l'université nantes angers le mans
PÔLE DE RECHERCHE ET D'ENSEIGNEMENT SUPÉRIEUR

UNIVERSITÉ DE NANTES

Thèse de Doctorat

Niels-Peter BRØCHNER NIELSEN

Mémoire présenté en vue de l'obtention du

grade de Docteur de l'Université de Nantes

sous le label de L'Université Nantes Angers Le Mans

École doctorale : *ED 504 « Cognition, Education, Interactions »*

Discipline : *Sciences et Techniques des Activités Physiques et Sportives, 74ème section*

Spécialité : *Biomécanique / Neurophysiologie*

Unité de recherche : *EA 4334 « Motricité, Interactions, Performance »*

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THE EFFECTS OF FATIGUE AND PAIN ON MUSCLE COORDINATION DURING A MULTIJOINT TASK

JURY

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Acknowledgements

The realization of this doctorate has been a great experience and a lot of this is due to the people that have been around me. I would first like to thank my supervisors, Sylvain Dorel, Francois Hug and Arnaud Guével for their guidance and support throughout my thesis. Their help has been invaluable. I would also like to thank Julien Lardy for his indispensable help with data collection. I enjoyed the countless hours in the lab. Also, a big thanks to Julien for his help with the data analysis in MatLab and to Vincent Fohanno and Floren Colloud for their work on inverse dynamics. Seven months of my PhD was spent at the University of Queensland, Australia. I would like to thank Kylie Tucker for her encouragement and advice during my stay and for making my stay an unforgettable experience. A lot of thanks also goes to all my colleagues and fellow PhD students with whom I have had the pleasure to work alongside for the past years. I learned a lot from our professional back-and-forth discussions and I also enjoyed the time spent outside work. The performed experiments in this thesis required a lot from the participants and the experience was not always pleasant. Therefore, a big thanks to the participants who volunteered, for their courage, time, and vital help. A special thanks also goes to the committee Pascal Madeleine, Serge Colson and Emilie Simoneau-Buessinger for their detailed reading and review of my work.

It goes without saying that this experience was a big personal challenge. My family and girlfriend stood by me at every step of the way, and was there when I needed it the most. *Thanks*.

Funding

Project support was provided by the Region Pays de la Loire (ANOPACy project) and the French Ministry of Sport (14- R- 23).

List of publications

1. Brochner Nielsen NP, Hug F, Guével A, Fohanno V, Lardy J, Dorel S.

   Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task.

   Scand J Med Sci Sports. 2016.

2. Brochner Nielsen NP, Hug F, Guével A, Colloud F, Lardy J, Dorel S.

   Muscle fatigue induces positive changes in coordination during a sprint cycling task

   MSSE. In review.

3. Brochner Nielsen NP, Tucker K, Dorel S, Guével A, Hug F.

   Motor adaptations to local muscle pain during a bilateral cyclic task.

   Exp Brain Res. 2016.

Conferences

Brochner Nielsen NP, Hug F, Guével A, Fohanno V, Lardy J, Dorel S.

Motor adaptations to localized fatigue during a bilateral cyclic task.

L'ACAPS (2015), Nantes, Symp. °11, Oral presentation.

Brochner Nielsen NP, Hug F, Guével A, Fohanno V, Lardy J, Dorel S.

Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task.

ECSS (2016), Vienna, Abstr.-ID: 21-1492, Oral presentation.

Author contributions to publications

Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task.

Brochner Nielsen NP: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Hug F: Conceptualization of the study, writing of the mauscript

Guével A: Conceptualization of the study

Fohanno V: Data analysis

Lardy J: Data collection, data analysis

Dorel S: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Muscle fatigue induces positive changes in coordination during a sprint cycling task.

Brochner Nielsen NP: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Hug F: Conceptualization of the study, writing of the mauscript

Guével A: Conceptualization of the study

Colloud F: Data analysis

Lardy J: Data collection, data analysis

Dorel S: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Motor adaptations to local muscle pain during a bilateral cyclic task.

Brochner Nielsen NP: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Tucker K: Conceptualization of the study, data analysis, writing of the mauscript

Dorel S: Conceptualization of the study, data analysis

Guével A: Conceptualization of the study

Hug F: Conceptualization of the study, data collection, data analysis, writing of the manuscript

Resumé

Le contrôle du mouvement humain nécessite la coordination de muscles multiples. La façon dont cette coordination est modulée face aux exigences changeantes telles que la fatigue et la douleur n'est pas bien comprise. C'est particulièrement le cas dans les tâches poly-articulaires en sport comme dans des activités de la vie quotidienne. Trois études ont été conçues pour approfondir cette question.

L'étude 1 vise à étudier comment la coordination motrice s'adapte à la fatigue unilatérale du quadriceps lors d'une tâche de pédalage bilatéral à charge constante. Nous avons d'abord émis l'hypothèse que cette fatigue locale ne serait pas compensée au sein des muscles fatigués conduisant à une diminution de l'extension du genou. Ensuite, nous avons cherché à déterminer si cette diminution serait compensée par des compensations entre articulations au niveau de la jambe ipsilatérale et/ou une augmentation de la contribution de la jambe contralatérale. Quinze volontaires sains ont été testés pendant le pédalage à 350 W avant et après un protocole de fatigue consistant en 15 minutes d'électromyostimulation des muscles superficiels du quadriceps. La coordination motrice a été évaluée à partir de l'activité myoélectrique (22 muscles) et des puissances articulaires calculées par dynamique inverse. Le couple maximal lors de l'extension du genou a diminué de 28,3% ± 6,8% (P <0,0005) immédiatement après l'électromyostimulation. Une diminution de l'extension du genou produite par la jambe ipsilatérale a été observée pendant le pédalage (-22,8 ± 12,3 W, -17,0% ± 9,4%, P <0,0005). Pour maintenir l'objectif de la tâche, les participants ont principalement augmenté la puissance produite par la jambe contralatérale non fatiguée pendant la phase de flexion. Ceci a été obtenu par une augmentation de la puissance de flexion de la hanche confirmée par une activation plus élevée du tenseur du fascia latae. Ces résultats ne suggèrent aucun ajustement de l’activation nerveuse centrale vers les muscles fatigués

et ne démontrent aucune compensation ipsilatérale concurrente par les muscles non fatigués impliqués dans la phase d'extension lors du pédalage. Bien qu'une variabilité interindividuelle ait été observée, les résultats montrent que les participants se sont principalement adaptés en compensant avec la jambe contralatérale pendant la phase de flexion lors du pédalage.

Les caractéristiques de la tâche (e.g., l'intensité) et l'objectif à atteindre lors d'une tâche sont importants et détermineraient les adaptations neuromusculaires à la fatigue. L'étude 2 visait à étudier les adaptations motrices à la fatigue unilatérale induite au sein des muscles superficiels du quadriceps, lors d'un pédalage « all-out » sprint. Quinze volontaires en bonne santé ont été testés lors d'un sprint complet avant et après un protocole de fatigue consistant en 15 minutes d'électromyostimulation appliqués sur les muscles superficiels du quadriceps. La coordination motrice a été évaluée à partir de l'activité myoélectrique (22 muscles) et des puissances articulaires calculées par dynamique inverse. Le couple maximal d'extension du genou a diminué de 28,3 ± 6,8% ($P < 0,0005$) immédiatement après l'électromyostimulation. Pendant le pédalage, l'activité musculaire du quadriceps fatigué est restée invariante, ce qui a entraîné une diminution de l'extension positive du genou (-34,4 ± 30,6W, $P = 0,001$). En outre, l'activité musculaire des synergistes sans fatigue et du muscle antagoniste biarticulaire a diminué, conduisant à une diminution de la puissance articulaire au niveau de la hanche (-30,1 ± 37,8W, $P = 0,008$) et de la cheville (-20,8 ± 18,7W, $P = 0,001$), mais aussi au maintien de la puissance appliquée au genou (moins de puissance négative) et de l'efficacité mécanique globale (66% pendant le contrôle et la fatigue). Des adaptations se sont également produites au niveau de la jambe contralatérale non fatiguée, montrant une puissance accrue pendant la phase de flexion (17,9 ± 28,3W, $P = 0,026$). Ces modifications sont associées à une amélioration significative de l'efficacité mécanique à la fois lors de l'extension (2,9 ± 3,3%, $P = 0,004$) et de la phase de flexion (17,9 ± 18,9%, $P = 0,0025$)

du genou. Globalement, les résultats suggèrent que le système de contrôle moteur adapte facilement la stratégie de coordination en modifiant l'activation des muscles non fatigués agonistes pour maintenir l'orientation de la force sur la pédale et par une amélioration globale de l'efficacité neuromusculaire. Enfin, d'amélioration non réalisé s'est manifesté pendant la phase de flexion du genou, bien qu'il s'agisse d'une tâche de pédalage à intensité maximale.

L'étude 3 visait à déterminer comment la douleur unilatérale, induite dans deux muscles extenseurs du genou, a affecté la coordination musculaire lors d'une tâche de pédalage bilatérale. Quinze participants ont effectué une tâche de pédalage de 4 minutes à 130 W dans deux conditions (Baseline *vs.* Pain). La douleur a été induite par injection d'une solution saline hypertonique dans les muscles vaste médian (VM) et vaste latéral (VL) d'une cuisse. La force appliquée pendant tout le cycle de pédalage a été mesurée à l'aide d'une pédale instrumentée et utilisée pour calculer la puissance développée au niveau de la pédale. L'électromyographie de surface (EMG) a été enregistrée bilatéralement à partir de huit muscles pour évaluer les changements dans les stratégies d'activation musculaire. En comparaison avec la ligne de base, l'amplitude EMG des muscles de la cuisse douloureuse (VL et VM - muscles douloureux, et rectus femoris (RF) – muscle sans douleur induite) était plus faible pendant la phase d'extension du genou [(moyenne ± écart-type) : VL : -22,5 ± 18,9%; P <0,001 ; VM : -28,8 ± 19,9% ; P <0,001, RF : -20,2 ± 13,9% ; P <0,001]. En accord avec cela, la puissance produite au niveau de la pédale par la cuisse douloureuse était plus faible pendant la phase d'extension du genou (-16,8 ± 14,2 W, P = 0,001) pendant la douleur par rapport à la condition « sans douleur ». Cette diminution a été compensée par une augmentation de 11,3 ± 8,1 W de la puissance au niveau de la pédale produite par la cuisse non douloureuse au cours de sa phase d'extension du genou (P = 0,04). Ces résultats soutiennent les théories de l'adaptation à la douleur, ce qui suggère que lorsqu'il y a une possibilité pour le système

neuromusculaire de compenser, alors des adaptations motrices à la douleur se produisent pour diminuer les tensions dans le tissu douloureux. Bien que la tâche de pédalage offre de nombreuses possibilités de compensation, seules les compensations entre jambes ont été systématiquement observées. Ce constat est discutée en relation avec les contraintes mécaniques et neuronales de la tâche de pédalage.

Dans l'ensemble, ces études ont démontré que le système de contrôle moteur adapte facilement la stratégie de coordination musculaire à la fatigue et à la douleur, et que des adaptations spécifiques ont été observées entre les études en fonction de la perturbation (fatigue ou douleur) et de l'intensité de la tâche. Ces adaptations ont été caractérisées par la nature cyclique bilatérale du pédalage et des adaptations neuromusculaires décrites entre les muscles et les jambes.

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List of Abbreviations

3D: Three dimensional

Ag/AgCl: Silver Chloride

ANOPACy: Analyse et optimisation de la performance en Aviron et en Cyclisme

BF: Biceps femoris

CNS: Central nervous system

DoF: Degrees of freedom

EMG: Electromyography

Ext: Extension

Flx: Flexion

GM: Gastrocnemius medialis

GMAX: Gluteus maximus

GL: Gastrocnemius lateralis

LSD: Least significant difference

M-max: Muscle compound potential

MVC: Maximal voluntary contraction

RF: Rectus femoris

RMS: Root mean squared

RT: Rest twitch

SOL: Soleus

ST: Semitendinosus

TA: Tibialis anterior

TDC: Top dead center

TFL: Tensor fascia latae

VA: Voluntary activation

VL: Vastus lateralis

VM: Vastus medialis

General introduction

Human movement is an integral part of daily life and has intrigued researchers for decades. To create skillful, goal-directed movement, the coordination of multiple muscles is required. The basis for this coordination is provided by simple reflex loops and complex neural network patterns working together at multiple levels within the nervous system. Prilutsky (2000) defined muscle coordination as the distribution of activation or force among individual muscles to produce a given combination of joint moments. This distribution, however, is not straightforward as the number of degrees of freedom (muscles, joints, etc.) exceeds what is required and can theoretically be used in a combination of ways to fulfil the requirements of the task. This excess was first proposed by Bernstein (1967) as the concept of redundancy. Importantly, the many degrees of freedom potentially allow for adaptation of the muscle coordination strategy when the control system is faced with changes in external (obstacles, forces, etc.) and/or internal constraints (fatigue, pain, etc.). This plasticity is a key feature of human movement, but the selection process determining which adaptations occur and how when many possibilities are available remains elusive.

Of special interest is how muscle coordination changes as a consequence of fatigue and pain, important internal constraints that occur frequently in everyday life, sports, and medicine. During fatigue, the force-generating capacity of the muscle is compromised due to peripheral changes at the working muscle (e.g. sarcolemma excitability, excitation-contraction coupling) and/or due to the integration of afferent feedback at spinal and supraspinal levels leading to a change in neural command (Enoka and Duchateau, 2008). Pain also involves significant constraints to movement. While the force-generating capacity of painful muscles is not affected per se, theories suggest that feedback from pain-sensitive afferents results in significant changes in the muscle coordination strategy to protect the painful tissue from further pain and/or injury

(Hodges and Tucker, 2011). These constraints necessitate a reorganization in muscle coordination to maintain key characteristics of the movement during both fatigue (Akima et al., 2002) and pain (Hug et al., 2014a).

The majority of studies that investigate this reorganization are focused on a single muscle group, and have limited transferability to the global and complex locomotor system. In this context, studies using single-joint tasks are constrained to observing changes at the perturbed muscle and/or at adjacent synergist muscles. During fatigue, an increase in activation of the fatigued muscle has been well established (Edwards and Lippold, 1956). In addition, some authors reported significant changes between some muscle pairs (Akima et al., 2002) as a strategy to maintain force, while others showed limited changes with high inter-individual variability (Bouillard et al., 2014). Similar inconsistency is also apparent for adaptations observed during pain; for example, studies reported both a decrease (Ciubotariu et al., 2004), increase (Fadiga et al., 2004) and no change (Farina et al., 2008a) in muscle activity for the painful muscle. Experimental evidence suggests that independent control between the affected muscles might be difficult (Hug et al., 2014b) or entail significant neurocomputational costs (Dounskaia and Shimansky, 2016), which could explain the different results found in the literature.

During multijoint movements, many more degrees of freedom are available, with the possibility to adapt between synergist muscles, at other muscles within a leg, and/or between legs in bilateral tasks. This adaptability might have important implications for the observed change in muscle coordination (Hug et al., 2014b). It remains unclear how previous results observed during single-joint tasks translate to more complex tasks with many degrees of freedom. For example, locomotion tasks are characterized by complex intralimb mechanisms responsible for the transfer of mechanical energy between joints and control of the orientation of force at the end point of the

movement chain (van Ingen Schenau et al., 1992, Raasch and Zajac, 1999). In addition, important inter-leg neural connections are controlled in distinct phases of the movement (flexion/extension) (Ting et al., 2000b). It is imperative to take these conditions into consideration when trying to understand adaptations to fatigue and pain, since they might have a significant impact on the observed changes in muscle coordination.

Changes in response to fatigue have been observed during different multijoint tasks such as hopping (Bonnard et al., 1994), repetitive lifting (Sparto et al., 1997), sawing/hammering (Cote et al., 2002, Cote et al., 2008) and pedaling (Dorel et al., 2009), suggesting that changes occur as a strategy to compensate for the decrease in force-generating capacity. However, these changes are difficult to interpret since fatigue might have occurred at multiple muscles; it is not possible to determine if adaptations occur in respect to the fatigued muscle, occur due to an actual decline in force-generating capacity, and/or reflect a purposeful change in motor control strategies to maintain or optimize some aspects of the task. Pain-induced changes in muscle coordination have been observed during gait (Henriksen et al., 2007, van den Hoorn et al., 2015), with activity of the painful area decreasing while other non-painful areas increase, possibly to compensate. Nevertheless, it is difficult to describe these changes as a purposeful strategy because they can be realized through variable mechanics such as a change in stride length or in the intensity of the task.

Altogether, clarification of the changes in muscle coordination during fatigue and pain is needed, particularly with regard to multijoint tasks. A better understanding of muscle coordination during these conditions might improve performance in sports, and have important implications in the development of rehabilitation programs. The overarching goal of the current dissertation was therefore to investigate changes in muscle coordination during multijoint tasks where many different possible adaptations are available in response to two main perturbations, fatigue and pain.

This dissertation was comprised of three studies. The first was designed to investigate how muscle coordination adapts to unilateral fatigue of the quadriceps during a constant load submaximal bilateral pedaling task. The second study aimed to investigate changes in muscle coordination with selective fatigue of the quadriceps during all-out sprint pedaling. Finally, the third study aimed to determine how unilateral pain induced in two knee extensor muscles affected muscle coordination during a bilateral pedaling task.

The following section will review the current literature on adaptions to fatigue and pain during both single and multijoint tasks. The main findings and current gaps will be outlined, forming the basis for this dissertation's aim and hypothesis, which will be presented in Chapter 1.4.

Chapter 1 – Literature review

1.1 Muscle coordination

The seminal work of Russian neurophysiologist Nikolai Bernstein (1967) posited a central issue in the study of muscle coordination that has long dominated the literature. He pointed out that any motor task can be executed in a large number of possible ways because of redundant degrees of freedom such as selection of muscles, joints and motor units. Although internal constraints, such as the involved muscles, joints, and neural connections, and external constraints, such as the support surface and load, limit the number of available solutions (Valero-Cuevas, 2016), the degrees of freedom and therefore solutions to how any given motor task is performed far exceed what is actually required. A complex neural computation of specific muscle coordination strategies between an infinite number of options might therefore be needed to produce all the biomechanical functions that a task requires. How this is done is still poorly understood.

Muscle coordination has been defined as the distribution of muscle activation or force among individual muscles to produce a given combination of joint moments (Prilutsky, 2000). Different approaches are classically used to study muscle coordination, including kinematics, electromyography (EMG), and inverse dynamics. EMG is related to the recruitment of motor units and their discharge rate (Kamen and Caldwell, 1996) and can be used to assess the grouping (d'Avella et al., 2003, Torres-Oviedo and Ting, 2007), magnitude, and timing of the neural output from the spinal cord (Farina et al., 2004), which are important characteristics of muscle coordination. Nevertheless, EMG data does have drawbacks that necessitate a careful interpretation of results, especially during dynamic multijoint tasks. This is due to factors such as the spatial variability of activity over the muscle, crosstalk between adjacent muscles, fatigue, or amplitude cancellation (Hug, 2011). It is therefore important to have additional outcome measures to improve interpretation of results in dynamic multijoint conditions. With inverse dynamics, it is

possible to estimate the torques produced around each of the involved joints (Martin and Brown, 2009). This information combined with EMG makes is possible to evaluate muscle coordination strategies in greater depth, relating muscle activity profiles with the torques produced around the spanned joints. A neuromechanical approach relying on EMG and inverse dynamics might therefore be a powerful tool for better understanding how the motor control system adapts muscle coordination strategies.

Although such information is valuable, it can be argued that these methods reveal little concerning why one solution is preferred over another. This is a critical issue that has led to a number of theories in the area of motor control. Among them, the optimal control theory (Todorov, 2004) is premised on the optimization of a cost function, such as effort (Fagg et al., 2002) and error (Harris and Wolpert, 1998), which combined with sensory feedback can predict muscle coordination strategies (Todorov and Jordan 2002). Both effort and error cost functions predict similar behavior and predict movements well, however other cost functions have also been used, such as minimal torque (Uno et al., 1989) and jerk (Hoff and Arbib, 1993). In everyday tasks such as locomotion, this prediction becomes increasingly complex since individual muscles have very different roles in the execution of the task, e.g. uni- vs. biarticular muscles (van Ingen Schenau et al., 1992), and therefore potentially necessitate different cost functions. This highlights a criticism of optimal control theory, the inability to *a priori* estimate the cost function for a movement task; as a result, behavior cannot be reliably predicted (Shadmehr and Krakauer 2008; Ajemian and Hogan 2010). Furthermore, recent studies have provided experimental evidence of sub-optimality in motor control, and suggest that memory takes precedence over optimal principles as a prerequisite for motor control (de Rugy, Loeb, and Carroll 2012; Ganesh et al. 2010; Raphael, Tsianos, and Loeb 2010). The above concepts are only described in brief, but they are important

to consider when investigating muscle coordination. However, the current dissertation focused on a neuromechanical approach and can only speculate on the influence of the different cost functions.

Redundancy of the motor control system is classically considered as a “problem” needing to be solved. This term is unfortunate as redundancy also might provide many advantages, for example when faced with changes in the task space. Here the many degrees of freedom allow for flexibility, which can be used to correct task error at one joint by adapting other unaffected joints to maintain task characteristics. Many different perturbations can affect muscle coordination, including internal constraints such as fatigue and pain, which are especially important from a clinical and sports point of view. Adaptations to these constraints will be discussed next.

1.2 Fatigue and muscle coordination

1.2.1 Fatigue

Fatigue is a condition common in both clinical settings and sports. While the term may encompass a variety of both psychological and physiological conditions (Enoka and Duchateau, 2016), the current work relates to the exercise induced impairment of motor performance (Enoka and Duchateau, 2008). Research has demonstrated multiple mechanisms, from cortical areas to contractile properties, that might affect the development of fatigue. In addition, these mechanisms change in regards to the requirements of the task.

Fatigue is often defined as an exercise-induced reduction in the ability of muscle to produce force, regardless of whether or not the task can be sustained (Bigland-Ritchie and Woods, 1984, Enoka and Duchateau, 2008). This means that fatigue develops continuously after the onset of exercise activity and is quantified by a decrease in maximal force capacity. For example, Bigland-Ritchie et al. (1986) showed a gradual decline in maximal voluntary force (MVC) during submaximal intermittent isometric contractions of the quadriceps, with a >50% decline at the end of the protocol. The association between a decrease in MVC force and fatigue has been shown repeatedly in the literature (Merton, 1954, Hunter et al., 2004, Levenez et al., 2005, Sogaard et al., 2006) (see figure 1).

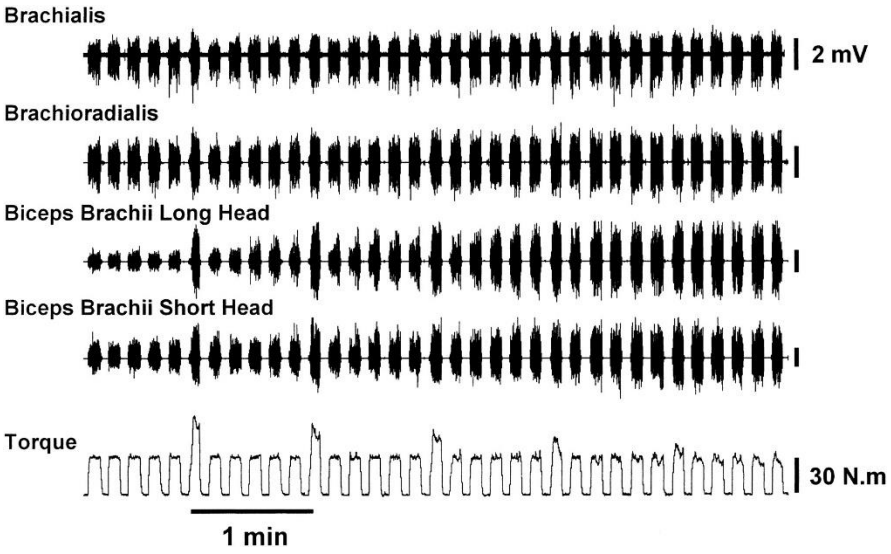

Figure 1. from Hunter et al. 2004. Shows the development of fatigue during intermittent contractions (elbow flexion) at 50% of maximum voluntary contraction (MVC). MVC's were performed each minute to evaluate the decrease in force generating capacity. Electromyography (EMG) was measured for the Brachialis, brachioradialis, biceps brachii long and short head.

Depending on the task, the decrease in MVC force and its time-course may vary significantly. In isometric MVC tasks fatigue develops rapidly whereas it slows in weaker submaximal contractions. In addition, the processes contributing to fatigue during these different contractions might vary (Taylor and Gandevia, 2008). One way to classify these processes is to divide them into central and peripheral fatigue. Central fatigue refers to an inability to drive the motoneurons voluntarily (Gandevia, 2001). This can be demonstrated by applying supramaximal nerve stimulation during a MVC (twitch interpolation technique). If the stimulation evokes an increase in force (superimposed twitch) it suggests that some motor units were not activated to generate a fused contraction (Merton, 1954). This has been demonstrated during maximal sustained contractions with stimulation of the peripheral nerve (Bigland-Ritchie et al., 1983b, Gandevia et al., 1996) indicating that central mechanisms proximal to the site of stimulation were involved in the loss of force generating capacity (figure 2). Central fatigue may include both cortical and spinal areas, as well as motor neurons leading to the muscle (Gandevia, 2001, Taylor and Gandevia, 2008). Thus other stimulation sites can be used as well such as the cervicomedullary

junction (Gruber et al., 2009) and transcranial magnetic stimulation of the motor cortex (Todd et al., 2003) to provide additional information about the locus of the central fatigue.

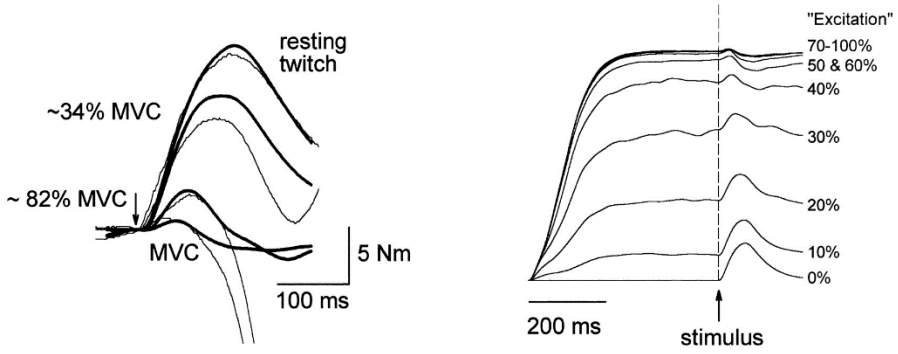

Figure 2. Adapted from Gandevia 2001. Displays the superimposed twitch at increasing contraction intensity. As the contraction intensity increases towards MVC the superimposed twitch is almost abolished.

Electrical stimulation elicited at the peripheral nerves can also be used to investigate changes in afferent feedback and reflexes. Modulation of group Ia and II afferent sensitivity have been demonstrated during fatigue (Duchateau and Hainaut, 1993) as well as activation of group III and IV afferents (Garland and Kaufman, 1995). The activation of group III and IV afferents is associated with changes in the metabolic and mechanical state of the muscle and has been linked to the depression in motor neuron excitability during fatigue (Duchateau and Hainaut, 1993).

Peripheral fatigue refers to processes at or distal to the neuromuscular junction that lead to a reduction in force generating capacity (Taylor and Gandevia, 2008). This may include an

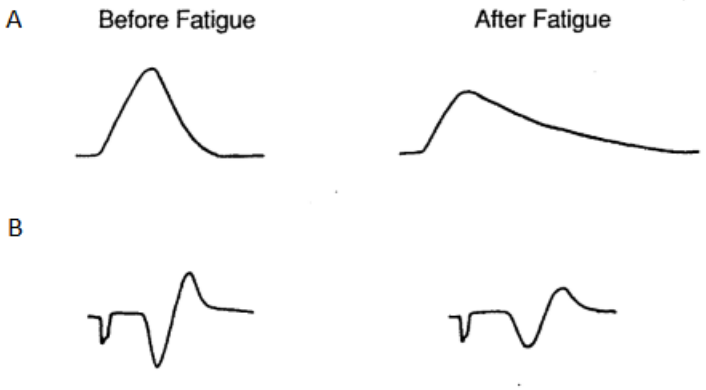

Figure 3. Adapted from Enoka 2002. Displays the influence of fatigue on the rest twitch (panel A) and the M-wave (panel B).

impairment of neuromuscular propagation. A typical way to test for peripheral fatigue is to elicit an electrical stimulation to the peripheral nerve and evaluate the surface electromyography (EMG) response at the muscle (compound muscle action potential) (Enoka, 2002). This is termed the Mwave (figure 3). During fatiguing submaximal sustained contractions, Fuglevand et al. (1993) demonstrated a significant decline in the M-wave response suggesting an impairment in neuromuscular propagation. This is likely caused by metabolic changes at the pre-synaptic terminal (Smith, 1984) and decreased efficiency of sodium channels (Juel, 1986). Peripheral fatigue can also be caused by changes in excitation-contraction coupling. This can be measured by evaluating the force response elicited during rest by electrical stimulation to the nerve, excluding neural factors. This indirectly assess excitation-contraction coupling mechanisms (rest twitch; figure 3). In this way, Bigland-Ritchie et al. (1986) demonstrated a significant decrease in twitch response after a fatiguing submaximal intermittent contraction of the quadriceps. These changes are associated with a decrease in Ca^{2+} release from the sarcoplasmatic reticulum or decreased sensitivity to Ca^{2+} at the myofibrils (Allen et al., 2011). Finally, a wide range of metabolic products and substrates are of significant importance during fatiguing contractions (Fitts, 1996). These include acidification of the muscle, Ca^{2+}, H^{+} and P_i concentrations, ATP, lactate - just to mention a few. Figure 4 outlines the major sites involved during neuromuscular fatigue.

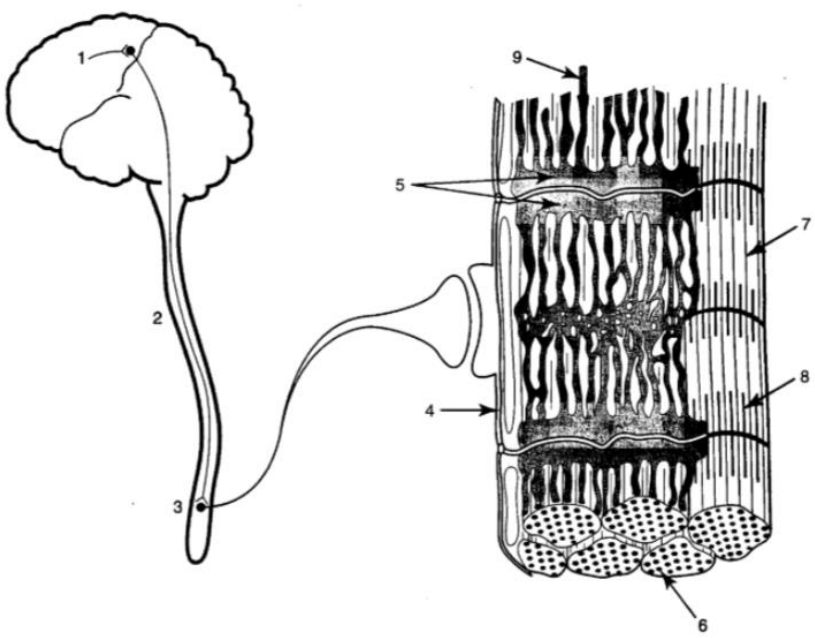

Figure 4. From Enoka 2002. Displays physiological sites relevant during neuromuscular fatigue. (1) primary motor cortex, (2) central drive to the motor neurons, (3) motor units, (4) neuromuscular propagation, (5) excitation-contraction coupling, (6) metabolic substrates, (7) intracellular milieu, (8) contractile properties, (9) muscle blood flow.

1.2.2 Within muscle adaptations

While the aforementioned mechanisms cause limitations in the muscles' ability to generate force, studies have demonstrated that submaximal contractions can be maintained at a constant force level for a period of time. This is, in part, because of the redundant degrees of freedom, present even during single-joint tasks. These can be used in a variety of ways and at many different levels (within the muscle and between adjacent and remote muscles), capable of counteracting the effects of fatigue. These different adaptations will be presented next.

During sustained submaximal isometric contractions of the calf Edwards and Lippold (1956) showed greater muscle activity (EMG) to maintain the same voluntary tension during fatigue (see also figure 1). This is an important and well known response that has been associated with a change in discharge rate and a recruitment of additional motor units. The latter has been demonstrated in numerous studies during fatigue (Bigland and Lippold, 1954, Enoka et al., 1989, Garland et al., 1994, Christova and Kossev, 1998, Adam and De Luca, 2003). Adam and De Luca (2003) measured the motor unit firing patterns of the vastus lateralis during fatiguing intermittent

knee extensions at 20% of MVC. Intramuscular EMG recordings revealed a progressive recruitment of additional motor units during fatigue. As the force generating capacity of the fatiguing muscle decreased, excitation of the muscle increased (lower recruitment thresholds), resulting in the recruitment of additional motor units. These results are further validated in an earlier study by Christova and Kossev (1998). The authors performed intramuscular EMG recordings of the biceps brachii during intermittent elbow flexion at approximately 10% of MVC. The data showed an increase in EMG activity during fatigue which was due to the recruitment of new motor units. This strategy appears to compensate for the decrease in force generating capacity during fatigue. An additional finding in this study was a concomitant decrease in discharge rate. Based on previous observations (Bigland-Ritchie et al., 1983a, Garland and McComas, 1990), the authors suggested that this decline was caused by inhibitory signals from small III/IV afferents. A decrease in discharge rate was also observed in (Bigland-Ritchie et al., 1983b, de Luca et al., 1996, Adam and De Luca, 2005, McManus et al., 2015). For example, de Luca et al. (1996) showed a change in motor unit discharge rates in isometric submaximal contractions of the first dorsal interosseous and tibialis anterior. This decline, in part, attributed to the decline in force. Other studies have shown both no change and an increase in discharge rate (Maton and Gamet, 1989, Miller et al., 1996, Adam and De Luca, 2005). This suggests that the discharge rate can also be used to maintain force during fatigue.

In addition to changes in motor unit recruitment and discharge rate, changes may also occur in respect to the spatial organization of muscle activation. Farina et al. (2008b) investigated these changes during a fatiguing contraction of the upper trapezius muscle. Participants performed a sustained isometric contraction at 15-20% of MVC until task failure and subsequently observed a

significant correlation between a shift in spatial distribution of the EMG and the development of fatigue (figure 5).

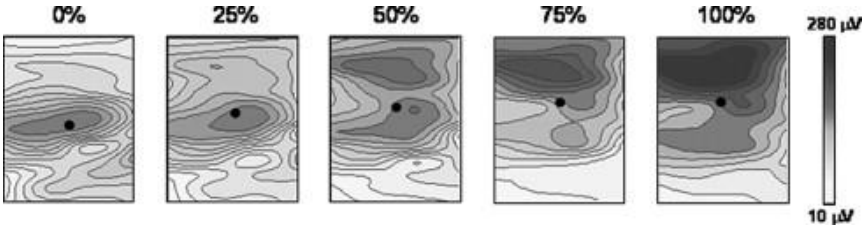

Figure 5. From Farina et al. 2008. Root mean square topographical map at 0, 25, 50, 75, and 100% of endurance time during a sustained fatiguing contraction.

This increase in heterogeneity for the spatial distribution of EMG activity was supported in a recent study by Staudenmann et al. (2014). The participants performed sustained fatiguing isometric contractions of the biceps brachii at 20% of MVC. The results showed an increase in global EMG activity during the fatiguing contraction, however this increase was not uniform across the whole muscle - suggesting a change in the spatial distribution of muscle activity. These studies suggest that the activation strategy within a single fatiguing muscle may change by sharing load between different regions within the fatiguing muscle to maintain the contraction (Holtermann and Roeleveld, 2006, Farina et al., 2008b).

1.2.3 Between muscle adaptations during singlejoint tasks

Generally multiple muscles contribute to the creation of movement. This is the case even during simple single-joint tasks. As fatigue develops, the relative contribution of synergist/antagonist muscles may change to adapt and to delay task failure.

Submaximal isometric contractions

During a sustained fatiguing isometric contraction at 5% of MVC, Sjogaard et al. (1986) measured intramuscular pressure and EMG of the knee extensors (vastus medialis, vastus lateralis and rectus femoris). Both intramuscular pressure and EMG recordings suggested that when the activity of a muscle decreased, the activity of other muscles increased. Confirming these results,

Kouzaki and Shinohara (2006) did a study where participants performed a low level (2.5% of MVC) sustained contraction of the knee extensors, measuring the EMG of the rectus femoris, vastus lateralis and vastus medialis. Alternate muscle activity was observed between some muscle pairs (vastus lateralis-rectus femoris; vastus medialis-rectus femoris) and an inverse relation was found between the frequency of this strategy and muscle fatigue. A similar study, at the same intensity, was recently performed by Akima et al. (2012), that also included the deeper located vastus intermedius muscle, showing alternate muscle activity between the muscle pairs including the rectus femoris and limited change between the vastus lateralis, medialis and intermedius. As a whole, the results from these studies suggest that adaptation between synergist muscles is possible and that the alternate activity between synergist possibly delay the effect of fatigue, by allowing for some recovery of the fatigued muscles. The data also suggest an important difference between the biarticular rectus femoris muscle and the monoarticular vastus lateralis, medialis and intermedius, e.g. alternate activity was observed between the uniarticular VM, VL, VI and the RF but not between the VM, VL, VI. This difference could be related to stronger monosynaptic Ia linkages between the uniarticular muscles as reported by Eccles et al. (1957) and/or a more specific neural control of biarticular muscles in relation to their to a functionally different role (van Ingen Schenau et al., 1995).

With these findings in mind Bouillard et al. (2012) investigated the adaptations to fatigue using a novel approach to measure load sharing. EMG interpretation can be challenging due to complex fiber membrane and motor unit properties, as well as difficulties with EMG cross talk, summation of action potentials and electrode positioning. For this reason, these authors utilized supersonic shear imaging (SSI), in addition to EMG, which provides shear elastic modulus, an estimate of stress within the muscle (for details see Hug et al. (2015)). The participants performed

sustained isometric knee extensions at 25% of MVC until exhaustion. The results, showed a significant increase of the EMG activity in the fatigued muscles across time, which was in accordance with previous findings (Edwards and Lippold, 1956, de Luca et al., 1996). In addition, a significant modulation of shear elastic modulus was observed for several participants, however the observed strategies in load sharing between muscles, were not consistent between participants. The high variability was explained by inter-individual differences and high task constraints limiting available solutions to adapt (figure 6).

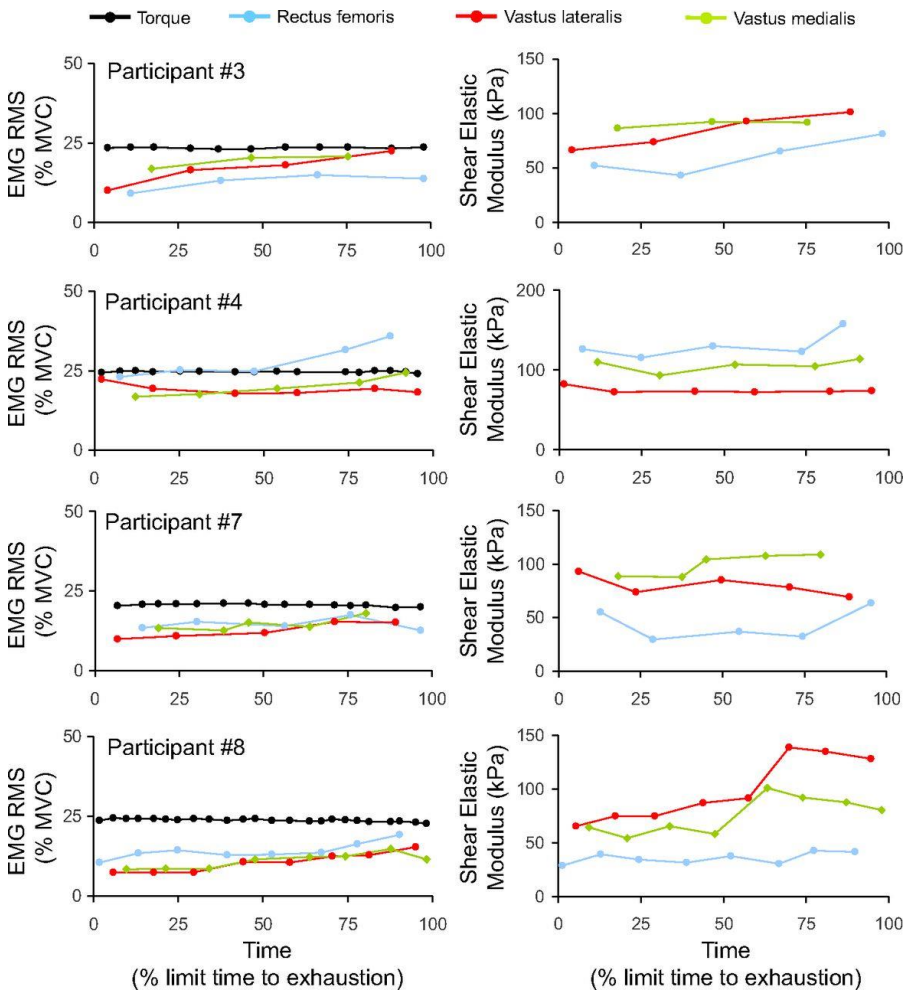

Figure 6. From Bouillard et al. 2012. Displays the EMG (left column) and shear elastic modulus (right column) ´for 4 participants in the rectus femoris, vastus lateralis and vastus medialis during a sustained contraction of the knee extensors at 25% of MVC to exhaustion.

Adaptations in response to selective fatigue during submaximal contractions

An issue in the study of fatigue is that it can be difficult to interpret the consequences of fatigue on force/activation sharing between synergists, when fatigue is not controlled. To circumvent this issue a different approach is to induce selective fatigue. This can be done by electrical stimulation, which involves intermittent electrical stimuli to the muscles to activate intramuscular nerve branches (Gagnon et al., 2009). Electrical stimulation can induce significant fatigue effects due to repeated activity in the same muscle fibers, disorderly recruitment of motor units and high metabolic demands. Besides being capable of fatiguing individual muscles electrical stimulation also limits the contribution of central mechanisms (Paillard, 2008, Maffiuletti, 2010). With this approach, Akima et al. (2002) aimed to clearly determine the force sharing between synergists in response to fatigue. The authors applied electromyostimulation to selectively fatigue the vastus lateralis before a submaximal (50% of MVC) dynamic knee extension task. Despite a significant loss of force production of the VL after the electromyostimulation protocol, the participants were able to maintain the required target force level. Using magnetic resonance images to evaluate the adaptations, the authors observed a contrast shift in transverse relaxation times (a measure correlated with integrated EMG activity) for the vastus medialis and rectus femoris. This suggested greater motor unit recruitment of these muscle, resulting in increased muscle activation. The results indicate that adaptations readily occur to compensate for selective decrease in force generating capacity in the vastus lateralis. It should be noted that all muscles showed increased activation, so compensation of individual muscles might not be as straightforward as the authors suggest. Interestingly, de Ruiter et al. (2008) reported similar findings during isometric voluntary knee extension at 20% of MVC. The authors induced selective fatigue by electrical stimulation

with occluded blood flow in the vastus medialis and as a consequence observed increased muscle activity and calculated force contributions of the vastus lateralis and rectus femoris.

In addition to these findings, Bouillard et al. (2014) induced selective fatigue by electrical stimulation in the vastus lateralis and used SSI to determine the change in muscle force sharing of the quadriceps muscles, during a sustained isometric knee extension task at 20% of MVC. The fatigued vastus lateralis muscle showed a significant decrease in shear elastic modulus compared to baseline. Despite of this, the task was maintained, suggesting that other muscles were recruited to compensate. However, no systematic change in strategy could be determined. Despite of this the individual data suggested that some compensation did occur, however it was not robust between the participants. As in their previous study (Bouillard et al., 2012), the acquired data showed high inter-individual variability in the adaptation strategy.

Maximal voluntary contractions

During a maximal voluntary contractions the EMG activity of the muscle usually decrease with fatigue, since no additional motor units can be recruited (Bigland-Ritchie, 1981). In this way, maximal contractions differ significantly compared to submaximal contractions. During a series of MVCs of the plantarflexors, Sacco et al. (1997) investigated the adaptations to selective fatigue of gastrocnemius lateralis (induced by electrical stimulation and ischemia). The authors reported a significant reduction in MVC (-29.7%) with a concurrent depression in EMG activity of the fatigued gastrocnemius lateralis, as well as in the non-fatigued synergist gastrocnemius medialis. Even though the gastrocnemius medialis muscle was not subjected to fatigue it was not possible to maintain the activation of this muscle. The authors argued that this was caused by inhibitory reflexes between synergists as previously suggested (Woods et al., 1987, Garland et al., 1988).

In a similar protocol, Stutzig and Siebert (2015) examined the muscle activation strategy of the triceps surae after selective fatigue of either the soleus, gastrocnemius lateralis or gastrocnemius medialis during MVC. Despite of significant changes in twitch torque and M-wave amplitude suggesting significant peripheral fatigue, the participants maintained MVC force levels. The authors argued that compensation occurred primarily at synergistic muscles but did show increased muscle activity for both synergists and the fatigued muscle. The increase was surprising since this indicates that the MVC task were in fact not maximal or maybe influenced by antagonist muscles, allowing for such adaptation which might also explain the contrast to the significant decrease in muscle activation observed in the aforementioned study (Sacco et al., 1997).

Adaptations of the antagonists

As described previously, the findings on adaptations to fatigue show considerable variability during both submaximal and maximal tasks. One possible explanation, often neglected, is the influence from the antagonist muscles (Smith, 1981, Kellis, 1998). For example, Bouillard et al. (2014) reported participant specific changes between synergists to compensate for fatigue and maintain target torque. Even though target torque remained unchanged the measured elastic modulus showed an overall increase, which would suggest an increase in force. To explain this change, the authors suggested that the muscle activity of the antagonist muscle might had increased. This increase in the mechanically opposing muscle would have necessitated the increase in the shear elastic modulus of agonists to maintain a constant torque output. A change in antagonist muscle activity has been shown in previous studies and has been termed coactivation (Smith, 1981, Psek and Cafarelli, 1993, Levenez et al., 2005). Levenez et al. (2005) investigated coactivation and the influence of spinal reflexes in the lower leg. During a sustained fatiguing isometric dorsiflexion at 50% of MVC the muscle activity (EMG) increased in both the agonist

(tibialis anterior) and antagonist (soleus, gastrocnemius lateralis). This finding was in line with other studies using submaximal isometric contractions, that generally show a parallel increased activity of both agonists and antagonists (Psek and Cafarelli, 1993, Ebenbichler et al., 1998, Hunter et al., 2003b). In contrast studies investigating adaptations during MVC show limited change (Patikas et al., 2002) or a decrease in coactivation (Mullany et al., 2002). Thus, although the activation of antagonist muscles might play a non-negligible role in providing joint stability during single joint movements, their activation may impede performance of the agonists during fatigue. This relationship is yet to be fully uncovered.

1.2.4 Multijoint tasks

Adaptations during submaximal tasks

The complexity during multijoint task is significantly higher compared to single joint tasks. Studies suggest that the distribution of muscle activation between individual muscles can be modulated to compensate for the loss of force generating capacity, by changing the interjoint coordination. This involves adaptations at multiple muscles because of the more degrees of freedom and differential adaptations at synergist/antagonist muscles. In this line, Forestier and Nougier (1998) investigated the reorganization of movement to fatigue during a forearm throw towards three specified targets. Fatigue was induced by sustained isometric contractions at 70% of MVC for the wrist muscles extensor digitorum communis and the flexor digitorum superficialis. Subsequently, the accuracy of the task decreased significantly. The successful throws showed a modulation of the inter-segmental organization to fulfil the task. More precisely, the movement showed increased rigidity by an absence of temporal delay between proximal and distal joints. This was explained by increased cocontraction between agonists and antagonists, simplifying movement control during the fatigue condition. Huffenus et al. (2006) also analyzed the throwing

task and tested the effects of local fatigue of proximal and distal joints respectively. Fatigue was induced via sustained isometric contractions at 70% of MVC in the triceps brachii (elbow extension) and extensor digitorum communis (wrist extension) respectively. The throwing task was performed across a horizontal plane (isolated elbow and wrist) with the aim to reach a specified target. In this study the participants were able to maintain the accuracy of the throwing task despite of fatigue. When fatigue was induced around the distal joints, a reorganization of temporal characteristics was observed. This resulted in increased rigidity of the movement, as was also reported by Forestier and Nougier (1998). In contrast, when fatigue was localized around the proximal joint a more significant change in the coordination of the movement occurred. This was expressed as a significant increase in wrist angular velocity, increased wrist flexor activity and greater use of the muscles viscoelastic properties. In a different study investigating the same task, the authors observed adaptations consistent with those reported here (Huffenus and Forestier, 2006). However, when fatigue was induced by electrical stimulation, the adaptation differed. This could indicate that important sensory information from spinal and supraspinal areas is lacking when fatigue is induced by electrical stimulation and that the active involvement of the central nervous system is important in the reorganization of movement during fatigue.

Adaptations during complex multijoint tasks

Significant changes in motor coordination strategies has also been observed in more complex tasks. Cote et al. (2008) investigated the reorganization of multijoint coordination with fatigue during a hammering task. Both muscle activity and kinematics were evaluated indicating fatigue at the upper trapezius muscle and also expressed as a decrease in displacement at the elbow joint. Nevertheless, the maximal speed of the hammer was maintained and task performance was prolonged despite of fatigue which was explained by additional recruitment of the external oblique

to increase trunk motion. This suggests that a redistribution of load took place, taking advantage of the redundant number of degrees of freedom, to prolong task performance. The study substantiated previously obtained results during a fatigued sawing task (Cote et al., 2002). Fatigue was induced by a combination of sawing and isometric contractions of the elbow flexors at 70% of MVC. Subsequently, the authors observed changes in movement amplitudes for the elbow (decrease) and for the wrist, shoulder and trunk (increase). The data indicated that the contribution to movement shifted towards non-fatigued joints, resulting in invariant endpoint trajectory and cycle duration. This was supported by Sparto et al. (1997), who showed that when participants fatigued during a repetitive lifting task, the relative work between joints remained invariant, with a higher reliance on passive forces in the spine by increased lumbar flexion. In this way, the participants were able to maintain mechanical effectiveness and lifting frequency despite of fatigue.

In the majority of these studies it is difficult to ascertain if the adaptation strategies occur as a result of a redistribution of load or due to changes in other movement characteristics (movements amplitude, produced force). Therefore, some advantages are afforded when the end-point is fixed and the force is constrained. Bonnard et al. (1994) investigated the adaptations to fatigue during hopping at a constant frequency and at 30% of maximal hopping height. The participants were able to maintain global power output by changing neural control strategies such as preactivation of the gastrocnemius muscle or increased activation of the knee extensors. A significant increase in muscle activity was also measured for the biarticular rectus femoris muscle. Biarticular muscles have been associated with specific roles in the execution of movement, such as control of orientation of force at the end-point (van Ingen Schenau et al., 1992, Prilutsky, 2000). As a result, the measured ground reaction force was modified depending on the compensation

strategy used. By increasing the gastrocnemius preactivation; a shorter duration ground reaction force profile was observed with higher peak force, suggesting an optimized bouncing process. Alternatively by increased knee extensor activity; a characteristic humb in the ground reaction force profile during the eccentric phase was observed suggesting increased reliance on the knee extensors. Although these strategies were observed independently of each other, lower limb kinematics remained unchanged for both.

Another convenient task in the investigation of motor coordination is cycling. Kinematic constraints due to the closed linkage result in fewer degrees of freedom, balance has negligible influence, the resistance at the pedal can be controlled and the circular pedal trajectory is constrained. Still it remains a complex task, with numerous effectors (muscles and joints) working together to produce force on the pedals and to control the direction of this force. This occurs via dynamic and bilateral interactions between individual muscles and joints. In addition pedaling is a relevant task that is similar to for example walking (Raasch and Zajac, 1999). Both tasks involve cyclical movements, with alternating extension and flexion phases, with phase dependent reflexes (Brooke et al., 1992). It is interesting to note that, in a pedaling task Raasch and Zajac (1999) identified six groups of lower limb muscles which in alternate phasing (extension/flexion) fulfilled

the requirements to perform both forward and backward pedaling. Similarly, Hug et al. (2011) found muscle synergies - groups of muscles coactivated over the course of the pedaling cycle. These synergies have been shown to be relatively robust across different mechanical constraints (Hug et al., 2011) and also to fatigue (rowing) (Turpin et al., 2011). Nevertheless some adjustments in muscle coordination have been demonstrated with the occurrence of fatigue. Mornieux et al. (2007) investigated the effects of fatigue by inducing hypoxia during pedaling at 150, 250 and 350W. The authors found that the relative contribution of joint torques remained invariant,

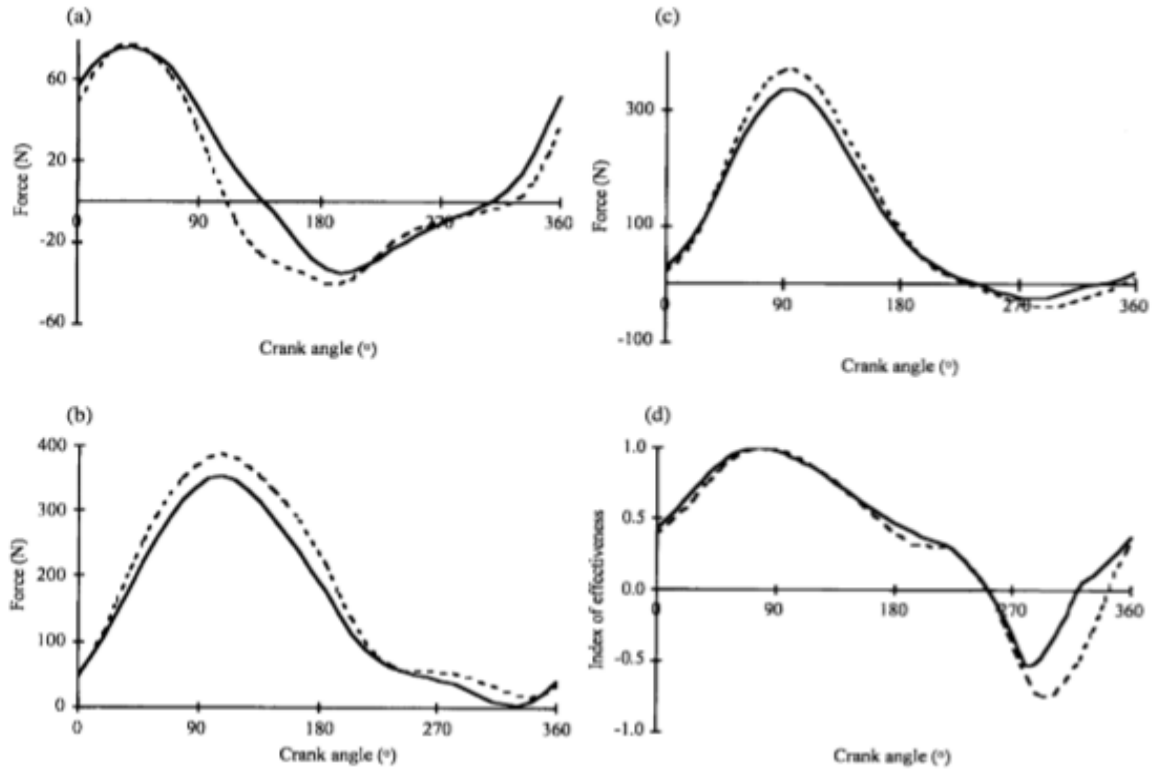

Figure 7. From Sanderson & Black 2003. Displays the forces at the pedal during a fatiguing pedaling task at 80% of maximum power output. A: tangential pedal force. B: normal pedal force. C: effective force. D: index of effectiveness (effective force / total force). The solid line corresponds to the first minute of the pedaling task and the broken line corresponds to the final minute of the pedaling task.

suggesting a robust coordination strategy despite of fatigue. Other authors, Sanderson and Black (2003) reported that when participants pedaled at 80% of maximum aerobic power output until exhaustion, the force applied to the crank changed. When fatigue occurred, the peak positive

effective force (the force applied perpendicular to the crank) increased and the peak negative effective force became more negative. This was explained by significant fatigue effects during the flexion phase of the pedaling cycle, which necessitated an increase during the extension phase to maintain power output. The authors suggested that focusing around the flexion phase of the pedaling cycle might improve performance during fatigue. In a similar study (Dorel et al., 2009), the participants performed constant-load pedaling at 80% of the maximum aerobic power until exhaustion. At the end of the exercise, the authors observed greater muscle activity in the gluteus maximus and biceps femoris to compensate for muscle activity of the knee extensors. A small change in the way participants exerted force on the pedal during the extension phase was also observed, as well as a change in muscle activity timing. These adjustments likely occurred as a result of fatigue, and might suggest a change in muscle coordination. The results strongly indicate that an adjustment of the muscle coordination strategy occurred during fatigue.

Maximal intensity tasks

During tasks performed at a maximal intensity a decrease in power is observed early due to fatigue, and adjustments to maintain power is generally considered to be limited, assuming that the main agonist muscles are maximally activated. Some changes in muscle coordination have been observed has been observed, however these have been interpreted differently and will be discussed next.

Rodacki et al. (2001) investigated the effects of fatigue during continuous maximal vertical jumps. During fatigue, the authors observed that the participants stiffened the leg segments, possibly to avoid muscle damage and improve movement control. The authors further interpreted these changes as a strategy to sustain maximal performance during fatigue. Surprisingly, the results also showed an increase in muscle activity for both the lower leg muscles

and knee extensors, despite of the task supposedly being performed at a maximal intensity. In addition, this was accompanied with an increased activation of the antagonist muscles, which was explained by a central coactivation mechanism. This in turn might have resulted in a suboptimal coordination strategy during fatigue. In an effort to investigate this further Rodacki et al. (2002), continued their study on maximal vertical jumps, however this time with local fatigue of the knee extensors/flexors respectively. While limited change occurred during flexor fatigue, significant changes were observed during extensor fatigue, highlighting their important role during vertical jumps. These changes included a reduction in peak joint angular velocity, peak joint net moment and power around the knee while the muscle activity profiles indicated that the muscle coordination strategy was similar irrespective of fatigue. Overall this confirmed their previous results, suggesting suboptimal muscle coordination strategies during fatigue.

Martin and Brown (2009) investigated the effects of fatigue during a maximal 30s isokinetic cycling exercise. The results showed a greater reduction in ankle joint power and range of motion compared to the knee and hip joints and an overall decrease in pedal power. The authors proposed that this was related to a more pronounced ankle joint fatigue and a strategy to stiffen this joint to minimize loss of power. This strategy could have simplified the task by decreasing the degrees of freedom which is in line with the previously discussed papers (Forestier and Nougier, 1998, Huffenus and Forestier, 2006, Cote et al., 2008), also showing increased rigidity during fatigue. In the same task O'Bryan et al. (2014a) reported significant reductions in muscle activity levels. Adding to this, the authors found significant changes in muscle activation timing for the biarticular rectus femoris and gastrocnemius muscles, resulting in decreased coactivation with the power producing muscles (vastus lateralis/medialis and gluteus maximus). This likely negatively influenced the joint power distribution and the transmission of force to the pedal.

Billaut et al. (2005) also observed significant changes between the force producing and biarticular antagonist muscles during fatiguing intermittent sprints. The authors reported that integrated EMG was maintained however muscle activation timings changed significantly. This involved a decreased delay between the vastus lateralis and biceps femoris muscle activation onset which suggests the inter-muscular coordination changed. The authors suggested that this relationship could have had negative implications for the power output produced during fatiguing sprints but importantly also noted that the changes could be explained by a change in pedaling frequency. Also during fatiguing intermittent sprints, Hautier et al. (2000) observed, that as fatigue developed the contractile force of the primary power producing muscles (vastus lateralis) decreased (based on increased EMG/force ratio during a submaximal condition). During this decrease in the intermittent sprint condition, the muscle activation of biarticular antagonists (biceps femoris and gastrocnemius lateralis) significantly decreased to account for the reduced force of the quadriceps.

The aforementioned studies highlight the complexity of a multijoint dynamic task, with differential effects between uni – and biarticular muscles. The uniarticular muscles are thought to primarily be involved in the production of force. On the other hand, the biarticular muscles have been suggested to i) ensure an effective transfer of mechanical energy between joints and ii) to maintain an effective orientation of the pedal resultant force (van Ingen Schenau et al., 1992, Raasch and Zajac, 1999, Prilutsky, 2000). Further research is needed to clarify these mechanisms further.

1.2.5 Summary

It is clear that depending on the complexity of the task, adaptations to muscle fatigue can occur at multiple levels ranging from within the fatigued muscle itself to within synergists of the same muscle group, within antagonists, and finally within other muscles at proximal and distal joints.

There is substantial evidence suggesting that when the force-generating capacity of a muscle decreases, the motor control signal from the central nervous system to this muscle changes. This involves both a change in motor unit recruitment strategy and in discharge rate. Recruitment of additional motor units to maintain force output is consistently observed in the literature (Enoka et al., 1989, Garland et al., 1994, Adam and De Luca, 2003). In contrast, effects on the discharge rate are more variable (Bigland-Ritchie et al., 1983a, Adam and De Luca, 2005, McManus et al., 2015), likely relating to different measuring techniques and protocols. In addition, the discharge rate may not be uniform between initial and newly-recruited motor units (Farina et al., 2009), due to a significant shift in the spatial organization of muscle activation as fatigue develops. This shift may aid in preserving force generation despite fatigue (Farina et al., 2008b, Staudenmann et al., 2014).

Adaptations occurring at other muscles involved in the task seem to strongly depend on the task and on the particular characteristics of fatigue. During sustained submaximal single-joint tasks, some studies show alternate activity between some muscle pairs (Kouzaki and Shinohara, 2006, Akima et al., 2012) and others show important inter-individual variability of the muscle coordination strategy with the same muscle pairs (Bouillard et al., 2012). There are several factors contributing to these inconsistent results. First, measuring techniques differed between studies. Second, different contraction levels were used, suggesting that as an adaptation strategy, alternate

activity between synergists might be limited to very low contraction levels. Finally, fatigue in these studies occurred in multiple muscles, which can make it difficult to dissociate the effects of fatigue from a purposeful adaptation strategy. Inducing selective fatigue in one muscle is an effective approach for further investigating adaptation to fatigue, yet findings remain variable (Akima et al., 2002, Bouillard et al., 2014). Within the same muscle group, changes especially occurred between the biarticular muscle and its synergists, while limited changes were observed between monoarticular synergists. This may indicate that strong neural connections exist between synergists (Schieppati et al., 1990, Bouillard et al., 2014), making it difficult to dissociate the drives of these muscles. Thus, single-joint tasks may involve important neural constraints. This is further emphasized in studies investigating adaptations to fatigue during contraction at maximal intensity. Here the activities of the fatigued muscle and its non-fatigued synergist change concurrently (Sacco et al., 1997, Stutzig and Siebert, 2015). Finally, coactivation of antagonist muscles was observed in a series of studies (Psek and Cafarelli, 1993, Patikas et al., 2002, Hunter et al., 2003b). This has important effects on the observed adaptations.

It seems that when adding more degrees of freedom (more muscles and joints) to a task, adaptations between muscles occur readily. This has been shown in different mulitjoint tasks such as throwing (Forestier and Nougier, 1998, Huffenus and Forestier, 2006), lifting (Sparto et al., 1997), hammering (Cote et al., 2008), and running (Kellis and Liassou, 2009). Studies showed increased rigidity of the task and increased activity for some muscles, suggesting that a task can be maintained despite fatigue by an adaptation in muscle coordination. Nevertheless, it remains difficult to dissociate many of the adjustments from changes in mechanical parameters (changes in intensity or frequency of the task or in kinematics). In more constrained multijoint tasks such as hopping (Bonnard et al., 1994) and cycling (Dorel et al., 2009), changes in muscle coordination

were also observed. These include change in muscle activation, change in timing of muscles, complex interactions between biarticular and monoarticular muscles, controlling the direction of force at the end-point, and transfer of mechanical energy between joints. These changes were suggested to have both positive and negative implications for the task. Overall, the main difficulty in these studies was that fatigue likely occurred in many muscles. Therefore, it was not possible to determine if changes occurred because of fatigue effects or as a purposeful adjustment to the muscle coordination strategy.

1.3 Pain and muscle coordination

1.3.1 Pain

Pain occurs in many everyday activities and can have significant implications on motor behavior, such as movement dysfunction. The International Association for the Study of Pain defined pain as an unpleasant sensory and emotional experience that is associated with actual or potential tissue damage or described in such terms. This definition highlights the subjectivity of pain, and is further part of multidimensional system, controlled at multiple levels in the nervous system. This includes excitatory and inhibitory spinal reflex circuits related to the activation of group III and IV nociceptive afferents (Mense, 1991), to various cortical areas such as the primary motor cortex, cerebellum and basal ganglia (Pierrot-Deseilligny and Burke, 2005). Musculoskeletal pain has been studied in clinical populations, such as osteoarthritis, fibromyalgia and low back pain (Mundermann et al., 2005, Graven-Nielsen and Arendt-Nielsen, 2008, Crossley et al., 2012) suggesting a reorganization of movement strategies when experiencing pain. Muscle weakness, disuse and changes in the structural tissue makes pain in clinical populations difficult to control, which makes interpretation difficult, in terms of underlying control of muscle coordination. This is further complicated by patient specific sensitization. Different models have been used to experimentally excite the nociceptors to induce muscle pain, the most popular one being injection of hypertonic saline (Graven-Nielsen and Arendt-Nielsen, 2008). This model creates localized pain with robust excitation of the nociceptors, and without any muscle toxicity. This model has made it possible to examine the modulation of muscle activity and movement characteristics during pain.

Different theories have been used to describe the adaptations to pain. The vicious cycle model suggested that muscle pain induces muscle hyperactivity due to fusimotor facilitation

(Roland, 1986). Although a few studies support the predictions made in the vicious cycle model numerous recent reports found no evidence suggesting muscle hyperactivity during musculoskeletal pain (Graven-Nielsen and Arendt-Nielsen, 2008, Hodges and Tucker, 2011, Bank et al., 2013). Alternatively, Lund et al. (1991) proposed the pain-adaptation model, predicting, decreased muscle activation of the painful muscle and increased activation of its antagonist. This serve to protect the painful tissue from further pain or injury. Numerous reports are in line with this model (Svensson et al., 1996, Martin et al., 2008), although considerable variability is observed between muscles and tasks. This lead Hodges and Tucker (2011) to suggest an alternative pain adaptation model taking these results into account (figure 8). This theory suggests, that a redistribution of activity occur in respect to the task and the individual and that changes occur to protect the painful muscle from further pain or injury. The literature is reviewed below.

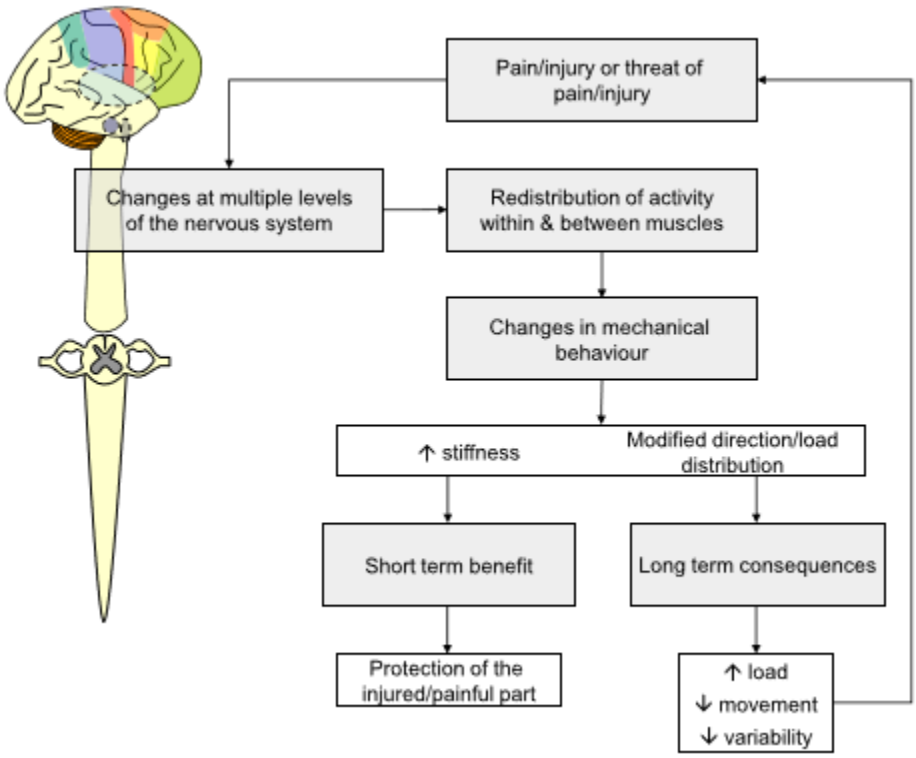

Figure 8. From Hodges 6 Tucker 2011. A schematic of the motor adaptations to pain

1.3.2 Within muscle adaptations

A variety of different tasks has been used to investigate the effects of musculoskeletal pain on muscle coordination (for review see Bank et al. (2013)). Even during high sensitization of musculoskeletal pain, adaptation can occur to maintain exercise performance. In this line, changes have been observed within the painful muscle. For example, after an injection of hypertonic saline into the tibialis anterior Graven-Nielsen et al. (1997) observed a significant decrease in MVC dorsi flexion and in muscle activity (EMG) levels during a sustained contraction at 80% of MVC. The EMG measurements further suggested that a given level of EMG activity produced a higher torque in the painful condition, possible explained by an additional recruitment of motor units within the painful muscle (Tucker et al., 2009). These results were confirmed by Ciubotariu et al. (2004). These authors induced pain by a hypertonic saline injection in either the tibialis anterior or the gastrocnemius lateralis. The participants were asked to perform sustained fatiguing isometric contractions of either the plantar (gastrocnemius lateralis pain) – and dorsi (tibialis anterior pain) flexors at 50 and 80% of MVC. Subsequently, a decreased EMG activity of the painful muscle and also decreased EMG/force ratios were observed. The decrease in muscle activity levels for the painful muscle could reflect limited motor unit recruitment and a reduction in motor unit discharge rates. However the fatigued condition is a confounding factor in this study as fatigue might involve additional, different changes in the distribution of muscle activity.

In contrast, both Farina et al. (2008a) and Hodges et al. (2008) showed no change in EMG activity for the painful muscle. Two important differences are worth noting – the contraction level was significantly lower and no fatigue was present. In Farina et al. (2008a) participants performed a sustained isometric dorsiflexion at 10 % of MVC. Pain was induced by hypertonic saline in the

tibialis anterior and the concomitant recording of both intramuscular EMG, multi-channel EMG and torque allowed for a thorough investigation of the motor unit recruitment strategies. The surface EMG showed no change during pain, however the discharge rate decreased significantly (figure 9), as also suggested by Ciubotariu et al. (2004).

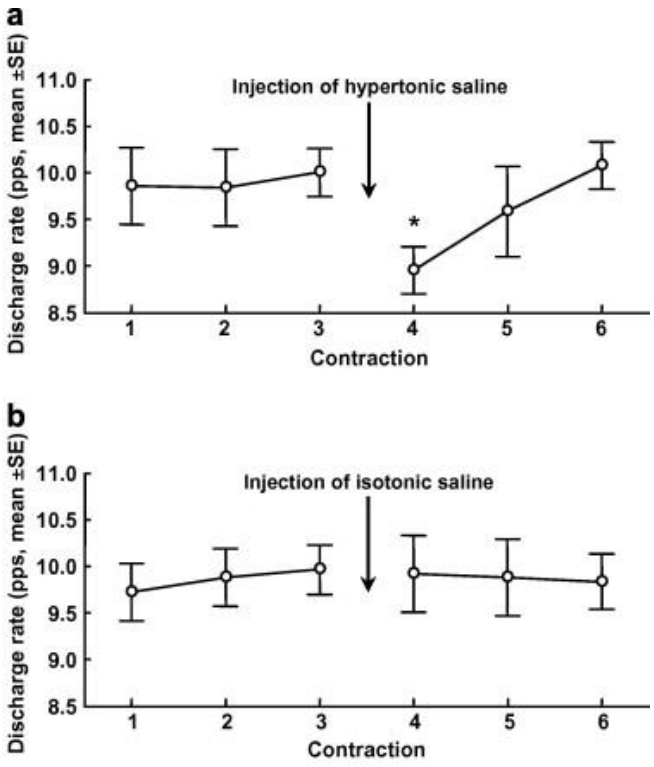

Figure 9. From Farina et al. 2008. The effect of hypertonic saline injection on motor unit discharge rate is displayed in panel A. Panel B shows the effect of isotonic saline (control). Participants performed a sustained isometric contraction of the dorsiflexors at 10% of MVC.

Hodges et al. (2008) induced pain in a different muscle, the gastrocnemius lateralis, to observe adaptations during submaximal isometric plantarflexions. Similar to Farina et al. (2008a) and in contrast to Ciubotariu et al. (2004), the results showed no change in surface EMG signal of the painful muscle but did report a significant decrease in discharge rate of the painful muscle and in addition its synergists. This is important because it shows that no change in surface EMG signal does not necessarily mean that the activation strategy is the same. These results also imply that compensatory mechanisms were necessary to complete the task. Compensatory mechanisms

responsible is still debated and might involve (1) an increased recruitment of higher threshold motor units, by a decrease in recruitment thresholds of those motor units (Masakado et al., 1991). (2) increased motor unit discharge synchronization. Multiple motor units have been shown to fire concurrently at fixed intervals, which can augment force output (De Luca et al., 1993). This is possibly by way of nociceptive afferents which are connected across the motor neuron pool. (3) Twitch potentiation has been shown to increase the force output due to a prior conditioning contraction increasing Ca^{2+} sensitivity (Vandervoort et al., 1983). (4) More recently Tucker et al. (2009) reported an alternative motor unit recruitment strategy that involved the recruitment of a new population of motor units within the painful muscle.

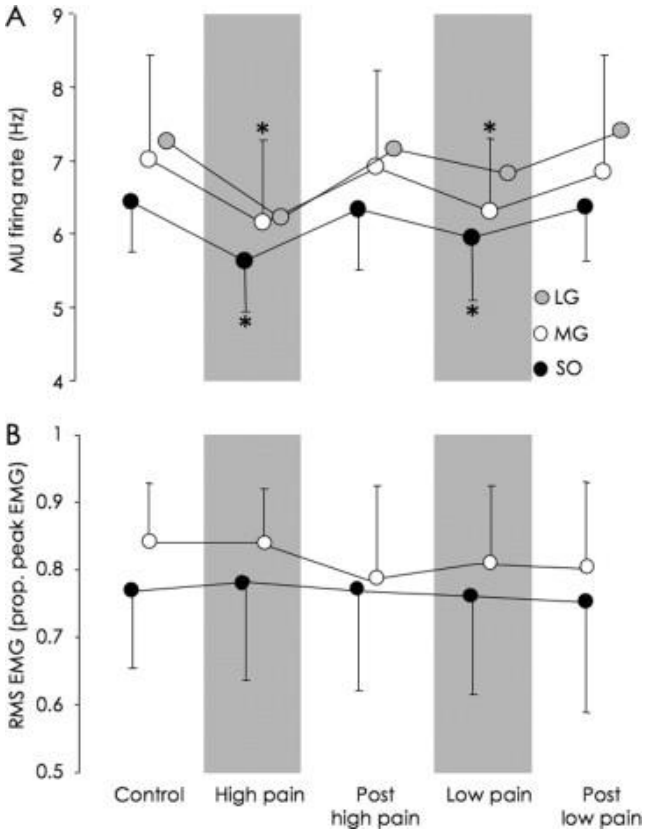

Figure 10. From Hodges et al. 2008. Displays the motor unit discharge rate (A) and rmg EMG (B) during low submaximal contractions of the plantar flexors.

To further understand these findings Tucker et al. (2014) used SSI to assess changes in regional muscle stiffness to pain during a knee extension task. The participants performed sustained isometric contractions at 10% of MVC and pain was induced by hypertonic saline injection in the vastus lateralis. Although some EMG studies showed both decreased EMG activity and discharge rate suggesting that changes occurred at the painful muscle, supposedly as a protecting strategy, the current study showed that the actual stress within the painful muscle did not systematically decrease. This was explained by significant inter-individual variability and high task constraints (adaptations limited to adjacent synergist muscles) that made it difficult to observe a redistribution of force within and between muscles.

Even though classical bipolar EMG techniques provide important information on the activity of a muscle, they only assess a small region of the muscle and cannot be used to assess local redistribution of motor unit activity. However, a spatial reorganization of activity may also occur within the painful muscle. This can be assessed by multiple EMG recordings within a muscle, using surface matrix electrodes, providing a topographical mapping of muscle activity. In this way Madeleine et al. (2006) measured the muscle activity of the trapezius muscle after injection of hypertonic saline. During a sustained contraction at 15-20% of MVC, they found a spatial redistribution of muscle activity within the painful muscle. Specifically, pain caused selective inhibition of motor neurons close to the injection site, as shown by a decrease in muscle activity and an increase at other non-painful areas. Later Falla et al. (2009), showed that the same reorganization of activity occurred with a different location of pain, suggesting that the spatial reorganization of activity occurs irrespective of the pain location. In support of these findings, Hug et al. (2013) used fine wire EMG and tested spatial organization of activity in the soleus during a low-force isometric plantarflexion. In contrast to Madeleine et al. (2006), the results did not show

a spatial reorganization of muscle activity in respect to pain location. In addition, gross EMG activity did not change however intramuscular fine wire EMG measurements did reveal a decrease in motor unit discharge rate. The discrepancy between studies is likely explained by the difference in task complexity and the involved muscles.

1.3.3 Between muscle adaptations

As suggested by several authors compensation to pain may occur at synergist/antagonist muscles and might also explain many of the findings within the painful muscle outlined in the above section. Ciubotariu et al. (2004), described previously, observed that in addition to the decreased activity of the painful muscle, the muscle activity of synergists also decreased. This suggests that these muscles were not able to compensate. Interestingly, previous experimental evidence suggests that the excitation of group III/IV afferents inhibits synergist α-motoneurons as well as the homonymous muscle (Kniffki et al., 1981, Hayward et al., 1988). In addition, the antagonist muscle activity did not change during pain which was in conflict with the increased antagonist muscle activation as proposed by Lund et al. (1991) and also suggests that modulation of the antagonist muscle is not used as a compensatory strategy. Hodges et al. (2008) (described previously), similarly reported a significant decrease in discharge rate for both the painful muscle and its synergists. Again, the additional decrease in discharge rate for the synergist muscles suggests that these were not recruited to maintain a constant force output. Thus it seems that these muscles behave in a similar way to the painful muscle itself.

To test this further, Hug et al. (2014c) investigated the adaptations during sustained isometric contractions of the knee extensors at 20% of MVC and at a low submaximal rms EMG target amplitude of the vastus lateralis. Pain was induced in either the rectus femoris or the vastus medialis by hypertonic saline injection to see if pain induce in different muscle types (mono - vs

biarticicular) showed different results. In addition, the adaptations were evaluated by both elastography and EMG. When pain was induced in the rectus femoris the results showed that the stress (estimated using elastography) and EMG decreased significantly in this muscle. This suggests that adaptations likely occurred at the other non-painful knee extensor muscles, VM and VL. In contrast, when pain was induced in the vastus lateralis the muscle stress and EMG activity in this muscle did not change systematically. The authors provided additional data concerning the participants' ability to control vastus medialis, vastus lateralis and rectus femoris activity independently of each other. This experiment, without pain, revealed that it was possible to voluntarily decrease the activity of the rectus femoris but not the vastus medialis – highlighting between muscle differences and possible neurophysiological constraints. This is an likely explanation (together with within-muscle changes in motor unit recruitment strategies) for the current variability in experimental findings, suggesting both increases (Fadiga et al., 2004), decreases (Graven-Nielsen et al., 1997) and no change (Farina et al., 2008a).

In a more complex task consisting of cervical flexion/extension ramped contractions to 60% of MVC, Falla et al. (2007) showed widespread effects to induced musculoskeletal pain. The authors induced pain by an injection of hypertonic saline into the sternocleidomastoid and the splenius capitis. The induced pain had significant effects on the agonist showing decreased muscle activity and this modulation seemed to depend on the contraction level, e.g. greater decrease of muscle activity with higher contraction level. The muscle activity of other muscles was also affected in the painful condition. During flexion both the agonist and antagonist muscles showed lower muscle activity level. During extension a different strategy was used, recruiting the synergist muscle trapezius while the activity of the antagonist remained invariant.

1.3.4 Multi-joint tasks

As previously implied, the constraints of a task may have important implications for the observed adaptations to pain. Hug et al. (2014b) compared the adaptations to pain during three force-matched isometric tasks with a varying number of muscles and joints involved (degrees of freedom); a single joint knee extension task, an isometric single leg squat and an isometric bilateral leg squat. When pain was induced by an injection of hypertonic saline in the vastus medialis the muscle stress of the painful vastus medialis muscle did not change during the knee extension task and the single leg squat. The authors suggested that this might be associated with an inability to dissociate the drive between synergist muscles. However, when the participants performed the bilateral squat a systematic decrease in muscle stress was observed in the painful vastus medialis and its synergist vastus lateralis. This study highlights the importance of the complexity of the task (degrees of freedom) and the muscles under investigation. When a clear solution to adapt as available this is chosen, as also shown in Hug et al. (2014a) studying the bilateral effects of pain in the soleus. Hypertonic saline was injected into the soleus muscle of one leg, subsequently, the participants performed submaximal force-matched isometric plantarflexions of both legs, with knee flexed (to minimize the contribution from GM and GL). The obtained results showed a clear tendency to change the relative force between the painful leg (decrease) and non-painful leg (increase) to reach target force. The muscle activity of the painful soleus muscle decreased, although with considerable inter-individual variability - especially at lower contraction levels. This variability in muscle activity underlines the complex adaptations within and between the muscles that cannot be captured be conventional surface EMG.

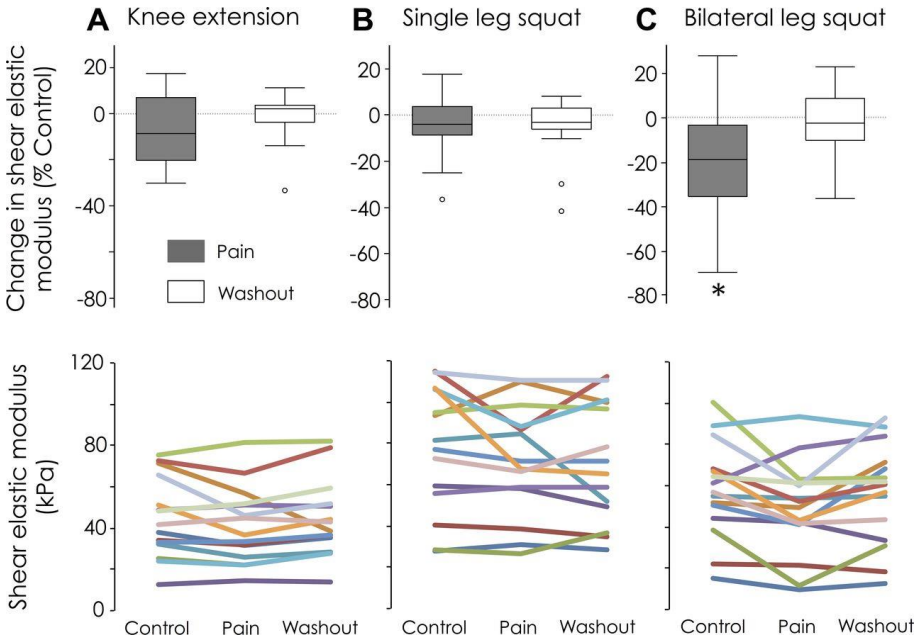

Figure 11. From Hug et al. 2014. The effect of hypertonic saline injection on average (top) and individual (bottom) shear elastic modulus during force matched knee extension (A), single leg squat (B) and bilateral squat (C).

During gait, van den Hoorn et al. (2015) investigated the adaptations to pain in the lower back and calf (gastrocnemius medialis). The results included an analysis of muscle activity patterns and kinematics. The muscle activity of the gastrocnemius medialis decreased during pain, as did the other lower leg muscles. In contrast, increased muscle activation was observed for the vastus medialis and vastus lateralis. Pain in the lower back resulted in decreased activity of the plantar flexors and a tendency to increase the activity of the muscles surrounding the trunk. Both conditions resulted in a modulation of muscle activity for a variety of muscles and decreases in stride time, despite of this muscle synergies remained relatively robust. The results highlighted the protection of painful tissues, decreased activity for the calf muscles (as shown by Graven-Nielsen et al. (1997)) and increased activity around the trunk to stabilize. At the same time the modulation showed considerable variability between participants due to individual experience and many different solutions to a problem (redundancy). These factors need to be taken into consideration during multi-joint tasks.

Focusing specifically around the knee joint, Henriksen et al. (2007) induced pain in the VM muscle with injection of hypertonic saline, to observe its effects during walking. The authors reported that when pain was induced in the vastus medialis, muscle activity of this muscle and the vastus lateralis decreased. As a result, the knee extension moment during the loading phase also decreased, and likely caused instability.

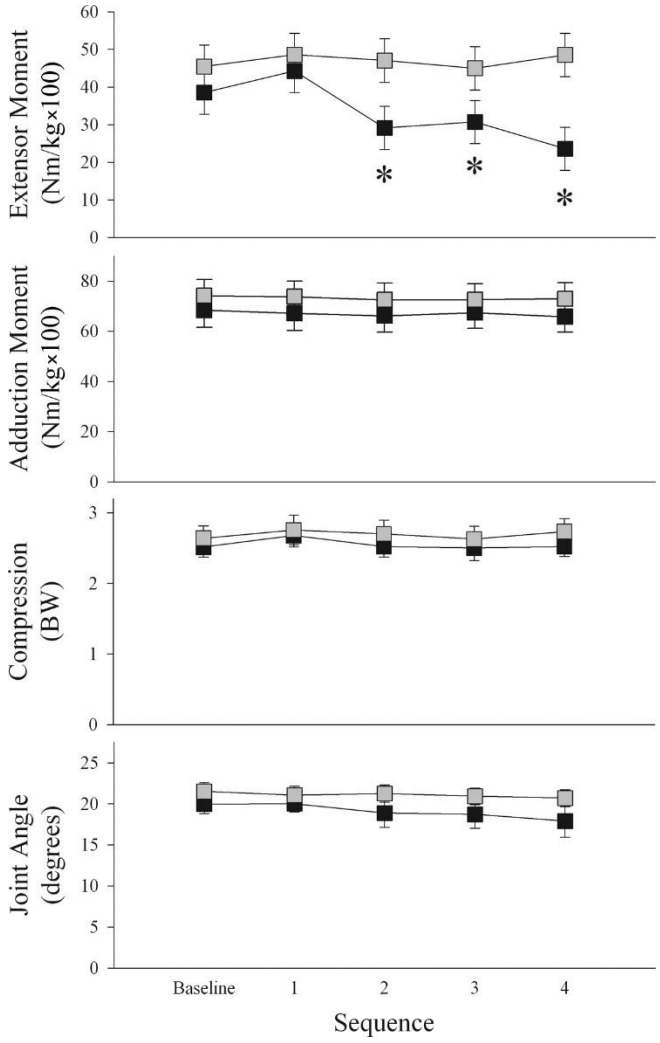

Figure 12. From Henriksen et al. 2007. This figure shows the effects of hypertonic saline injection on knee joint function during gait. Top-down: the extension moment, adduction moment, compression and joint angle. The grey squares denotes the effects of isotonic saline (control) and the black squares denotes the effects of hypertonic saline (pain). Each sequence (x-axis), consisted of gait cycle and each sequence was separated by 5 mins.

Despite of these changes kinematics (knee joint angle) remained unchanged, together with hamstring muscle activity and knee flexion moment. Henriksen et al. (2009) later repeated the induced pain in the vastus medialis during a forward lunge task, to observe adaptations in a task

with higher demands on the knee joint dynamics. Again, the authors reported a significant reduction in knee extension moment, associated with decreased vastus medialis and lateralis muscle activity. In addition, this study also showed a decrease in muscle activity for the antagonists. Thus, even during tasks with high demands on the painful muscles, changes occur that might not benefit function over longer periods of time. This may have important consequences for injury susceptibility.

1.3.5 Summary

Experimental evidence of adaptations to pain varies significantly depending on the method and protocol used. In force-matched single-joint tasks, both a decrease (Ciubotariu et al., 2004), increase (Fadiga et al., 2004), and no change (Farina et al., 2008a) in activity of a painful muscle have been reported. In addition, spatial organization has been shown to change in respect to the pain location (Madeleine et al., 2006), although the results are not consistent (Hug et al., 2013) and Falla et al. (2009) showed that spatial redistribution might depend on which location pain was induced at in the muscle.

The observed changes in muscle activity seem to depend on contraction intensity. Studies using high intensities (80% of MVC) show decrease in muscle activity (EMG) in response to an injection of hypertonic saline (Graven-Nielsen et al., 1997, Ciubotariu et al., 2004). In contrast, at lower intensities (10-20% of MVC) the activity of the painful muscle does not change (Farina et al., 2008a, Hodges et al., 2008). Nevertheless, a decrease in discharge rate was observed in these studies. Thus, changes in muscle activity may occur even though EMG amplitude remains invariant. Compensating mechanisms which maintain activity levels or force output are not agreed upon, but most likely include motor unit recruitment and synchronization.

Changes also involve synergist and antagonist muscles. The painful muscle and its synergists seem to behave in a similar manner (Ciubotariu et al., 2004, Ervilha et al., 2004, Falla et al., 2007) but this is not always the case for biarticular muscles (Hug et al., 2014c). However, antagonist muscles show more variable results, showing both no change (Ciubotariu et al., 2004), decreases in activity (Falla et al., 2007), and increases (Graven-Nielsen et al., 1997). Again, the constraints of the task seem to have an important influence on observed results (Hug et al., 2014b), possibly due to difficulties dissociating the drive between synergist muscles. In contrast, studies using experimental pain during gait show a variety of changes. The muscle activity of the painful muscle and its synergists decrease (Henriksen et al., 2007, van den Hoorn et al., 2015), while increased muscle activity is observed elsewhere to stabilize and maintain gait characteristics. The adaptations observed in multijoint tasks tend to show high variability, which is associated with the participants' individual histories and the complexity of the task (many different options for adaptation).

1.4 Aim and hypotheses

As the above review indicates, there is a gap in the current understanding of adaptations of muscle coordination to fatigue and pain, specifically how muscle activation and force change at the perturbed muscle and how such change affects other muscles relevant for the task. This is particularly important where multiple effectors work in concert to maintain a task goal, such as in multijoint tasks. Although studies have been performed on such tasks, it remains difficult to interpret their results because of changing mechanics (ex. changing joint angles or forces) or a lack of control of the perturbation itself (e.g. fatigue occurring at multiple muscles).

Therefore, the overarching goal of the current dissertation was to observe changes in muscle coordination in response to fatigue and pain during a bilateral multijoint pedaling task, where it was possible to control power and pedaling frequency. Careful control of induced selective fatigue and pain in a muscle group allowed for interpretation of adaptations occurring 1) between synergist muscles, 2) between muscles/joints within the same leg, and 3) between legs. Several hypotheses needed to be tested to further understand the impacts of fatigue and pain on muscle coordination during a complex multijoint task, and these were assessed through three separate studies. **Study 1 - Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task** investigated adaptations to fatigue during pedaling at submaximal intensity with fatigue selectively induced in the quadriceps. The aim was to determine adaptations occurring at the level of the fatigued muscle when other solutions exist. It was hypothesized that in this situation, fatigue would induce a decrease in the contribution of knee joint power at the ipsilateral leg. This would necessitate a change elsewhere to maintain overall power. A second aim was therefore to determine which muscle coordination strategy was preferably used among possible options of the antagonist, synergists within the leg, or between legs. In this regard, it was

hypothesized that a change in muscle coordination would occur that increased the contribution of the contralateral (non-fatigued) leg to maintain the task.

Adaptations are likely to depend on the goal of the task and furthermore on the available degrees of freedom. Increased intensity imposes increased constraints on the motor control system which could significantly limit the possible adaptations. Nonetheless, intricate changes might occur related to control of pedal forces or forces transferred between joints. In addition, some muscles might not be maximally activated during specific phases of the movement and might therefore have the potential to compensate (Dorel et al., 2009). **Study 2 – Muscle fatigue induces positive changes in coordination during a sprint cycling task** therefore investigated adaptations to fatigue during pedaling at maximal intensity. Fatigue would result in a decrease in knee joint power at the fatigued leg. The aim was therefore to investigate the consequences of this decrease on muscle coordination strategy. Since the task was performed at maximal intensity, it was hypothesized that little change would/could occur at the non-fatigued muscles and joints, while significant changes in co-activation of the biarticular hamstring and gastrocnemii muscles were expected.

Pain is another internal constraint that the control system regularly needs to adapt for. Pain often occurs in conjunction with fatigue but is significantly different as it does not impair the muscle's force-generating capacity. Studies have suggested a decrease in muscle activity to protect the tissue from further pain and injury, but this decrease is not consistently observed. When observed, the redistribution of muscle activation to maintain task characteristics has considerable interindividual variability. One explanation is the fact that the majority of studies have been performed during single-joint tasks with few degrees of freedom or otherwise with a study design lacking control of the task mechanics. **Study 3 – Motor adaptations to local muscle pain during**

a bilateral cyclic task therefore investigated adaptations to selective pain in the vastii muscles during pedaling at submaximal intensity. The first aim of this study was to determine adaptations in the painful muscles. Where many available compensatory solutions were available, it was hypothesized that the painful muscles would show a consistent decrease in activity. As a result, a redistribution of muscle activity was necessary to maintain the task. A second aim was therefore to determine the most common compensatory strategy during bilateral pedaling; we hypothesized it would occur at the contralateral leg.

The following chapters will present each study separately in the form of articles submitted to and/or published in peer-reviewed international scientific journals.

Chapter 2 - Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task

Accepted: 31 October 2016

DOI: 10.1111/sms.12811

ORIGINAL ARTICLE

WILEY

Motor adaptations to unilateral quadriceps fatigue during a bilateral pedaling task

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Funding information
Region Pays de la Loire (ANOPACy project); French Ministry of Sport, Grant/Award Number: 14-R-23; European Union; Regional Development European Funds

This study was designed to investigate how motor coordination adapts to unilateral fatigue of the quadriceps during a constant-load bilateral pedaling task. We first hypothesized that this local fatigue would not be compensated within the fatigued muscles leading to a decreased knee extension power. Then, we aimed to determine whether this decrease would be compensated by between-joints compensations within the ipsilateral leg and/or an increased contribution of the contralateral leg. Fifteen healthy volunteers were tested during pedaling at 350 W before and after a fatigue protocol consisting of 15 minutes of electromyostimulation on the quadriceps muscle. Motor coordination was assessed from myoelectrical activity (22 muscles) and joint powers calculated through inverse dynamics. Maximal knee extension torque decreased by 28.3%±6.8% ($P<.0005$) immediately after electromyostimulation. A decreased knee extension power produced by the ipsilateral leg was observed during pedaling (−22.8±12.3 W, −17.0%±9.4%; $P<.0005$). To maintain the task goal, participants primarily increased the power produced by the non-fatigued contralateral leg during the flexion phase. This was achieved by an increase in hip flexion power confirmed by a higher activation of the tensor fascia latae. These results suggest no adjustment of neural drive to the fatigued muscles and demonstrate no concurrent ipsilateral compensation by the non-fatigued muscles involved in the extension pedaling phase. Although interindividual variability was observed, findings provide evidence that participants predominantly adapted by compensating with the contralateral leg during its flexion phase. Both neural (between legs) and mechanical (between pedals) couplings and the minimization of cost functions might explain these results.

KEYWORDS
compensation strategy, interlimb coupling, joint-specific power, multijoint task, muscle coordination, redundancy

1 | INTRODUCTION

Muscle coordination is defined as the distribution of muscle activation or force among individual muscles to produce a given combination of joint moments.[1] As the motor system has many more degrees of freedom than needed to generate basic movements, even single-joint motor tasks can be theoretically produced by an infinite number of muscle force combinations. There is a lack of knowledge in regard to how the central nervous system (CNS) adapts coordination among the numerous muscles that are involved in the task when the force-generating capacity of one muscle (or one muscle group) is decreased.

Motor adaptations to fatigue have been extensively studied during force-matched isometric single-joint tasks.[2–4] Beyond the established increased activation of the fatigued

muscle,[5] between-muscle compensations can theoretically occur to maintain the task goal. Although some studies reported alternate activity or adaptation between some muscle pairs [eg, vastii and rectus femoris[2]], more subtle adaptations have been reported by others.[3] For example, some evidence for compensation between the heads of the quadriceps muscle was reported during an isometric knee extension task,[3] but this was not observed in all participants. In addition, when this adaptation was observed, participants did not exhibit the same strategies; that is, the adaptations did not systematically occur between the same muscles.

More consistent motor adaptations to fatigue have been reported during dynamic multijoint tasks such as pedaling,[6,7] hopping,[8] repetitive lifting,[9] and sawing/hammering.[10] Using indirect (kinematics, kinetics) or more direct (EMG) measures of muscle coordination, they suggested between-muscle adaptation as an effective strategy to maintain the task goal. However, the location of fatigue was not controlled implying that fatigue might have occurred in one or more muscles. Therefore, along with the difficulty of interpreting changes in EMG amplitude in a fatigued muscle,[11] the aforementioned studies cannot determine whether motor adaptations are organized with respect to the fatigued muscle(s) and whether they can be considered as compensation strategies.[6] This is crucial to address because it would provide a deeper understanding of the underlying control principles of muscle coordination during fatiguing tasks.

One solution to address this question is selectively to fatigue one muscle/muscle group.[2,12] These authors used electrical stimulation selectively to fatigue the vastus lateralis muscle. Akima et al.[2] reported a small contribution of the VL and an increased use of the other quadriceps muscles during an isometric task, which was explained by an increase of central command to the quadriceps muscle group as a whole. Although Bouillard et al.[12] observed a systematic decrease in the force produced by VL (assessed using shear wave elastography) during a subsequent isometric force-matched task, the adaptation strategy varied between individuals. Similarly, de Rugy et al.[13] showed that when one agonist muscle was fatigued by electrical stimulation, the activation of all agonist muscles was increased instead of recruiting only the effective muscles. Overall, this absence of systematic and predictable compensation strategies during single-joint tasks might be explained by the limited ability to dissociate neural drive between some agonist muscles or by the high control cost associated with such dissociation.[14]

It is unclear how muscle coordination preferentially adapts to unilateral localized fatigue during a constant-load bilateral dynamic task in which numerous possibilities of adaptation are available. When considering unilateral multijoint tasks, compensatory strategies to local fatigue involving a greater contribution of torque produced by non-fatigued muscles were observed in some[15] but not all studies.[16] During pedaling, it is well established that complex intralimb mechanisms are involved in muscle coordination (eg, transfer of mechanical energy between joints by biarticular muscles, necessity to effectively orientate the force at the endpoint).[1,17–19] In addition, studies performed on bilateral cyclic tasks have provided evidence that some neural pathways participate to regulate the ipsilateral muscle activity using contralateral sensorimotor information.[20,21] This suggests that adaptations to unilateral fatigue would possibly involve between-leg adaptations to compensate for functional changes within-leg. To the best of our knowledge, there is no experimental evidence whether one strategy (ie, within or between legs) is more consistently used during a bilateral cyclic task.

Here, we studied motor adaptations to an unilateral fatigue of the quadriceps muscle during a constant-load bilateral pedaling task. We used a neuromechanical approach that combined recording of EMG activity of 11 muscles, the measurement of pedal forces, and inverse dynamics modeling for both lower limbs. The first aim was to test the hypothesis that local quadriceps muscle fatigue would induce a decrease in the contribution of the knee joint power. The second aim was to determine whether motor adaptations to this reduced knee joint power would be compensated by (a) a concurrent modulation of power produced at the other joints within the ipsilateral fatigued leg; and/or (b) an increased contribution of the contralateral leg. We hypothesized that the induced fatigue would result in a decreased knee joint power of the ipsilateral leg that would be consistently compensated by increasing the contribution of the contralateral (non-fatigued) leg.

2 | METHODS

2.1 | Participants

Fifteen healthy active males (sports science students) with no history of lower limb injury and no history of specific cycling training volunteered to participate to this experiment [mean±SD: age 23.7±3.3 years, height 1.80±0.08 m, body mass 72.7±8.9 kg]. They provided their written informed consent. All procedures were approved by the local ethics committee (CPP Ouest V: n°2013-A01714-41) and were conducted according to the Declaration of Helsinki.

2.2 | Experimental protocol

Participants performed a series of submaximal and maximal pedaling tasks both before (Pre) and after (Post) an electromyostimulation protocol that selectively fatigued the knee extensor muscles of one leg (Figure 1).

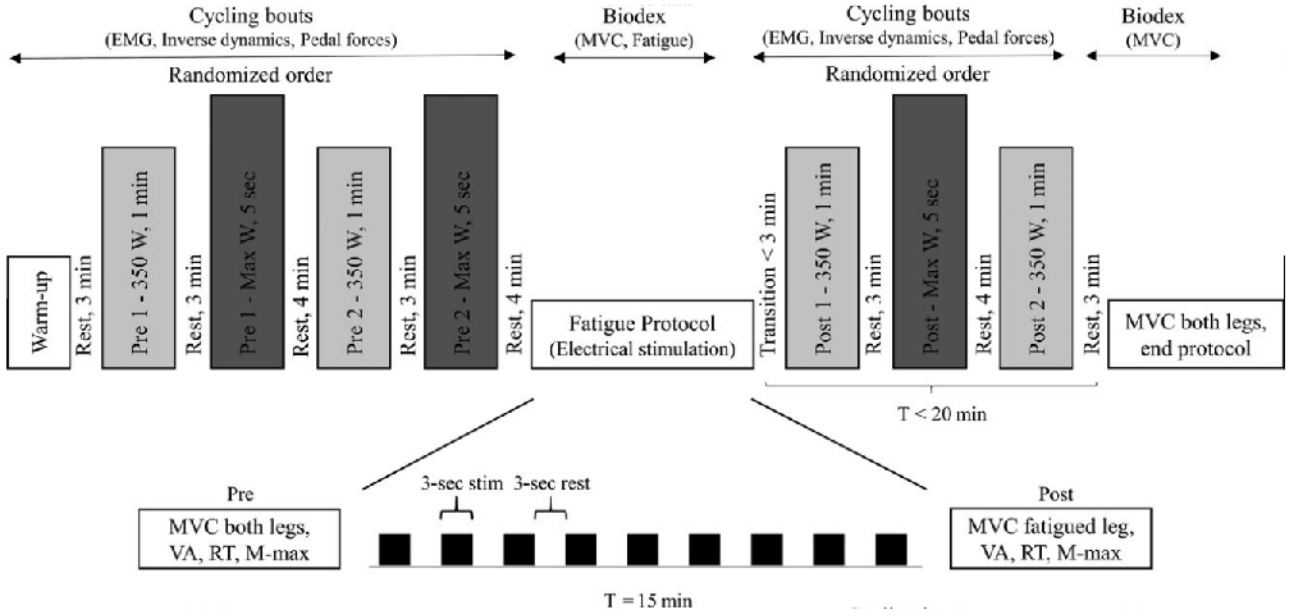

FIGURE 1 Experimental setup. Participants performed a series of pedaling tasks both before (Pre) and after (Post) an electromyostimulation protocol that selectively fatigued the knee extensor muscles of one leg. The order of the cycling tasks (ie, 350 W vs MaxW) was randomized. MaxW, all-out sprint exercise; MVC, maximal voluntary contraction (knee extension, for the fatigued leg or both legs); VA, voluntary activation; RT, resting twitch; M-Max, maximal M-wave (for the fatigued leg). The MaxW bouts were not included in the current study

2.2.1 | Pedaling task (pre- and post-fatigue)

All pedaling exercises were performed on an electronically braked cycle ergometer (Excalibur Sport; Lode, Groningen, the Netherlands) equipped with standard cranks (170 mm). The cycle ergometer was adjusted to fit the preferences of the participants, who were instructed to maintain their seated position throughout the tests. After a standardized warm-up (10 minutes of pedaling at 100 W followed by 1 minute 30 seconds at 250 W), participants performed two bouts at 350 W (1 minute duration). The pedaling rate was freely determined by the participants during the warm-up and was held constant throughout all the following bouts. Note that two 5-second all-out sprints were also performed to address a specific different research question (ie, the effect of fatigue on maximal explosive multijoint performance) and were therefore not considered for the present study. The order of all the cycling bouts was randomized to avoid any confounding effects from repetition of the exercises. These cycling bouts were repeated immediately after the fatigue protocol following a transition <3 minutes corresponded to the time necessary to change position from the single-joint ergometer to the cycle ergometer. The short duration of the bouts (5 seconds for sprint and 1 minute for 350 W) and the associated rest periods (3-4 minutes) were chosen to limit the occurrence of additional fatigue during the cycling protocol which lasted for <20 minutes. For the same reason, only one all-out sprint was completed during this post-fatigue cycling session. Forces on the pedals, lower limb kinematics and myoelectrical activity of lower limb muscles were recorded throughout the pedaling exercises and used to assess the motor adaptations. Note that the first 350 W pedaling bout performed before fatigue was considered as a familiarization to the task and therefore was not used for further analysis. Therefore, only the second 350 W pedaling bout was considered as the Pre condition. Both bouts performed after the fatigue protocol were considered (Post 1 and Post 2) to test a possible practice time effect of the motor adaptations. Note that, although a longer exposure to the fatigue stimulus (ie, longer than 1 minute) would have been preferable to observe the possible time effect, this was not possible given that potential additional fatigue induced by the cycling bouts was to be avoided.

2.2.2 | Fatigue protocol

To induce selective fatigue to the quadriceps muscle group, participants sat on an isokinetic dynamometer (Biodex System 3 research, Biodex Medical, Shirley, NY, USA) with their trunk and legs flexed at 90° and 80°, respectively (0° being full extension of the trunk and knee). The torso and the waist were strapped to the chair. Transcutaneous electromyostimulation was applied to the quadriceps muscle group of one leg (side randomized, right side n=8 and left side n=7) with the intent of fatiguing this muscle group. Rectangular electrodes (Stimex 50×90 mm, Monath Electronic, Rouffach, France) were placed over the expected motor points of the vastus lateralis (VL), vastus medialis (VM), and rectus femoris (RF) (determined using Botter et al.[22]) and one over their proximal insertion (anode;

Stimex 80×130 mm, Monath Electronic). A constant current stimulator (DS7A, Digitimer, Letchworth Garden City, UK) coupled with a train/delay generator (DG2A, Digitimer) was used to deliver a train of rectangular pulses at 70 Hz (pulse duration=450 μs). Each evoked contraction lasted for 3 seconds, followed by 3-second rest. An initial 150 contractions were induced (ie, 15 minutes), followed by a single maximum voluntary contraction (MVC) to evaluate the level of strength loss. If this MVC did not decrease by ≥30% of the initial MVC, an additional 50 contractions were induced and no more. During the protocol, the stimulation intensity was adjusted continuously to the maximal tolerable level. To characterize the fatigue induced by the protocol, MVC torque, voluntary activation level (VA), and M-waves were assessed before and after the electromyostimulation trial on the ipsilateral leg. VA is a measure of the descending drive, modulated at cortical and spinal levels, whereas the M-wave is a measure of sarcolemma excitability at the level of the muscle. In addition, to confirm that fatigue persisted throughout the entire experiment on the ipsilateral leg, two maximal knee extensions were performed at the end of all procedures. To check that fatigue was absent on the contralateral leg, participants performed two maximal knee extensions before and at the end of all procedures.

2.3 | Materials and procedures

2.3.1 | Electromyography

Electromyography (EMG) was used to record myoelectrical activity from 11 muscles bilaterally (total=22 muscles): tibialis anterior (TA), soleus (SOL), gastrocnemius medialis (GM) and lateralis (GL), VM, VL, RF, biceps femoris—long head (BF), semitendinosus (ST), gluteus maximus (GMax), and tensor fascia latae (TFL). Pairs of surface Ag/AgCl electrodes (diameter of the recording area: 5 mm; Covidien, Kendall, Mansfield, MA, USA) were attached to the skin (~20 mm interelectrode distance). Electrodes were placed according to SENIAM recommendations when available. The skin was shaved and cleaned with alcohol to reduce impedance. Electrode cables were well secured to the skin with adhesive tape to minimize movement artifacts. EMG signals were pre-amplified close to the electrodes (×1000) and digitized at 1000 Hz using two synchronized EMG amplifier units (ME6000, Mega Electronics Ltd., Kuopio, Finland).

2.3.2 | Assessment of muscle fatigue

Neuromuscular fatigue was evaluated before and immediately after the electromyostimulation protocol. More precisely, both VA and the M-wave (for both the VL and VM) were assessed from supramaximal stimulation of the femoral nerve. An electrical stimulus of 1000-μs duration and 400 V amplitude was delivered by a Digitimer DS7AH constant current stimulator (Digitimer) through a cathode (diameter: 20 mm, Covidien, Kendall) placed on the femoral triangle and an anode on the gluteal fold (Stimex 50×90 mm, Monath electronic). The resting twitch of maximal amplitude was determined by applying a stimulus of increasing intensity in increments of 5 mA, until knee extension torque and M-wave amplitude plateaued despite an increase in current intensity. A light pressure was applied on the cathode to stimulate close to the nerve. To ensure a maximal response throughout the testing, supramaximal stimulus intensity was used, corresponding to 120% of the intensity that evoked a maximal resting twitch response [50-125 mA]. A single stimulus was delivered to elicit the maximal M-wave at rest. A doublet stimulus (interspaced by 10-ms) was delivered during the plateau of MVC and within 5 seconds in the following rest period to elicit a superimposed and resting twitch, respectively. Force and EMG data during the fatigue trial were recorded in LabChart 8 (AD Instruments Pty. Ltd., Castle Hill, NSW, Australia) and digitized at 2000 Hz (Powerlab 16/35, AD Instruments Pty. Ltd.).

2.3.3 | Pedal forces

The cycle ergometer was equipped with instrumented pedals (VélUS group, Sherbrooke, Canada), as described elsewhere.[6] Briefly, the pedals measured the Cartesian components, corresponding to the horizontal (Ft) and vertical (Fn) components of the force on the pedal. The pedal angle in respect to the crank was measured using a motion capture system as described in the next paragraph. The top dead center (TDC) was measured by way of transistor-transistor logic rectangular pulses delivered at the highest position of the right pedal. The pedals were compatible with clipless pedals using LOOK KEO cleats allowing a solid shoe-pedal interface. All data from the instrumented pedals were digitized at 1000 Hz with the same acquisition units as those used for EMG (ME6000, Mega Electronics Ltd.).

2.3.4 | Kinematics

Three-dimensional (3D) kinematic data were recorded using an optoelectronical motion capture system composed of nine cameras (Flex 13, 1.3 Mpx, OptiTrack, Natural Point, Corvallis, OR, USA). Twenty-eight retroreflective markers (diameter: 10 mm) were attached to the skin with double-sided tape on relevant anatomical landmarks, bilaterally, that is, the superior iliac spine, iliac crest, greater trochanter region, thigh (5 cm above the center of the patella; the patella was located with the knee in an extended position), lateral and medial femoral condyles, tibial tuberosity and distal tibia (20 cm below the center of the patella), lateral and medial malleoli, posterior facet of the calcaneus, first and fifth metatarsophalangeal joints, and front tip of the cycling

shoe. The kinematic data were recorded at 100 frames per second. Individual anthropometric measures including leg length and circumference, and overall body fat estimation were measured to better estimate participant specific joint moments, in inverse dynamics calculations. The estimation of body fat was based on skinfold measurements from the biceps, triceps, subscapular, and suprailiac regions.[23] Prior to the cycling measurements, three kinematic setup bouts were recorded. First, a static bout was recorded while the subject maintained an upright standing position. Then, the subject performed four hip extensions/flexions, four hip abductions/adductions, and four circumductions to locate both the right and left hip joint centers.[24] Afterward, six reflective markers were removed bilaterally (medial malleolus, medial femoral condyles, and first metatarsophalangeal joint), such that the participants were able to pedal on the ergometer without discomfort. EMG, force, and kinematic signals were synchronized using a trigger signal from the OptiTrack system.

2.4 | Data analysis

All data were processed using MATLAB R2013a (The Mathworks Inc., Natick, MA, USA) using custom-written scripts.

2.4.1 | Fatigue

At each time point (Pre, Post, and at the end of the whole experiment), the maximal torque measured during the two maximal knee extensions was averaged to obtain the MVC torque. The percentage of voluntary activation was estimated according to the equation given by Todd et al. (2004)[25]: Voluntary activation (VA)=100×[1-(superimposed twitch/resting twitch)]. The superimposed twitch amplitude was defined as the difference between the peak torque induced by the stimulation and the voluntary torque averaged over a period of 100 ms before the stimulus artifact during MVC. The resting twitch was defined as the difference between the peak torque induced during rest after MVC and the baseline. For both the VL and VM, the amplitude of the M-waves was measured as the peak-to-peak value, and M-wave duration was measured as the peak-to-peak time difference.

2.4.2 | Motor coordination

The force signals at the pedal were low-pass-filtered at 10 Hz (third-order Butterworth filter). The total force was calculated using trigonometric procedures and resolved so that the effective force (ie, the force applied perpendicular to the crank) could be derived. The power was calculated for each leg as the product of the effective force and the linear velocity of the pedal (derived from the position of a crank axis marker).

Kinematics were low-pass-filtered at 8 Hz (fourth-order Butterworth filter). The kinematic setup bouts described above were used to determine the right and left hip joint centers using the SCoRE algorithm [26] and a specific biomechanical model including seven rigid body segments (pelvis, thighs, shanks, and feet). The biomechanical model constituted 24 degrees of freedom (DoF). Three translations and three rotations were assigned to the pelvis segment. The hip, knee, and ankle joints were modeled as ball-and-socket joints, that is, three rotational DoF. Flexion-extension, abduction-adduction, and internal-external joint angles were described by the *XYZ* Cardan sequence as proposed by the International Society of Biomechanics. The biomechanical model included the 3D local marker coordinates. A forward kinematic function was established to determine the 3D coordinates of these model-determined markers in the global bike frame as a function of the 24 unknown variables, that is, the hip, knee, and ankle joint angles and the position and orientation of the pelvis. Then, an extended Kalman filter algorithm was used to estimate the 24 unknown variables at each time step by minimizing the distance between the model-determined and actual markers measured by the motion capture system.

After having determined the position of joint centers, segment lengths and linear/angular velocities utilizing the position data from the kinematic model, the moment of inertia, segment masses, and segment centers of mass were calculated using the regression equations defined by Zatsiorsky and Yakunin.[27] Sagittal plane joint reaction forces and joint moments at the hip, knee, and ankle were then calculated by way of a conventional inverse dynamic method similar to that published by van den Bogert & De Koning.[28] Joint power was calculated as the dot product of net joint moments and joint angular velocities.

The raw EMG data were band-pass-filtered (bandwidth 10-500 Hz) and low-pass-filtered at 24 Hz (third-order Butterworth filter). The root mean square (RMS) EMG was then calculated using a 25-ms window with a 24-ms overlap for each muscle.

All EMG, kinetic, and kinematic data were resampled to obtain one value for each 5 degrees of crank displacement. Thirty consecutive pedaling cycles (selected after the first 40 cycles) were averaged to obtain representative profiles of EMG activity, pedal, hip, knee, and ankle joint power. Mean values were calculated over the full pedaling cycle and for both the extension and flexion phase determined from kinematics. The extension phase was defined as an increase in the distance between the pedal and the hip joint, and the flexion phase was defined as a decrease in this distance.[29]

2.5 | Statistics

All statistical tests were performed using SPSS 22 (IBM, Armonk, NY, USA). Data were tested for a normal distribution

using the Shapiro-Wilk test. Data violating this criterion were transformed (logarithmic, square root, or reciprocal transformation, depending on the skew). The sphericity was tested by Mauchly's sphericity test for all repeated measures ANOVA and a Greenhouse-Geisser correction for sphericity violation.

A repeated measures ANOVA was used to test the effect of the electromyostimulation protocol on MVC torque of the ipsilateral leg [within-subject factor: Time (Pre, immediatly Post, and end of the protocol)]. A paired samples *t* test was used to compare the MVC torque produced by the contralateral leg between Pre and the end of the protocol values. A paired samples *t* test was used to compare the M-wave, resting twitch, and voluntary activation level between Pre and immediatly Post on the ipsilateral leg. Because artifacts were found for three participants in the VL M-wave data and for six participants in the VM data, these data were excluded. Similarly, the VA and rest twitch data were excluded for one participant due to an artifact for the resting twitch measured post-fatigue.

To test the effect of localized quadriceps fatigue on the mechanical output during pedaling and whether this effect differed between legs, a two-way repeated measures ANOVA was performed on pedal power [within-subject factors: Leg (Ipsilateral and Contralateral) and Time (Pre, Post 1, Post 2)]. To further test the effect of fatigue on motor adaptations, an ANOVA with repeated measures (within-subject factor: Time [Pre, Post 1, Post 2]) was performed on EMG amplitude and joint power calculated over the complete cycle for each muscle/joint and leg separately. To determine where the alterations appeared during the cyclic movement, a similar repeated measures ANOVA was performed on the averaged data measured over the extension and flexion phases.

A least significance difference (LSD) adjustment was applied for all statistical tests to identify at which time point a difference occurred. The results are presented as the mean±SD. The significance level for all statistical tests was set to $P<.05$. Partial eta-squared values were calculated as effect size. Benchmarks define the effect size as small ($\eta^2=0.01$), medium ($\eta^2=0.06$), and large ($\eta^2=0.14$).[30] Individual changes for the pedal power, ankle, knee, and hip joint power between the three time points (Pre, Post 1, and Post 2) were also presented and defined as a difference larger than the typical error (SEM) calculated between the two bouts performed before the fatigue protocol.

3 | RESULTS

3.1 | Fatigue induced by the electromyostimulation protocol

Knee extension MVC torque produced by the ipsilateral leg (ie, fatigued leg) was significantly affected by the fatigue protocol (main effect of Time: $P<.001$, $\eta^2=0.585$; Figure 2A). We observed a decrease of −28.0%±6.8% ($P<.001$) immediately after the electromyostimulation protocol. Although the M-wave amplitude of the VL muscle decreased significantly post-fatigue (−12.7%±18.5%, $P=.03$, $\eta^2=0.362$, n=12), M-Wave amplitude of VM did not change significantly ($P=.113$, $\eta^2=0.284$, n=9). The M-wave duration of the two muscles remained unchanged (VL: $P=.663$, $\eta^2=0.069$, n=12; VM: $P=.624$, $\eta^2=0.031$, n=9; Figure 2C). Resting twitch amplitude decreased by −24.8%±23.4% ($P=.032$, $\eta^2=0.288$, n=14) immediatly Post. VA remained unchanged (Pre 92.9%±5.9%, immediatly Post 92.7±5.2; $P=.869$, $\eta^2=0.002$, n=14; Figure 2B).

At the end of the whole protocol, the ipsilateral leg exhibited a similar decrease in MVC torque (−21.1%±10.5%; $P=.006$) than that observed post-fatigue. The MVC torque produced by the contralateral leg was also significantly decreased, albeit much less than the ipsilateral leg (−5.9%±8.2% of Pre, $P=.02$).

3.2 | Pedal power

The chosen pedal power (350 W), normalized to the maximal power produced during the all-out sprint, corresponded to a mean relative intensity of 40.5%±5.3%. There was no effect of time ($P=.414$, $\eta^2=0.056$) on the total power output (sum of both legs; Pre: 348.5±10.8 W, Post 1: 347.8±10.9 W, and Post 2: 346.3±14.5 W). There was a significant main effect of time ($P=.004$, $\eta=0.411$) on the pedaling rate. Although the pedaling rate was similar between Post 2 (92.0±1.1 rpm, $P=1$) and Pre (91.7±1.5 rpm), it was slightly lower during Post 1 (91.2±1.2 rpm) compared with both Pre ($P=.032$) and Post 2 ($P<.001$). When the power produced by each leg was considered, a significant interaction Leg×Time was found for the power output averaged over the complete crank cycle ($P<.001$, $\eta^2=0.579$).

3.2.1 | Ipsilateral Leg

When averaged across the whole cycle, the power produced by the ipsilateral leg was significantly altered by fatigue (main effect of Time: $P<.0005$, $\eta^2=0.666$). More precisely, power was lower during Post 1 (−6.1±5.4 W; $P=.001$) and Post 2 (−9.8±5.9 W; $P<.001$) than Pre. In addition, the power output measured during Post 2 was significantly less than the power output measured during Post 1 ($P=.003$). When considering each phase separately, the power produced by the ipsilateral leg was significantly affected by fatigue during the extension phase (main effect of Time: $P<.001$, $\eta^2=0.66$, Figures 3 and 4A). The power was less during both Post 1 (−17.0±15.9 W; $P=.001$) and Post 2 (−26.0±13.9 W; $P<.0005$) than Pre and during Post 2 than Post 1 (−9.0±11.5 W, $P=.003$). The power produced by the ipsilateral leg during the flexion phase remained unchanged (main effect of Time: $P=.195$, $\eta^2=0.110$).

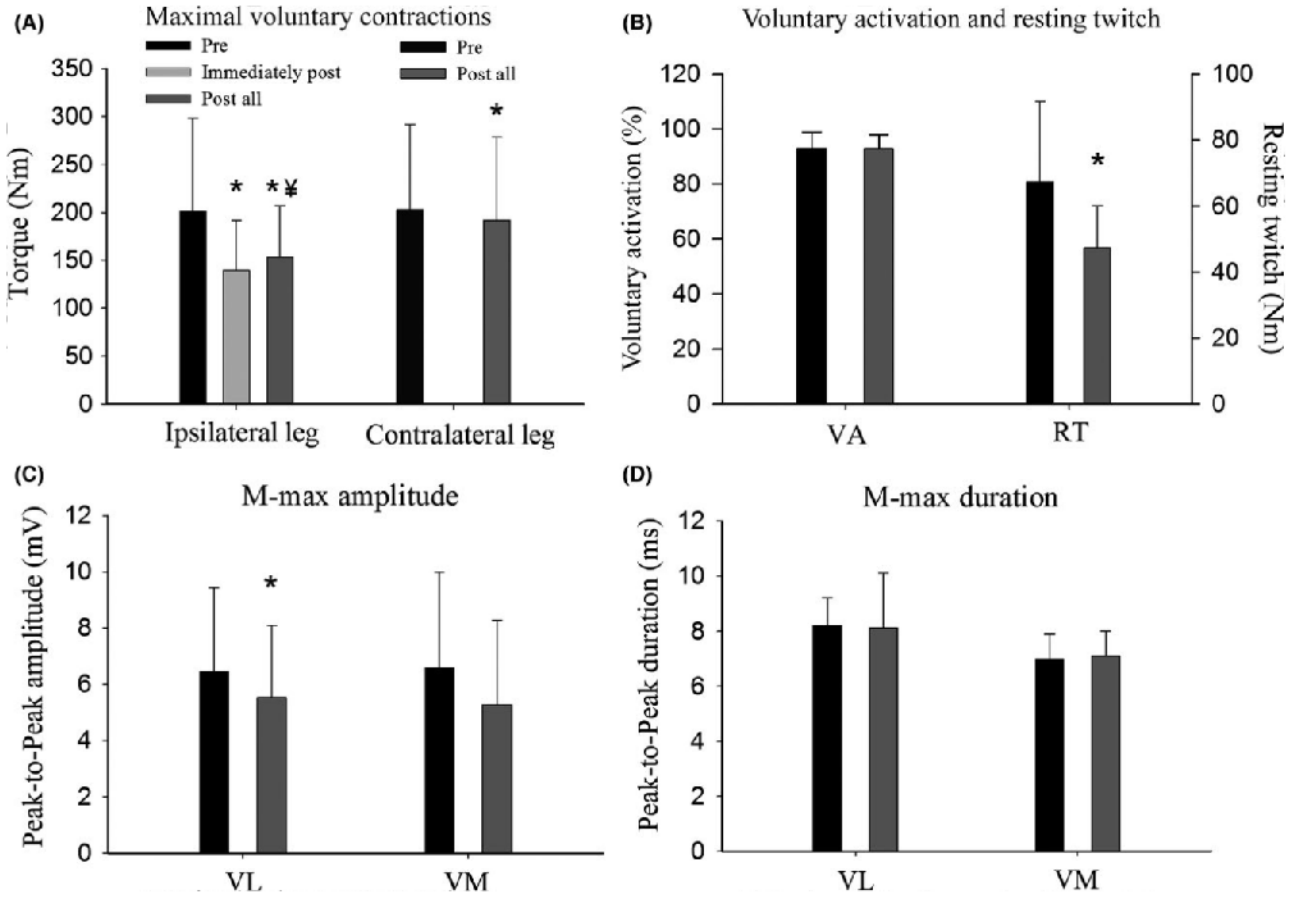

FIGURE 2 Effect of the fatigue protocol on neuromuscular function. Data were measured before (Pre; black for both legs), immediately after the fatigue protocol (light grey for the ipsilateral leg), and at the end of the whole protocol (dark grey for both legs). Panel A: MVC knee extension torque on both legs. Panel B, C, and D: neuromuscular parameters measured on the ipsilateral (fatigued) leg. Panel B: voluntary activation and resting twitch; Panel C: peak-to-peak amplitude of the M-wave measured for the vastus lateralis (VL, n=12) and vastus medialis (VM, n=9); Panel D: peak-to-peak duration of the M-wave measured for the VL and VM. *P<.05 for comparison with Pre and ¥P<.05 for comparison with immediately after the fatigue protocol

3.2.2 | Contralateral leg

When averaged across the whole cycle, the power produced by the contralateral leg was significantly altered by fatigue (main effect of Time: P<.001, η^2=0.487). The power was significantly higher during Post 1 (+5.4±5.8 W; P=.003) and Post 2 (+7.6±6.6 W; P=.001) than Pre. Although there was no significant effect of time on the power produced during the extension phase (P=.393, η^2=0.064), a significant effect was found for the flexion phase (main effect of Time: P=.004, η^2=0.323). More precisely, the power increased during Post 2 compared with Pre (+10.2±10.7 W, P=.002, Figures 3 and 4A). Note that Post 1 did not differ from Post 2 (P=.055) and Pre (P=.186).

3.3 | Joint-specific power

3.3.1 | Ipsilateral leg

There was a decrease in the knee power produced during the extension phase (main effect of Time: P<.001, η^2=0.502; Figures 3 and 4C). Knee power produced during Post 2 was less than that produced during both Pre (−22.8±12.3 W; P<.001) and Post 1 (−12.1±14 W; P=.005). The knee joint power produced during the flexion phase was not altered at any time point (main effect of Time: P=.752, η^2=0.02; Figures 3 and 4C).

The ankle joint power decreased during the extension phase (main effect of Time: P=.025, η^2=0.232), but only during Post 1 compared with Pre [−5.3±8.4 W, P=.029] (Figures 3 and 4B). No changes were observed during the flexion phase (main effect of Time: P=.281, η^2=0.087).

There was no change in hip joint power during the extension phase (main effect of Time: P=.919, η^2=0.006; Figures 3 and 4D). However, there was a significant effect of time for the flexion phase (P=.017, η^2=0.252). Hip joint power measured during both Post 1 (+6±8.1 W, P=.013) and Post 2 (+6.1±8.9 W, P=.019) was significantly higher than that measured during Pre.

3.3.2 | Contralateral leg

Knee joint power measured during the extension phase was not significantly altered by fatigue (main effect of

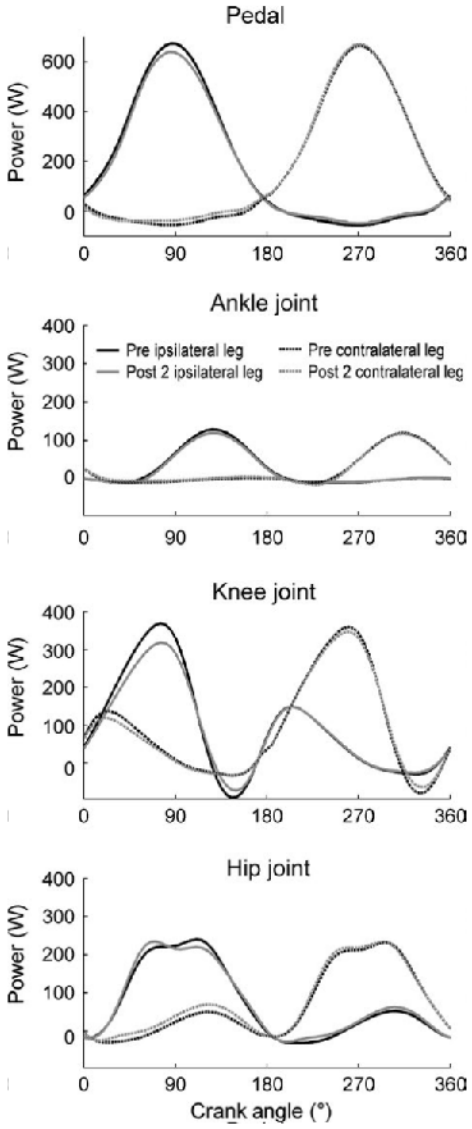

FIGURE 3 Profiles of pedal and joint power. The profile of pedal power and specific joint power at the ankle, knee, and hip level on both legs was obtained by averaging 30 pedaling cycles during the Pre (before fatigue; solid black for the ipsilateral leg and dotted black for the contralateral leg) and Post 2 bouts (after fatigue; light grey for the ipsilateral leg and dotted grey for the contralateral leg) performed at 350 W. Zero degrees corresponds to the top dead center (TDC) of the ipsilateral pedal (and hence bottom dead center of the contralateral pedal). Profiles are displayed as mean (without SD, for the sake of clarity)

Time: P=.403, η^2=0.063). A significant main effect of time was found for the flexion phase (P=.002, η^2=0.362), indicating that the knee power was less during Post 1 than both Pre (−9.4±9.6 W, P=.002) and Post 2 (−4.2±6.9 W, P=.034). No other differences were found (all post-hoc: P>.76).

The ankle power was affected by fatigue during both the extension (main effect of Time: P=.03, η^2=0.222) and the flexion phase (main effect of Time: P=.003, η^2=0.337). The ankle power produced during the extension phase was higher during Post 2 than Post 1 (+3.6±3.9 W, P=.003) but remained unchanged between all other time points (all post-hoc: P>.08). For the flexion phase, both Post 2 (+2.9±3.4 W, P=.005) and Post 1 (+2.5±3.8 W, P=.023) were higher than Pre.

There was no change in the hip joint power during the extension phase (main effect of Time: P=.28, η=0.087). In contrast, an increase in hip power was observed during the flexion phase (main effect of Time: P<.001, η^2=0.661) where both Post 1 (+12.9±9.1 W, P<.001) and Post 2 (+14.9±8.6 W, P<.001) exhibited significantly higher power than Pre. Post 1 and Post 2 were not different (P=.341).

3.4 | EMG activity

EMG data were used to determine the coordination strategies that were used to achieve the changes in kinetics presented above. Data are reported for the phase of the pedaling cycle (flexion or extension) in which the muscle under consideration was active (one phase for monoarticular muscles and both phases for biarticular muscles; Figure 5). For example, since the VM is active only during the extension phase (Figure 5), only this phase was used for the analysis and the flexion phase was neglected, and for the biarticular RF, both phases were included and used separately.

3.4.1 | Ipsilateral leg

There was a main effect of time on EMG amplitude for VM (P=.039, η^2=0.25), ST (P=.006, η^2=0.304), BF (P=.034, η^2=0.214), and TFL (P=.037, η^2=0.21). The EMG amplitude averaged over the extension phase (Figure 6) was significantly lower during Post 1 than Pre for VM (−7.1%±13.2%, P=.029), ST (−6%±7.9%, P=.005), and BF (−6.2%±9.2%, P=.009). No change was observed between Post 2 (VM, P=.074; ST, P=.107; BF, P=.31) and Pre. In contrast, the TFL EMG amplitude during the flexion phase was significantly higher during Post 2 than Pre (+10.7%±14.8%, P=.022), but Post 1 and Pre were not different (P=.216).

Finally, the EMG for the VM and VL was normalized to the M-max. As a result, no significant change was observed for either the VM/M-max (P=.867, η^2=0.007) or the VL/M-max (P=.168, η^2=0.159).

3.4.2 | Contralateral leg

Both the BF EMG amplitude and ST EMG amplitude were significantly altered by time during both the extension phase (BF: P=.047, η^2=0.223; ST: P=.023, η^2=0.237) and the flexion phase (BF: P<.001, η^2=0.507; ST: P=.003, η^2=0.347, Figure 7). When considering the extension phase, the BF EMG amplitude decreased during Post 1 compared with Pre (−6.2%±7.8%, P=.005), but no difference between Post 2 and Pre was found (P=.284). The ST EMG amplitude decreased

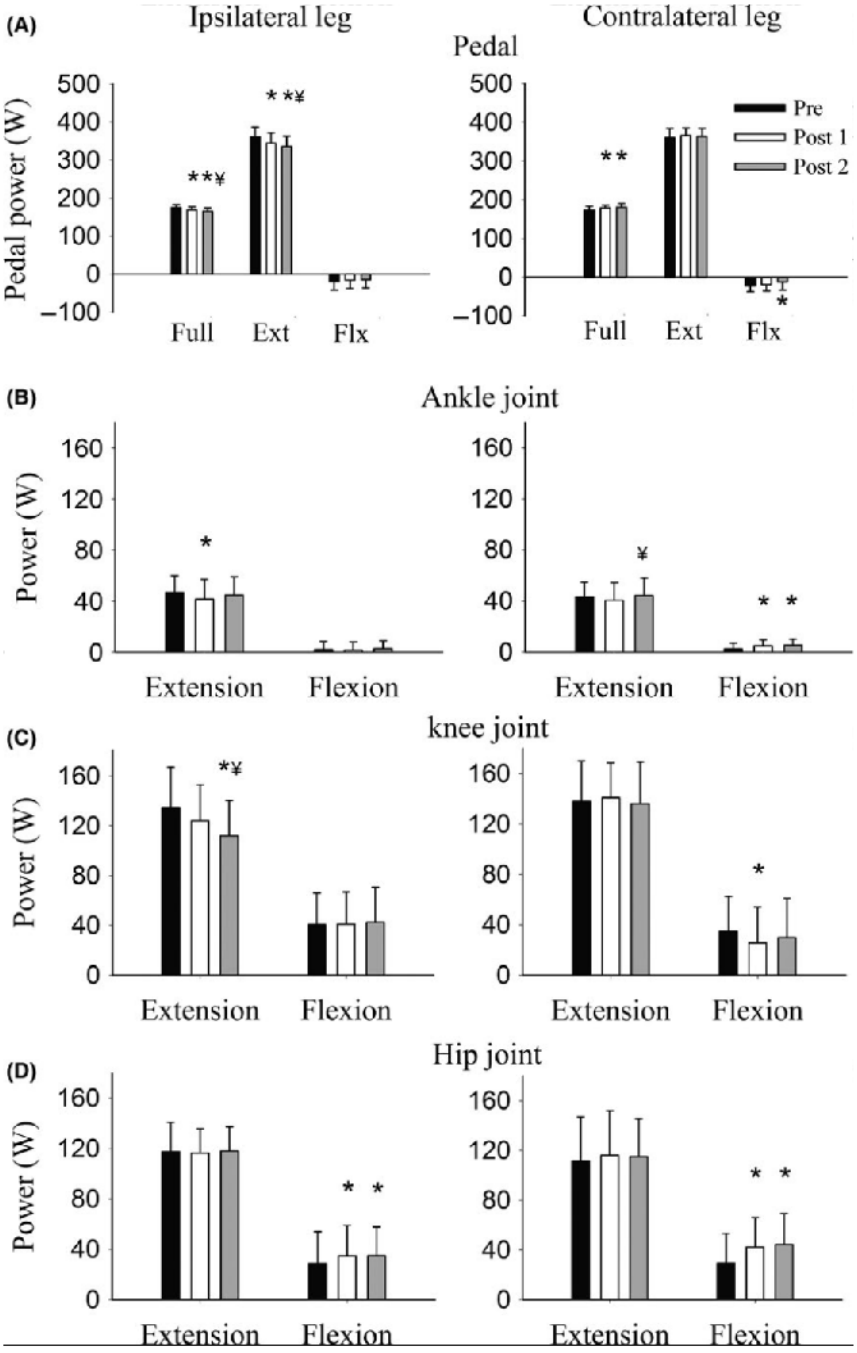

FIGURE 4 Pedal and joint power. Pedal power (Panel A) was averaged across the full pedaling cycle, the extension, and the flexion phase. Joint-specific power measured at the ankle (Panel B), knee (Panel C), and hip (Panel D) level was averaged across the extension and flexion phases. Data measured before (Pre, black) and after the fatiguing protocol (Post 1, white, Post 2, grey) for ipsilateral (left) and contralateral leg (right) are shown. *$P<.05$ for comparison with Pre and $^{¥}P<.05$ for comparison with Post 1. All tasks were performed at a constant power of 350 W

during both Post 1 (−8.4%±7.1%, $P<.001$) and Post 2 (−7.2%±8.7%, $P=.002$) compared to Pre. When considering the flexion phase, BF also decreased during Post 1 compared to Pre (−4.1%±6.7%, $P=.017$), but no difference between Post 2 and Pre was found ($P=.156$). ST EMG amplitude decreased during both Post 1 (−6.8%±8.7%, $P=.006$) and Post 2 (−4.4%±7.5%, $P=.024$) compared with Pre. A significant effect of time was found for GM EMG amplitude only during the flexion phase ($P=.039$, $\eta^2=0.206$). Specifically, there was a decrease in the EMG amplitude during Post 1 compared with Pre (−1.9%±3.4%, $P=.017$), but there was no change between Post 2 and Pre ($P=.214$). A main effect of time was found for TFL ($P=.003$, $\eta^2=0.342$) during the flexion phase with a significant increase in the EMG amplitude during Post 2 compared to both Pre (+17.7%±17.1%, $P=.003$) and Post 1 (+10.1%±15.95%, $P=.045$).

4 | DISCUSSION

This study explored the adaptations of motor coordination to unilateral quadriceps fatigue during a submaximal bilateral pedaling task. There were three major findings. First, there was no increase in activation of the fatigued muscles during the pedaling task leading to a large decrease in knee joint extension power produced by the ipsilateral leg. Second, no

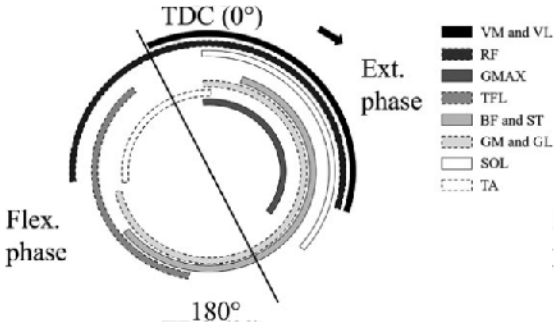

FIGURE 5 Schematic representation of the activation period of the muscles during the pedaling cycle. 11 muscles: VL, vastus lateralis and VM, vastus medialis; RF, rectus femoris; GMax, gluteus maximus; TFL, tensor fascia latae; BF, biceps femoris and ST, semitendinosus; GL, gastrocnemius lateralis and GM, gastrocnemius medialis; SOL, soleus; and TA, tibialis anterior. TDC (0°): top dead center. The extension phase (Ext. phase) and flexion phase (Flex. phase) were defined as an increase and a decrease in the distance between the pedal and the hip joint center, respectively

consistent between-joints compensation was observed within this ipsilateral leg, therefore leading to a decrease in the total pedal power produced during the extension phase. Third, to maintain the task goal (total power output and pedaling rate), participants primarily increased the power concurrently produced by the contralateral leg, during the flexion phase. Other compensations were also observed during the second phase of the pedaling cycle for both legs in some, but not all, participants.

4.1 | Fatigue induced by the electromyostimulation protocol

Knee extension MVC torque declined by >28% after the electromyostimulation protocol. It was associated with a significant decrease in both resting twitches and M-wave amplitude of the VL (Figure 2). In regard to the unchanged maximal voluntary activation, this result confirms that this protocol was effective in inducing substantial local peripheral fatigue of the knee extensor muscles with negligible effects of central mechanisms. Moreover, knee extension MVC torque remained very low at the end of the experiment, indicating that local fatigue induced persisted and remained relatively stable during the whole cycling protocol (ie, with a MVC torque decrement between 22% and 28%, Figure 2). This findings are in agreement with previous studies using electromyostimulation to induce fatigue, which showed a decrease in maximal voluntary force for >45 minutes after the fatigue protocol.[31–33] It makes us confident that fatigue lasted

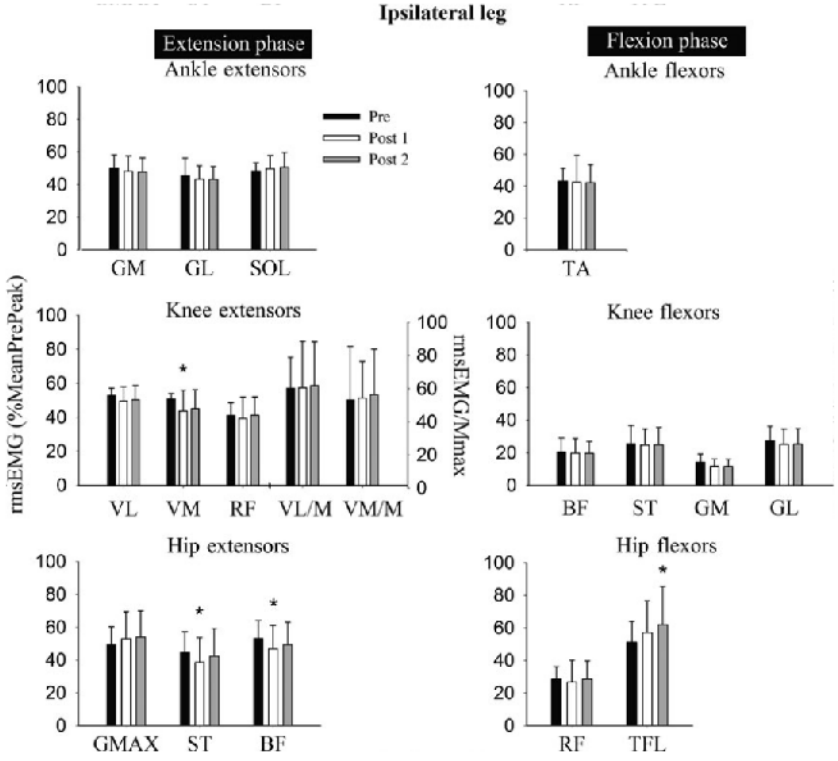

FIGURE 6 Muscle activation, ipsilateral leg. The RMS EMG data for 11 muscles averaged on both functional phases are presented. For the sake of clarity, data are only reported for the phase of the pedaling cycle (flexion or extension) during which the muscle was active (one phase for monoarticular muscles and both phases for biarticular muscles). Data were normalized to the peak value of the mean EMG pattern (30 pedaling cycles) obtained before fatigue (%MeanPrePeak) and also to M-max for VL and VM (rmsEMG/M-max). Data measured before (Pre, black) and after the fatiguing protocol (Post 1, white; Post 2, grey) are depicted (power output: 350 W). *P<.05 for comparison with Pre. BF, biceps femoris; GL, gastrocnemius lateralis; GM, gastrocnemius medialis; GMax, gluteus maximus; RF, rectus femoris; ST, semitendinosus; SOL, soleus; TA, tibialis anterior; TFL, tensor fascia latae; VL, vastus lateralis; VM, vastus medialis

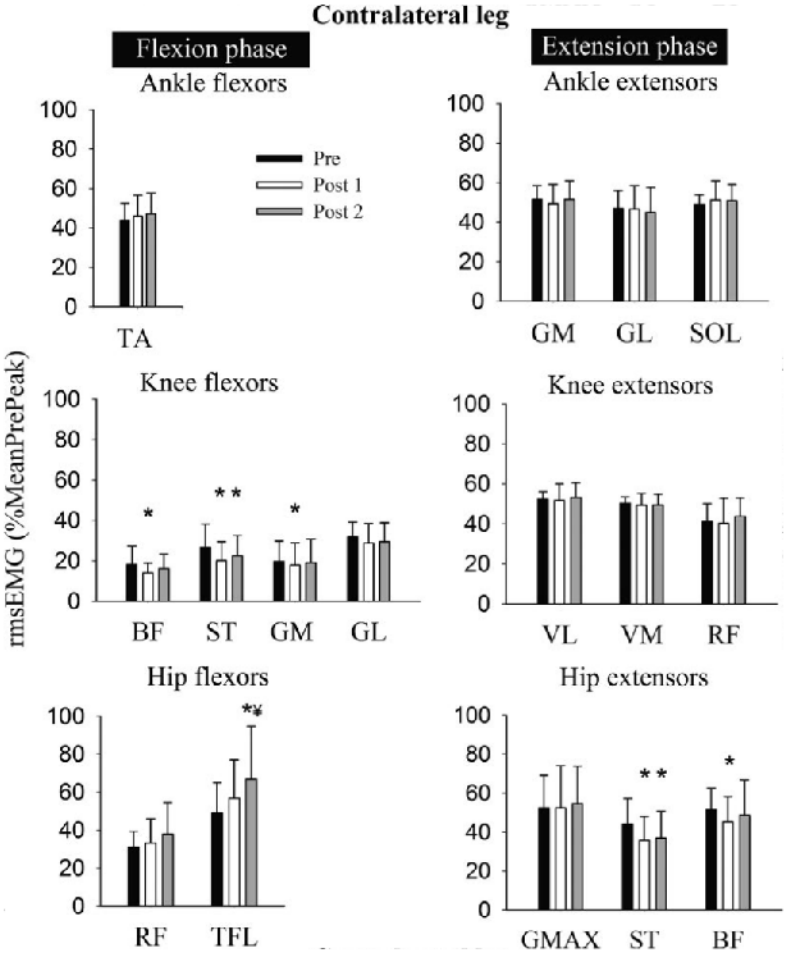

FIGURE 7 Muscle activation, contralateral leg. See caption of Figure 6 for details of abbreviations and symbols. $^{*}P<.05$ for comparison with Pre and $^{¥}P<.05$ for comparison with Post 1.

during the whole protocol and therefore that the changes in motor coordination we report originated from the unilateral quadriceps peripheral fatigue. A slight (<6%) but significant decrease in knee extension MVC torque was observed at the contralateral leg at the end of the protocol. Because no significant decrease in voluntary activation was observed, and because this fatigue was of much smaller amplitude than that observed for the ipsilateral leg, we do not believe that it interfered with the conclusions of the present study.

4.2 | Adaptations at the fatigued muscle group level

Because of the decreased force-generating capacity of the knee extensor muscles, a significant decrease in the knee extension power produced by the ipsilateral leg was observed during Post 2 (−22.8±12.3 W, Figures 3 and 4C). It is well documented that information about neural drive cannot be directly inferred from surface EMG amplitude when neuromuscular fatigue occurs.[11] We therefore considered both the amplitude and the duration of the M-wave to account for possible changes in the shape of muscle action potentials. Neither the ratio between EMG amplitude and M-wave amplitude nor the M-wave duration of the VL and VM was altered after the fatigue protocol. In line with our first hypothesis, this strongly suggests that the neural drive to these fatigued muscles did not increase during the pedaling task, thus explaining the observed decrease in knee joint extension power.

This absence of increased drive to the fatigue muscles is in discrepancy with other studies that focused on more simple tasks. For example, de Rugy et al.[13] showed during single-joint wrist movements that when the force-generating capacity of a muscle was acutely decreased, the activation of all synergist muscles (including the fatigued muscle) increased rather than increasing the recruitment of only the non-fatigued muscles. It is possible that single-joint tasks do not allow for dissociation of activation between the synergist muscles or that such dissociation requires high control costs.[14,34] Here, we studied a bilateral multijoint task that offered further solutions to the CNS, and our results demonstrate that altering the activation at the fatigued muscles is not a preferred compensation strategy during such a task. The optimal feedback control theory considers that motor coordination is optimized by minimizing a cost function, for example, energetic or effort.[35,36] Our results suggest that some optimization of effort might have occurred to avoid the increased recruitment of already fatigued (less efficient) muscles and then to prioritize other possibilities of

increasing the activation of more effective (ie, non-fatigued) muscles that are available within or between legs.

4.3 | Absence of between-joints compensation in the ipsilateral leg

It is important to consider that the decreased power of knee extensors in Post 2 led to a similar decrease in the total pedal power produced by the ipsilateral leg during the extension phase (−26.0±13.9 W). This indicates that although within-leg compensation to maintain the total power produced by the ipsilateral leg was theoretically possible (by increasing the extension power at the two other joints), this was not observed. We even observed a small decrease in the ankle extension power (only significant at Post 1; Figures 3 and 4B). This was associated with decreased activation of the biarticular muscles crossing the knee during the extension phase (significant for ST and BF at Post 1, and only trends for GM and GL, Figure 6). Overall, this result seems in line with the mechanisms underlying the reciprocal coordination of one- and two-joint muscles crossing the joint from opposite sides [1] and, more precisely, the assumption that the primary roles of biarticular muscles during a multijoint task such as cycling are (a) to distribute and transfer the net moments from proximal to distal joints; and (b) to participate in effectively orientating the force on the pedals.[19,37,38] Because the knee extension power decreased after fatigue, a lower mechanical energy needed to be transferred from the knee to the ankle, likely explaining the trend of decreased activation of the gastrocnemii muscles. Similarly, the decrease in hamstring activity in this phase might have occurred to maintain the same orientation of the force on the pedal. Overall, these results are interesting because they provide evidence that when one muscle group is functionally impaired, the strategy to compensate by simultaneously increasing the recruitment of the non-fatigued muscles within the same limb is not straightforward when other solutions exist. A similar observation was reported when pain was induced in VM.[14] In this study, no systematic compensation was observed during isometric single-leg squats despite the fact that within-leg compensation was theoretically possible between joints. Interestingly, in our study, the decrease (significant or trend) in biarticular muscle activation was not accompanied by a decrease in activation of their monoarticular synergists (Gmax and SOL). Instead, these muscles exhibited no change (or a small increase—albeit no significant), which might explain why the joint power at the hip and the ankle did not change during Post 2. Overall, this result might be related to the fact that the neural cost to redistribute the drive to different joints within the same leg is higher than that needed to change the force sharing between the legs.[14]

Note that two post-cycling bouts were used to allow for sufficient practice time for the participants to adapt to the cycling task after the fatigue protocol. The results showed that the decrease in knee joint power and in the total pedal power produced by the ipsilateral leg was larger during Post 2 than Post 1 (Figure 4A,C). Moreover, individual changes in pedal power for each respective pedaling phase were investigated during Post 1 and Post 2, based on differences larger than the typical error (SEM) calculated between Pre 1 and Pre 2. This analysis revealed that the decrease in extension pedal power produced by the ipsilateral leg was more consistently observed during Post 2 (14/15 participants) than Post 1 (12/15 participants). This practice time effect is in line with previous results showing that the recalibration of motor strategies to fit the constraints and requirements of a novel environment can require >50 cycles during gait.[39] In our study, the participants performed almost 40 pedaling cycles before the measurement period at Post 1. At Post 2, they had performed >130 cycles and, thus, might have had time of practice at this specific power to optimize the adaptation strategy. Consequently, we will only focus on the interpretation of Post 2 in the following parts of the discussion.

4.4 | Compensation strategies

Because of the reduction in the ipsilateral extension pedal power, other compensation strategies were necessary to maintain the task goal. We observed a significant increase in power produced by the contralateral leg (Figures 3 and 4A). This result is in line with our hypothesis that between-leg compensation would be a consistent strategy used by the CNS to compensate for unilateral fatigue of the knee extensors. The significant increase in power was observed during the flexion phase through an increase in hip flexion and ankle dorsiflexion power (Figures 3 and 4A). These mechanical data were confirmed by EMG data showing an increase in TFL activation and a tendency for an increase in activation of the ankle dorsiflexors (Figure 7). Inspection of data for individual participants (Figure 8) confirmed that this strategy to increase the flexion power produced by the contralateral leg was the primarily used compensation strategy (ie, observed for 11/15 participants).

There are three hypotheses for interpreting the bilateral compensation strategy observed during the flexion phase. First, as a strategy to control the numerous degrees of freedom, each leg might be controlled as a functional unit in which joints are coupled and oscillators control the flexion and extension phases.[40] In support of this neural organization, Haddad et al.[41] observed that when a unilateral additional load was applied during locomotion, participants adapted bilaterally but maintained unilateral coordination patterns. Similarly, when fatigue was induced unilaterally in our study, compensation occurred bilaterally rather than modulating individual joints within the ipsilateral leg. Second, it is important to consider that each leg participated

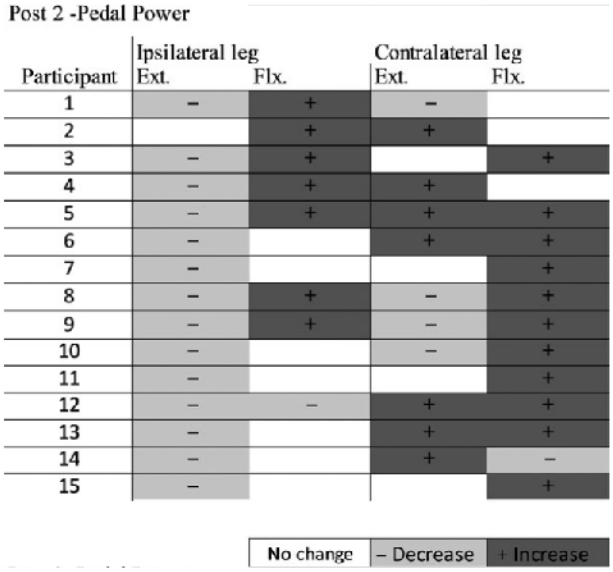

FIGURE 8 Individual changes in pedal power. For each participant, pedal power values measured after the fatiguing protocol (Post 2 at 350 W) were defined as increased (+, dark gray) and decreased (−, light gray) if they changed by more than the typical error calculated between the two bouts performed before the fatigue protocol. White denotes no change

in the net torque produced at the crank level and that the force produced by one leg was transmitted to the contralateral leg. Referring to this mechanical coupling, when unilateral localized fatigue was introduced, motor adaptations within the same temporal phase might have helped to maintain the symmetry and smoothness imposed by the task's goal (ie, maintain a constant pedaling rate and power output). This might ultimately have allowed the participants to better maintain the efficiency of movement.[42] It is important to note that because of this mechanical coupling at the crank level, a decrease in force produced by the ipsilateral leg might have been directly detected by the contralateral, non-fatigued leg. Third, this adaptation might originate from a strong neural linkage between the legs.[21,43] Considering an uncoupled pedaling task, Ting et al.[21] demonstrated that ipsilateral sensorimotor activity affects the contralateral mechanics. These authors suggested that the muscles involved in the flexion phase of the contralateral leg (ie, hip and ankle flexors) decrease their activity in response to the increased activity of those involved in the extension phase of the ipsilateral leg (knee extensors). This is in accordance with our results showing that the increased activity of the hip and ankle flexors (TFL and a tendency for TA) of the contralateral leg during its flexion phase would be related to the decreased knee joint power produced by the ipsilateral leg (Figure 4). In contrast, we did not observe any change at the knee level of the contralateral leg in which BF activity was unaffected and ST activity even decreased. This might be explained by the fact that these biarticular muscles (BF and ST) primarily act to accelerate the limb posteriorly to initiate the extension-to-flexion transition [37] and, hence, that their onset of activation precedes the observed decrease in the extension power produced by the ipsilateral leg. It is further supported by previous data demonstrating that contralateral hip/ankle flexors and hamstring muscles are differently affected by the ipsilateral sensorimotor activity.[21,44] As a whole, these results provide evidence that these hamstring muscles are controlled in such a specific way that they are not actively involved in the compensation strategy.

Because pedaling is composed of two distinct phases (extension and flexion) and the contralateral leg moves in antiphase (180°) with the ipsilateral leg, further compensation strategies were theoretically available: (a) during the flexion phase of the ipsilateral leg; and (b) the extension phase of the contralateral leg. Regarding the first possibility, we observed an increased hip joint flexion power (Figures 3 and 4D) produced by the ipsilateral leg in 7/15 participants (Figure 8). This was associated with a significant increase in TFL activation (Figure 6). However, despite the trend, this strategy did not induce a significant increase of the total flexion power on the pedal (Figure 4A). Second, no significant increased power was observed during the extension phase (ie, the most powerful phase) in the contralateral leg (Figure 4A). Indeed, inspection of individual results (Figure 8) revealed that 7/15 participants exhibited an increase in extension pedal power while 4/15 exhibited a decrease and 4/15 no change. It has been suggested that individuals use trial-and-error learning to acquire a repertoire of individual sensorimotor behaviors.[44] This in turn leads to different solutions to the problem explaining why some participants adopted these additional adaptation strategies (ie, in antiphase within the fatigued and non-fatigued legs), whereas the majority compensated during the same time phase with the contralateral leg (during the flexion of this leg).

With the results obtained in the current study, we cannot definitely conclude whether the observed between-leg compensation originates from a bilateral neural and/or the mechanical coupling imposed by the task. Whatever the origin of the observed adaptations, we believe that the fact that adaptations occurred during the flexion phase of the contralateral leg is an interesting result. When participants are asked to voluntarily increase the contribution of this phase during a submaximal non-fatiguing cycling exercise, they are consistently less energetically efficient [ie, higher metabolic cost [45]]. On the one hand, this suggests that the adaptation observed in the present study cannot be considered optimal when considering the energetic cost.[35] On the other hand, it is important to note that in addition to not being fatigued, the hip flexor muscles are known to be activated at a very low level compared with the other muscles at the submaximal power output maintained in the current study (ie, almost 15%-20% of their maximal level vs 40%-50% for the quadriceps [46]). Thus, the between-legs compensation strategy observed herein cannot definitively be considered

to be in disagreement with the minimization of the energetic cost functions. Overall, we should keep in mind that a trade-off between control costs, such as variability (smoothness) and effort (de Rugy, [13,45,48]) together with a complex interaction between the biomechanics of the task (mechanical coupling at the pedals and biphasic aspect of the task) and the underlying neural organization (neural coupling), might ultimately result in this relatively consistent strategy adopted by the participants.

5 | CONCLUSION AND PERSPECTIVES

The current study was performed to investigate whether, in a bilateral submaximal pedaling task, adaptations occurred to compensate for unilateral local muscle fatigue and maintain the task goal. Results showed that the muscle activation of the fatigued quadriceps was not altered and, consequently these muscles failed to maintain their mechanical output leading to a decrease of the knee extension power. As a result, no concurrent between-joints compensation by the non-fatigued muscles of the ipsilateral leg was observed. Then, some between-leg compensation appeared in response by predominantly increasing recruitment of non-fatigued muscles of the contralateral leg and hence the power produced simultaneously during its flexion phase. Other compensations were also observed during the opposite phase of the pedaling cycle (in both legs), but to a much lesser extent and not in all participants.

Having determined a preference to adapt between the legs in response to local muscle fatigue during this specific pedaling task, further studies are necessary to generalize this finding to other multijoint cyclical tasks; specifically by better dissociating the respective roles of the neural and mechanical couplings between the legs. Moreover, the non-negligible variability of compensation among the subjects is likely related to some differences in controlling the different cost functions such as variability (smoothness) and effort (energy cost). As a consequence, the robustness of this between-legs coordination strategy needs to be further tested, by comparing the effects of the amount of fatigue, the muscle type/group, and the intensity of the tested task as well as the influence of other perturbations such pain. This is crucial to provide a deeper understanding of the principles underlying human motor control. It is important when determining appropriate training and rehabilitation programs.

ACKNOWLEDGEMENTS

Project support was provided by the Region Pays de la Loire (ANOPACy project) and the French Ministry of Sport (14-R-23). ANOPACy is cofunded by the European Union. Europe commits itself to Pays de La Loire through Regional Development European Funds.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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Chapter 3 – Muscle fatigue induces positive changes in coordination during a sprint cycling task.

Submitted to Medicine & Science in Sports & Exercise

Research paper

Muscle fatigue induces positive changes in coordination during a sprint cycling task

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Abstract (252 words)

Purpose: This study investigated how muscle coordination is adjusted in response to a decrease in force-generating capacity of one muscle group during a sprint cycling task. **Methods:** Fifteen participants were tested during a sprint before and after a fatigue electromyostimulation protocol was conducted on the quadriceps of one leg. Motor coordination was assessed by measuring myoelectrical activity, pedal force orientation and specific power at each joints. **Results:** The decrease in the force-generating capacity of quadriceps (-28.0±6.8 %) resulted in a decrease in positive knee extension power during the pedaling task (-34.4±30.6 W; P=0.001). The activity of the main non-fatigued synergist and antagonist muscles (plantar flexors, hip extensors and hamstrings) of the ipsilateral leg decreased, leading to a decrease in joint power at the hip (-30.1±37.8 W; P=0.008) and ankle (-20.8±18.7 W; P=0.001). However, the net power around the knee was maintained during the extension phase by reducing the negative power as was the ability to effectively orientate the pedal force. Adaptations also occurred in the non-fatigued leg, exhibiting an increased power during the flexion phase (+17.9±28.3 W; P=0.026), associated with an improvement in mechanical effectiveness during both the extension and flexion phases. **Conclusion:** These results demonstrate that the nervous system readily adapts the coordination in response to peripheral fatigue. Herein, it was achieved by altering the activation of adjacent non-fatigued muscles to maintain an effective orientation of force on the pedals and by increasing the neural drive to muscles involved in the flexion phase such that the total pedal power was optimized.

Keywords: Adaptation, Multi-joint task, Joint-specific power, Motor control, Mechanical energy transfer, mechanical effectiveness

Introduction

Muscle coordination adaptations to muscle fatigue have been extensively studied during intensity-matched submaximal tasks (Bigland-Ritchie and Woods, 1984, Enoka and Duchateau, 2008). In contrast, motor adaptations in response to muscle fatigue during maximal multi-joint tasks has received much less attention. During such maximal, all-out exercises, decreased performance is classically observed early as fatigue occurs (Martin and Brown, 2009, O'Bryan et al., 2014b). To identify the muscles most affected by fatigue during a fatiguing sprint cycling exercise, studies have described either changes in electromyography (EMG) amplitude of the main lower limb muscles or changes in the power production at each joint (Hunter et al., 2003a, O'Bryan et al., 2014b). Although these studies observed a comparable decrease in muscle activation or power in specific joints, they have interpreted these adaptations differently. For Martin and Brown (2009), the larger decrease in extension power at the ankle joint reported at the end of a 30-s sprint cycling exercise would be explained by a greater reduction in the force-generating capacity of the plantar flexors compared to the other muscles. For others (Hautier et al., 2000, O'Bryan et al., 2014b), the related decreased activation of the plantar flexors and the hamstrings with fatigue would also be a consequence of the decreased force-generating capacity of the quadriceps muscles. This latter interpretation is supported by the assumed primary roles of the bi-articular muscles making: i) the observed decreased activation of gastrocnemii a possible consequence of a lower mechanical energy to be transferred from the fatigued quadriceps to the ankle joint (between-joint energy transfer principle), and ii) the observed decreased activation of hamstring, a strategy to maintain an effective orientation of the pedal force (directional constraint principle) (van Ingen Schenau et al., 1992, Raasch and Zajac, 1999).

In the aforementioned studies (Hautier et al., 2000, Martin and Brown, 2009, O'Bryan et al., 2014b), fatigue was not controlled in the sense that it was unknown which muscles were affected by fatigue and to what extent. In addition, both peripheral and central components might have been involved (Fernandez-del-Olmo et al., 2013). These are critical issues because it is not possible to determine whether a change in the activation of a specific muscle occurred as a result of an actual decrease in its force-generating capacity and/or to maintain or optimize some biomechanical characteristics of the task. Although the two control principles of bi-articular muscle coordination (i.e., between-joint energy transfer and directional constraint of force application) are widely reported and supported by simulation studies (Raasch and Zajac, 1999, Prilutsky, 2000), there is a lack of experimental evidence. Specifically, it remains unclear whether an energy transfer principle exists such that the central nervous system would decrease the drive to bi-articular muscles as a result of the decreased force-generating capacity of associated main power–producer muscles. One original approach to address these issues would consist of inducing selective fatigue in one muscle group (de Rugy et al., 2012, Bouillard et al., 2014). Furthermore, no previous studies have quantified the effect of motor adaptations on pedal force orientation, making it difficult to experimentally test the directional constraint principle.

Assuming that the main agonist muscles are maximally activated during a maximal multi-joint task, it is classically thought that the fatigue-induced decrease in force cannot be theoretically compensated by an increase in neural drive to these muscles or adjustments in motor coordination, leading to decreased performance. However, as mentioned above, the decreased activation of some bi-articular muscles may not necessarily be considered detrimental. Moreover, although some extensor muscles (quadriceps, gastrocnemii) are maximally activated during an all-out sprint cycling task, other muscles, such as the hamstrings and hip flexors, are not (Dorel et al., 2012).

These muscles are not considered to be the main contributors to cycling power, but they do contribute significantly, notably to actively pull on the pedal in the upstroke phase (Martin and Brown, 2009, Dorel et al., 2010). It is unclear whether they can maintain their activity and exhibit compensatory strategies to partly counteract the decreased force produced by the main agonists.

In the present study, we induced selective fatigue of the quadriceps muscle group. A neuromechanical approach (EMG, pedal force and estimation of joint power) was used to describe motor coordination during a sprint cycling task. We aimed to investigate whether a reorganization of the neural command to fatigue-free muscles would occur and whether such a reorganization may act to maintain some mechanical characteristics of the task such as mechanical effectiveness. In accordance with the assumed roles of bi-articular muscles in energy transfer between joints and directional constraints of force application (van Ingen Schenau et al., 1992, Hautier et al., 2000, Prilutsky, 2000, O'Bryan et al., 2014b), we hypothesized that a significant decrease in the activation level of bi-articular muscles would occur in response to decreased power at the knee. We also predicted that flexor muscles, which are not initially activated at their maximal level, would exhibit an increased activation which could be considered as a positive adaptation to limit the decrease in performance.

Method

Participants

Fifteen active and healthy male volunteers participated in this study (mean ± SD: age 23.7 ± 3.3 years, height 180.1 ± 8.1 cm, body mass 72.7 ± 8.9 kg). They had no prior cycling training experience and no history of lower limb injury. The experiment was approved by the local ethics

committee (CPP Ouest V: n°2013-A01714-41) and was conducted according to the Declaration of Helsinki. The participants provided their written informed consent.

Experimental protocol

The participants performed a series of submaximal and all-out sprint pedaling tasks before (Control) and after (Fatigue) selective fatigue was induced in the knee extensors of one leg via electromyostimulation (Figure 1). Results obtained during the submaximal pedaling tasks have been published elsewhere (Brochner Nielsen et al., 2016).

Fatigue protocol

As previously described in detail (Brochner Nielsen et al., 2016), participants sat on an isokinetic dynamometer (Biodex System 3 research, Biodex Medical, Shirley, NY, USA) with their hip and knee flexed at 90° and 80°, respectively (0° being full extension of the hip and knee). The torso and waist were strapped to the chair. Transcutaneous electromyostimulation was applied to the quadriceps muscle group of one leg (side randomized; right side n = 8 and left side n = 7) with the intent of fatiguing the whole muscle group. Electrodes (Stimex 50×90 mm, Monath Electronic) were placed over the motor points of the vastus lateralis (VL), vastus medialis (VM) and rectus femoris (RF). A fourth electrode (Stimex 80×130 mm, Monath Electronic) was placed over their proximal insertion (anode). A constant current stimulator (DS7A, Digitimer, Letchworth Garden City, UK) coupled with a train/delay generator (DG2A, Digitimer) was used to deliver a train of rectangular pulses (pulse duration = 450 μs) at 70 Hz within 3 s. Each stimulation was followed by a 3-s rest. After 15 min of stimulation (i.e., 150 contractions), a single isometric maximum voluntary contraction (MVC) was performed to assess loss of strength in the quadriceps. If the maximal torque during MVC did not decrease by ≥30% of the MVC performed before the fatigue

protocol, a final set of 50 contractions was induced. The stimulation intensity was adjusted throughout the protocol to match the maximal tolerable level. Fatigue was characterized through the assessment of MVC torque, voluntary activation (VA) level and M-waves before and after this protocol. To confirm that fatigue persisted in the leg throughout the entire experiment, two additional MVCs were performed at the end of all procedures. To check that fatigue was absent in the contralateral leg, participants performed two maximal knee extensions before the stimulation protocol and at the end of all procedures.

Pedaling task

The pedaling exercises were performed on an electronically braked cycle ergometer (Excalibur Sport; Lode, Groningen, the Netherlands). The positions of the handlebar and saddle were adjusted to fit the preferences of the participants. After a standardized warm-up (10 min pedaling at 100 W followed by 1 min 30 s at 250 W), participants performed two submaximal tasks of 1 min duration at 350 W and two 5-s all-out sprints at a fixed cadence of 90 rpm (isokinetic mode) while in a seated position. The order of the cycling bouts was randomized to avoid any confounding effects related to the repetition of the exercises. Note that the two 350-W bouts were performed to address a different research question (Brochner Nielsen et al., 2016) and were therefore not considered for the present study. The same pedaling tasks were then repeated within a period of 3 min after the fatigue protocol, but only one all-out sprint was performed to avoid additional fatigue. The 2D pedal forces, lower limb kinematics and myoelectrical activity of 11 muscles (bilaterally) were recorded during the pedaling tasks.

Materials and procedures

Neuromuscular tests. VA and M-wave were measured using supramaximal stimulation of the femoral nerve and concurrent measurements of torque and the EMG signal of vastus lateralis (VL) and vastus medialis (VM). Because these data have been reported in a previous paper (Brochner Nielsen et al., 2016), they are not presented in detail herein, but they are discussed in the Discussion section.

Pedal forces. The ergometer was equipped with instrumented pedals to measure 2D forces (VélUS group, Canada; for details, see Dorel et al., 2009). Briefly, cartesian components of the force on the pedal corresponding to the horizontal and vertical components were measured during the cycling trials. To create a solid shoe–pedal interface, the pedals had a clipless configuration compatible with LOOK KEO cleats. All data from the instrumented pedals were digitized at 1000 Hz with a Mega data logger (ME6000, Mega Electronics Ltd.).

Kinematics. Three-dimensional kinematic data were recorded using an optoelectronic motion capture system composed of nine cameras (Flex13, 1.3 Mpx, OptiTrack, Natural Point, USA). Twenty-eight retro-reflective markers (diameter: 10 mm) were attached to the skin with double-sided tape on relevant anatomical landmarks bilaterally (i.e., the anterior-superior iliac spine, postero-superior iliac spine, greater trochanter region, thigh [5 cm above the center of the patella and located with the knee extended], lateral and medial femoral condyles, tibial tuberosity and distal tibia [20 cm below the center of the patella], lateral and medial malleoli, posterior facet of the calcaneus, first and fifth metatarsophalangeal joints and front tip of the cycling shoe). Additional markers were placed on the frame of the ergometer and on both pedals.

The kinematic data were recorded at 100 Hz. Body fat was estimated and segment length/circumference was measured (Zatsiorsky and Seluyanov, 1985), and both were included in

the inverse dynamics model. The estimation of body fat was based on skinfold measurements from the biceps, triceps, subscapular and supra-iliac regions (Durnin and Womersley, 1974). At the beginning of the experimental session, three kinematic setup bouts were recorded. First, a static bout was recorded while the participants maintained an upright standing position. The participants then performed four hip extensions/flexions, four hip abductions/adductions and four circumductions to locate both the right and left hip joint centers (Begon et al., 2007). Afterward, six reflective markers were removed bilaterally (medial malleolus, medial femoral condyles and first metatarsophalangeal joint) to enable the participants to pedal on the ergometer without discomfort. EMG, force and kinematic signals were synchronized using a trigger signal from the optoelectronic motion capture system.

Electromyography. Myoelectrical activity of 11 muscles was recorded bilaterally using surface electromyography electrodes (diameter of the recording area: 5 mm; Covidien, Kendall; inter-electrode distance of 20 mm) placed over the tibialis anterior (TA), soleus (SOL), gastrocnemius lateralis (GL), GM, VM, VL, RF, BF, semitendinosus (ST), GMax and tensor fascia latae (TFL). Before electrode application, the skin was shaved, abraded and cleaned to reduce impedance. All cables and electrodes were well secured to the skin using adhesive tape. The EMG signals were pre-amplified close to the electrodes (×1000) and digitized at 1000 Hz using two synchronized EMG amplifier units (ME6000, Mega Electronics Ltd.).

Data analysis

All data were processed in MatLab R2013a (The Mathworks Inc., USA) using custom-written scripts. The force and kinematic signals were low-pass filtered at 10 Hz with a second-order Butterworth filter. The effective force (the force applied perpendicular to the crank) was derived using trigonometry using 2D pedal forces and pedal angle in the sagittal plane measured by

reflective markers placed on the pedal and a potentiometer. The index of mechanical effectiveness (IE) was calculated as the ratio between the effective force and the norm of the total force applied to the pedal. The external power generated at each pedal (pedal power) was calculated as the product of effective force and the norm of the velocity of the pedal. A biomechanical model consisting of 24 degrees of freedom was created. Joint centers were determined using the SCoRE algorithm (Ehrig et al., 2006), and joint angles were described using an XYZ Cardan sequence, following the recommendations of the International Society of Biomechanics. The local 3D marker coordinates in the biomechanical model were used to estimate marker positions in the global bike frame by way of a forward kinematic function and an extended Kalman filter (Fohanno et al., 2014). The 2D joint reaction forces and net torque for the ankle, knee and hip were derived using a conventional inverse dynamics method (for details, see (Brochner Nielsen et al., 2016). The specific-joint power at each joint was calculated as the dot product of the joint moment force and joint angular velocity.

The raw EMG data were band-pass filtered (bandwidth 10-500 Hz), root mean squared (RMS, 25-ms window) and low-pass filtered at 24 Hz (second-order Butterworth filter). All EMG data and data issued from the inverse kinematics and dynamics methods were resampled to obtain one value for every 5 degrees of crank displacement. Pedaling cycles were detected using transistor–transistor logic rectangular pulses at the highest position of the right pedal (top dead center). The five most powerful pedaling cycles (excluding the first one) then were extracted from each sprint trial and averaged to obtain representative profiles of i) pedal power, ii) index of effectiveness, iii) muscle EMG amplitude and iv) specific-joint power. To provide a deeper understanding of the overall coordination strategy, data were also averaged in each phase (i.e., extension and flexion of the lower limb). Based on classical data reported in the literature (Elmer et al., 2011, Dorel et al.,

2012), extension was defined as a crank angle between 340° and 160° and flexion as between 160° and 340°; with 0° indicating the vertical position of the crank. For the sake of clarity, EMG data are only reported for the phase in which the muscle under consideration was active (one phase for mono-articular muscles, two phases for bi-articular muscles).

Statistics

Statistical tests were performed using STATISTICA (V8, StatSoft, Inc., USA). The Shapiro-Wilk test was used to test for a normal distribution. Data violating this criterion were transformed depending on the skew (logarithmic, square root or reciprocal transformation). A repeated-measures analysis of variance was used to test the effect of the fatiguing protocol on the MVC torque of the fatigued leg (within-subject factor: Time [Control, Fatigue and end of the protocol]). A paired samples *t*-test was used to compare the Control and end of protocol MVC torque values of the non-fatigued leg. A paired samples *t*-test was also used to compare the Control and immediately post–fatigue protocol M-wave, resting twitch and voluntary activation level of the fatigued leg.

For the pedaling task, a paired samples *t*-test was used to determine whether the total pedal power output (sum of both legs) was affected by condition (Control, Fatigue). A two-way repeated-measures analysis of variance was used to determine the effects of legs and conditions on pedal power and IE averaged over the full pedaling cycle (within-subject factors: Leg [fatigued and non-fatigued] and Condition [Control, Fatigue]). Post hoc analyses were performed using the Bonferroni adjustment for multiple comparisons. To further determine the effect of fatigue on muscle coordination and where the alterations occurred during the crank cycle, paired samples *t*-tests were used to compare data averaged over the extension and flexion phases (pedal power, IE, EMG activity and specific-joint power) between Control and Fatigue conditions. An additional paired sampled *t*-test was performed specifically for the average positive and negative knee joint

power over the extension phase between Control and Fatigue conditions. The significance level was set to $P < 0.05$. All results presented below are presented as mean ± SD.

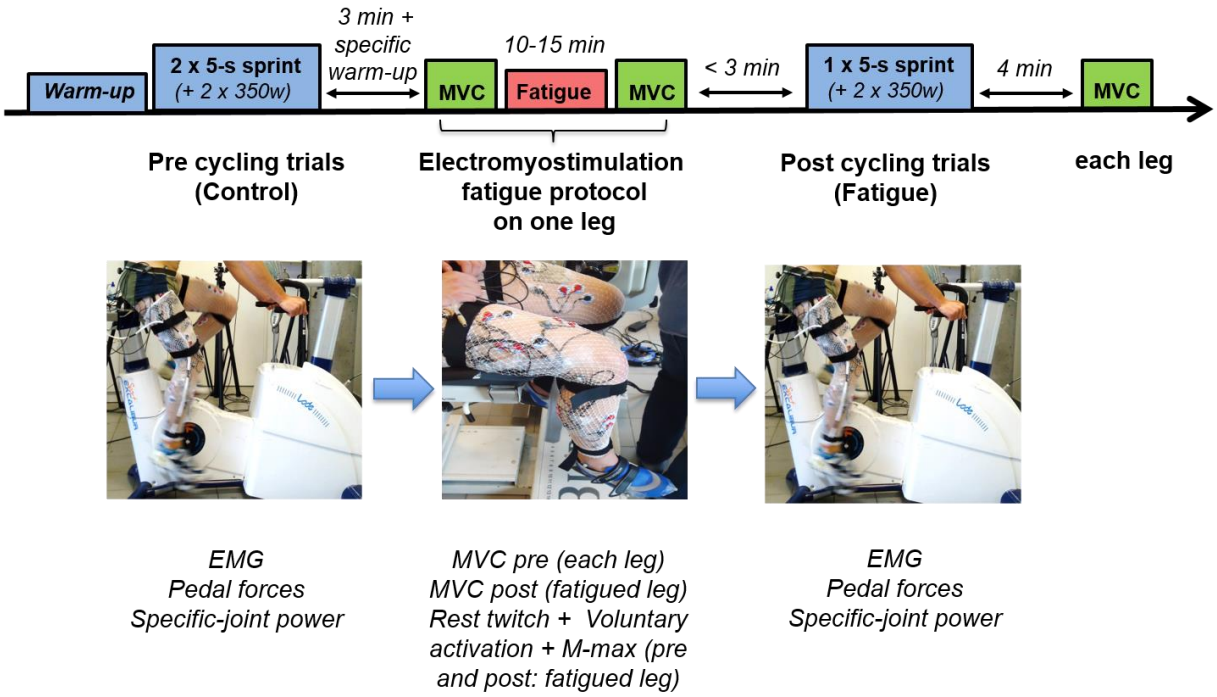

Figure 1: Experimental setup. Participants performed an all-out pedaling sprint both before (Control) and after (Fatigue) an electromyostimulation protocol that selectively fatigued the knee extensor muscles of one leg. The order of the cycling tasks (i.e. 350 W vs. Sprint) was randomized. The submaximal bouts at 350w was not included in the current study.

Results

Neuromuscular fatigue

Data have been reported in detail in a previous paper (Brochner Nielsen et al., 2016). Briefly, and in relation to the specific aim of this study, knee extension MVC torque produced by the fatigued leg decreased by 28.0 ± 6.8% ($P < 0.001$) immediately after the fatigue protocol and remained at this low level at the end of the entire protocol (–21.1 ± 10.5%; $P = 0.006$ compared to Control). At the end of the fatigue protocol, resting twitch amplitude decreased by 24.8 ± 23.4% ($P = 0.032$), but voluntary activation was unchanged ($P = 0.869$). The MVC torque produced by the non-

fatigued leg was slightly decreased at the end of the protocol when compared to Control (–5.9 ± 8.2%; P = 0.020).

Table 1: Pedal power, index of effectiveness, specific-joint power and range of motion at the ankle, knee and hip. Data are displayed as mean±SD during both the Fatigue and Control condition at both the fatigued (left panel) and non-fatigued leg (right panel). Change signifies the difference between the Control and Fatigue condition (Fatigue-Control) and P-values are provided in bold.

	Fatigued leg				**Non-fatigued leg**			
Pedal power (W)	Control	Fatigue	Change	P	Control	Fatigue	Change	P
Full cycle	443.9 ± 59.8	418.4 ± 50.9	**-25.5 ± 22.5**		433.2 ± 78.2	433.5 ± 68.7	0.3 ± 25.6	
Extension phase	762.9 ± 88.6	696.0 ± 78.4	**-66.9 ± 34.3**	**<0.001**	752.3 ± 112.9	736.4 ± 95.7	-15.9 ± 38.2	
Flexion phase	97.6 ± 66.1	117.1 ± 54.5	**19.5 ± 21.9**	**0.004**	86.8 ± 69.7	104.7 ± 66.3	**17.9 ± 28.3**	**0.026**
IE (%)	Control	Fatigue	Change		Control	Fatigue	Change	
Full cycle	58.7 ± 17.3	64.7 ± 14.2	6 ± 5.7	**<0.001**	53.5 ± 14.8	63.7 ± 13.5	10.1 ± 9.7	**<0.001**
Extension phase	66.3 ± 5.6	66.0 ± 6.2	-0.3 ± 2.5		65.2 ± 7.6	68.1 ± 6.4	**3 ± 3.3**	**0.004**
Flexion phase	50.5 ± 33.5	63.2 ± 28.2	**12.7 ± 10.4**	**0.001**	40.9 ± 27.9	58.8 ± 24.9	**17.9 ± 18.9**	**0.003**
Ankle joint power (W)	Control	Fatigue	Change		Control	Fatigue	Change	
Extension phase	139.8 ± 34.2	119.0 ± 25.2	**-20.8 ± 18.7**	**0.001**	128.8 ± 34.4	117.0 ± 32.6	**-11.8 ± 15.5**	**0.011**
Flexion phase	12.5 ± 13.1	11.2 ± 10.6	-1.3 ± 6.7		15.7 ± 12.8	15.0 ± 13.5	-0.7 ± 7.8	
Knee joint power (W)	Control	Fatigue	Change		Control	Fatigue	Change	
Extension phase	136.7 ± 55.8	121.5 ± 40.8	-15.2 ± 47.4		149.9 ± 47.3	160.2 ± 43.5	10.3 ± 26.8	
Positive ext.	203.2 ± 35.8	168.8 ± 35.9	**-34.4 ± 30.6**	**<0.001**	213.1 ± 43.8	213.5 ± 43.0	0.4 ± 17.9	
Negative ext.	-66.5 ± 36.2	-47.2 ± 21.5	**19.3 ± 23.8**	**0.009**	-63.2 ± 24.6	-53.3 ± 18.3	**9.9 ± 17.8**	**0.048**
Flexion phase	170.7 ± 63.7	167.4 ± 62.2	-3.3 ± 20.8		158.0 ± 52.0	143.0 ± 61.2	**-15.0 ± 27**	
Hip joint power (W)	Control	Fatigue	Change		Control	Fatigue	Change	
Extension phase	329.9 ± 71.6	299.8 ± 64.3	**-30.1 ± 37.8**	**0.008**	317.2 ± 48.3	298.2 ± 46.8	**-18.9 ± 27.2**	**0.017**
Flexion phase	5.4 ± 55.7	18.2 ± 53.2	12.8 ± 25.2		8.8 ± 49.0	39.8 ± 48.5	**31.0 ± 25.2**	**<0.001**
Range of motion (°)	Control	Fatigue	Change		Control	Fatigue	Change	
Ankle joint	49.9±8.2	48.8±8.3	-1 ± 4.5		48.3±10.7	47.5±12.1	-0.8 ± 3.9	
Knee joint	84.2±8.4	79.3±7.2	**-5 ± 3.8**	**<0.001**	83.9±7.2	82.9±6.1	-1 ± 3.6	
Hip joint	43.7±4.4	41.5±4.8	**-2.1 ± 2.8**	**0.01**	43.8±4.5	43.4±3.5	-0.4 ± 2	

Pedal power and index of effectiveness

The total pedal power output (sum of both legs) during the cycling sprint was significantly reduced after the fatigue protocol (Control: 877.2 ± 132.5 W; Fatigue: 851.9 ± 115.9 W; P = 0.033). We observed a significant interaction of Leg × Condition (P < 0.001) on the power output averaged over the whole crank cycle (Table 1; Figure 2). The power produced by the fatigued leg was lower

during the Fatigue condition than Control (–25.5 ± 22.5 W; $P < 0.001$), whereas the power output produced by the non-fatigued leg did not change significantly ($P = 1.0$). Further analysis showed that the power produced by the fatigued leg during the extension phase significantly decreased (–66.9 ± 34.3 W; $P < 0.001$) during the Fatigue condition, whereas the power produced during the flexion phase increased (+19.5 ± 21.9 W; $P = 0.004$). The power output produced by the non-fatigued leg during its extension phase was not significantly altered ($P = 0.195$) during Fatigue compared to Control, and the pedal power during flexion significantly increased during Fatigue (+17.9 ± 28.3 W; $P = 0.026$).

There was neither a main effect of Leg ($P = 0.4$) nor an interaction of Leg × Condition ($P = 0.07$) on IE averaged over the full pedaling cycle. However, a main effect of Condition ($P < 0.001$) was observed, showing a higher IE (fatigued leg: +6.0 ± 5.7%; non-fatigued leg: +10.2 ± 9.7%) during Fatigue than during Control. Inspection of each phase of the pedaling cycle revealed that the IE of the fatigued leg did not change ($P = 0.643$) during the extension phase, but it significantly increased during flexion in Fatigue compared to Control (+12.7 ± 10.4%; $P < 0.001$). For the non-fatigued leg, IE significantly increased during both the extension (+2.9 ± 3.3%; $P = 0.004$) and the flexion phase (+17.9 ± 18.9%; $P = 0.003$).

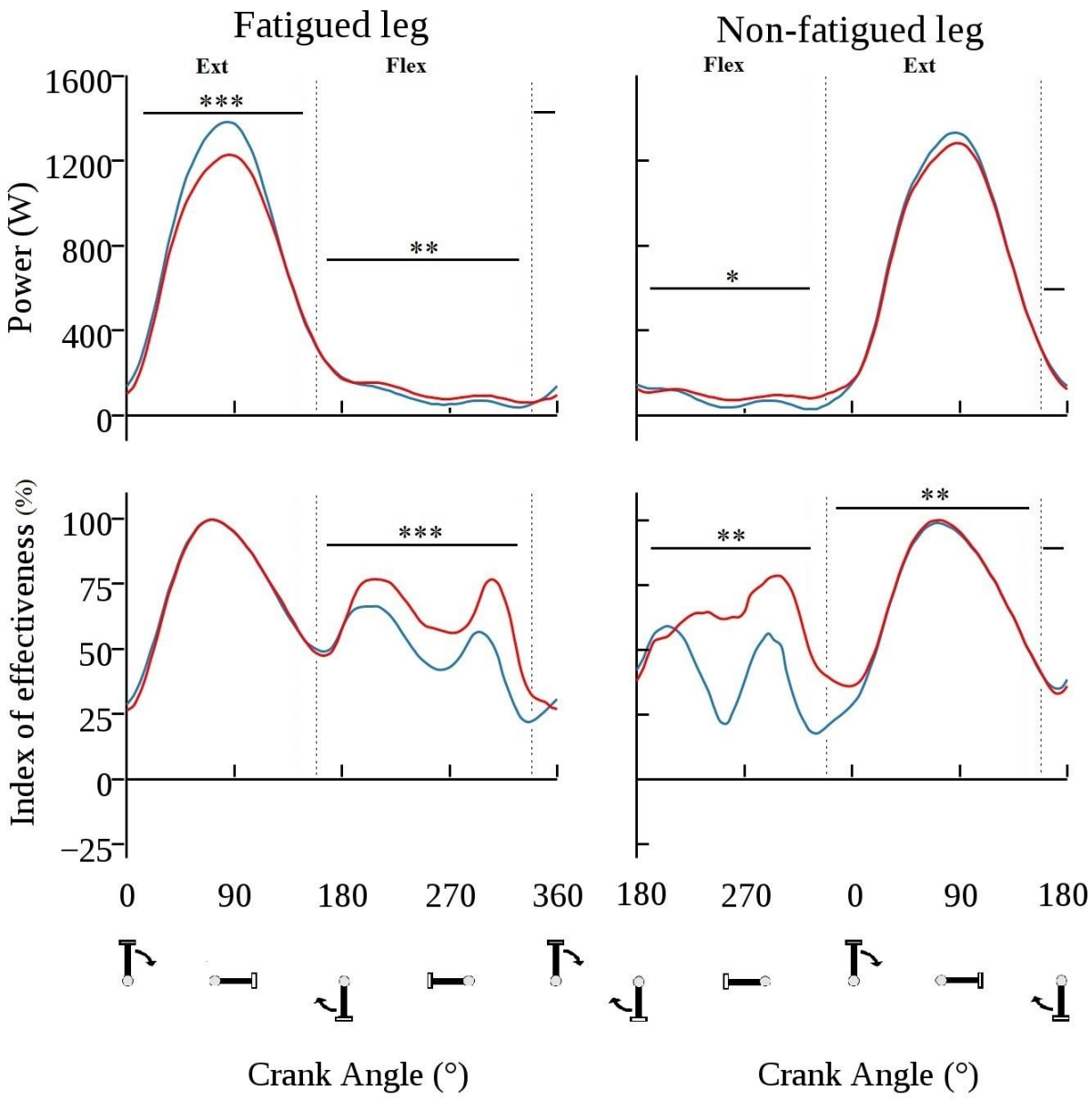

Figure 2: Pedal power and IE. The profile of pedal power and index of effectiveness level on both legs was obtained by averaging 5 pedaling cycles during the Control (blue) and Fatigue bouts (red). Zero degrees corresponds to the top dead center (TDC) of the pedal at the fatigued leg (and hence bottom dead center of the non-fatigued leg). The pedal position is indicated below the x-axis. Profiles are displayed as mean (without SD) for the sake of clarity. * signifies P<0.05, ** P<0.005, *** P<0.0005 for the results averaged during the extension and flexion phase (as indicated by the solid black line)

Joint-specific power

Fatigued leg. When considering the extension phase, the hip joint power was lower during Fatigue than Control (-30.1 ± 37.8 W; P = 0.008). No change was observed during the flexion phase (P = 0.068) (Table 1; Figure 3). The mean power produced by the knee joint during the extension phase was not affected by Fatigue (P = 0.236). Of note, during this phase, the knee joint power exhibited both a positive and negative component (Figure 3); the positive component significantly decreased (–34.4 ± 30.6 W; P < 0.001), whereas the power in the negative component increased (i.e., became less negative: +19.3 ± 23.8 W; P = 0.007). The knee joint power produced during the flexion phase remained unaltered by Fatigue (P = 0.546) (Table 1; Figure 3). The ankle joint power produced during the extension phase significantly decreased during Fatigue (–20.8 ± 18.7 W; P = 0.001), but no changes were observed during the flexion phase (P = 0.469).

Non-fatigued leg. When considering the extension phase, the hip joint power was lower during Fatigue than Control (–19 ± 27.2 W; P = 0.017; Table 1; Figure 3). In contrast, during the flexion phase, the hip joint power was higher during Fatigue than Control (+31 ± 25.2 W; P < 0.001). The knee joint power did not change during the extension phase in the Fatigue condition (P = 0.158). The positive component of the knee extension power also did not change, but the power in the negative component increased significantly (i.e., became less negative: +9.9 ± 17.8 W; P = 0.048). When considering the flexion phase, the knee joint power did not change significantly during Fatigue despite a tendency to decrease (–15 ± 27 W; P = 0.051). The ankle joint power produced during Fatigue was lower during the extension phase (–11.8 ± 15.5 W; P = 0.011) and remained unchanged during the flexion phase (P = 0.737).

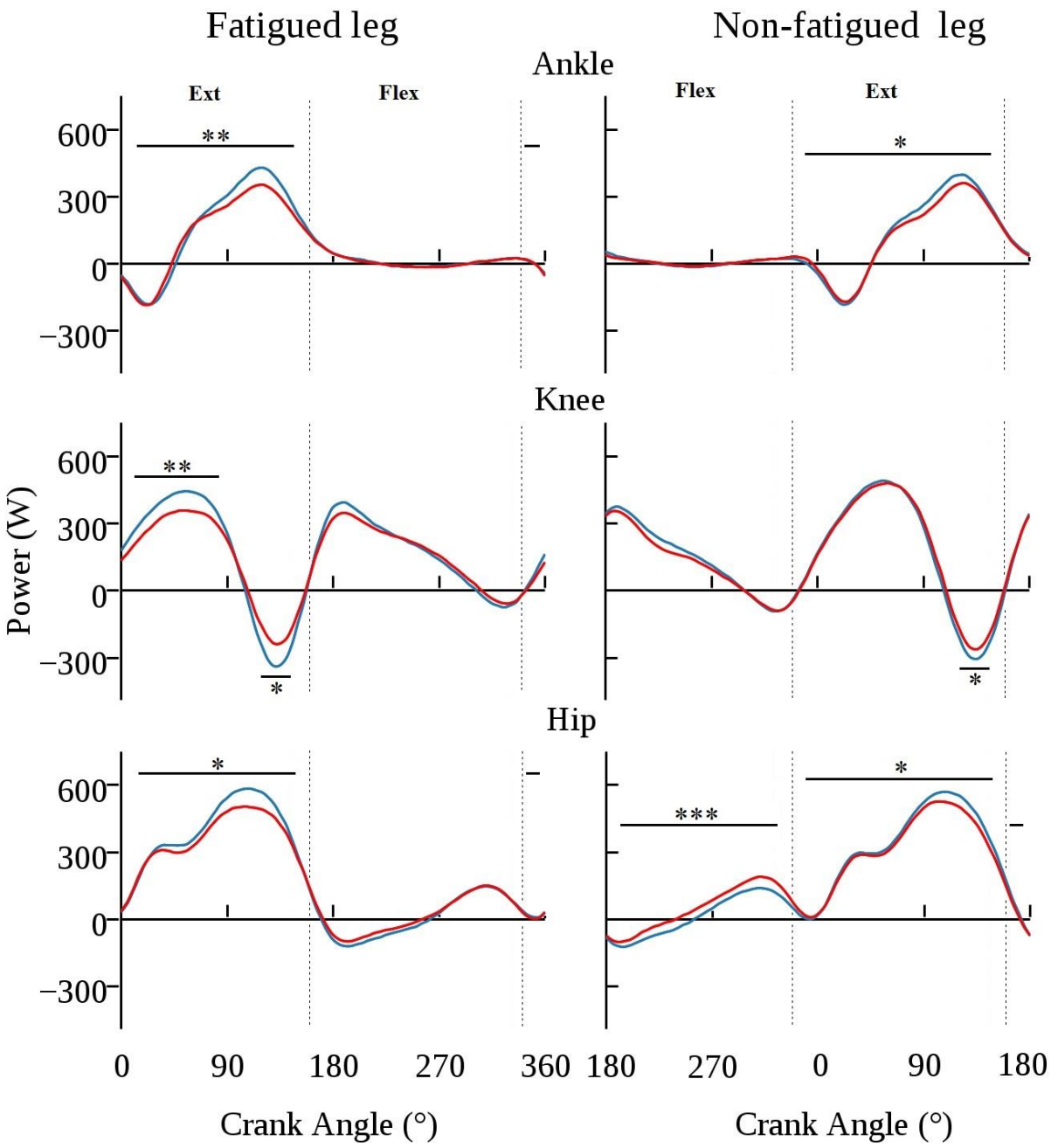

Figure 3: Joint power. The profile specific-joint power at the ankle, knee and hip level on both legs was obtained by averaging 5 pedaling cycles during the Control (blue) and Fatigue bouts (red). Zero degrees corresponds to the top dead center (TDC) of the pedal at the fatigued leg (and hence bottom dead center of the non-fatigued leg). Profiles are displayed as mean (without SD) for the sake of clarity. * signifies $P<0.05$, ** $P<0.005$, *** $P<0.0005$ for the results averaged during the extension and flexion phase (as indicated by the solid black line). An additional calculation was performed for the knee joint, averaging positive and negative power respectively.

EMG activity

Fatigued leg. When considering the extension phase of the fatigued leg, we observed a decrease in EMG amplitude during Fatigue compared to Control for all muscles (range: –5.8 % to –19.2 %; VL [P = 0.02], VM [P = 0.009], RF [P < 0.001], GMAX [P = 0.008], ST [P = 0.001], GM [P = 0.035], GL [P = 0.009] and SOL [P = 0.046], except for BF [P = 0.090]; Table 2; Figure 4). During the flexion phase, only the RF muscle exhibited a decrease in EMG amplitude after fatigue (–17.5 ± 17.6%; P < 0.001).

Non-fatigued leg. When considering the extension phase of the non-fatigued leg, a decrease in EMG amplitude was observed during Fatigue for some muscles (range: –6.9 % to –19.5 %; VM [P = 0.014], GMAX [P = 0.004], BF [P = 0.002], ST [P < 0.001], GL [P = 0.001] and SOL [P = 0.027]) but not all (VL, RF and GM; all P values >0.102; Table 2; Figure 4). During the flexion phase, the EMG amplitude of both BF (–13.0 ± 16.4%; P = 0.004) and ST (–10.9 ± 26.1%; P = 0.038) was lower during Fatigue than Control. The EMG amplitude of RF (P = 0.102), GM (P = 0.103), GL (P = 0.139) and TA (P = 0.150) remained unchanged. Only the activity level of TFL increased significantly during this phase (+27.5 ± 37.6%; P = 0.015) (Table 2; Figure 4).

rms EMG (au.)	**Fatigued leg**		**Non-fatigued leg**	
EXTENSION	Change (%)	P	Change (%)	P
SOL	**-5.8 ± 10.8**	**0.046**	**-6.9 ± 12.1**	**0.027**
GL	**-6.9 ± 10.5**	**0.009**	**-11.3 ± 11.2**	**0.001**
GM	**-8.8 ± 13.9**	**0.035**	-5.2 ± 9.4	
VL	**-11.7 ± 16.5**	**0.02**	-5.2 ± 15	
VM	**-18.5 ± 23**	**0.009**	**-7.6 ± 11**	**0.014**
RF	**-19.2 ± 12.8**	**<0.001**	-4.9 ±12.5	
BF	-8.2 ± 14.1		**-10.4 ± 9.9**	**0.002**
ST	**-15.7 ± 14.4**	**0.001**	**-19.5 ± 13.3**	**0**
GMAX	**-15.4 ± 18.4**	**0.008**	**-7.8 ± 12**	**0.004**

rms EMG (au.)				
FLEXION	Change (%)	P	Change (%)	P
TA	-7.1 ± 16.6		5.3 ± 14.3	
GL	-4.7 ± 15.2		-6.9 ± 13.8	
GM	-2.5 ± 27		-9.9 ± 19.1	
RF	**-17.5 ± 17.6**	**0.003**	-8.6 ± 22.9	
BF	-0.9 ± 26.9		**-13 ± 16.4**	**0.004**
ST	0.0 ± 26		**-10.9 ± 26.1**	**0.038**
TFL	9.5 ± 23		**27.5 ± 37.6**	**0.015**

Table 2: EMGrms data for all muscles active during the extension (top panel) and flexion (bottom panel) phase respectively. Data are displayed as mean±SD during both the Fatigue and Control condition at both the fatigued (left panel) and non-fatigued leg (right panel). Change signifies the difference between the Control and Fatigue condition (Fatigue-Control) and P-values are provided in bold. Muscles included the tibialis anterior (TA), soleus (SOL), gastrocnemius medialis (GM), gastrocnemius lateralis (GL), vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), biceps femoris (BF), semitendinosus (ST), tascia fascia latae (TFL), gluteus maximus (GMAX).

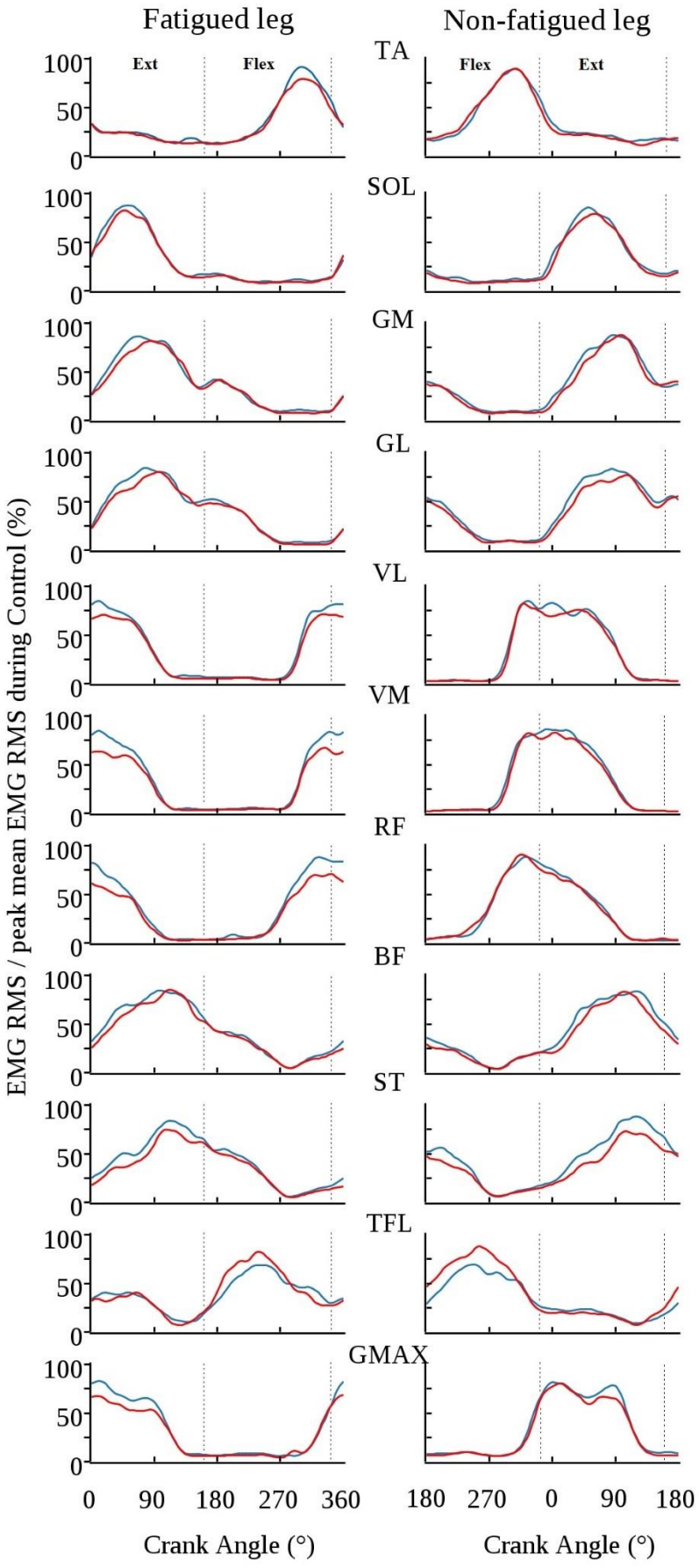

Figure 4: Muscle activity patterns. The profile 11 muscles on both legs (22 in total) was obtained by averaging 5 pedaling cycles during the Control (blue) and Fatigue bouts (red). From the top and down; tibialis anterior (TA), soleus (SOL), gastrocnemius medialis (GM), gastrocnemius lateralis (GL), vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), biceps femoris (BF), semitendinosus (ST), tascia fascia latae (TFL), gluteus maximus (GMAX). Data was normalized to the peak mean EMGrms during Control. Zero degrees corresponds to the top dead center (TDC) of the pedal at the fatigued leg (and hence bottom dead center of the non-fatigued leg). Profiles are displayed as mean (without SD) for the sake of clarity. flexion phase (as indicated by the solid black line). An additional calculation was performed for the knee joint, averaging positive and negative power respectively.

Discussion

The present results highlight two major adjustments of motor coordination that occurred during an all-out sprint pedaling task when the force-generating capacity of the quadriceps of one leg was experimentally decreased. First, in the leg affected by the fatigue protocol, the reduction in positive knee extension power observed during the extension phase was accompanied by decreased activation of the bi-articular hamstrings and gastrocnemii as well as the monoarticular gluteus maximus and soleus muscles. Although these adaptations led to decreased hip and ankle extension power, they might have participated in limiting the decrease in total pedal power by maintaining the net knee joint power and mechanical effectiveness during this powerful phase. Second, a significant increase in both muscle activation and pedal power was observed during the flexion phase of both legs. Interestingly, all the adjustments observed in the non-fatigued muscles of both legs were associated with improved mechanical effectiveness. Taken together, these findings suggest that the nervous system modulates the coordination strategy by decreasing the activation of synergist muscles that could restrain effective force orientation at the pedal and by increasing the activation of other muscles that could enhance the total force produced at the crank level.

Adaptations of synergist/antagonist muscles within the fatigued leg

As detailed elsewhere (Brochner Nielsen et al., 2016), the electromyostimulation protocol was effective in inducing substantial peripheral impairment in the force-generating capacity of the quadriceps muscles. This led to a decrease in knee extension positive power (–34.4 ± 30.6 W) during the subsequent sprint pedaling. The unchanged maximal voluntary activation of the quadriceps muscles during MVC performed at the end of the fatigue protocol confirmed that central fatigue mechanisms did not contribute to the loss of force and that the ability of the central nervous system to drive the quadriceps maximally was maintained. Because the presence of fatigue

makes EMG amplitude difficult to interpret (Farina et al., 2004, Keenan et al., 2006), especially due to an alteration in membrane excitability, VL and VM EMG activity level was normalized to the maximal M-wave amplitude (M_{max}) to better represent the neural drive to these muscles (Hureau et al., 2016). Interestingly, the EMG/M_{max} did not significantly change during the sprint performed in the Fatigue condition ($P = 0.31$ and $P = 0.82$ for VL and VM, respectively). These findings suggest that peripheral quadriceps fatigue was responsible for the observed reduction in knee extension power during the sprint pedaling task, preventing the muscle from responding to an identical central motor drive to the same extent.

Along with the decreased power produced by the knee extensor muscles, muscle activity decreased for most of the muscles involved in this extension phase. This included both the mono-articular (GMax, SOL) and the bi-articular muscles (ST, GM, GL) and logically resulted in decreased hip and ankle power. This finding represents the first experimental evidence that the drive to some unfatigued synergist and antagonist muscles may be reduced in response to the decreased force-generating capacity of distant muscles. In the absence of global neural inhibition due to central fatigue mechanisms, these findings are in accordance with our first hypothesis that selective peripheral fatigue would result in a reorganization of motor control strategy through reduced recruitment of unfatigued muscles. Consequent to the decreased knee extension power, less mechanical energy needed to be transferred from the knee toward the ankle joint and from the limb to the crank. In line with previous work suggesting that calf muscles play a key role in this energy transfer, this might explain the decreased activation of gastrocnemii and soleus (van Ingen Schenau et al., 1992, Fregly and Zajac, 1996, Raasch and Zajac, 1999). Similarly, decreased activity of the mono-articular GMax muscle and hip extension power could be explained by the altered capacity of fatigued RF muscle to transfer hip extension torque to the knee. Overall, these adaptations

provide experimental evidence of the role of the mechanical energy transfer principle in the control of muscle coordination during a multi-joint task (van Ingen Schenau et al., 1992, Prilutsky, 2000).

On one hand, the decreased activation of the gastocnemii, soleus and GMax can be considered ineffective for performance because it led to an inability to maintain extension power at the ankle and hip and might participate in decreasing pedal power. On the other hand, joint torque produced by each muscle group participated in the magnitude of total force exerted at the pedal and in the ability to effectively orientate this force perpendicularly to the crank. Previous studies highlighted the role of bi-articular muscles in ensuring this function during pedaling (Neptune et al., 2000, Prilutsky, 2000). Overall, the results of the current study support the hypothesis that alterations in activation of muscles at adjacent joints can be seen as an interesting strategy regarding this force orientation task's constraint. First, the decreased activation of the hamstrings appears to be a strategy to limit the decrease in knee joint power during extension by producing less negative knee joint power during this phase (+19.3 ± 23.8 W). This explanation is supported by the observation that this decreased activation is limited to the phase in which hamstrings are co-activated with quadriceps (i.e., 0-120° in the extension phase) and is not observed during the beginning of the flexion phase (Table 2; Figure 4). This finding confirms previous studies suggesting that the decrease in hamstrings activity accounts for the loss of force produced by the quadriceps during a fatiguing repeated sprint cycling task (Hautier et al., 2000). Second, adjustments in muscle coordination led to an invariant relative contribution of each joint to the total power produced during the extension phase (23% for the ankle, 23% for the knee and 54% for the hip in control vs. 22%, 23% and 55% during Fatigue, respectively). Finally, the absence of changes in the index of effectiveness between Control and Fatigue conditions (~66%) demonstrates that the orientation of the total force on the pedal was maintained. This supports the hypothesis that in the presence of

quadriceps fatigue, the adaptation strategy of decreasing synergist and antagonist activity is useful in maintaining the ability to effectively orientate force at the pedal.

Adaptations in other muscles in both legs

No change was detected in the mean pedal power for the non-fatigued leg over the full pedaling cycle. This is in accordance with previous results showing an unchanged maximal pedal power for the contralateral leg after a fatiguing single-leg pedaling task, which suggests that no crossover fatigue effect occurred between legs (Elmer et al., 2013). Nevertheless, we observed a significant increase in power during the flexion phase of this non-fatigued leg (Table 1). This was mainly explained by an increase of about 31 W in the hip-specific joint power (associated with increased TFL activity), resulting in a larger relative contribution of the hip to the total pedal power produced during this flexion phase (from 4.8% during Control to 20.1% during Fatigue). Moreover, a significant increase in pedal power was also observed during the flexion phase for the fatigued leg (~20 W). This finding confirms that even during a brief all-out exercise, not all muscles are maximally activated (Dorel et al., 2012). More importantly, it shows that the central nervous system is able to increase the neural drive to these muscles in the presence of peripheral fatigue of another muscle group. This result supports our second hypothesis that despite an observable decrease in performance during a maximal multi-joint task, neural strategy can partly compensate for the loss of power produced by the fatigued muscles.

Previous findings suggest that between-leg adaptations could be mediated via interlimb neural pathways and/or could originate from the mechanical coupling at the crank level (Ting et al., 2000a, Alibiglou et al., 2009, Brochner Nielsen et al., 2016). In the present study, because of the use of an isokinetic cycling mode, the mechanical coupling at the crank level certainly would have been limited, which means that the decrease in force produced by the fatigued leg at the pedal

might not have been directly detected by the non-fatigued leg at the contralateral pedal. Thus, it is reasonable to argue that owing to interlimb neural pathways, the sensorimotor activity of the fatigued quadriceps would have directly affected the contralateral mechanics by increasing activity in the non-fatigued leg muscles involved in the flexion phase. Additionally, note that some muscles of the non-fatigued leg exhibited a slight decrease in activity. These adaptations mainly concerned hamstrings muscles involved in the extension–flexion transition; less uniform changes also appeared in some muscles involved in the extension phase (Table 2). This finding is quite surprising because numerous studies using split-belt treadmills have shown that each leg can be controlled independently of the other, suggesting the use of separate pattern-generating circuits (Reisman et al., 2005, Rossignol et al., 2006). Although unexpected, this result provides further evidence that strong neural connections between legs are involved in the performance of locomotion tasks characterized by symmetric and phasic movements of the two limbs (Ting et al., 2000a).

Although this mechanism was beneficial for muscle activity in the flexion phase, it may be considered unfavorable in this case by making it critical to maintain pedal power during the extension of the non-fatigued leg. However, it confirms that two-joint hamstrings muscles (activated in the antero-posterior transition of the pedal) are particularly sensitive to this interlimb neural coupling, particularly to the sensorimotor state of two joint muscles involved in the postero-anterior transition in the opposite leg (i.e., RF) (Kautz et al., 2002). In response to the fatigue state induced in RF in the fatigued leg, this mechanism would participate in the decreased activation of the contralateral non-fatigued BF and ST muscles.

Practical implications

In the fatigued leg, the general decreased activation of the main non-fatigued muscles during the extension phase suggests that the activation of each muscle during a multi-joint cycling task depends not only on each muscle's own sensorimotor status but also on the status of other muscles. This would mean that during such a maximal multi-joint exercise, the activation level of *stronger* muscles would be limited by the *weakest* muscles. The question remains as to whether this strategy should be considered detrimental to overall performance during a fatiguing exercise. First, the observed decrease in pedal power during the extension phase (–8.9%) was only moderate, considering the larger decrease in isometric quadriceps MVC (–28%). Second, the decreased activation of all antagonist (except BF) and synergist muscles is an appropriate neural strategy to maintain the orientation of pedal force. This result is important because, contrary to the submaximal pedaling task, the ability to effectively orientate force has been demonstrated as a key factor in power production in maximal sprint conditions (Dorel et al., 2008, Dorel et al., 2010). In this line, a significant increase in pedal power and effectiveness was even observed in the fatigued leg during the opposite flexion phase, which represented a means of limiting the decrease in total power produced over the full cycle (only –5.8%). In the non-fatigued leg, while the adaptations during the extension phase led to a small decrease in ankle and hip joint power, the knee joint power tended to increase, and the increase in the index of effectiveness led to a constant pedal power. Combined with the increase in the power produced during the flexion phase, the capacity to effectively orientate the total force on the pedal over the full cycle is clearly improved for this leg (Table 1; Figure 2). Finally, although these adjustments actually represent a decrease in activation of the non-fatigued leg (i.e., almost –6% in total EMG activity and a significant decrease

in the activity of 6 of 11 muscles in the extension phase), participants were able to maintain exactly the same mean pedal power with this leg.

Taken together, one can interpret these results as an *optimization* of muscle coordination during Fatigue conditions for several reasons. First, adaptations led to an acute improvement in the technical aspects of the cycling task, evidenced by both an increase in the ability to orientate pedal force and an increased power production in the initially non-optimized flexion phase for both legs. Second, it is interesting to note that all these adjustments induced only a small decrease in total cycling power (–2.8%; $P = 0.03$), although a global decrease in activation was observed for almost all muscles (significant for 14 of 18 muscles involved in the extension phase in both legs; Table 2). By considering total EMG intensity as a proxy for the metabolic power required for pedaling, some authors recently proposed to estimate a relative efficiency, calculated as the ratio of mechanical power output measured at the pedals to the sum of the total EMG activity levels across all muscles (Wakeling et al., 2011, Blake and Wakeling, 2015). Applied to the results of the current study, this ratio was clearly improved (i.e., an approximately 6% increase in both fatigued and non-fatigued legs between Control and Fatigue conditions), which ultimately suggests better "neuromuscular efficiency" in the Fatigue condition. However, muscle fatigue was often demonstrated to impair inter-segmental or limb coordination (Samaan et al., 2015), which is traditionally considered to be a drawback to learning a new skill or working to improve the effectiveness of a movement. The present results are exciting because they raise the possibility, using a pre-fatigue training strategy on extensor muscle groups, to partially optimize muscle coordination during the sprint cycling task by the additional recruitment of flexor muscles. Further studies are needed to determine: i) if other positive adaptations would be induced in response to fatigue of a different muscle group and ii) if these adaptations would still occur in a population of

well-trained sprint cyclists. A promising perspective is to determine whether the central nervous system would retain these locomotor parameters after a learning period for use in "normal" conditions to enhance performance.

Conclusion

The current study shows that in response to local fatigue of one muscle group, activity of all the co-activated synergist and antagonist muscles and joint-specific power at adjacent joints are decreased. This study demonstrates that it is questionable to interpret a decrease in EMG activity or joint-specific torque produced by one particular muscle group as evidence of a reduction in its force-generating capacity during a global fatiguing multi-joint task. Alternatively, despite a slight decrease in activity for some muscles in the non-fatigued leg, positive adaptations occur by increasing the neural drive to flexor muscles and increasing the mechanical effectiveness and power produced by both legs in the flexion phase. These findings provide evidence that in response to peripheral fatigue, the nervous system modulates the coordination strategy by decreasing the activation of non-fatigued synergist and antagonist muscles to ensure an effective orientation of pedal force and by increasing the neural drive in the direction of muscles involved in other specific parts of the task to optimize the power produced at the crank level. These results support the notion that fatigue, contrary to what is traditionally assumed, could also represent an interesting paradigm and local fatigue a promising perspective in optimizing some aspects of motor performance during a multi-joint cycling task.

Acknowledgements

Project support was provided by the Region Pays de la Loire (ANOPACy project) and the French Ministry of Sport (14-R-23). The authors are grateful to the subjects for having agreed to participate in this study.

Conflict of Interest

The authors report no conflict of interest. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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Chapter 4 - Motor adaptations to local muscle pain during a bilateral cyclic task.

Exp Brain Res
DOI 10.1007/s00221-016-4826-y

RESEARCH ARTICLE

Motor adaptations to local muscle pain during a bilateral cyclic task

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Received: 23 August 2016 / Accepted: 5 November 2016

Abstract The aim of this study was to determine how unilateral pain, induced in two knee extensor muscles, affects muscle coordination during a bilateral pedaling task. Fifteen participants performed a 4-min pedaling task at 130 W in two conditions (Baseline and Pain). Pain was induced by injection of hypertonic saline into the vastus medialis (VM) and vastus lateralis (VL) muscles of one leg. Force applied throughout the pedaling cycle was measured using an instrumented pedal and used to calculate pedal power. Surface electromyography (EMG) was recorded bilaterally from eight muscles to assess changes in muscle activation strategies. Compared to Baseline, during the Pain condition, EMG amplitude of muscles of the painful leg (VL and VM—the painful muscles, and RF—another quadriceps muscle with no pain) was lower during the extension phase [(mean ± SD): VL: −22.5 ± 18.9%; $P < 0.001$; VM: −28.8 ± 19.9%; $P < 0.001$, RF: −20.2 ± 13.9%; $P < 0.001$]. Consistent with this, pedal power applied by the painful leg was also lower during the extension phase (−16.8 ± 14.2 W, $P = 0.001$) during Pain compared to Baseline. This decrease was compensated for by an 11.3 ± 8.1 W increase in pedal power applied by the non-painful leg during its extension phase ($P = 0.04$). These results support pain adaptation theories, which suggest that when there is a clear opportunity to compensate, motor adaptations to pain occur to decrease load within the painful tissue. Although the pedaling task offered numerous possibilities for compensation, only between-leg compensations were systematically observed. This finding is discussed in relation to the mechanical and neural constraints of the pedaling task.

Keywords Muscle coordination · Pedaling · Force · Electromyography

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Introduction

When maintaining a net torque during an isometric single-joint task, decreased activation of one muscle must be compensated for by increased activation of its synergist muscle(s), or a decrease in antagonist muscle activity. This is particularly important when considering the motor adaptations to pain, which are often associated with decreased activation of the painful muscle, to protect this tissue from further pain or injury (Lund et al. 1991; Hodges and Tucker 2011). This seems logical; however, experimental data that consider myoelectrical activity alone do not systematically support this assumption (Bank et al. 2013). When net torque is maintained during Pain, decreased activation of the painful muscle is observed during some isometric single-joint tasks (Graven-Nielsen et al. 1997; Ciubotariu et al. 2004). However, other studies report no change (Farina et al. 2008; Hodges et al. 2008) or even increased muscle activation (Fadiga et al. 2004). Furthermore, spatial changes in activation within a painful muscle are not organized with respect to the pain location (Falla et al. 2009; Hug et al. 2013). These conflicting findings might originate from constraints that affect the

Published online: 12 November 2016

possibilities of compensation in the presence of pain (Hug et al. 2014a, b, c).

Considering the quadriceps muscle group, when pain was induced in the rectus femoris (RF) muscle during a force-matched isometric knee extension task, tension estimated by shear wave elastography was systematically reduced within this muscle (Hug et al. 2014b). This result suggests that when neural drive can be disassociated between synergist muscles (e.g., between the bi-articular RF and the mono-articular vastii muscles), compensation strategies successfully reduce tension in the painful tissue. However, during the same task, when pain was induced into the vastus medialis (VM) muscle, the systematic decrease in tension within the painful muscle was not observed (Hug et al. 2014b). This is likely because VM and VL share most of their neural drive (Laine et al. 2015) making it difficult for the nervous system to independently control these muscles. Such independent control would have been required to compensate for a decrease in VM contribution, especially because the force-generating capacity of the RF muscle is not sufficient to compensate for a large reduction in tension produced by Vastii muscles. Motor adaptations to pain are also influenced by the possibilities of compensation offered by the motor task. For example, tension is systematically reduced within the VM when pain is induced unilaterally in this muscle during an isometric bilateral leg squat, i.e., when the reduction in force may be compensated for by the contralateral side. However, a systematic decrease in tension within a painful VM is not observed during a single leg squat task (Hug et al. 2014a). Taken together these results suggest that motor adaptations to pain need to be considered with direct reference to the muscle(s) and the degrees of freedom present within the motor task being performed.

van den Hoorn et al. (2015) studied the effect of unilateral pain in the medial gastrocnemius muscle on coordination during walking and observed decreased activation in the whole *triceps surae* during Pain rather than a selective decreased activation of the painful muscle. This was associated with participant-specific changes in muscle synergies. However, interpretation of these changes in terms of underlying motor control principles or biomechanical effects is not straightforward. This is because a significant decrease in both stride time and stance time was also observed, which influence the mechanics of the task, and may have altered passive forces during Pain.

The aim of this study was to determine the effect of unilateral pain, induced in two knee extensor muscles (VL and VM), on muscle coordination during a pedaling task. Pedaling on a cycloergometer provides a good experimental model because lower limb movement is constrained and the total mechanical power output can be well controlled by fixing the resistance and maintaining a particular pedaling rate. In addition, this task theoretically allows for various possibilities of compensation, for example: (1) between synergist muscles, (2) between joints within the same limb, and/or (3) between limbs. The tested hypothesis was that activation of the painful muscles would decrease when pedal power is maintained. In the case that this hypothesis was supported, the second aim was to determine the preferred (or most common) compensation strategy.

Methods

Participants

Fifteen healthy males (mean ± SD: age 22.9 ± 4.2 years, height 176.9 ± 5.9 cm, body mass 77.6 ± 10.3 kg) with no history of lower limb pain participated in this study. All participants provided their written informed consent. The experimental procedures were approved by the local ethics committee (The University of Queensland), and all of the procedures conformed to the Declaration of Helsinki. The synchronization of data failed for one participant and the data were therefore excluded. Data are thus reported for 14 participants.

Experimental protocol

Participants performed a pedaling task on a cycloergometer (Monark 828E, Monark, Sweden) equipped with standard cranks (170 mm) and instrumented clipless pedals, i.e., pedal and shoe attached with cleats (VélUS group, Canada). The saddle height was set at 109% the participants' inseam length. First, they performed a standardized warm-up consisting of 5 bouts of 1-min cycling followed by 4-min cycling, with ~30-s rest between each cycling bout. Throughout the warm-up, the power output and the pedaling rate were fixed at 130 W and 80 rpm, respectively. Then, a 4-min cycling bout was performed (with the same power output and pedaling rate) during two experimental conditions: Baseline and Pain. Each cycling bout was separated by ~3 min. As motor adaptation to pain does not totally resolve after pain ceases (Henriksen et al. 2009; Hug et al. 2014a), the Baseline condition was always performed before the Pain condition. Feedback of the pedaling rate was provided by a digital display on the cycloergometer, and participants were asked to maintain the pedaling rate at all times during the cycling tasks.

Experimental pain

Pain was induced unilaterally in two major knee extensor muscles, i.e., the VL and VM muscles with two injections of hypertonic saline. A 0.5-mL bolus of 6.7% NaCl was

injected into each muscle using 25 G × 25 mm hypodermic needles (Terumo, Japan). The painful side was randomly assigned prior to the beginning of testing. The injection location was ~1 cm distal to the VL and VM electromyography (EMG) electrodes (placement described below). Global pain intensity from both sites was reported verbally every 30 s during the Pain condition and every minute during the Baseline conditions using an 11-point numerical rating scale, anchored with 0 = "no pain" and 10 = "worst pain imaginable." Note that isotonic saline was not used as a control in our experiment for two reasons: (1) It has been previously demonstrated that injection of non-painful saline (isotonic saline) did not alter the force sharing between limbs during a bilateral isometric task (Hug et al. 2014c) and (2) an injection of isotonic saline is often associated with low level pain likely explained by the needle insertion (Farina et al. 2005; Gizzi et al. 2015) and is therefore not appropriate for a pain-free control condition. Cycling during the Pain condition started within 30 s of the saline injection used to induce local muscle pain.

Mechanical data

The force applied at the shoe–pedal interface during cycling was measured using an instrumented pedal equipped with eight strain gauges (VélUS group; Department of Mechanical Engineering, Sherbrooke University, Canada) as described in Dorel et al. (2008). The Cartesian components force in the horizontal axis (Ft) and in the vertical axis (Fn) and the pedal angle with respect to the crank were measured. Data were digitized at 1000 samples/s (PowerLab/16SP, AD Instruments Pty. Ltd., Castle Hill, Australia). The position of the axis of both the pedal and the crank was recorded using an optoelectronic motion capture system (OptiTrack, Natural Point, USA).

Surface electromyography

Myoelectrical activity was recorded from eight muscles bilaterally (total of 16 muscles): tibialis anterior (TA), soleus (SOL), VM and VL, RF, biceps femoris—long head (BF), gluteus Maximus (Gmax) and tensor fascia latae (TFL). Skin was first shaved and cleaned with abrasive gel (Nuprep; D.O. Weaver & Co.) and alcohol to reduce impedance. Subsequently wireless surface electrodes (Delsys, Trigno™, Boston, MA, USA) were attached to the skin at sites recommended by SENIAM (Hermens et al. 2000), except for the SOL which was placed at two-thirds of the line between the lateral condyle of the femur and the lateral malleolus (to ensure that the electrodes did not strike the crank of the cycloergometer during the cycling task). The myoelectric signals were amplified, band-pass-filtered (20–450 Hz), digitized at 1000 samples/s (CED Power 1401, CED Ltd, Cambridge, UK) and recorded in Spike2 (V7, CED Ltd, Cambridge, UK). To synchronize kinematic, force and EMG data, a Transistor–Transistor Logic trigger signal was sent simultaneously to the force and EMG data acquisitions systems from the optoelectronic data acquisition systems, at the start and continuously until the end of each bout.

Data processing

The data were processed using MatLab R2013a (The Mathworks Inc., USA) and Mable 13 (Maplesoft, Waterloo Maple Inc., Canada) using custom scripts. The force components measured using the instrumented pedals were low-pass-filtered at a cutoff frequency of 10 Hz using a third-order Butterworth filter. The total force (the vector sum of Ft and Fn) applied to the pedal was calculated using standard trigonometric calculations and resolved to derive the effective force, i.e., the force applied perpendicular to the crank. Finally, the pedal power was calculated as the product of effective force and velocity of the pedal.

The root mean square (RMS) of the EMG signal was calculated using a 25-ms moving window (24-ms overlap). Then, a third-order butterworth low-pass filter (24 Hz) was applied. A spline interpolation was used on force and EMG data to have equal data points for both data sources. All data were divided into pedaling cycles using the top dead center (TDC; highest point of the cycle as determined by kinematics) and resampled to obtain one value each 5°.

Pedal power and RMS EMG for all muscles were extracted from 30 consecutive cycles, from the end of the first minute for the Baseline condition and from the period of peak pain rating for the Pain condition. EMG signals were visually inspected for movement artifacts. If 30 consecutive cycles were not available without artifacts, recording for that muscle was discarded from further analysis for that participant. The number of participants considered for the analysis is depicted for each muscle/condition in Table 1. Mean RMS EMG values are reported for the full cycle, as well as for both the extension (between 340° and 160°) and flexion phase (between 160° and 340°). For the sake of clarity, RMS EMG of each muscle is reported only for the phase(s) of the pedaling cycle where it is active [one phase for mono-articular muscles (extension for VL, VM, Gmax, SOL and flexion for TFL, TA), both phases for bi-articular muscles (RF, BF)]. Because of the within-subject design of this experiment, RMS EMG was not normalized.

Table 1 Number of participants considered for the EMG analysis after checking for motion artifacts

Muscle	Painful leg	Non-painful leg
VL, VM, RF, BF, SOL	14	14
TFL	12	12
Gmax	10	8
TA	12	14

Statistics

All statistical tests were performed using STATISTICA (V8, StatSoft. Inc., USA). A Shapiro–Wilk test was performed to test for a normal distribution. Some data were not normally distributed, and a box-cox test was performed to determine the appropriate data transformation. An inverse transformation was thus applied on the mean power (full cycle), RF EMG RMS (extension phase) and on the BF (flexion phase) of the non-painful leg. A squared root transformation was applied on the VL, TFL and SOL EMG RMS of the non-painful leg.

A paired *t*-test was used to check that the total power output (sum of both legs) did not change between conditions. A repeated measures ANOVA was performed to test the effect of pain on pedal power calculated over the whole pedaling cycle [within-subject factors: Leg (painful leg and non-painful leg), Condition (Baseline, Pain)]. To locate the changes within the two main phases of the pedaling cycle, a repeated measures ANOVA was performed on pedal power averaged over the extension and the flexion phases [within-subject factors: Leg (painful leg and non-painful leg), Phase (extension, flexion), Condition (Baseline, Pain)]. Post hoc analyses were performed using the Bonferroni adjustment for multiple comparisons (corrected P values are reported within the "Results" section). Finally, RMS EMG for each muscle (separately) was compared between Conditions (Baseline and Pain) using paired *t*-tests. The significance level was set to $P < 0.05$. All results presented below are presented as mean ± SD.

Results

The leg in which pain was induced is referred to as the "painful leg" and the leg for which no pain was induced is referred to as the "non-painful leg." This is the case regardless of the experimental condition (Baseline—where no pain was present, and Pain—where pain was present).

Pain intensity

During the Pain condition, pain intensity peaked within the first minute for all participants (4.4 ± 1.4) and declined toward the end of the bout (1.4 ± 1.6 at 4 min). The mean pain rating for the period of EMG and force data analysis was 4.4 ± 1.5 out of 10. The painful area was recorded in five participants who drew the area with pain directly on the leg. The area was close to the injection site for both the VM and VL. As expected, there was no pain reported (i.e., 0/10) during the Baseline condition.

Pedal power output

Total power output (Baseline: 129.1 ± 3.7 W and Pain: 130.1 ± 3.9 W; $P = 0.44$) and pedaling rate (Baseline: 80.5 ± 0.8 rpm and Pain: 80.4 ± 1.1 rpm; $P = 0.79$) were not significantly different between conditions. These results confirm that the task goal was maintained.

When considering the power output produced by each leg, a significant Leg × Condition interaction was observed ($P < 0.001$). The power produced by the painful leg was significantly lower during Pain than during Baseline (−7.3 ± 6.6 W, $P = 0.002$), and the power produced by the non-painful leg was significantly higher during Pain than during Baseline (+8.2 ± 5.4 W, $P = 0.004$) (Figs. 1, 2). To explore these results further, the pedaling cycle was divided into the extension and flexion phase. This analysis revealed a significant Leg × Phase × Condition interaction ($P < 0.001$). Pedal power applied by the painful leg was lower during the extension phase (−16.8 ± 14.2 W, $P = 0.001$) and remained unchanged during the flexion phase (+3.1 ± 5.8 W, $P = 1.0$) (Fig. 2). Pedal power applied by the non-painful leg was significantly greater during its extension phase (+11.3 ± 8.1 W, $P = 0.04$) and remained unchanged during the flexion phase (+4.9 ± 4.6 W, $P = 1.0$) (Fig. 2). Consequently, a significant difference ($P < 0.001$) in extension power was

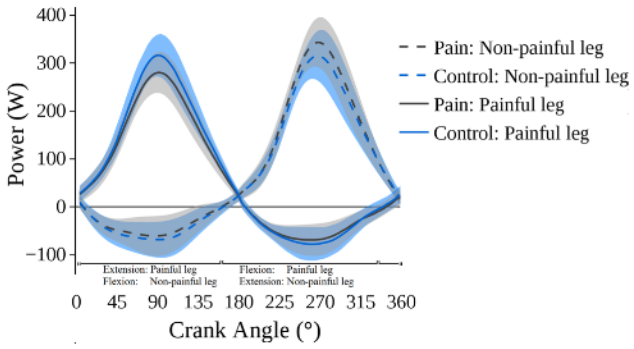

Fig. 1 Averaged profiles of the pedal power. The profiles were calculated by averaging 30 pedaling cycles during control (*blue*) and Pain conditions (*black*) for both the painful (*solid curve*) and non-painful legs (*dashed curve*). Zero degree represents the highest position of the crank for the painful leg. The profiles are mean data of 14 participants (color figure online)

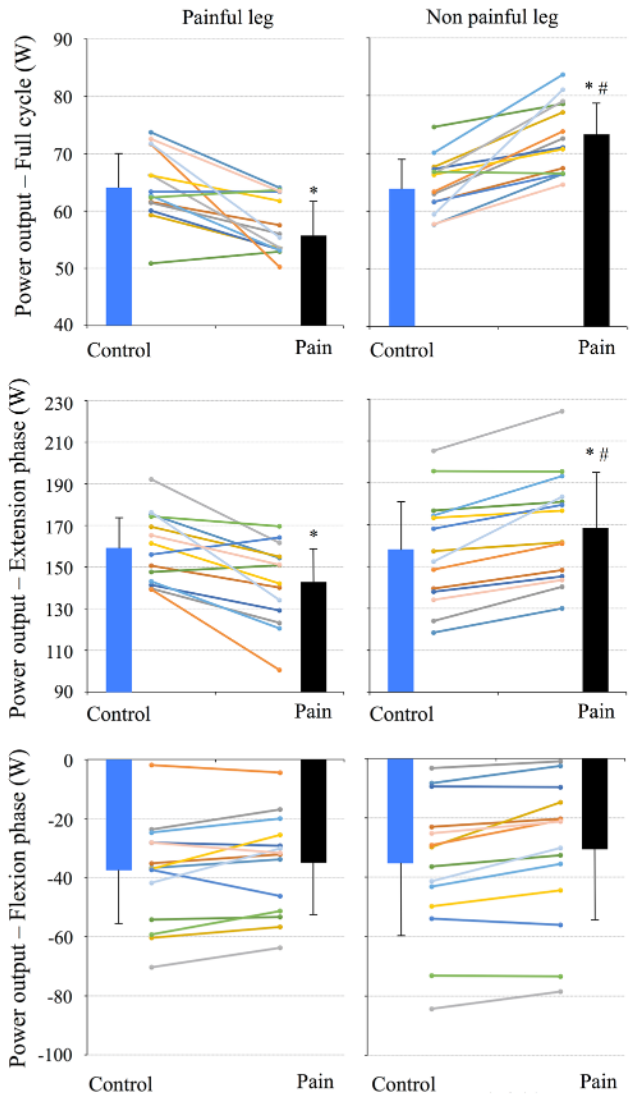

Fig. 2 Pedal power. The power measured at the pedal was averaged across the full pedaling cycle (*upper panel*), the extension phase (*middle panel*) and the flexion phase (*lower panel*). Each participant is depicted in a *different color*. The *bar graph* indicates the mean data over the whole population. $^{*}P < 0.05$ for comparison between Pain and Control. $^{\#}P < 0.05$ for comparison between the painful and non-painful legs (color figure online)

observed between the legs during Pain, whereas it was not observed during Baseline ($P = 1.0$). No between-leg difference in flexion power was observed during either the Pain ($P = 1.0$) or the Baseline condition ($P = 1.0$) (Fig. 2).

RMS EMG

Painful leg

Electromyographic signal amplitude of VL and VM (the painful muscles) and RF (another quadriceps muscle with no pain) was lower during the extension phase of the Pain condition compared to Baseline (VL: $-22.5 \pm 19\%$; $P < 0.001$; VM: $-28.8 \pm 19.9\%$; $P < 0.001$, RF: $-20.2 \pm 13.9\%$; $P < 0.001$) (Fig. 3). No other muscles differed significantly between Pain and Baseline during the extension phase (Gmax: $P = 0.82$; BF: $P = 0.29$; SOL: $P = 0.78$). No change in RMS EMG was observed between conditions during the flexion phase of the painful leg for the RF ($P = 0.71$), BF ($P = 0.86$) TFL ($P = 0.25$) and TA ($P = 0.08$).

Non-painful leg

A significant increase in RMS EMG was observed during the extension phase with Pain for the VM ($+19.4 \pm 17.3\%$; $P = 0.008$), VL ($+18.9 \pm 13.3\%$; $P = 0.002$), RF ($+15.6 \pm 18.8\%$; $P = 0.004$), SOL ($+18.5 \pm 20.2\%$; $P = 0.004$) and Gmax ($+25 \pm 30.3\%$; $P = 0.03$) (Fig. 3). The BF did not differ between conditions during the extension phase (BF: $P = 0.59$) but increased significantly during flexion ($+13.5 \pm 23.9\%$; $P = 0.04$). No significant change was observed for any other muscle of the non-painful leg during the flexion phase although the RF was close to being higher during the pain condition (RF: $P = 0.06$; TFL: $P = 0.2$; TA: $P = 0.09$) (Fig. 3).

Discussion

This study had two main findings. First, when pain was induced unilaterally in the VM and VL muscles, activation of these painful muscles reduced considerably, while total pedaling power and pedaling rate were maintained. This reduced activation was associated with decreased pedal power produced by the painful leg during the extension phase of the cycle. Second, the decrease in pedal power produced by the painful leg was mainly compensated for by increased activation of hip, knee and ankle extensor muscles of the non-painful leg leading to an increased power produced during its extension phase. These results support the theory that when there is an obvious opportunity to compensate, the motor adaptations to pain involve decreased activation of the painful muscle (Lund et al. 1991; Hodges and Tucker 2011). Putting this together, although this cycling task allows for numerous compensation possibilities (e.g., between muscles within a limb, between joints within a leg, and between-leg), only between-leg compensations were systematically observed. This finding is discussed in relation to the neural and mechanical constraints of the task.

Decreased activation of the painful muscles

It is commonly thought that the activation of painful agonist muscles decreases during Pain [e.g., the pain

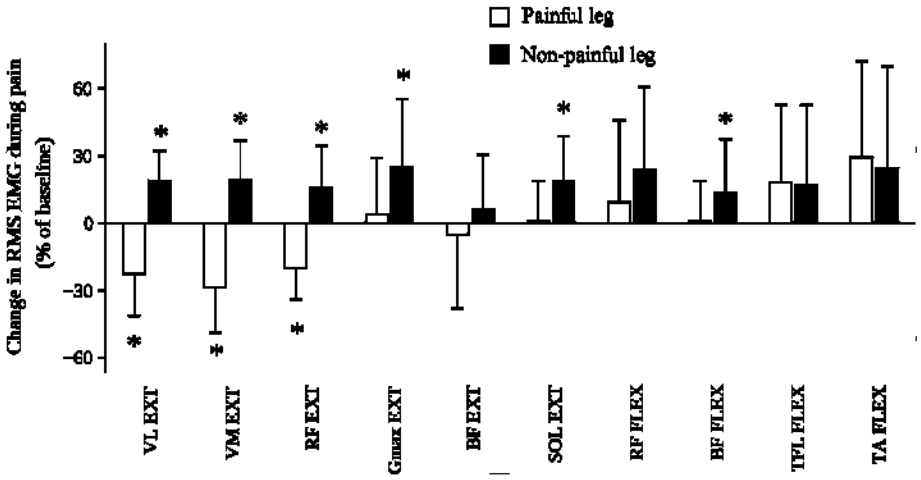

Fig. 3 Muscle activation. RMS EMG mean differences between the Pain and Control conditions are presented for eight muscles for the phase(s) of the pedaling cycle where they are active (extension and/or flexion) for both the painful (*white*) and non-painful legs (*black*). $^*P < 0.05$ for comparison between the Control and Pain conditions (color figure online)

adaptation theory, Lund et al. (1991)]. However, human studies investigating simple force-matched isometric single-joint tasks do not always report decreased activation of the painful agonist muscle. For example, Hodges et al. (2008) reported no change in surface EMG amplitude of the painful lateral gastrocnemius muscle during isometric plantar flexion. Similarly, Hug et al. (2014b) reported no change in VM surface EMG during isometric force-matched knee extension when this muscle was made painful by injection of hypertonic saline. Here, we report a large decrease in RMS EMG of the two painful muscles (VM and VL, between −22 and −29%) during the extension phase of the pedaling cycle, which was associated with a significant decrease in pedal power produced by the painful leg during the same phase. Discrepancies between our results and those obtained during isometric single-joint tasks may be explained by the fact that pedaling is a dynamic task that offers number of available degrees of freedom to compensate for the decrease in force produced by the painful muscle. For example, Hug et al. (2014a) showed that when pain was induced into the VM during tasks with few degrees of freedom, i.e., isometric knee extension and isometric single leg squat, no systematic reduction in EMG was observed. However, a systematic decrease in VM EMG amplitude was observed during an isometric bilateral leg squat.

Consistent with many studies (Hug et al. 2014b, c; Tucker et al. 2014), pain was experienced locally in the VM and VL in the current study, i.e., close to the site of the injection. We have shown that although the RF muscle was not painful in the current study, decreased activation of this muscle was also observed during the extension phase of the Pain condition. This is somewhat surprising as results from Hug et al. (2014b) showed that it is possible to voluntarily dissociate neural drive of the vastii and RF, i.e., participants were able to voluntary decrease RF activation and increase VM activation while matching an isometric knee extension torque. As such, the decrease in force produced by the vastii could have been theoretically compensated (at least in part) by an increased RF force. This result might be accounted for the higher neural *cost* of disassociating the drive to synergist muscles than that of compensating between legs during such a multi-joint task. If we consider this neural *cost* as the neurocomputational effort required for the coordination of joint motions (Dounskaia and Shimansky 2016), activating a group of muscles (referred to as synergy or motor primitive) by a single neural command would be an effective strategy to decrease the neural *cost*. This is in line with previous data that show RF, VL and VM belong to the same muscle synergy during pedaling (Hug et al. 2010). Therefore, a selective reduction of drive to the painful muscles (VL and VM) but not their non-painful synergist (RF) may be associated with higher *cost* for the central nervous system, than using a strategy of increasing drive to the opposite limb. Of note, the neural cost of motor control strategies difficult to quantify. As such, the underlying neurophysiological mechanisms behind the observed motor adaptations to pain cannot be inferred from the results of the current study and therefore remain speculative. Further research is needed to understand the mechanisms behind the observed pain adaptations.

In addition, because of the RF's lower force-generating capacity than that of vastii muscles, this muscle is unlikely to be able to compensate for a large decrease in force produced by the vastii. A similar reduction in the activity of three muscles from the same muscle group (gastrocnemius lateralis, gastrocnemius medialis and SOL) was observed during gait, while acute pain was experienced in the gastrocnemius medialis muscle (van den Hoorn et al. 2015) and during isometric planter flexion acute pain was experienced in the gastrocnemius lateralis (Hodges et al. 2008).

Compensation strategies

As a result of the decreased quadriceps activation, compensations were necessary to maintain the task goal. Inspection of data for individual participants (Fig. 2) revealed that 11/14 participants exhibited a decrease in power produced by the painful leg (-7.3 ± 6.6 W), while 13/14 participants exhibited an increase in power produced by the non-painful leg ($+8.2 \pm 5.4$ W). Therefore, a very large majority of the participants exhibited a similar compensation strategy even though standard deviation of these changes revealed a variability of the magnitude of these adaptations. Although possibilities to compensate were available within the painful leg during extension, no systematic compensation was observed. For example, it is theoretically possible to increase the power produced by the non-painful hip extensor muscles (e.g., Gmax, BF) during this phase of the cycle to compensate for a reduction in knee extension power. The lack of within-leg compensations is in line with previous studies showing that unilateral coordination patterns remain largely unchanged during walking when a unilateral load is placed on the lower leg (Haddad et al. 2006) or when cutaneous pain is induced unilaterally (Bouffard et al. 2014). It might be explained by an additional neural cost associated with altering muscle coordination strategies within the leg in the same phase. Compared to the aforementioned study that focused on walking, the current study provided an additional possibility to produce power, and thus to compensate, during the flexion phase of the painful leg (i.e., increased power during the flexion phase by increasing activation of the hip flexor muscles). However, it was not observed. This could be explained by the fact that increasing the power produced during the flexion phase of the pedaling cycle would decrease the overall gross efficiency of the task (Korff et al. 2007).

Although there is evidence that neural coupling may exist between legs throughout the involvement of neural networks located in the spinal cord (Hansen 2015), it remains unclear how these centrally generated signals are integrated with peripheral afferent information to produce coordinated bilateral tasks. Studies performed on bilateral cyclic tasks have provided evidence that some neural pathways participate to regulate the ipsilateral muscle activity using contralateral sensorimotor information (Ting et al. 2000). During Pain, we observed a significant increase in pedal power produced by the non-painful leg during its extension phase. As the extension is the primary phase for force production, compensation during this phase may be a very effective compensation strategy. Interestingly, the increase in activation of knee extensor muscles in the non-painful limb was less (<20%) than the decrease observed in the painful limb (22–29%). Further, we observed increased Gmax and SOL muscle activation during the extension phase of the non-painful limb. More precisely, Gmax, which is known to be a powerful hip extensor muscle, but only activated at a low level during such a low power output [about 10% of its maximum, Hug and Dorel (2009)], increased its activity by ~25% during Pain. We therefore contend that this is likely to be an efficient strategy to compensate for a decrease in force produced by the painful leg as Gmax has a huge activation reserve during submaximal cycling.

Some compensation occurred during the flexion phase as demonstrated by the significant increase in BF activation. However, this did not lead to a significant increase in pedal power. This could be explained by between-subject variability. For example, 4 participants exhibited a >15% increase for the BF muscle, 5 participants exhibited a 0–15% increase and 5 participants did not change BF activity during Pain compared to Baseline. Such a variability of pain adaptations was similarly reported during trunk movements (Hodges et al. 2013) and walking (van den Hoorn et al. 2015) and is thought to be related to participant's prior experience and subtle differences in the pain experienced during the experiment.

Pain adaptation theories

It is well accepted that movement behavior changes in response to pain. However, the purpose of these adaptations is not well understood. Although it is generally assumed that motor adaptations aim to unload the painful tissue, there is a lack of experimental evidence (Bank et al. 2013). More precisely, a number of studies do not report a decrease in activation (Hodges et al. 2008) or decrease in tension (Tucker et al. 2014) within the painful muscle during force-matched tasks with pain. Further, a significant proportion of work in this field considers isometric single-joint tasks. A key finding of the present study is that during multi-joint bilateral tasks, similar to daily life activities, the activation of the painful muscles does decrease. This decrease appears to be most often compensated for, with an increase in activation of muscles within the contralateral leg. The previous studies that do consider multi-joint tasks do not account for adaptations between the legs, nor do they control for changes in the mechanical output (Henriksen et al. 2007; van den Hoorn et al. 2015). If studies do not account for the adaptations between legs, it could mask the primary adaptation strategies to pain, compromise the interpretation of the results in relation to existing pain theories, and ultimately explain much of the variability between findings reported in the literature. Overall this study demonstrates that pain adaptations need to be interpreted in relation to the available options to compensate. Future studies need to account for the mechanics of the task and the involved muscles, when trying to determine underlying neural strategies associated with motor adaptation to pain.

Acknowledgements Project support was provided by the Region Pays de la Loire (ANOPACy project) and the French Ministry of Sport (10-R-019). ANOPACy is co-funded by the European Union. Europe commits itself to Pays de La Loire through Regional Development European funds.

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Chapter 5 – General discussion & perspectives

5.1 General discussion

This dissertation provided additional insight into adaptations to local fatigue or pain occurring at the perturbed muscle(s) and at other unaffected muscles during a bilateral multijoint task. It aimed to investigate adaptations to selective fatigue or pain in a muscle group and to see whether compensations would occur between synergists/antagonists, between muscles within the leg, or between legs. Three experiments were designed and the results have been reported and addressed in detail in three manuscripts. The focus of this section is to (1) consider each individual finding in respect to the overall aim and hypotheses, (2) compare the three experiments, and (3) conclude and give perspectives.

Adaptations at the fatigued or painful muscles

The experiments in the current dissertation stand out for investigating a bilateral multi-joint task while controlling the important parameters of fatigue and pain. In both studies 1 and 2, selective peripheral fatigue was induced in the quadriceps muscle group using an electromyostimulation protocol. The resulting decrease in force-generating capacity, exhibited as a decrease in knee extension MVC, was associated with peripheral fatigue as shown by a decrease in M-wave and rest twitch, and not central fatigue (i.e. constant voluntary activation). The majority of studies investigating adaptations to fatigue induce widespread fatigue, making it difficult to determine if changes in muscle coordination occur because the muscles fatigue or because of a purposeful change in muscle coordination strategy. Our selective approach was advantageous because it made it possible to determine both local adaptations occurring at the fatigued muscle and adaptations occurring at other non-fatigued muscles.

Study 1 investigated adaptations to local fatigue in a submaximal pedaling condition. Adaptations at the fatigued muscle(s) during submaximal single-joint tasks generally involve

increased muscle activity as a strategy to recruit additional motor units (Edwards and Lippold, 1956, Adam and De Luca, 2003). Interestingly, this study showed a different adaptation, as the estimated neural drive to the fatigued quadriceps muscles did not change. As a consequence, knee joint power decreased during the extension phase of the pedaling cycle. Some interesting aspects can be considered in explaining this result. Muscle coordination strategies have been suggested to depend on the optimization of different cost functions such as effort and variability (Todorov, 2004). As muscle fatigue has been associated with a decrease in mechanical efficiency (Woledge, 1998), it could therefore be a more optimal strategy to recruit other muscles rather than additional units within the fatigued muscle. However, it is crucial for such a strategy that other unaffected muscles be available. Single-joint tasks have a low number of degrees of freedom, and the possible adaptations are limited to changes in muscle activation strategies within the fatigued muscles or at the adjacent synergist muscles. In this regard, it has been reported that it might be difficult to dissociate activation between synergist muscles (Laine et al., 2015), which could explain the inconsistent results between some single-joint studies (Akima et al., 2002, Bouillard et al., 2014). In the current study, fatigue was induced in the whole quadriceps muscle group, but the bilateral pedaling task allowed for many possible adaptations, resulting in no activation change for the fatigued muscles and possibly a preference to adapt using other muscles. It should be noted that it was not possible to measure effects on the vastus intermedius because of its deep location. Some adaptations might have occurred in this muscle, but are likely negligible because knee joint power decreased and because of the aforementioned difficulty in dissociating activity between synergists.

Study 2 investigated adaptations to local fatigue during pedaling at maximal intensity, with the primary goal of producing the maximal power output possible over a short period of time. This intensity significantly limited available adaptations, since theoretically all motor units were

recruited. Moreover, a decrease in muscle activity is commonly observed in similar studies (Taylor and Gandevia, 2008). Despite this, the results of this study showed that activation of the fatigued muscles remained unchanged. It can be argued that because the induced fatigue primarily consisted of peripheral fatigue rather than central fatigue, it was possible to maintain the same activation level for the fatigued muscles to get their maximum possible force output. This highlights a possible change in task goal, where a cost such as effort might have had negligible influence on the chosen muscle coordination strategy.

A change in task goal likely also occurred in study 3, which investigated adaptations to pain. Although fatigue and pain share some neural pathways (III/IV afferents), there are important differences; for example, fatigue (comprised by a peripheral component) implies a loss of force-generating capacity at the level of the muscle, while during pain this is not the case. The painful muscle can produce the same amount of force if, for example, it is electrically stimulated. However, an inhibition occurs at cortical levels, reducing the drive to the muscles (Lund et al., 1991, Graven-Nielsen et al., 1997). Considerable variability considering activation of the painful muscle has been observed in the literature (for review see Bank et al. (2013)). The results reported in Hug et al. (2014b) indicated that the constraints of the task, such as available degrees of freedom, could be key to the observed variability. In the current study, when local pain (vastii muscles) was experienced during a bilateral cyclic task, the participants consistently decreased activity of the painful muscles. It has been suggested that this might occur to protect the painful tissue from further pain and/or injury, as in the pain adaptation theory (Lund et al., 1991). The results in the current study partially supported this theory; the many degrees of freedom in the pedaling task might have provided an obvious solution for compensation, allowing for consistent results (decreased activation of the painful muscles) between participants. An additional observation in

this study was, that the activity of the biarticular synergist RF muscle also decreased. Other studies showed that it is possible to independently control this muscle (Hug et al., 2014c), therefore some compensation could have occurred in it. Nevertheless, such independent control was not observed and the RF muscle activation decreased alongside the painful VM and VL. It was hypothesized that this could be explained by neurocomputational costs, the neurocomputational effort required for coordination of joint motions. It is possible that neural cost during pain can be effectively decreased by activating a group of muscles at once rather than each muscle independently. This grouped control has also been observed during gait (van den Hoorn et al., 2015) and bilateral squat (Hug et al., 2014b).

Overall, it appears that the availability of many possible adaptations during pedaling, had a significant effect on adaptations observed at the perturbed muscles. During fatigue, this involved the use of muscles not affected by fatigue, whereas limited adaptations were observed at the fatigued muscle itself. During submaximal intensity, this reliance on non-fatigued muscles might have served to decrease strain on the fatigued muscle and decrease overall effort, whereas during maximal intensity, activity in the fatigued muscle was maintained to produce as much force as possible. During pain, the number of available adaptations possibly allowed for protection of the painful muscles, as shown by the consistent decrease in muscle activity.

Adaptations at non-perturbed muscles within the affected leg

Pedaling requires specific coordination of certain muscles and involves coactivation between agonists at different joints (ex. GMAX, vastii, SOL) as well as biarticular antagonists (ex. vastii and hamstrings) (Raasch and Zajac, 1999). Importantly, the fatigue induced in both studies 1 and 2 significantly decreased the muscle activity of biarticular BF and ST within the fatigued leg, which are antagonists to the perturbed quadriceps muscles. A complex interaction exists

between monoarticular agonist and biarticular antagonist muscles during movement. In classic single-joint tasks, activation of Ia inhibitory interneurons during activation of the agonist muscle has been shown to inhibit the antagonist alpha-motoneurons (reciprocal inhibition), minimizing opposing action of the antagonist muscles (Levenez et al., 2008, Duchateau and Baudry, 2014). Although this minimization might favor the intended action of the monoarticular agonist muscles, multi-joint tasks are a different case, where cocontraction of the antagonist provides stability and control of the orientation and transfer of joint forces (Prilutsky, 2000). During pedaling, power is influenced by forces produced by all the muscles about any given joint and, in addition, by forces interacting across all the segments in the movement chain (Gribble and Ostry 1999; Dounskaia et al. 1998). The bi-articular muscles are thought to i) have a bifunctional role, capable of exerting force around both joints they span; ii) distribute and transfer net moments from proximal to distal joints; and iii) participate in effectively orientating the force on the pedals (van Ingen Schenau et al., 1992, Raasch et al., 1997, Raasch and Zajac, 1999). In study 1 (submaximal intensity), the force-generating capacity of the quadriceps muscles decreased due to fatigue. As a result, activation of the biarticular antagonists BF and ST decreased, possibly to ensure similar orientation of force on the pedal. This was in turn associated with a decrease in activation of the distal GM and GL muscles to accommodate for loss of power around the knee joint, i.e. less transfer of mechanical force between joints.

These results and the importance of these mechanisms became even more evident in study 2 during pedaling at maximum intensity (significant for all muscles), confirming the specific role of the biarticular muscles. Moreover, as fatigue included the RF muscle, this muscle's capacity to transfer extension torque produced at the proximal hip joint might have been compromised (van Ingen Schenau et al., 1992). This in turn could have caused the decrease in GMAX muscle activity

observed during this intensity. Furthermore, activity of the biarticular muscles BF and ST decreased significantly to accommodate for the loss of power at the quadriceps, similar to but more strongly than in the submaximal condition. The increased power needed in the maximal condition likely increased the importance of maintaining mechanical effectiveness. In addition, coactivation of the biarticular antagonists BF and ST accounted for the negative component in knee joint power observed during the last part of the extension phase and the extension-flexion transition phase, where the pedal force was to be directed in a posterior direction (Raasch and Zajac, 1999). When activation of the BF and ST muscles decreased during maximal intensity pedaling, it resulted in a decrease in negative power and thus an overall increase in power for the knee joint, alongside a constant mechanical effectiveness. A similar compensatory strategy was suggested in a previous study (Hautier et al. 2000) to limit the decrease in pedal power during fatigue. The current study confirms this hypothesis, and for the first time adds additional experimental evidence for its importance in mechanical effectiveness. The results in both study 1 and 2 suggest that the dynamic interactions between muscles acting in synergy might play an important role in maintaining a proper orientation of force on the pedal during fatigue, particularly in regards to the biarticular antagonist muscles. The results further indicate that this parameter becomes more important at higher intensities.

In addition to the above changes observed in the biarticular muscles, study 2 showed that activation of adjacent non-fatigued synergists within the fatigued leg decreased as well, concurrent with the decrease in force-generating capacity of the quadriceps. This result is interesting because it suggests that one muscle group potentially limited the overall performance of synergist muscles. Previous studies have shown that integrative sensory information from Ia and Ib afferents can inhibit synergist muscles and that this inhibition might occur across joints (Eccles and Lundberg,

1958, Ross and Nichols, 2009). In addition, it has been suggested that synergist muscles might be controlled in groups (modules/synergies) by a common control signal, relative to the flexion and extension phase during both pedaling and locomotion (Kautz and Patten, 2005, Hug et al., 2011, van den Hoorn et al., 2015). This could also explain why the changes in hip extensors and plantar flexors within the fatigued leg occurred concurrently with the active phase of the fatigued muscles (extension). Overall, these findings suggest that data on the alteration of muscle activation obtained during global uncontrolled fatigue should be interpreted with caution. Even though the force output of a muscle decreases, this does not necessarily imply fatigue. Moreover, fatigue of a single muscle might inhibit the performance of other unaffected muscles. Note that this inhibition did not occur during a submaximal intensity condition. The higher constraints at higher intensities might augment the impact of fatigue, which in turn necessitated changes in motor control strategies (Enders et al. 2015; Nichols 1994). It has also been suggested that the afferent interactions between joints are weaker during tasks at lower intensity, providing more flexibility to the task (Nichols, 1994).

Interestingly, the biarticular BF showed no adaptations during pain (study 3), despite a significant decrease in activation of the painful vastii muscles. This might seem counterintuitive considering the results in study 1 and 2, however previous authors found that cocontraction of the antagonist muscles provides stability around the affected joint (Lund et al., 1991). This is an important aspect to consider and might be preferentially employed during pain as a protective mechanism for the painful muscles.

Adaptations between legs

The primary adaptation in all studies occurred at the contralateral leg. In study 1, during which submaximal pedal power was maintained, adaptation occurred primarily by an increase in

power at the non-fatigued leg during the flexion phase, concurrent with the decrease in extension for the fatigued leg. The primary joint involved was the hip, showing increased hip joint power and increased muscle activity of the tensor fascia latae. This between leg adaptation might be explained by the mechanical coupling between pedals, due to which any change at one pedal would inherently affect the contralateral pedal. This relationship might also favor adaptations within the same phase of movement to maintain symmetry and smoothness, which were part of the task goal (i.e. maintain constant pedaling rate and power). In addition, studies using decoupled cranks demonstrated a neural coupling between legs (Ting et al., 2000b, Kautz and Patten, 2005) which could also explain adaptations occurring between legs. Afferent information on the fatigued state could have been mediated through these neural interlimb coupling mechanisms to ensure proper compensation at the contralateral leg. Finally, each leg might be controlled as a functional unit. Central pattern generators at a spinal level have been shown to utilize sensory afferent information and descending inputs to generate bilateral activity during locomotion (Rossignol, Dubuc, and Gossard 2006; Lajoie et al. 1996; Pearson, Misiaszek, and Hulliger 2003). These might maintain muscle coordination at the ipsilateral leg and prefer to adapt bilaterally.

Between leg adaptions were also observed in study 2 during pedaling at maximal intensity. In this study, flexion power also increased at the contralateral leg, which was somewhat surprising since the task was performed at maximal intensity. Moreover, this increase of power output during the flexion phase was also clearly observed at the ipsilateral leg. Interestingly, some authors suggested that even though the task is maximal, some muscles might not be maximally activated (Dorel et al., 2009). This could be the case for the hip flexors muscles, whose contribution to overall power is also relatively low. This reserve might allow for an increase in muscle activation during this phase. Note that muscle activity decreased slightly for a number of muscles, especially

those active during the extension-flexion transition and extension phase of the contralateral leg. Although studies suggest that independent control of each lower limb is possible, these results suggest an inherent and dependent relationship between the two. It could be explained in part by a bilateral neural coupling between the biarticular muscles responsible for the extension-flexion transition phase of one leg and flexion-extension at the contralateral leg (Kautz et al., 2002). Despite the decrease in activity, the overall power of the non-fatigued leg remained unchanged, which was associated with increased power during flexion and an increase in the index of effectiveness during both flexion and extension.

In study 3, adaptations to pain consistently occurred at the contralateral non-painful leg during the extension phase, with increased activation of the contralateral extensor muscles to maintain target power and pedaling frequency. The extension phase of the pedaling cycle is particularly well-suited for force production, but the adaptation observed was completely different to what was observed in study 1. The difference in strategies between study 1 and study 3 is difficult to explain from the data obtained in these studies, and its cause can only be speculated upon. One explanation is the differences between fatigue (loss of force generating capacity) and pain. However, a more likely explanation is the significant difference in intensity levels. Study 1 was performed at 350 W, which is a relatively high submaximal intensity (vastii and GAS muscle activity levels around 40-50% of their max (Dorel et al., 2012)) In a comparable low intensity experiment (150 W) obtained during the same experimental session, adaptations to fatigue were limited and occurred during the extension phase if at all (unpublished data). This confirms the results obtained during pain and might indicate that intensity of the task is an important parameter in determining adaptations. Further studies are needed to determine if the strategy chosen depends on a specific threshold related to the intensity of the task. At higher intensities, as muscles

activation levels increase, adaptations in other phases than extension might become increasingly attractive to avoid excessive activation of some muscles. Indeed, the flexion phase normally contributes very little to the overall production of power (Raasch and Zajac, 1999), suggesting that this phase could have unused potential for improvement. An increase in flexion power has been stated to play an important role during high intensity pedaling (Raasch et al. 1997) and also when the force produced during the extension phase is inadequate in regards to the given requirements (Kautz and Brown, 1998).

It should be noted that considerable inter-individual variability was an important feature in all the studies. It is likely that in the initial search for an alternative muscle coordination strategy, the exploration might be suboptimal (de Rugy, Loeb, and Carroll 2012), and may entail increased purposeful variability (Raphael, Tsianos, and Loeb 2010). Studies suggest that the adaptation strategy is chosen within a range of acceptable behaviors, which could be chosen stochastically (Ganesh et al., 2010, Kodl et al., 2011). This might explain the observed inter-individual variability.

Overall, the studies showed that adaptations preferably occurred at the unaffected contralateral leg. Furthermore, specific adaptations in this leg might depend on a trade-off between some control costs such as variability and effort, together with a complex interaction with the task mechanics and underlying neural organization.

5.2 Perspectives

Research ideas and possible applications in sports

The findings are applicable to areas in both sports and medicine. Study 1 showed that selective fatigue resulted in an increase in power during the flexion phase. This could potentially

attenuate fatigue effects during prolonged submaximal cycling by redistributing the workload to flexor muscles, or by a more even distribution of work between extensors and flexors. The flexion phase during pedaling has been subject to some controversy. Studies have reported that an acute increase in flexion power might come at higher metabolic cost (Korff et al., 2007). The advantages of this strategy are therefore not very clear. Nevertheless, Theurel et al. (2012) showed that when this strategy was used during prolonged pedaling, efficiency was maintained while muscular strain on knee extensor muscles decreased. This could possibly help attenuate fatigue effects during prolonged pedaling. Considering these results, training interventions designed to force the subject to use alternative pedaling strategies could have major practical applications for cycling performance. An interesting future project could use a longitudinal study design to investigate whether these pedaling strategies would produce even better results, and if the same results are obtained in a well-trained population.

It would also be interesting to test this strategy during pedaling at maximal intensity. Pedaling technique is an important parameter for high performance in cycling, especially during sprint. Study 2 showed that even during pedaling at maximal intensity, there is potential to increase the power contribution in the flexion phase. In addition, the index of effectiveness increased during both flexion and extension as a result of induced fatigue, providing evidence of changes in muscle coordination strategy. These changes included optimization of the way forces were directed on the pedal, possibly resulting in increased total power output. Further studies are needed to determine if pre-induced fatigue can be used as a strategy to augment these changes, improving overall performance, and also to perhaps provide additional positive adaptations by fatiguing different muscle groups.

Research ideas and possible clinical applications

The results in the current dissertation might also have important implications for the diagnosis and rehabilitation of patients. Pain and fatigue are issues in several clinical conditions such as fibromyalgia, arthritis, and chronic musculoskeletal pain. It is well known that, for example, pain has a significant impact on motor and postural control (Heredia Jimenez et al., 2009, Jones et al., 2011), which is related to the findings reported in study 3. In this study, activation of the painful knee extensor muscles decreased. While this strategy protects the painful tissue from additional pain, it might also result in decreased stability around the knee joint. Although this strategy did not cause issues in the cycling task used in our study, decreased stability could increase susceptibility to injury and risk of falls during locomotion (Henriksen et al., 2009, Leveille et al., 2009). Evidence also suggests that adaptations might persist even after pain has disappeared; this could induce an asymmetry and lead to problems elsewhere, such as lower back pain. The application of selective pain to develop a better understanding of muscle coordination could help identify both strong and weak links during movement with pain. This could help develop appropriate rehabilitation techniques and prevent translation from acute to chronic musculoskeletal problems.

In general, results in the current dissertation showed that the motor control system readily adapts to fatigue and pain. This plasticity is an impressive feature in the human motor control system, and studies suggest that this capacity is intact in patients with post stroke hemiparesis or spinal cord injury, despite diminished compensatory capabilities (Dietz & Colombo 1998; Wezel et al. 2000). Appropriate rehabilitation strategies are needed to assist in regeneration of neural circuits. By restoring appropriate patterns of neural activity, synaptic connections might be improved and modified to enhance recovery, especially for locomotion tasks. This can be attained

by manipulating load levels, weight-supported treadmill training, and/or functional electrical stimulation. The results also suggest that selective fatigue/pain, could potentially target specific muscle groups, which might help patients with neuropathy in regaining locomotor patterns through a reorganization of spinal circuits. It remains to be seen how and if this strategy could be used in a clinical framework. Finally, pedaling could have a practical advantage in severe cases, since factors such as balance and gravity have negligible influence. Studies showed a strong correlation between hemiparetic severity and deviant motor activity (Kautz and Patten, 2005), suggesting that some patients may benefit from an approach using pedaling.

Adaptations to fatigue and pain and existing motor control theories

Although important features were identified for adaptions to pain and fatigue, it was not possible to investigate specific underlying neural control mechanisms. The results suggest that when a muscle group is fatigued, compensatory adaptations preferentially occur in other muscles when this obvious solution is available, rather than inside the perturbed muscle. How this fits into existing motor control theories, such as optimal control, is difficult to ascertain. Optimization likely occurred, as shown by an increase in contralateral flexion/extension; however, it was not clear if this was the result of optimization of a cost function such as effort and/or variability. Theurel et al. (2012) recently demonstrated that an increase in mechanical effectiveness had the potential to attenuate effects of fatigue. Thus, it might be that adaptations in other muscles are in accordance with minimization of effort or fatigue. A similar proposition was made by Prilutsky (2000), though others highlight that no single factor can be the governing mechanism in muscle coordination (Kautz et al., 2000). In this line, considerable inter-individual variability was observed in muscle coordination strategies; this could indicate that multiple good-enough solutions were available, from which the adaptation strategy was chosen stochastically. The variability could

also reflect emergent motor control strategies based on a multitude of individual constraints at any given point in time, including individual history, body characteristics, environment, and task characteristics such as the level of fatigue and the subjective sense of effort/pain. The influence of these constraints was further emphasized by the influence of task intensity on adaptation strategies. While adaptations occurred readily during the flexion phase at higher intensities, data at lower intensities suggested that adaptations primarily occurred during extension. This could be explained by a tradeoff between different cost functions, such as effort and error, changing in relation to the mechanics of the task and the underlying neural organization. A clarification of how the motor control system arrives at a specific muscle coordination strategy is one of the main issues in the study of motor control, with major implications in medicine and for the development of prosthetics and robotics. To investigate further, simulation studies manipulating factors such as effort and variability could be used to observe how muscle coordination changes in respect to these parameters; the simulations would also be compared to actual measurements.

One important aspect emphasized throughout the dissertation was that the majority of studies on muscle coordination are focused around subsystems, such as a single muscle group, studied in isolation from the complex global locomotor system. Little knowledge is available regarding overall function and how these subsystems are connected. Although studying the global system involves a range of experimental challenges, such research is imperative. The specificity the adaptations to fatigue and pain observed in the current dissertation highlights important limitations in transferring traditional findings (single-joint tasks) to daily life activities where between joint and leg adaptations might play a key role.

5.3 Conclusion

The purpose of this work was to investigate adaptations to fatigue or pain occurring during a multijoint task with many degrees of freedom. In general, the results showed that the motor control system readily adapts its muscle coordination strategy to both fatigue and pain. Specific adaptations were observed between studies depending on the perturbation (fatigue/pain) and the intensity of the task. During pedaling at maximal intensity with selective fatigue of the quadriceps muscle, results suggest that the central motor drive to the fatigued muscles is not impaired, likely as a strategy to produce the highest amount of force possible. In contrast, during pedaling at submaximal intensity, the activity of the fatigued muscle remained unchanged. This resulted in a decrease in power, necessitating a change elsewhere to maintain total power. These results suggest that the muscle coordination strategy exploited additional degrees of freedom (other non-fatigued muscles) rather than the fatigued muscle itself. In the submaximal condition, a factor such as effort might play a more important role. A similar muscle coordination strategy, exploiting additional degrees of freedom, was observed during pain; this allowed a decrease in muscle activity at the painful muscles, likely as a strategy to protect the painful tissue from further pain and/or injury.

In all studies, changes at the perturbed muscles had a significant impact on other unaffected muscles. During both submaximal and maximal pedaling, fatigue resulted in important changes within the fatigued leg to accommodate for loss of power and to maintain the direction of force. The biarticular muscles were especially involved. During maximal pedaling, additional changes were observed for synergist muscles within the affected leg; these did not maintain muscle activation levels despite not being fatigued.

Consistent adaptations were observed between legs, regardless of perturbation and intensity. This might suggest that when adjusting to local unilateral perturbations during a bilateral

mulitjoint task, a preference exists to adapt between legs. This can be explained by both mechanical (coupling between the pedals) and neural factors (inter-leg neural coupling and control of muscles in functional groups/synergies). A difference was observed concerning which phase of the pedaling cycle bilateral adaptations occurred in. With fatigue and either submaximal or maximal intensity pedaling, adaptations primarily occurred during the flexion phase at the contralateral leg. This increase during flexion was explained by its increased importance and advantage during higher intensities. In the pain study, which was performed at a much lower intensity, the between leg adaptations occurred during the extension phase, the most efficient and powerful phase.

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PÔLE DE RECHERCHE ET D'ENSEIGNEMENT SUPÉRIEUR

UNIVERSITÉ DE NANTES

Thèse de Doctorat

Niels-Peter BRØCHNER NIELSEN

THE EFFECTS OF FATIGUE AND PAIN ON MUSCLE COORDINATION DURING A MULTIJOINT TASK

Summary

Movement requires the coordination of multiple muscles. How this is done during fatigue and pain is not well understood, particularly in multijoint tasks. This thesis investigated muscle coordination and the adaptations to local fatigue or pain during pedaling. Fatigue and pain was induced unilaterally on the quadriceps, which made it possible to determine the adaptations at these perturbed muscles, as well as between synergists, and muscles within the same leg and between legs. The thesis demonstrated that during submaximal pedaling, the unilateral pre-fatigue results in a predominant redistribution of muscle activity towards unaffected muscles at the contralateral leg. Another study performed in the same pre-fatigue condition but at maximal intensity, provided evidence that muscle coordination changes to decrease activation of ipsilateral synergist muscles allowing to maintain an effective force orientation at the pedal. Interestingly, we also observed an increase in activation of other muscles which participated to improve the total force produced during the flexion phase of both legs. Finally, another study that induced unilateral local pain, supported pain adaptation theories suggesting that when there is a clear opportunity to compensate, adaptations to pain occur to decrease load within the painful tissue. Overall this thesis demonstrated that muscle coordination readily adapts exploiting the many degrees of freedom available during pedaling. Both neural (between legs) and mechanical (between pedals) couplings in this specific task and the minimization of cost functions (neural, energetic, mechanical) or pain adaptation theories might explain these results.

Keywords
Fatigue, Pain, Muscle coordination, Pedaling, Multi-joint, Adaptation

Résumé

Le mouvement nécessite la coordination de nombreux muscles. La manière dont le système nerveux adapte la commande motrice sous l'effet de contraintes telles que la fatigue ou la douleur n'est pas encore bien comprise, en particulier lors des tâches multi-segmentaires. Ce travail a démontré que lors d'une tache de pédalage sous-maximale, une pré-fatigue unilatérale du quadriceps entraîne une redistribution préférentielle de l'activité musculaire vers la jambe controlatérale pour compenser. Une seconde étude réalisée à puissance maximale (i.e sprint) a mis en évidence une diminution de l'activation des muscles synergistes, mais permettant le maintien de l'efficacité de pédalage. De façon originale, une amélioration de l'activation d'autres muscles a été observée, participant à augmenter la force produite lors de la phase de traction de la pédale pour les deux jambes. Enfin, en réponse à une douleur locale, les résultats d'une dernière étude suggèrent que, lorsqu'il existe une opportunité claire de compenser, des adaptations se produisent dans le but de diminuer la charge dans le tissu touché. Dans l'ensemble, cette thèse a démontré que les coordinations musculaires s'adaptent à la fatigue et à la douleur en exploitant les nombreux degrés de liberté disponibles dans cette tâche. Ces adaptations ont été discutées au regard des théories et lois de contrôle proposées dans la littérature incluant la minimisation de « fonctions de coût » (énergétique, mécanique et/ou nerveux) ou d'adaptation à la douleur, mais aussi des contraintes spécifiques de la tâche (orientation de la force externe à la pédale, transferts inter-segmentaires, couplage mécaniques et nerveux inter-jambes).

Mots clés
Fatigue, Douleur, Coordination musculaire, Multi-articulaires, Pédalage, Adaptation