the touchdown (flight phase) and until the first point crossing a threshold of body weight ± 2.5% following a minimum in the vertical GRF after the touchdown (stance phase). Marker trajectories were filtered using a 4th order Butterworth low-pass filter with a cut-off frequency of 18 Hz[581]. Sagittal kinematics of the ankle, knee and hip joints from the landing-leg and the resultant internal joint moments for the aforementioned joints were calculated using a custom Matlab (v. R2012a, The MathWorks, Natick, MA) inverse dynamics procedure[582] with segmental masses and inertial parameters derived from literature[7]. Kinematics and resultant joint moments were time-normalized to 300 points with 100 points assigned to the flight and 200 points to the stance phase, pasted one after another (i.e., concatenated) and kept for further analysis. We calculated the Euclidean norm of the GRF and time-normalized it in the same way as the kinematic and resultant joint moments data. The 2D centre of pressure (CoP) data was used to analyse the effect of the ground (SG vs. UG) on the postural sway during the stance phase of each landing. The CoP's 95% confidence ellipse area (CoP area), representing the area of the smallest ellipse able to contain 95% of all the measured CoP points, was calculated using a custom Matlab script.

4.3.3. Muscle synergies

EMG signals were filtered with a 4th order IIR Butterworth zero-phase high-pass filter with a cut-off frequency of 50 Hz full-wave rectified and low-pass filtered with a cut-off frequency of 20 Hz[437]. The amplitude of the EMG signal was then normalized to the maximum activity of each muscle in the SG series of each participant. Lastly, all intervals of interest were time-normalized in the above-mentioned manner. Thus, all variables were time-normalized in a similar manner. The rationale for this normalization (i.e., 100 and 200 points to the flight and stance phase respectively) was to respect the time structure of each landing (i.e., roughly a 1:2 ratio for the flight and the stance), and provide a common time reference for all landings (i.e., the touchdown) whilst allowing any time-dependent modulation that could have occurred independently of the absolute duration of the events. All EMG off-line processing and further analysis on all variables were performed in R (R v4.0.3, R Core Team, 2020, R Foundation for Statistical Computing, Vienna, Austria).

Muscle synergies were extracted from the filtered and normalized EMG signals and classified using the open source script musclesyneRgies v0.7.1-alpha[583] based on the classical Gaussian non-negative matrix factorisation (NMF) algorithm[435,437]. It is to be mentioned, that several other factorisation methods have been used in the literature to extract muscle synergies as principal component analysis, independent component analysis, or factor analysis[430,434]. Nonetheless, NMF has been reported to provide a more intuitive physiological representation of synergies compared to other factorisation methods[434] and as the best factorisation method for identifying muscle synergies in dynamic tasks with different levels of muscle contraction[436]. The concatenated EMG data vectors were grouped in an m × n matrix V, where m = 13 (number of muscles) and n = number of points (300). This matrix was factorized such that $V \approx V_R = MP^T$, where V_R represents a new reconstructed matrix that approximates the original matrix V, while M and P describe the synergies necessary to accomplish a movement. M represents the m × p motor modules matrix[437,554], containing the time-invariant muscle weightings. P represents the p × n time-dependent coefficients (motor primitives) matrix[437,451], where p represents the number of synergies necessary to reconstruct the signal and n the number of data points. The number of synergies p was defined as the amount of synergies that did not improve the reconstruction of the signals with the addition of an extra module and it was calculated using the R^2 between V and VR. When the mean squared error of a linear regression model fitting the curve of R^2 values vs. synergies for all the synergies fell below 10^{-5}, we assumed that the addition of an extra synergy did not improve the quality of the reconstruction[12,437]

In order to compare the extracted synergies and give them a functionally meaningful interpretation, we classified them using an unsupervised method based on k-means clustering, with the aim to reduce possible operator-dependent bias in the classification. The algorithm initially clusters the average motor primitives (i.e., one primitive of 300 points per series, average of all the 52 obtained for that series) for each condition separately. This is done for a number of clusters going from one until the number of muscles, with 20 random start sets and using the Hartigan and Wong algorithm[584]. Then, a curve "number of clusters vs. within-cluster sum of squares" is built and normalized between zero and one. The minimum number of clusters (or their centroids) is then selected as the number of muscles minus the number of points on the curve that can be linearly interpolated with a mean squared error lower than 10^{-3}. Motor modules are then clustered by imposing the number of centroids thus obtained with the analysis on motor primitives. The average full width at half maximum (FWHM) and centre of activity (CoA) of the motor primitives are then summed and normalized by the number of

points (i.e., 300) and this value is used as a score to compare the k-means classification of modules and primitives. The FWHM was calculated as the number of points exceeding each cycle's half maximum, after subtracting the cycle's minimum[574] and the CoA is defined as the angle of the vector (in polar coordinates) that points to the centre of mass of that circular distribution and its calculation method has been previously described. Common classifiers identify fundamental synergies, while discording classifiers return combined (i.e., spurious) synergies. If no matching is found, only primitive-based classification is retained. Motor primitives between SG and UG condition were compared across condition by means of the FWHM. Further, we calculated the overlapping intervals of the motor primitives for each synergy per every landing trial and then averaged for each participant and surface condition. An overlap is happened when at least two motor primitives were exceeding half maximum at the same time.

To compare motor modules across conditions, we assessed the distribution of muscle contributions for each synergy separately. We defined the ratio of flexor and extensor muscle contribution to each joint in a specific motor module as the coactivation index (CaI). For its calculation, we considered the tensor fasciae latae and rectus femoris as hip flexors and the gluteus medius and gluteus maximus as hip extensors. For the knee, the flexors were the semitendinosus and biceps femoris and the extensors the rectus femoris, vastus medialis and vastus lateralis. For the ankle, only the tibialis anterior was considered as flexor (i.e., foot dorsiflexor) and the peroneus longus, gastrocnemius medialis, gastrocnemius lateralis and soleus as extensors (i.e., foot plantar flexors). For each joint, the mean of the flexor contributions Flex and the mean of the extensor contributions Ext were forced to sum to 1:

$$CaI = \overline{Flex}/\left(\overline{Flex}+\overline{Ext}\right) \textit{ (eq. 4.1)}$$

Hence, the CaI is equal to: a) zero when only extensors are contributing to the considered joint; b) one when only flexors are giving their contribution; c) 0.5 if flexors and extensors are equally contributing (i.e., full coactivation of flexors and extensors).

4.3.4. Statistical analysis

After removing the first and last landing, the remaining 50 landings were used to create a representative dataset for each participant on each ground condition of the following variables: FWHM, maximum range of joint angles (defined as the difference between minimum of the joint angle and angle at touchdown), maximum of joint moments and GRF, rate of joint moment development (defined as the ratio between joint moment maxima and the time interval

between touchdown and time to maxima), joint moments' lever arm, and CoP area. Then the mean of the 50 repetitions of each subject was used as the subject's data for the statistical test. We tested the homogeneity of variances on the residuals of each aforementioned variable using the Levene's test. If the variables were normally distributed, we used a parametric test to investigate the effect of ground condition on variable. Hence, we performed a one-way ANOVA for repeated measures on each of the following variables: GRF maxima, CoP area, and FWHM of the synergies. Correspondingly, we used a two-way ANOVA for repeated measures on the joint kinematics, resultant moments, joint moment's lever arm and joint moment's rate using ground (SG – UG) and variable (i.e., ankle, knee hip joint angle or moment) as within-subjects variables. The same two-way ANOVA for repeated measures was used for each synergy using ground (SG – UG) and muscle or CaI, for the motor modules as within-subjects variables. When normality conditions on the residuals were not met (i.e., joint range of motion, resultant joint moment maxima and FWHM of the touchdown synergy), we used a rank-based robust ANOVA from the R package "Rfit" (v 0.24.2, function "raov")[585]. If an interaction of main effects was observed, we performed a Tukey post-hoc analysis with false discovery rate α-value adjustment. All the significance levels were set at 0.05.

Moreover, we adopted a similar approach using the statistical parametric mapping (SPM) on all the aforementioned continuous variables (i.e., time-normalized vectors). Correspondingly, the individual time-normalized joint kinematics, resultant joint moments, GRF, EMG and overlaps curve for each landing were averaged to create a representative dataset of each participant on each ground condition. We tested for normality using a D'Agostino-Pearson test corrected for arbitrary one-dimensional domains using random field theory[586]. If non-parametric test were needed the corresponding two-way ANOVA for repeated measures Permutation test[587]was used. SPM allow us to analyse the entire time-series by using Random Field Theory[588]. Based on the temporal smoothness of the data (i.e., each time-normalized dataset) residuals trajectory a critical threshold f* was calculated. Then a test statistics SPM{F} was evaluated at each point of the time series. In the case that SPM{F} exceeded f*, a significant difference was detected. Similar to the above described analyses, significance level was set at 0.05. In case of finding an interaction of main effects, we conducted a SPM two-tail paired t-test with significance t* level Bonferroni corrected for multiple comparisons (n = number of levels in the variable) between each relevant pair of variables as a post-hoc analysis. All SPM calculations were performed in using the open-source package spm1d (v 0.4.3).

4.4. Results

Participants needed a longer time to reach their body weight threshold (i.e., stabilization) when landing on UG. This led to a significantly longer stance phase after landing onto the unstable ground compared to the stable condition (SG: 0.491 ± 0.062 s, UG: 0.629 ± 0.085 s, $t(1,13) = -5.611$, $p < 0.001$). Two participants were excluded from the kinematic analysis due to poor reconstruction of the markers' trajectories. The SPM-analysis revealed a significant main effect of the ground type on joint kinematics during the flight ($F^* = 9.877$, $p = 0.012$) and the first half of the stance phase ($F^* = 9.877$, $p = 0.034$). An interaction of ground by joint was found shortly before touchdown and during the entire stance phase ($F^* = 5.724$, $p < 0.001$). The post-hoc analysis revealed no differences in the flight phase in a specific joint but showed that landing on UG led the participants to reach a less dorsiflexed position at the ankle joint after the touchdown ($35 - 55\%$ of the task duration, $t^* = 3.618$, $p = 0.010$) and in the middle of the stance phase ($59 - 78\%$ of the task duration, $t^* = 3.618$, $p = 0.007$, Figure 4.2). Landing on UG also had a significant main effect on the joint range of motion ($F(1,11) = 5.48$, $p = 0.023$), and a significant interaction of ground by joint ($F(2, 22) = 9.81$, $p < 0.001$). The post-hoc analysis showed that landing on UG resulted in a less range of dorsiflexion at the ankle joint during the stance phase (UG: $37.19 \pm 12.76°$, SG: $52.03 \pm 6.45°$, $p < 0.001$).

There was a significant ground effect on the internal resultant joint moments shortly after the touchdown ($F^* = 17.500$, $p = 0.003$) and an interaction of ground by joint in the swing phase ($\sim 20 - 25\%$ of the task duration, $F^* = 8.572$, $p = 0.025$), around touchdown ($F^* = 8.572$, $p = 0.012$), and during three periods of the stance phase: between the 36 and 40% ($F^* = 8.572$, $p = 0.023$), $45 - 75\%$ ($F^* = 8.572$, $p < 0.001$) and between the 60 and 76% of the task duration ($F^* = 8.572$, $p < 0.001$). The post-hoc analysis showed lower a plantar flexion moment at the ankle joint ($\sim 30 - 40\%$ of the task duration, $t^* = 4.097$, $p = 0.002$) in UG compared to SG (Figure 4.2). At the knee joint the extension moment was also lower in UG during the flight phase ($20 - 25\%$ of the task duration, $t^* = 4.118$, $p = 0.017$) and around the touchdown ($28 - 34\%$ of the task duration, $p = 0.010$, Figure 4.2). A lower hip flexion moment in UG condition around the touchdown ($\sim 30\%$ on the task duration, $t^* = 4.166$, $p = 0.008$) was found (Figure 4.2). Further, the maximum resultant ankle ($p = 0.002$) and hip ($p = 0.004$) joint moment and the rate of moment development in all joints ($p = 0.029$ at the knee and $p < 0.001$ for the ankle and hip) were significantly lower in UG compared to SG (table 4.1). The lever arm of ankle joint centre to GRF-vector at moment maximum was also lower in the UG condition (table 4.1). The SPM-analysis identified a significantly lower GRF after touchdown in UG ($t^* = 3.305$, $p = 0.013$, Figure 4.3), however, the maximum of the GRF did not differ ($F(1,13) = 2.025$, $p = 0.178$,

figure 4.3) between the two ground conditions. CoP area during the landing was smaller in UG (F(1,14) = 7.527, p = 0.020) compared to SG (Figure 4.3).
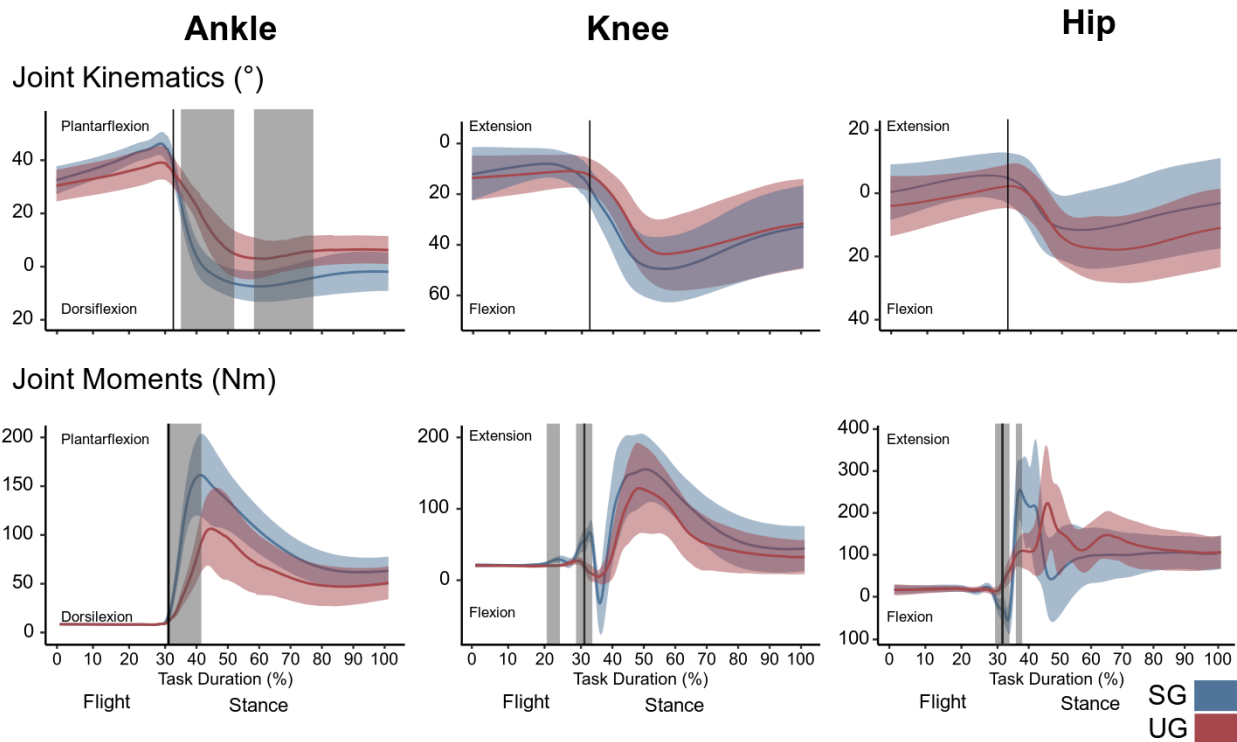
Figure 4.2. Lower limb kinematics and internal resultant joint moments of the single-leg drop landing (from 300 ms previous to the touchdown until the first point crossing a threshold of body weight ± 2.5% following a minimum in the vertical ground reaction force after the touchdown). Each panel shows the mean values and standard deviation bands for the ankle, knee and hip joint angles and moments for the stable (SG—blue) and unstable (UG—red) ground condition. Panels are presented in a time normalized base, vertical lines represent the touchdown. Gray vertical bands highlight time periods of significant differences assessed by statistical parametric mapping.

Table 4.1. *Maxima of the resultant joint moment, lever arm at moment maxima and rate of moment development for the ankle, knee and hip joint during a single-leg drop landing on stable (SG) and unstable ground (UG). Values are presented as mean ± standard deviation. Asterisks denote statistically significant (p < 0.05) difference between the two ground conditions.*

| Joint	Parameter	SG	UG
Ankle	Moment Max (Nm) *	183.7 ± 46.5	142.4 ± 41.4
	Lever arm (m) *	0.102 ± 0.02	0.079 ± 0.02
	Rate of Moment (Nm/s) *	2665.7 ± 487.0	1094.1 ± 275.4
	Time to Peak torque (ms)	56.1 ± 14.7	60.6 ± 21.7
Knee	Moment Max (Nm)	136.6 ± 41.1	118.5 ± 53.2
	Lever arm (m)	0.093 ± 0.02	0.077 ± 0.03
	Rate of Moment (Nm/s) *	1593.7 ± 554.4	788.6 ± 260.0
	Time to Peak torque (ms)	73.3 ± 11.2	86.4 ± 22.4
Hip	Moment Max (Nm) *	261.6 ± 78.1	207.5 ± 92.1
	Lever arm (m)	0.104 ± 0.02	0.090 ± 0.01
	Rate of Moment (Nm/s) *	4514.7 ± 1923.7	1610.0 ± 806.5
	Time to Peak torque (ms)	77.1 ± 13.5	78.4± 23.1
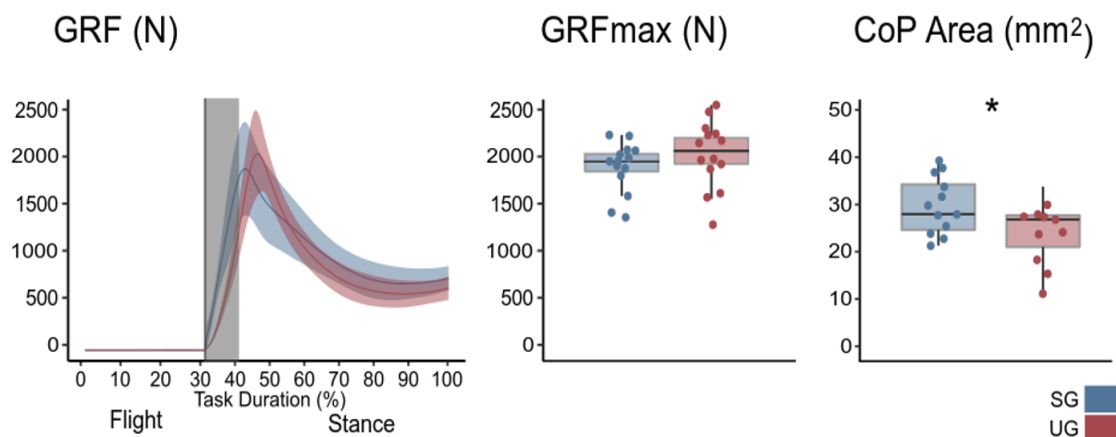
Figure 4.3. *Right panel presents the mean Euclidean norm and standard deviation bands of the ground reaction force (GRF) during a single-leg drop landing for the stable (SG) and unstable ground conditions (UG). Vertical lines represent touchdown, gray vertical bands highlight time periods of significant differences assessed by statistical parametric mapping. Central panel represent the maximum of the GRF with points denoting single trials. Left panel shows the CoP 95% confidence area for the stance phase with points denote single trials. Asterisks denote statistically significant differences between the two conditions.*

The ground condition affected the EMG activity during the second half of the swing (F* = 14.364, p < 0.001), and in three brief periods of the stance phase (p = 0.049, 0.014 and 0.029). There was also a significant interaction between ground and muscle in both the flight (F* =

2.718, p < 0.001) and stance (F* = 2.718, p = 0.001) phase. The post-hoc analysis revealed lower EMG activity before touchdown in the gastrocnemius medialis (~25 - 33% of the task duration, t* = 4.544, p < 0.001) and gastrocnemius lateralis (~25% of the task duration, t* = 4.447, p = 0.004) and after the touchdown in the soleus (~45% of the task duration, t* = 4.709, p = 0.020, Figure 4.4) in the UG condition.
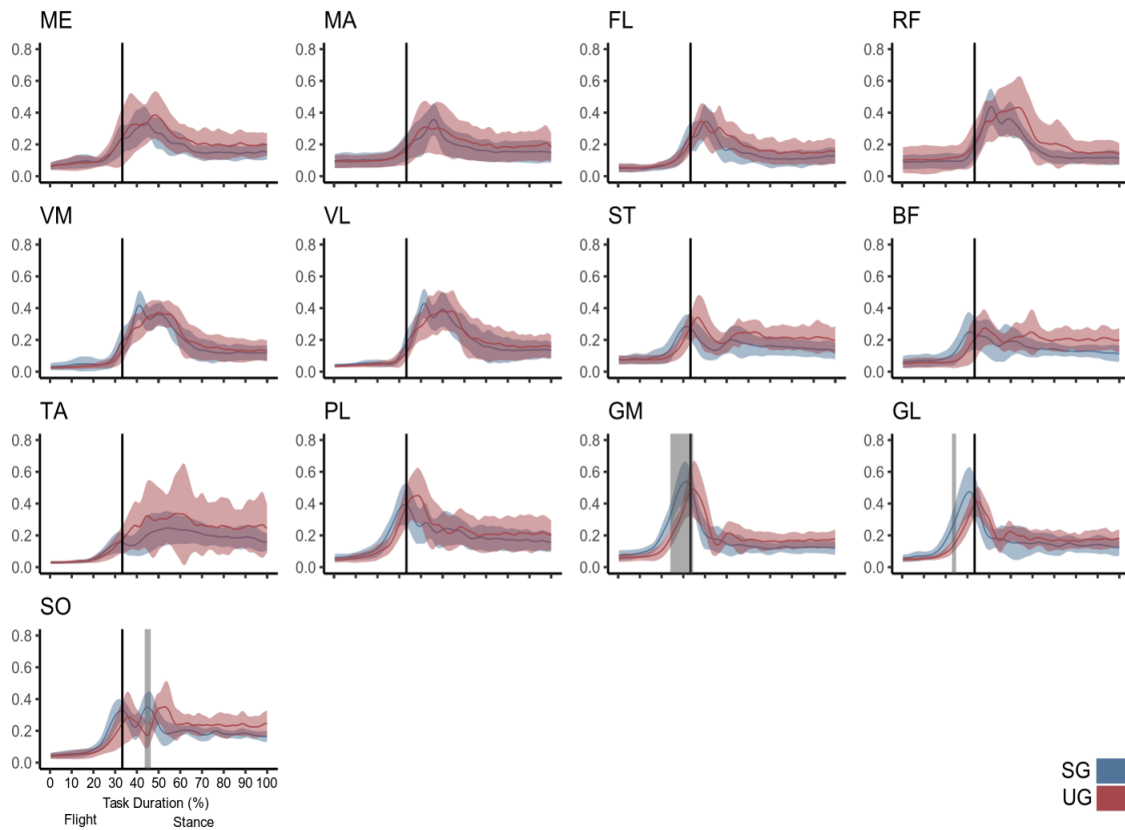

Figure 4.4. Mean values and standard deviation bands for the EMG activities for a single-leg drop landing on stable (SG, blue) and unstable ground condition (UG, red) normalized to the maximum activity of each muscle on the SG condition. Vertical lines represent touchdown. Gray bands denote time periods of significant difference found by the statistical parametric mapping analysis. ME: Gluteus Medius MA: Gluteus Maximus, FL: Tensor Fascia Latae, RF: Rectus Femoris, VM: Vastus Medialis, VL: Vastus Lateralis, ST: Semitendinosus, BF: Biceps Femoris (long head), TA: Tibialis Anterior, PL: Peroneus Longus, GM: Gastrocnemius Medialis, GL: Gastrocnemius Lateralis, SO: Soleus.

The number of extracted synergies that sufficiently reconstructed the original EMG signals did not differ between the two ground conditions (SG = 4.64 ± 0.49, UG = 4.85 ± 0.53, p = 0.282). We identified three fundamental synergies on both SG and UG (Figure 4.5). The first synergy was functionally related to the preparation of touchdown and showed a major contribution of plantar flexors. The second synergy presented its main activity shortly after the touchdown, thus it was functionally related to the weight acceptance and showed a main contribution of

knee extensors. The third synergy represented the stabilization phase after landing and was characterized, in SG, by a major contribution of the muscles acting around the ankle joint, whilst in UG we observed a main contribution of hamstrings, tibialis anterior and peroneus longus. A significant interaction of
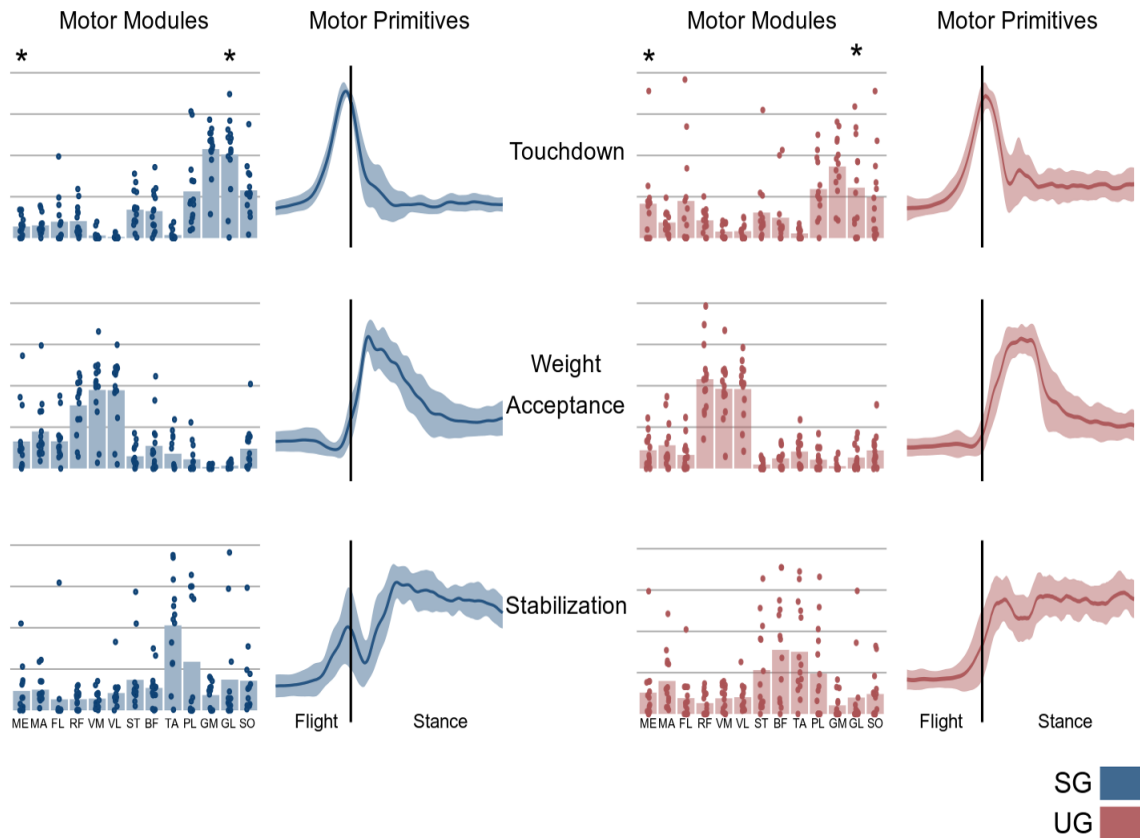

Figure 4.5. Average and individual motor modules values and average with their standard deviation bands motor primitives of the fundamental synergies classified from a single leg drop landing on stable (SG, blue) and unstable (UG, red) ground. The vertical lines in the primitive panels indicate the touchdown. ME: Gluteus Medius MA: Gluteus Maximus, FL: Tensor Fascia Latae, RF: Rectus Femoris, VM: Vastus Medialis, VL: Vastus Lateralis, ST: Semitendinosus, BF: Biceps Femoris (long head), TA: Tibialis Anterior, PL: Peroneus Longus, GM: Gastrocnemius Medialis, GL: Gastrocnemius Lateralis, SO: Soleus. Asterisks denote post-hoc (p<0.05) differences in the motor modules and width on the motor primitives between stable (SG) and unstable (UG) condition.

ground by muscle was observed in the motor module of the touchdown synergy (F(12, 144) = 2.594, p = 0.004). The post-hoc analysis showed a higher contribution of gluteus medius (p = 0.015) and a lower contribution of gastrocnemius lateralis (p < 0.001) when landing on UG compared to SG (Figure 4.5). An interaction of ground by joint (F(2, 24) = 6.347, p = 0.006) was observed in the CaI of muscles in the touchdown synergy. The post-hoc analysis showed that landing on UG significantly increased coactivation around the knee joint compared to SG

(p = 0.001, Figure 4.6). The FWHM of the touchdown primitive was in UG on average 61 ± 17 points and was significantly greater ($F(1,13) = 11.27$, $p = 0.005$) than in SG (48 ± 7 points).
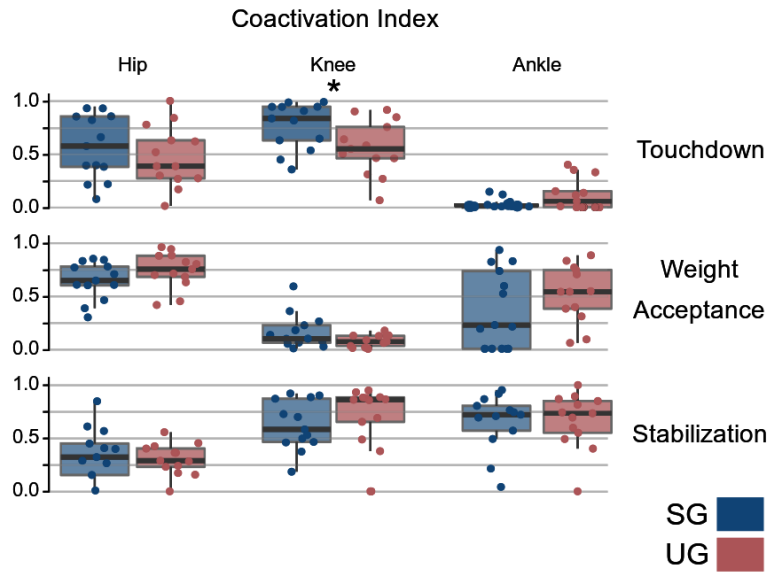

Figure 4.6: Coactivation Index (CaI) for the motor modules for the recognized synergies. The CaI may vary from 0 (exclusive contribution of extensors) to 1 (exclusive contribution of flexors). A CaI of 0.5 indicates equal contribution of flexors and extensors for that motor module. Points denote single trials and asterisks denote statistically significant (p<0.05) differences between stable (SG) and unstable (UG) conditions.

The overlaps of the motor primitives showed a statistically significant difference ($t^* = 4.752$, $p < 0.049$) only at about 90% of the task duration (Figure 4.7).
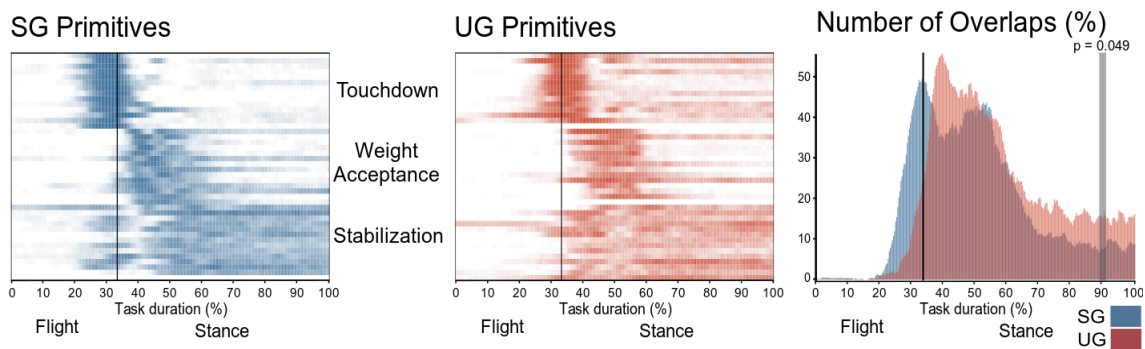
Figure 4.7. Overlapping time intervals of motor primitives for the single-leg drop landings on stable (SG, right-panel blue) and unstable ground (UG, middle panel red). Each row of the heat maps represents a single motor primitive. A colored time-point indicates the primitive is exceeding half maximum. Darker colors indicate higher number of occurrences across all cycles per participant. At the right panel the average number of overlaps across all trials and all participants per ground condition with gray bands denoting time period of significant difference found by the statistical parametric mapping. For all graphs the x-axis full scale represents one trial time-normalized to 300 points. The vertical line indicates the touchdown.

4.5. Discussion

We investigated the effects of perturbations induced by unstable surfaces on the mechanical loading and modular organization of leg muscles during single-leg landings. We hypothesized a modulation of the neuromotor control when landing on UG resulting in an increase of leg muscle loading. When landing on UG, the participants modulated the spatiotemporal structure of muscle synergies mainly in the touchdown phase, indicating a proactive adjustment to the unstable surface and confirming our first hypothesis. The experience-based proactive control in combination with the deformation characteristic of the soft surface resulted in a lower maximum resultant ankle and hip joint moment, lower rate of joint moment development and no increase in muscle EMG-activity observed during the landing phase. Thus, the hypothesis of an increased muscle loading was rejected. Our results show that the participants managed to use their experience and awareness of the unstable ground characteristics to proactively deal with the predicted perturbation before touchdown, minimizing the consequences of the perturbation.

The modulation of the spatiotemporal structure of the touchdown synergy (i.e., widening of the motor primitive and modified contribution of gluteus medius and gastrocnemius medialis muscles) indicates proactive adjustments in the neuromotor control of landing on UG. Proactive control strategies have been shown to be very effective to support stability in the presence of perturbations and to prevent a fall[75,88,572]. Moreover, proactive adjustments have been proposed to successfully compensate proprioceptive impairments[589] and enhance passive stabilizing mechanisms[590,591]. In our experiment, the landings were performed with open eyes and participants had previously acquired knowledge about the ground and task characteristics during the familiarization trials. Therefore, it is likely that the spatiotemporal modifications found in the touchdown synergy reflect a proactive strategy driving the preparation to the predictable perturbation. Widening of motor primitives is a phenomenon commonly associated with the presence of perturbations which has been proposed to reflect a mechanism that increases the robustness of neuromotor control[12,498,551,573]. The reduced CoP area when landing on UG indicates that the proactive control successfully predicted most of the challenges induced by the compliant surface, facilitating landing stability[590].

It is to mention that motor control can be quickly improved and the experience of just one or two trials in a predicted perturbation modifies significantly proactive strategies[88,302]. In our statistical analysis we used 50 landing trials in each condition and therefore the repeated experience on the unstable ground might introduce an acute, trial-dependent modification of the temporal structure of muscle synergies, potentially biasing the findings. In order to check

for possible acute adaptations in the neuromotor control due to the repeated execution of the landings, we tested the FWHM of the motor primitives during the 50 repetitions using a linear mixed model. We did not find any effect of repetition on the FWHM of any of the three synergies: an indication that the basic activation patterns were not influenced by the landing repetitions (Figure 4.8). The participants performed some familiarization trials that were not included in this analysis. These initial repetitions might also have played a role in reinforcing previous knowledge of the landing characteristics initiating possible acute modifications in the modular organization and providing an adapted neuromotor control of the task.
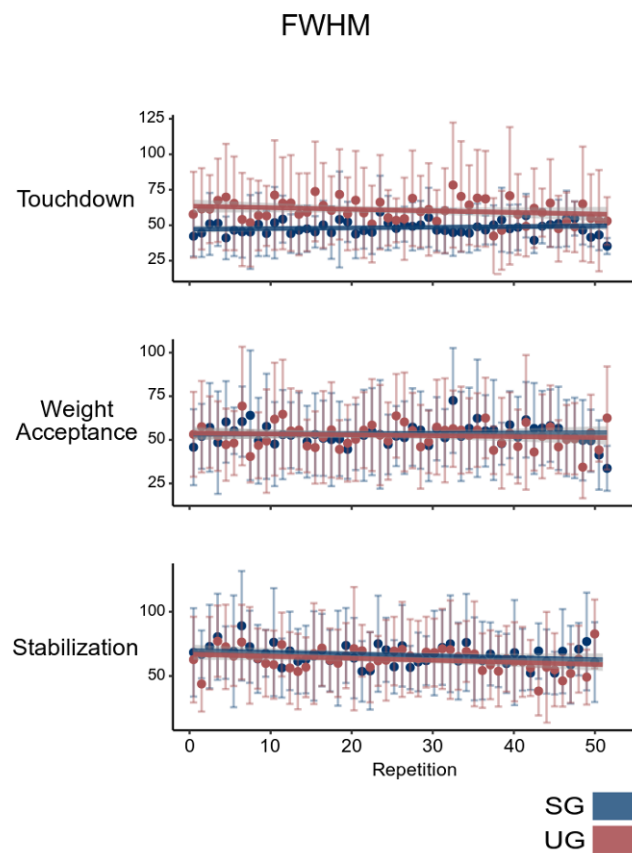
Figure 4.8. Mean value and standard deviation of full width at half maximum (FWHM) of the classified motor primitives for every single-leg landing on stable (SG) and unstable (UG) ground. Lines represent the linear interpolation of each data set.

When landing on UG, we observed a decreased CaI at the knee joint in the touchdown synergy indicating a higher contribution of the knee extensors compared to SG. Looking at the motor modules of the touchdown synergy, it is however visible that both knee flexors and extensors showed an almost negligible contribution to this synergy. Thus, the decreased CaI can be interpreted as functionally irrelevant. The knee joint plays a critical role during the landing

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phase in order to absorb the kinetic energy of the body[562,592,593]. The contribution of knee extensor muscles to the weight acceptance synergy is very high and the knee extension moment achieved its maximum in this phase, evidencing the importance of the knee joint for the kinetic energy dissipation during landings.

The weight acceptance and stabilization synergies were not modified in the UG condition and the overlapping of the motor primitives showed a short and small difference indicating a negligible influence of the unstable surface on the neuromotor control of the stance phase. Hence, it seems that that predictive adjustment made by the participants during the single-leg landings were sufficient to cope with the UG and the unstable ground did not trigger reactive modulations of the neuromotor control which might be elicited if the difficulty of the task is increased. The result of our present setup is somewhat in disagreement with our previous findings during forward and backward lunging onto a foam beam – with similar mechanical characteristics to the current UG surface - where we found a modulation of the touchdown as well as the weight acceptance and stabilization synergies leading to a higher frequency of overlaps in the unstable condition[577]. From a biomechanical point of view, a basic difference between single-leg landings and lunges is the dynamic state of the body mass at touchdown. Landings were characterized by a vertical movement of the body centre of mass with negligible components in the horizontal direction. On the other hand, the body mass moved in both horizontal and vertical direction during the forward and backward lunges. It seems that the two-dimensional body motion during the lunges was challenging to a greater degree the neuromotor control of the task in the presence of perturbations. This shows that the consequences of perturbations present a task specificity that should be accounted for when designing perturbation-based balance interventions. Sufficient reactive balance control after unpredicted perturbations is very important to maintain or even regain balance and avoid a fall. One of the main purposes of perturbation-based interventions is to improve balance reactive control, especially in older adults[254,300,303,354]. Our results show that the unstable ground used for single-leg landings did not trigger reactive modulations of the neuromotor control and that predictive adjustment were sufficient to cope with the UG. Thus, we can argue that the use of unstable surfaces does not necessarily challenge reactive control. Challenging dynamic tasks (i.e., including anteroposterior and mediolateral body motion) or including a large catalogue of unstable conditions to increase the unpredictability of perturbations[302] are key points in the design of perturbation-based interventions.

We expected an increase in the muscle activity and resultant joint moments as indicators of increased muscle loading in the UG condition. However, the ankle and hip maximum resultant

joint moment and rate of moment development for all three joints were higher in SG. The damping behavior of the foam pads due to its viscoelastic properties might explain the significantly lower development of the GRF after touchdown and the reduced rate of joint moment development, the shorter lever arm of the GRF at the ankle joint, however, indicates an additional mechanism that explains the lower maximum ankle joint moment in UG. We found similar results (i.e., scarce differences in the EMG activity and a tendency towards lower resultant joint moments in the lower extremities) during forward and backward lunges on stable and unstable surfaces[577]. Therefore, we can conclude that using unstable surfaces does not necessarily increase muscle loading per-se. We should remark that estimating resultant joint moments and the electromyographic activity of a muscle are indirect estimators of the mechanical demands for a muscle group. Nonetheless, both methods are valid and highly reliable and therefore provide an accurate estimation of the training stimuli. We should also remark that the foam pads used in the UG condition were bigger than the force plate and this might have transmitted a small portion of the landing forces to the ground. The size choice was dictated by the fact that pads as small as the force plate would show different mechanical properties and would lift their perimeter so strongly after landing that the foot would be completely enveloped and the effect of the foam strongly affected. Yet, our main focus was on the modular organization, thus we decided to use a bigger foam pad size, despite the potential bias in the measured GRF. In any case, we observed from the data that the vertical GRF at steady state was similar between SG and UG (i.e., body weight), indicating that the force dissipation due to the extra size might be negligible despite the acknowledged limitation.

In conclusion, our results provide evidence that the neuromotor system relied on a proactive control to modulate the spatiotemporal structure of muscle synergies during perturbed landing, particularly in the touchdown synergy. These modulations allowed the participants to deal with the predictable perturbation before touchdown and minimize the mechanical consequences of the perturbation. Moreover, our results show that the use of unstable surfaces did not challenge reactive motor control, nor increase muscle loading per se. Since perturbation-based interventions aim to improve reactive balance, the task characteristics and the intensity of the challenge imposed by the unstable surface should be carefully designed when planning this kind of intervention programs.

5. Epilogue and conclusions

The theoretical framework of the present thesis, presented in chapter one, covered the incidence, causes and consequences of falls. This review summarised how most falls result from a failed response to unexpected perturbations such as a trip or slip[594]. Consequently, those with a diminished response capacity exhibit an increased risk of falling and getting injured[595]. Furthermore, the individual, social and economic outcomes of fall-related injuries transform falls into a significant public health problem[596].

Amid many existing intervention paradigms targeting the causes and risk of falls, exercise-based interventions are the most cost-effective[597]. Since the mid-2000s, perturbation-based balance training has gained interest as an efficient and effective alternative to prevent falls. Under this scope, inducing reactive balance reactions through perturbations is suggested as a task-specific training approach that might represent a change of paradigm in fall prevention[598]. Nonetheless, such high specificity difficult the transfer of the trained gains into non-trained perturbations. Thus, issues such as transfer, retention and dose-response relationship are yet to be determined. Alternatively, training the execution of the fundamental balance recovery mechanism (i.e., counterrotating body segments and increasing the base of support) in the presence of perturbations has been reported to improve balance recovery performance in both trained and non-trained situations as well as increase the force generating capacities of the lower limb muscles further promoting the execution of balance recovery reactions.[302,354].

Based on these promising results, this thesis endeavoured to provide an insight into the fundamental elements promoting the neuromechanical adaptations underpinning the reported advantages of training the fundamental balance recovery mechanism in the presence of perturbations for reducing falls, with the perspective that this knowledge could improve tailoring the design of effective training interventions for reducing fall in both healthy elderly and clinical populations. Concordantly, this thesis assessed a series of exercises promoting the execution of the aforementioned balance-recovery mechanism under two different ground configurations, a hard solid surface and an unstable ground.

5.1. Summary of findings

Overall, performing the exercises encompassed in this dissertation on unstable surfaces did not induce a change in any indicator of mechanical demand that could be related to increased muscle activity. Yet, the unstable surfaces systematically evoked modulations in the muscular

synergies. Although the characteristics of such modulations differed among exercises, they allowed the trainees to maintain functionality despite the presence of perturbations and, consequently, increased the robustness of the neuromuscular control.

Based on a standing balance task to elicit the counter-rotating balance recovery mechanism, Chapter 2 showed that while the neuromuscular organisation did not differ between ground configurations when standing with a bipedal stance, maintaining a single-leg stance onto an unstable surface evoked the addition of an extra synergy, compared to performing the same task on solid ground. Also, the unstable ground enhanced the stabilisation of proximal over distal body segments expressed by the maximal Lyapunov's exponent.

A subsequent study targeting the increase of the base of support was presented in chapter 3. There, participants elicited a reactive step by leaning and then maintained the achieved lunge position in a forward and backward direction. In the perturbed condition, foam surfaces induced minor differences in the resultant joint moments and EMG activity. Hence, the compliant surface did not influence the muscle's mechanical loading. On the contrary, the perturbations induced a modulation in the time-dependent structure of the muscle synergy responsible for the stabilization of the body in both directions. The centre of activity of this synergy shifted towards a later moment in the forward lunge and towards an earlier time in the backward lunge. Moreover, instead of the four in the unperturbed counterpart, only three synergies were recognised in the perturbed backward lunge. This dimensionality reduction appeared to result from a redistribution of the body weight acceptance into the touchdown and stabilisation synergies.

In chapter 4, a single-leg drop landing enhanced the use of the counter-rotational mechanism and the effect of the perturbations induced by compliant surfaces during the contact phase. Yet, the primary effects of the unstable ground occurred during the flight phase. The observed adjustments in EMG activity and joint kinematics were associated with a modulation of the muscle synergy responsible for controlling the touchdown. These modulations, combined with the viscoelastic properties of the soft surface, reduced the mechanical loading in the lower leg muscles during the stabilisation phase. Thus, the participants relied mainly upon a proactive strategy to adjust the neuromotor control of landings, minimising the demands of the weight acceptance and stabilization phase. These results also indicated that using unstable surfaces does not necessarily challenge reactive motor control nor increase muscle loading per-se.

5.2. General discussion and conclusions

Albeit the reported increased muscle force after training the fundamental balance-recovery mechanism onto unstable surfaces[302,354], the overall results of chapters 3 and 4 showed no indication of an increased mechanical demand on the lower limb muscles when performing such exercises in the presence of perturbations. Neither the EMG activity nor the resultant joint moments increased when performing the exercises on unstable surfaces in the aforementioned experiments. These results contradict earlier reports of increased EMG activity when performing a standing balance task on compliant surfaces[568,576]. The overall intensity of the activity might relate to a plausible explanation for the different outcomes. Whereas maintaining balance on a compliant surface is more demanding than standing on stable ground, it is not comparable to the demands imposed by the exercises encompassed in this dissertation and the training interventions that motivated it. For example, the movement's velocity of the single-leg landing in chapter 4 and the reactive stepping task in chapter 3 is considerably higher than the velocity of a standing balance task. Thus, performing the exercises in both experiments conveyed higher resultant joint moments. Consequently, if the perturbations increased the demands during the exercise, the magnitude of this demand was small compared to those resulting from the landing or the ground contact. Correspondingly, the large kinematic modulation in the ankle joint observed in chapter 4 during the impact phase of the single-leg landings suggests that controlling the impact itself was far more relevant than the instability induced by the compliant surface at that highly demanding phase. In a similar direction, Voloshina and Ferris reported a relevant role of the ankle in coping with uneven grounds during running with a minor effect on muscle activity and joint moments[599]. Altogether, these reports and the results encompassed in this dissertation demonstrate that using compliant surfaces does not increase muscle activity nor the mechanical demand on the muscle per-se.

On the other hand, training on unstable surfaces decreases spinal excitability and modulates the level of co-contraction and H-Reflex gains[148,268,273]. These neural adaptations are proposed to reflect an attempt to improve movement control instead of the enhanced motoneuron output observed after strength training[268]. In light of the foregoing and considering that in the interventions that motivated this dissertation, muscle strength did not increase simply by training the balance-recovery mechanism on compliant or unstable surfaces[351], but only when the exercise was tailored to further challenge balance and evoke a larger involvement of the active muscle groups[302,354], the reported increments in muscle strength after training the fundamental balance recovery mechanism in the presence of perturbations[302,354] are likely to have a neural origin rather than an adaptation to increased mechanical demand on the muscle.

The perturbations induced by the unstable surfaces evoked modulations of the muscle synergies in every exercise of the present dissertation. As mentioned in the introduction, based on the reported widening of the motor primitives observed during perturbed locomotion[12,498] and the proposed role of this modulation as an acute strategy to cope with the presence of perturbations[12], I expected the unstable surfaces to evoke modulations in the form of a widening of the motor primitives in all the experiments encompassed in this dissertation. Yet, such widening of primitives was not always present, and performing the requested exercises in unstable conditions resulted in the recognition of different modulations. Modulating the activation of muscle synergies can account for immediate adjustments of the motor output[482] and the structure of muscle synergies has been reported to change after undergoing perturbation-based training in a standing paradigm[600]. Thus, this dissertation provides evidence that the neuromotor system is able to modulate synergies in ways that differs from the widening of the primitives as a response to external perturbations. The time-dependent modulations observed in chapter 4 also suggest that these modulations change over time as a response to the training.

Considering muscle synergies as a simplified representation of the organisation of the neuromuscular system, it follows that they reflect all the sensorimotor transformations related to a task. Hence, it is likely that the sensorimotor transformation differed between the experiments depending on elements such as the characteristics and the timing of the perturbation as well as the characteristics of the task, its constraints and the perceived challenge, yielding different modulations in every task. This idea is akin to the reported modulations of muscle synergies for accommodating the motor output to changes in load which depended on elements such as the direction, amplitude and phase of the performed movement[482].

Moreover, the exercises of the present dissertation imposed different constraints for recovering balance. As the participants had to choose a strategy that could account for the perturbations and the task constraints, the task constraints may have provided them with alternatives for every task, modifying their coordination and control strategies[601,602]. The challenge presented by the exercise also seems to play a critical role in the magnitude of the observed modulations of the muscle synergies. Thus, in the aforementioned perturbed walking experiments[12,441,498], the dynamic of gait might have provided the participants with enough inertia to manage the perturbations through multiple steps, a possibility allowed by the experimental design. On the other hand, the experiments contained in this dissertation constrained the trainees to transition and maintain the achieved position while coping with the perturbations. These constraints

challenged dynamic and static balance control, calling for a different solution. Concordantly, controlling a single-leg stance on an unstable surface as in chapter 2, changed the mechanical demands of the task compared with standing on solid ground. The neuromuscular system solved the challenge by adding a temporally co-existing synergy that accounted for the displacement of the surface. In the same direction, the presence of a foam beam when lunging backwards in chapter 3 not only induced perturbations once the trainees stepped onto it but, probably, also limited the visual inflow and changed the perception of the risk in case of missing the target compared to the unperturbed setting. These challenges resulted in a reduction of the number of synergies and a widening of the chronologically adjacent primitives. On the contrary, a simple temporal modulation and redistribution of the motor modules allowed the participants to cope with the perturbations induced by the compliant surfaces in the forward lunges. The trainees' experience on landings allowed them to successfully predict the behaviour of the compliant surface during the single-leg landings in chapter 4, minimising its perturbing effect. This proactive strategy also resulted in a very simple temporal modulation and redistribution of the motor modules. Thus, whereas exercises presenting habitual situations to the trainees resulted in smaller or simpler modulations when perturbed, larger modulations were evoked when the characteristic of the perturbed task differed significantly from the unperturbed version. These results concur with the fact that control strategies are selected depending on the perceived difficulty of a task, the available neural resources and other elements such as the perception of potential injuries[165,166,603,604], and suggest that supra-spinal control played an important role in modulating the muscles synergies and deciding the control strategy to cope with both the constraints of the task and the perturbations.

Regardless of the extension and characteristic of the observed modulations for each exercise, they allowed the trainees to cope with the perturbations and execute the requested set of exercises despite being perturbed. Maintaining functionality notwithstanding external and internal perturbations is a fundamental property of all complex biological systems known as biological robustness[26]. As aforementioned in Chapter 1, widening the motor primitives during perturbed locomotion is proposed to reflect a transition towards a fuzzier control modality[12]. By providing a "buffer of muscle activity", this buffer facilitates transitioning to another synergy and increases the system's robustness[12,441]. Though some of the perturbed exercises comprising this dissertation also exhibited a widening of motor primitives, this was not the only observed modulation. Thus, the corresponding chapters resulted in a rejection of the working hypothesis. Yet, in every experiment, the modulations tended to overlap the

chronologically adjacent primitives. Thus, these modulations also created a fuzzier strategy of control. This overlapping effect was particularly enhanced when the perturbations induced larger modulations, as in chapters 2 and 3. Under a system's control perspective, fuzzy control is sub-optimal and decreases performance[605]. Nonetheless, perturbations could also promote robust neural networks[291] and the presence of perturbations might endorse variability to modify the basin of attraction of muscle synergies and improve performance[504]. In this direction, all the modulations observed in this dissertation allowed the trainees to perform the exercises on unstable ground. Thus, they can represent different strategies to cope with perturbations and increase robustness.

The comprising results of this dissertation also suggest that muscle synergies provided the neuromuscular system with many alternatives to cope with the perturbation while performing a task. From a conceptual point of view, evolution often selects the attributes enhancing robustness due to their capacity to allow a system to function in unpredictable environments[26,501,545]. Consequently, they also tend to be an organisational principle in biological and engineering systems[26,545,606]. Assuming the existence of muscle synergies, they provide the neuromotor system with at least two principles that promote robustness: modularity itself and the decoupling of functions. These two principles are effective mechanisms to isolate the effect of a perturbation on a local scale, minimizing its effect on the entire system and preserving high-level functionalities[26]. Hence, as each synergy is able to function autonomously, it can also respond and adapt swiftly to a perturbation occurring within its scope. Then, such perturbation might disturb only the specific sub-task related to the synergy and not the entire motor output. Modularity (i.e., a modular organisation) also provides a coherent structure that accounts for variations of the individual modules[26]. Thus, as observed in chapter 2 and 3, other synergies can compensate or complement the modulations of the perturbed synergy, further promoting robustness. Cross-modulating synergies require a rich neural connectivity capable of generating and coordinating complex interactions between the synergies. Concordantly, proprioceptive afferents are crucial in the neuroanatomy and recruitment of muscle synergies[411,496] and loop-driven activities among several areas of the central nervous system, including the associative and motor cortex, might participate in the modulation of synergies[463,468,469]. As the role of cortical activity scales with the difficulty of the perturbation and the functional ability of the participant[607,608], the results of this dissertation suggest that both proprioceptive information and supraspinal control played a crucial role in the observed modulations. Moreover, this dissertation indicates that modularity presented the

trainees with different alternatives to solve the challenge presented by the exercises and minimise the effects of the perturbations at a macro level.

Henceforth, the main conclusion of this dissertation is that robustness does not emerge as a consequence of widening the primitives, but as a consequence of different modulations of synergies that depends on several factors such as the characteristics of the task and the individual capacities. Furthermore, the neuromotor system exploits the alternatives provided by its modular organisation to adapt the control of a task in the presence of perturbations, further ensuring robustness.

Additionally, this dissertation provides evidence that anticipatory and reactive strategies might account for the perturbations during a training session. Moreover, training on unstable surfaces does not increase the mechanical demands upon the leg muscles per-se. Thus the gains in muscle force observed after training the fundamental mechanism of balance recovery onto unstable surfaces are likely a consequence of neural adaptations.

5.3. Practical implications and open questions

The evidence provided in this dissertation might improve the design of effective fall reduction interventions in both healthy and clinical populations with an increased risk of falling. From the discussion above, it follows that tailoring the challenges imposed by the task is of crucial importance for attaining the objectives of the training intervention. Thus, planning a training session requires careful consideration of the characteristics of the task, its predictability and the intensity of the perturbation. Yet, adjusting the intensity of the perturbation is no trivial task, as the challenge imposed by the training exercise might differ depending on the level of activity, functional capacities and social context of the trainees. Moreover, there is still a need for developing a valid test, or battery of tests, that can assess every aspect of balance with respect to daily life[609–611]. A fast and reliable method for checking if reactive balance is being challenged during a training session is also needed.

Considering the promising reported outcomes of training the fundamental balance-recovery mechanism in the presence of perturbations, determining if the magnitude of the fall-preventing effect correlates with the magnitude of the challenge, as the reported larger protective effects for highly challenging perturbation-based training[181,307,320], is necessary. Studies with a large number of participants and long follow-ups are also certainly needed to assess its fall-preventing effects.

Quantifying balance-recovery performance and the challenge imposed by the exercise is critical for tailoring a training session. Yet, there is a lack of a simple and valid estimator for

the magnitude of the challenge, balance-recovery performance and predictors of falls. In this direction, whilst assessing the magnitude of the synergies' modulation deserves to be explored to quantify the challenge, the work by Rieger et al.[612] and Meurisse et al.[613] appear as attractive alternatives for quantifying the training effect on reactive balance.

The observed task-specificity in the modulation of muscle synergies in the present dissertation should also be considered. Albeit specificity is a desired characteristic in training programmes[298] it also conveys a challenge to generalise the training effect to daily life and untrained tasks[301,305,614]. Concordantly, perturbation-based training interventions have shown to be highly effective in optimising the response to perturbations similar to those trained but to have little effect on those untrained[181,240,598]. The specificity of muscle synergies in diverse perturbation responses can inhibit the inter-task generalisation of adaptations in stability control[615]. Yet, this dissertation might present an alternative view. Training the fundamental balance recovery mechanism might provide the trainees with the possibility of exploring different alternatives to cope with a perturbation in different situations, expanding their repertoire of solutions. This idea is supported by the diverse synergies and modulation strategies observed in the experiments of this dissertation and those previously reported for perturbed locomotion[441,615]. Considering the manifold nature of perturbations and falls, some of the observed modulations might be sub-optimal. Yet, they are useful and might be adequate to adapt to untrained situations. This scope agrees with the so-called "good-enough" control strategy[616], in which an organism acquires a repertoire of sensorimotor behaviours through trial-and-error learning that results in a diversity of solutions that tends to confer robustness. Furthermore, good-enough control is proposed to be more consistent with the capabilities of higher sensorimotor structures, such as the cerebral cortex, which seems designed to classify and recall complex sets of information and learn from experience, rather than to compute new strategies online[616].

Considering the above, the overall effectiveness of fall-preventing programmes might increase with a mixed approach. As classical perturbation-based training is reported for improving the reaction to the most prevalent types of perturbations (i.e., slips and trips)[598], it can be complemented with sessions promoting the execution of the fundamental balance-recovery mechanism onto unstable surfaces. As the result of the present dissertation hints at the importance of supra-spinal control and higher process like decision-making when coping with perturbations, other alternatives such as foot positioning and gait adaptability should also be considered. Consequently, this mixed approach might provide the trainees with different alternatives that can be flexibly used to cope with the manifold perturbations in daily life.

It follows that much more research is needed to translate this alternative view into an evidence-based conclusion. A large number of elements still need to be further investigated to improve our understanding of the mechanism underpinning the adaptations promoting effective fall reduction. For example, fundamental neurophysiological studies pinpointing the neural mechanism of the observed modulations or the role of supra-spinal control in modulating synergies.

Moreover, the long-term adaptation of training and its reach in other domains of fall prevention such as self-confidence is also needed. The latter, calls for further multidisciplinary research that can bring together biomechanical, psychological and neurophysiological metrics to fully assess the puppeteer mastering motor control.

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