Control of Trunk Muscle Force in Individuals with Low Back Pain: New Insights Revealed by High-Density Surface Electromyography

By

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A thesis submitted to the University of Birmingham

for the degree of

DOCTOR OF PHILOSOPHY

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July 2024

Abstract

Low back pain (LBP) is a leading cause of disability worldwide, with chronic non-specific LBP (CLBP) accounting for most cases. It is well-recognised that individuals with LBP exhibit different movement patterns compared to those without pain. Extensive research has examined motor adaptations in individuals with CLBP, highlighting alterations in trunk muscle strength, muscle activity, movement patterns, and proprioceptive acuity. Recent studies have also shown that musculoskeletal pain, including CLBP, can impair muscle force control. However, the concept of force or torque steadiness as a motor adaptation in people with CLBP has been relatively understudied and therefore requires further investigation. This thesis presents research that focuses on enhancing our understanding of motor adaptations in people with CLBP, specifically in relation to changes in the control of trunk muscle force/torque steadiness and the potential underlying neuromuscular mechanisms. To achieve this, it examines the relationship between trunk high-density electromyography (HDsEMG) signals and torque using cross-correlation and coherence analyses, and principal component analysis (PCA) to improve these estimations. The *first study* examined the control of trunk muscle force and EMG-torque relationships during isometric trunk extension contractions, revealing that individuals with CLBP have poorer control compared to pain-free individuals. People with CLBP performed the contractions with altered recruitment strategies, including a higher contribution of more cranial regions of the lumbar erector spinae (ES) to the resultant torque and a failure to increase the contribution of the lumbar ES to the resultant torque with an increase in load. The *second study* extended these findings to dynamic trunk flexion/extension concentric and eccentric contractions, showing that the control of trunk muscle force is also impaired during these movements alongside altered recruitment patterns. These involved a

higher contribution of the thoracolumbar ES to torque, as observed in the first study during trunk extension contractions, and increased abdominal muscle activity, with the centre of activation being more cranial and a higher contribution of this musculature to the resultant torque (particularly the external oblique muscle) during trunk flexion. In contrast, the *third study*, which investigated the effects of acute low-back soreness induced by delayed onset of muscle soreness (DOMS) on trunk muscle function, recruitment behaviour, movement patterns, and underlying neuromuscular mechanisms, showed that DOMS did not impair trunk force control. However, EMG-torque relationships and kinematics were altered in a contraction-dependent manner. During eccentric contractions, a decrease in the thoracolumbar ES contribution to the resultant torque was observed, and individuals showed increased lumbar flexion during the more demanding contractions. During concentric contractions, a reduction in thoracolumbar range of motion in the sagittal plane was observed, suggesting the maintenance of a more neutral lumbar spine posture, but no alterations in HDsEMG-torque relationships were observed in the presence of DOMS. These findings suggest that pain-free individuals could adapt their motor strategies and maintain muscle performance despite DOMS. The *fourth study* was a systematic review and meta-analysis that explored the influence of clinical and experimental musculoskeletal pain on the control of muscle force. The findings of this review suggested that the persistent, multidimensional nature of clinical musculoskeletal pain is related to more pronounced impairments in force control compared to the temporary nature of experimental pain, particularly for the trunk. The results of this thesis underscore the importance of evaluating torque steadiness in individuals with CLBP. The findings indicate that people with CLBP exhibit impaired force control and altered trunk muscle recruitment strategies. Future research should explore the value of torque steadiness training and HDsEMG-based biofeedback for enhancing torque steadiness performance in this patient population.

These interventions could lead to better-targeted therapies that address the specific neuromuscular deficits associated with CLBP.

Acknowledgements

Firstly, I would like to thank my supervisors, Dr. Eduardo Martinez-Valdes and Prof. Deborah Falla, for all their support, invaluable guidance, and dedication to my academic and personal growth. I could not have asked for a better supervisory team. The number of opportunities and the breadth of knowledge you have imparted to me—in terms of academic, technical, management, and organisational skills, as well as in teaching—is something I never anticipated when I arrived in the United Kingdom. Thank you for everything; you have been exceptional! I am looking forward to our future research endeavours.

I would also like to express my thanks to Dr. Andy Sanderson for his support and input as a second reviewer of the systematic review and meta-analysis in this thesis. I extend my gratitude the participants of my studies. Thank you to all my colleagues from the CPR Spine team for their ongoing support and for assisting me in the lab whenever I needed it. Specifically, I would like to thank my friends Nadège Haouidji-Javaux (a.k.a *"keep calm and ask Nadège"*) for collecting most of the data with me, for her help with the MATLAB scripts, for being always one step ahead and organising the best birthday parties; David Jiménez-Grande for his contribution to the signal analysis of my data, which significantly advanced the output of my work as well as for our runs and training moments, and Ignacio Contreras-Hernandez for his help with the data collection, discussions on the interpretation of data and easy cooking tips. Thank you all for the great moments we have shared and for those that will come!

To my girlfriend, Katerina, thank you for always being there for me and consistently believing in me, even when I doubted myself. Your patience has been tremendous on this journey. I am sorry that I have not been there for you as much as I wanted. I love you!

Lastly, all of this would not have been possible without the support of my family. My dear dad (Dinos), mother (Anna), and brother (Efthymis), you have always been there for me,

even reading my manuscripts and identifying my mistakes. With your support and encouragement, you made this incredible dream a reality and have shaped me as a person. I will be forever grateful, and I do not know what I would do without you. I am so lucky to have you. I would also like to thank my grandparents (whom I call my second parents) for all the lessons they taught me from an early age and for making all my wishes come true. Grandpa, I know that these last years were not easy for you. I wish I could have been by your side, and I am sorry that I could not. This Ph.D. is dedicated to you. I love you all.

List of Papers and Conference Abstracts

This thesis includes papers that have been published, presented at conferences, or are currently under review. A detailed summary of these papers and their relevance to this thesis will be provided at the beginning of each chapter as needed. Therefore, some sections of this thesis are written verbatim from these published works. Other sections are developed based on published work and thus may share similarities in structure and content with these sources. To maintain conciseness and avoid repetition, parts of the introduction and methodology sections have been significantly reduced, with readers referred to earlier chapters for detailed discussion.

Published Articles (Related to the thesis)

Arvanitidis M, Falla D, Sanderson A, Martinez-Valdes E. Does pain influence control of muscle force? A systematic review and meta-analysis. *Eur J Pain*. 2024.

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Eccentric exercise-induced delayed onset trunk muscle soreness alters high-density surface EMG-torque relationships and lumbar kinematics. *Sci Rep*. 2024;14(1):18589.

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Low Back Pain-Induced Dynamic Trunk Muscle Control Impairments Are Associated with Altered Spatial EMG-Torque Relationships. *Med Sci Sports Exerc*. 2024;56(2):193-208.

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. People with chronic low back pain display spatial alterations in high-density surface EMG-torque oscillations. *Sci Rep*. 2022;12(1):15178.

Arvanitidis M, Falla D, Sanderson A, Martinez-Valdes E. Does pain influence force steadiness? A protocol for a systematic review. *BMJ Open*. 2021;11(1):e042525.

Conference Presentations (Presenter is highlighted in bold)

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Associations between delayed onset trunk muscle soreness, altered EMG-torque relationships, and lumbar kinematics in dynamic contractions. XXIV Congress of the International Society of Electrophysiology and Kinesiology (ISEK). Oral presentation, Nagoya, Japan, June 26 - 29, 2024.

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Associations between impaired dynamic trunk muscle control in people with chronic low back pain and altered spatial EMG-torque correlations. XXIV Congress of the International Society of Electrophysiology and Kinesiology (ISEK). Poster presentation, Nagoya, Japan, June 26 - 29, 2024.

Arvanitidis M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Lumbar extensor muscle isometric torque steadiness and torque-HDsEMG coherence is altered in

individuals with chronic low back pain. XXVIII Congress of the International Society of Biomechanics (ISB). Digital Congress, July 25 - 29, 2021.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

Acronym	Definition
1D	One-Dimensional
2D	Two-Dimensional
3D	Three-Dimensional
ADM	Abductor Digiti Minimi
ANOVA	Analysis of Variance
APAs	Anticipatory Postural Adjustments
AUC	Area Under the Curve
AU	Arbitrary Units
ASIS	Anterior Superior Iliac Spine
BIC	Biceps Brachii
CLBP	Chronic Low Back Pain
CNS	Central Nervous System
CoV	Coefficient of Variation
CON	Concentric
CPAs	Compensatory Postural Adjustments
CIs	Confidence Intervals
CSA	Cross-sectional Area
CLE	Chronic Lateral Epicondylitis
CNP	Chronic Neck Pain
DASH	Disabilities of the Arm, Shoulder and Hand
DOMS	Delayed Onset of Muscle Soreness
DYN	Dynamic
ECG	Electrocardiogram
ECC	Eccentric
EMG	Electromyography
EO	External Oblique
ECT	Extramuscular Connective Tissue
ES	Erector Spinae
F	Females
FIHOA	Functional Index of Hand Osteoarthritis
GCPS	Graded Chronic Pain Scale
GDNF	Glial Cell Line-derived Neurotrophic Factor
GLMM	Generalised Linear Mixed-Effects Model
GM	Gastrocnemius Medialis
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDsEMG	High-density Electromyography
IAT	Insertional Achilles Tendinopathy
ICC	Intraclass Correlation Coefficient
IO	Internal Oblique
IPAQ	International Physical Activity Questionnaire
IQR	Inter-quartile Range
ISO	Isometric

IVDs	Intervertebral Discs
JFLS-20	Jaw Functional Limitation Scale
JPF	Jaw Pain and Function
LBP	Low Back Pain
M	Males
MD	Mean Difference
METs	Metabolic Equivalents
MeSH	Medical Subject Headings
MSC	Magnitude Squared Coherence
MVC	Maximal Voluntary Contraction
MNF	Mean Power Frequency
N/A	Not Applicable
NGF	Nerve Growth Factor
NDI	Neck Disability Index
NOS	Newcastle-Ottawa Scale
NPRS	Numerical Pain Rating Scale
NSLBP	Non-specific Low Back Pain
OA	Osteoarthritis
OBC	Oral Behavioural Checklist
ODI	Oswestry Disability Index
PCA	Principal Component Analysis
PCs	Principal Components
PCS	Pain Catastrophising Scale
PFP	Patellofemoral Pain Syndrome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PPT	Pressure Pain Threshold
RA	Rectus Abdominis
RAND	Research and Development
RMS	Root Mean Square
RM-ANOVA	Repeated Measures Analysis of Variance
ROM	Range of Motion
SampEn	Sample Entropy
SAPS	Sub-Acromial Pain Syndrome
SE	Standard Error
SF-36	36-Item Short Form Health Survey
SIS	Shoulder Impingement Syndrome
SMD	Standardised Mean Difference
STAI	State-Trait Anxiety Inventory
SD	Standard Deviation
TA	Tibialis Anterior
TF	Target Force
TMDs	Temporomandibular Disorders
TSK	Tampa Scale for Kinesiophobia
TrA	Transverse Abdominis
VAS	Visual Analogue Scale

VM	Vastus Medialis

Chapter 1

GENERAL INTRODUCTION

1.1 Low Back Pain – an Overview

1.1.1 Definition, Epidemiology & Economic Burden

Low back pain (LBP) is typically defined as pain, muscle tension, or stiffness localised in the posterior aspect of the body, extending from the lower margin of the 12th ribs to the lower gluteal folds, with or without referred lower limb pain, and lasting for at least one day (Chiarotto and Koes, 2022, Hoy et al., 2014, Koes et al., 2006). LBP is exceedingly common and is the leading cause of years lived with disability worldwide, with an average global lifetime prevalence of approximately 40% in adults (Ferreira et al., 2023, Hoy et al., 2012, Hoy et al., 2010). In 2020, there were over 500 million prevalent cases of LBP globally, with projections suggesting that by 2050, the number could exceed 800 million, primarily due to population growth and aging in certain regions (Ferreira et al., 2023). LBP affects individuals across all ages and socioeconomic strata (Fatoye et al., 2023b), with its prevalence peaking at approximately 85 years of age and being more common in females and those aged 40 to 69 years old (Ferreira et al., 2023, Hoy et al., 2012, Maher et al., 2017).

Beyond its impact on health, LBP extends into societal and economic realms due to its high prevalence and considerable burden, particularly among working-age individuals. Consequently, this often results in significant work-related consequences, including absenteeism and premature retirement (Ferreira et al., 2023). The financial implications of LBP

are substantial, encompassing both direct costs (e.g., expenses for diagnosis and treatment), and indirect costs (e.g., early retirement pensions and premature mortality) (Fatoye et al., 2023b). Notably, in high-income regions such as America, Europe, and the Western Pacific, the average annual direct and indirect costs per population for LBP can reach up to €2.6 billion and €8.15 billion, respectively (Fatoye et al., 2023b). Meanwhile, in lower- and middle-income countries, including Argentina, Brazil, and Ethiopia, annual costs can reach up to US$2.2 billion (Fatoye et al., 2023a). In the UK, the annual direct healthcare costs of chronic LBP (CLBP) were estimated to be £1.5-£2.8 billion, primarily due to people with CLBP accruing double the yearly healthcare cost of pain-free individuals (Hong et al., 2013). On the other hand, historically, the annual indirect costs of CLBP were estimated at £10.7 billion in 2000 (Maniadakis and Gray, 2000).

The high and escalating rates of LBP, alongside its significant financial impact, underscore the need for comprehensive strategies that refine assessment protocols, enhance intervention methods, and effectively integrate prevention, assessment, and management to improve outcomes and quality of life for affected populations globally. Given the profound impact and complexity of LBP, an understanding of its classification is crucial for tailoring effective assessment protocols and interventions.

1.1.2 Classifications of LBP

Diagnostic triage in clinical practice classifies LBP into three categories based on the cause of pain: (i) specific pathology (spinal or non-spinal) (ii) nerve root/radicular pain, and (iii) non-specific LBP (Chiarotto and Koes, 2022, Koes et al., 2006). Specific spinal causes include herniated disks, spinal stenosis, fractures, tumours, infections, and axial spondyloarthritis, while non-spinal causes may involve hip conditions, pelvic organs diseases,

such as prostatitis and endometriosis, and vascular (e.g., aortic aneurysm) or systemic disorders (Chiarotto and Koes, 2022, Koes et al., 2006, Nijs et al., 2024). LBP conditions with radicular pain due to nerve-root involvement have a higher prevalence (5 to 10%) compared to other spinal causes, with the two most frequent causes of such LBP being disk herniation and spinal stenosis (Foster et al., 2018). However, the majority (80-90%) of LBP cases are classified as *"non-specific"*, suggesting that in most individuals with LBP a specific pathoanatomical cause explaining pain or disability cannot be identified, and LBP probably develops from the interplay of biologic, psychological and social factors (Chiarotto and Koes, 2022, Nijs et al., 2024).

Recent criticism of the term *"non-specific"* LBP has prompted a shift toward pain phenotyping, such as *"nociplastic pain"*, to prevent stigmatization and nocebo effects (Nijs et al., 2023, Nijs et al., 2024). Pain phenotyping categorises pain based on its predominant source into (i) nociceptive (i.e., pain resulting from the activation of the peripheral sensory endings of primary afferent neurons by noxious mechanical, thermal of chemical stimuli or pain arising from actual or threat of non-neural tissue damage caused by activation of nociceptors) (Merskey, 1986), (ii) neuropathic (i.e., pain caused by a lesion or disease of the somatosensory nervous system (Scholz et al., 2019) and (iii) nociplastic (i.e., pain due to altered nociception despite no clear evidence of actual or threatened tissue damage, which causes the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain) (Kosek et al., 2016). This classification allows for the recognition of mixed pain presentations which might be the case in people with CLBP (i.e., a mixture of nociceptive, neuropathic and/or nociplastic pain) (Nijs et al., 2024). LBP is further classified by the duration of symptoms, as acute (<6 weeks), subacute (6 to 12 weeks) and as chronic, which is defined as pain every day for 3 months or pain for at least half the days in the last 6 months, allowing

some flexibility when considering people with recurrent LBP (Deyo et al., 2014, Ferreira et al., 2023).

This thesis focuses specifically on individuals with non-specific CLBP, hereafter referred to simply as *"CLBP"*. According to recent guidelines, this category of CLBP may involve mechanisms of nociplastic and/or nociceptive pain, or potentially a combination of both (Nijs et al., 2023, Nijs et al., 2024). Understanding the detailed classifications and underlying pain mechanisms of LBP sets the stage for exploring the lumbar spine's anatomy, which is crucial for comprehending how anatomical dysfunctions contribute to the condition.

1.2 Anatomy of lumbar spine

1.2.1 Structural anatomy

The lumbar region encompasses a complex anatomical configuration, which contributes to the structural stability of the upper torso and to a modest range of movement between the thorax and the pelvis (Bogduk and Endres, 2005, Moore et al., 2014). A dysfunction in this region can play a significant role in the aetiology of CLBP (Ebraheim et al., 2004). Hence, an in-depth understanding of the anatomy of the lumbar spine is important for elucidating the mechanisms potentially contributing to the perpetuation of symptoms.

The lumbar spine consists of five lumbar vertebrae (L1 to L5) that are followed by the sacrum (Bogduk and Endres, 2005). Movement and stability in the lumbar spine is facilitated by its structural design, which features each lumbar vertebra consisting of two main parts, the vertebral body anteriorly and the neural arch posteriorly (Ebraheim et al., 2004). This configuration supports articulations through intervertebral discs (IVDs) located anteriorly between the vertebral bodies, and pairs of zygapophyseal joints found posteriorly (Ebraheim et al., 2004). The IVDs, being avascular structures, permit flexion, extension, and lateral bending

movements by allowing the vertebral bodies to move relative to each other (Ebraheim et al., 2004). Similarly, the zygapophyseal joints, composed of adjacent inferior and superior articular processes and an articular capsule, enable a sliding motion within the posterior part of the spinal column (Ebraheim et al., 2004). Thus, the combined function of these components allows for the range of movements observed in the lumbar spine. Except of the vertebral column, passive stability in the lumbar region as a unit also originates from other non-contractile tissues, such as the anterior and posterior longitudinal ligaments, ligamenta flava or yellow ligaments, supraspinous and interspinous ligaments (Ebraheim et al., 2004). Beyond the passive structural support, the muscles provide the functional mechanism for movement and stability of the spine by allowing for smooth, controlled movement in all functional planes (Gilchrist et al., 2003).

1.2.2 Lumbar extensor muscles

The anatomy of the muscles that surround the lumbar spine is complex, likely due to the diversity of their numerous attachments (Bogduk, 2016). In the posterior part of the lumbar spine the primary muscle groups responsible for controlling lumbar movement and forward inclination of the trunk are the erector spinae (ES) and multifidus muscles (Gilchrist et al., 2003, Mawston and G. Boocock, 2015). The lumbar ES which is enveloped by the posterior layer of the thoracolumbar fascia, consists of two divisions, the iliocostalis lumborum and the longissimus thoracis, both of which have two components, (i) a lumbar part which consists of fascicles arising from lumbar vertebrae and (ii) a thoracic part with the fascicles arising from thoracic vertebrae or ribs (Bogduk and Endres, 2005, Macintosh and Bogduk, 1987, Mawston and G. Boocock, 2015). Therefore, these four muscles are commonly referred to as longissimus thoracis *pars lumborum*, iliocostalis lumborum *pars lumborum*, longissimus thoracis *pars thoracis* and iliocostalis lumborum *pars thoracis*. On the other hand, the multifidus muscle is

located more medially to the ES and is composed of both deep and superficial short muscle fibres organised in densely packed bundles (Hodges and Danneels, 2019, Mawston and G. Boocock, 2015, Ward et al., 2009) (**Figure 1.1**). This arrangement results in a physiological cross-sectional area (CSA) that is twice as large as that of other ES muscles, despite having a similar mass (Mawston and G. Boocock, 2015). The large CSA, combined with the muscle's short fibre length, enables the multifidus to generate substantial forces across a limited range of motion (ROM) (Mawston and G. Boocock, 2015). Such characteristics render the multifidus better suited for providing stability to individual spinal segments rather than contributing to lumbar spine movement (Hodges and Danneels, 2019, Mawston and G. Boocock, 2015, Ward et al., 2009).

Contrary to the multifidus, which is primarily involved in providing stability to individual spinal segments due to its large CSA and short fibre length (Hodges and Danneels, 2019, Mawston and G. Boocock, 2015, Ward et al., 2009), the ES contributes significantly to concentric extension, eccentric flexion, and both concentric and eccentric axial rotation and lateral flexion during functional movements (Lee et al., 2005, Shojaei et al., 2017). This specific functionality is particularly relevant given that individuals with CLBP often report exacerbation in symptoms during such movements (Hanney et al., 2013). While the multifidus muscle is indeed crucial for lumbar spine stability is has been previously extensively studied (Hodges and Danneels, 2019), its deep location poses challenges for non-invasive investigation techniques, such as surface electromyography (EMG). In contrast, the ES muscles, due to their more superficial location, are more accessible for non-invasive measurement with such techniques. Consequently, the emphasis of this thesis is on investigating the thoracolumbar ES muscles.

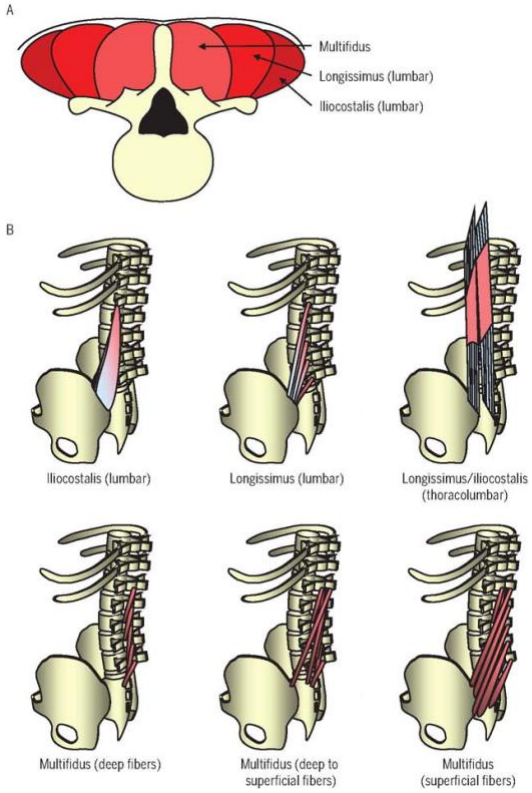


Figure 1.1: **Depicting the anatomical layout of the lumbar paraspinal muscles through (A) a cross-sectional view and (B) an in-situ perspective, emphasizing the orientation of the muscle fibres. The area marked by brackets represents the origin of the muscle fibres, commonly referred to as the pars region. Reproduced with permission from Hodges and Danneels (2019), DOI: 10.2519/jospt.2019.8827. Copyright ©Journal of Orthopaedic & Sports Physical Therapy®, Inc.**

1.2.3 Lumbar flexor muscles

Though not directly attached to the lumbar spine, the abdominal muscles are instrumental in controlling its movement. The abdominal wall is a complex structure that houses critical muscle groups such as the external and internal abdominal obliques (EO and IO), transverse abdominis (TrA), and rectus abdominis (RA) (Arslan, 2005) (**Figure 1.2**). These muscles are key to generating intra-abdominal pressure, aiding in expiration by compressing the thorax, and enabling movements of the thorax relative to the pelvis, thereby influencing lumbar spine mechanics indirectly (Arslan, 2005, Gilchrist et al., 2003).

The IO and TrA muscles, deeper within the anterolateral abdomen, are often referred to as local muscles due to their significant role in providing segmental control and enhancing lumbar stability. Conversely, the more superficial EO and RA muscles contribute to torque generation across multiple segments, facilitating load transfer between the thoracic cage-upper limbs and the pelvis-lower limbs (García-Jaén et al., 2020). Cadaveric studies have indicated that the RA and EO possess the longest fascicle lengths among the abdominal muscles, which allows them to generate force over a broad ROM, supporting various lumbar spine movements including flexion and lateral flexion (Brown et al., 2011). The function of these muscles is relevant for people with CLBP, since they commonly experience pain during these movements (Jung et al., 2018). Moreover, the superficial positioning of the RA and EO facilitates their assessment through techniques such as surface EMG, which is described in **Section 1.5**. Therefore, this thesis will focus on the roles of the RA and EO muscles in relation to CLBP.

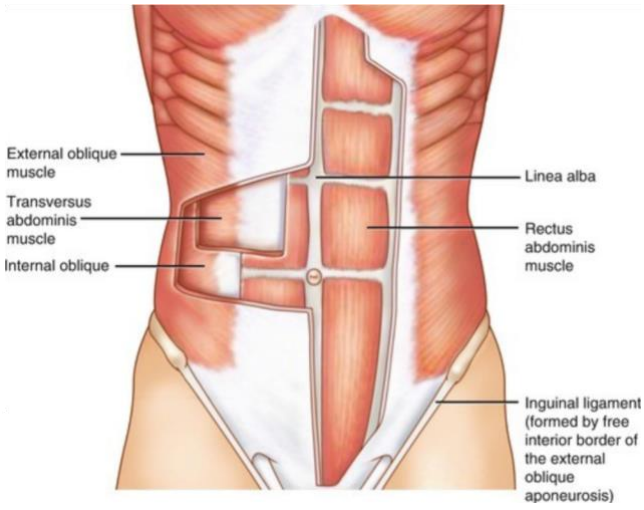


Figure 1.2: **This illustration offers a detailed view of the abdominal muscle layers, showing the EO, IO, TrA, and RA muscles, along with the linea alba and inguinal ligament. Material from: (García et al., 2014), Advances in Laparoscopy of the Abdominal Wall Hernia, © 2014 Springer-Verlag London**

Considering the complex anatomy of the trunk, it is important to understand how CLBP influences motor control and what impairments are commonly observed in this population.

1.3 Motor Control Adaptations in People with Low Back Pain

Motor control is the process by which the nervous system orchestrates posture and movement to accomplish specific motor tasks, integrating motor, sensory, and integrative functions (van Dieën et al., 2019). The redundancy within the musculoskeletal system, particularly in the trunk, affords the nervous system flexibility in utilising various muscles and joints for task execution. This adaptability is crucial for motor adaptation and learning and becomes particularly relevant in the context of pain (Bastian, 2008, Hodges and Tucker, 2011, van Dieën et al., 2019). Motor adaptation is the gradual modification of movement patterns through repeated trials, where these alterations become the new default, making the original patterns less accessible without gradual de-adaptation practices (Bastian, 2008, Martin et al., 1996). Conversely, motor learning is defined as the development of new movement patterns through sustained practice, resulting in the long-term storage of these patterns. Unlike motor adaptation, once a new movement pattern is learned, it can be recalled and utilised when needed, allowing for efficient transitioning between different learned patterns (Bastian, 2008).

In the presence of pain, individuals initially adjust the way they move to alleviate pain or discomfort, a process consistent with the concept of motor adaptation (Hodges and Tucker, 2011). This adaptation involves minor, trial-specific modifications that gradually become more permanent through repeated practice. Once these pain-induced altered movement patterns are firmly established, they transition into a phase of motor learning. During this phase, the new movement patterns are practiced extensively and become embedded within the nervous system, making them readily accessible and usable within appropriate contexts. This demonstrates the

individual's ability to adapt to and incorporate new movement strategies to avoid pain (Hodges and Tucker, 2011). Although, this can be beneficial in the short-term, the long-term utilisation of these adapted movement strategies may become maladaptive, potentially contributing to the perpetuation of symptoms (Hodges and Smeets, 2015, van Dieën et al., 2017, van Dieën et al., 2019).

Assessing motor adaptations to pain is essential for understanding their correlation with clinical symptoms and, more importantly, for identifying the precise nature of these motor control changes. This can inform the development of targeted intervention strategies that aim to alter maladaptive patterns and restore original motor control patterns, which may not be achievable without specific motor control restoration interventions (Falla and Hodges, 2017). Importantly, these interventions might differ considering the redundancy of the trunk and the large inter-individual variability in motor control impairment presentations as detailed below (van Dieën et al., 2019).

1.3.1 Movement Adaptations in people with LBP

Multiple adaptations contribute to the development and persistence of LBP, and their interactions are highly complex (Cholewicki et al., 2005). One such adaptation involves altered movement patterns (Hodges and Tucker, 2011).

People with LBP typically exhibit reduced lumbar ROM and slower movements in all lumbar directions compared to asymptomatic individuals (Laird et al., 2014). Movement alterations in individuals with CLBP are also evident during everyday activities like walking, where they often move slower, take shorter steps, and show disrupted trunk-pelvis coordination compared to those without LBP (Smith et al., 2022). Additionally, trunk kinematics during sit-to-stand-to-sit movements are affected; individuals with CLBP may experience reduced lumbar

ROM, slower displacement velocities, decreased acceleration, and increased kinematic variability of the trunk (Alsubaie et al., 2023, Sedrez et al., 2019).

However, it is important to note that there are inconsistencies in the direction of findings, which can be attributed to methodological differences, trunk redundancy, variation in symptom severity among LBP participants, and the lack of patient subgroups (van Dieën et al., 2019). The adaptations observed in CLBP extend beyond movement changes and are further explored in subsequent sections.

1.3.2 Trunk Muscle Performance Adaptations in LBP

In 2014, a narrative review concluded that people with CLBP demonstrate decreased strength, endurance, and atrophy of the lumbar extensor muscles (Steele et al., 2014). Even though muscle strength and endurance are typically reduced in people with CLBP, there is strong inter-individual variability (Matheve et al., 2023) and this is not supported by all studies (Pranata et al., 2017, Rostami et al., 2015, Tavares et al., 2020). The alterations in muscle strength and endurance might be explained to an extent by differences in muscle structure that are commonly observed in many but not all individuals with CLBP (Matheve et al., 2023). Specifically, a reduced CSA of the multifidus muscle has been noted, although it remains uncertain whether the lumbar ES and other back muscles are similarly affected (Matheve et al., 2023). There is also an increased fatty infiltration in the multifidus muscle and, to a lesser extent, in the lumbar ES (Matheve et al., 2023).

Interpreting the influence of CLBP on back muscle strength and endurance is challenging due to inconsistent findings. These inconsistencies may arise from methodological differences across studies and the multi-joint nature of the trunk, which can lead to compensatory actions by hip musculature during trunk extension contractions, thus

confounding assessments of muscle strength and endurance (Matheve et al., 2023). Additionally, as described in the next section, individuals with CLBP may also exhibit reduced proprioceptive acuity, leading to more subtle changes in motor performance, such as impairments in the control of trunk muscle force.

1.3.3 Proprioceptive and Force Control Adaptations in LBP

Proprioceptive deficits, frequently observed in individuals with CLBP either through active assessment in sitting positions or by measuring the threshold for detecting passive motion compared to asymptomatic controls, are likely significant contributors to the motor impairments seen in this population (Tong et al., 2017). Proprioception, a crucial element of our sensory system, involves the detection of joint position and movement, as well as sensations of force, heaviness and effort (Proske and Gandevia, 2012). These latter proprioceptive inputs are essential for smooth force production and overall motor control (Proske and Allen, 2019).

Pain can disrupt the ability to control muscle force through altered afferent inputs or neuroplastic changes in the central nervous system (CNS), which affect the integration of nociceptive and proprioceptive signals (Ager et al., 2020, Brumagne et al., 2019). Despite the pivotal role of proprioception in motor function, research has predominantly focused on conscious repositioning tasks, often neglecting how proprioceptive changes affect trunk muscle force control (Coppieters et al., 2021, van Dieën et al., 2019). This highlights a gap in our understanding of how proprioceptive changes influence the control of trunk muscle force in people with CLBP.

Neuromuscular control is the interaction between the nervous and muscular systems aimed at controlling movement (Clark et al., 2023). The ability to generate smooth trunk muscle force output, is crucial for protecting tissues from excessive mechanical stress. Skeletal muscles

protect the bones and cartilage via absorption of vibration and compression forces (Pain and Challis, 2006, Rudenko et al., 2016), and ligaments and joint capsules by resisting excessive tension forces (Olmstead et al., 1986). Since the skeletal muscle *"stress-shields"* the articular tissues from potentially damaging forces, the joint health relies on optimal neuromuscular and muscle force generation appropriate for a specific dynamic task (Clark et al., 2023). Therefore, optimal activation of the abdominal and paraspinal muscles, including the RA, EO, and ES, is vital for maintaining smooth force output and preventing lumbar spine overload.

An under-investigated aspect of neuromuscular control in people with CLBP is force or torque steadiness, defined as the ability of an individual to exert constant force output during a sustained submaximal contraction (Tracy and Enoka, 2002). This measurement is typically assessed through submaximal contractions against resistance provided by a dynamometer, using magnitude-based measures like standard deviation (SD) and coefficient of variation (CoV) of force to quantify absolute and relative variability (Clark et al., 2023, Enoka and Farina, 2021). Previous studies have demonstrated that lumbar extensor muscle force accuracy (i.e., measuring the difference between sub-maximal force output generated by an individual and a target force) is impaired in individuals with CLBP and that it predicts LBP-related disability (Pranata et al., 2017). Another study also observed that people with CLBP have worse isometric trunk extension force steadiness, but only at moderate force levels (Miura and Sakuraba, 2014).

These preliminary findings indicate potential impairments in force control during isometric trunk extension. However, it remains uncertain whether similar impairments are present during dynamic trunk movements. Understanding the underlying neuromuscular mechanisms responsible for these impairments is crucial, as it can inform targeted intervention strategies for individuals with CLBP. Therefore, this thesis aims to assess both trunk flexor and

extensor muscle torque steadiness and muscle activity in individuals with CLBP, employing the techniques outlined in the subsequent sections. In particular, this thesis will explore the EMG-torque relationships to understand how muscle recruitment affects the transmission of trunk muscle force. By investigating how muscle activity translates into force output, we aim to uncover specific neuromuscular patterns that contribute to impaired force control in CLBP and provide a more comprehensive understanding of the motor control deficits associated with this condition. As described in the next section, emphasising the interactions between muscle activity and force production is crucial, considering the alterations in trunk muscle activity observed in this population.

1.3.4 Trunk Muscle Activity Adaptations in LBP

Previous studies have explored muscle activation patterns during the control of trunk when challenged by (i) predictable and (ii) unpredictable perturbations, as well as (iii) during steady-state posture or movement (van Dieën et al., 2019). There is substantial evidence of muscle activation changes in individuals with CLBP, although findings vary.

A previous systematic review and meta-analysis found that trunk muscle responses to both predictable and unpredictable disturbances were delayed in people with CLBP compared to healthy individuals (Knox et al., 2018). This delay was not observed in those with acute LBP, indicating altered anticipatory postural adjustments (APAs) and compensatory postural adjustments (CPAs) in the CLBP population (Knox et al., 2018). Variability is also evident in the amplitude of muscle activation (root mean square; RMS), with some studies reporting no changes (Arvanitidis et al., 2021a, Larivière et al., 2000, Lisiński, 2000, Nouwen et al., 1987), others noting decreased (Ahern et al., 1988, Cassisi et al., 1993, Sihvonen et al., 1991), or increased (Balasch-Bernat et al., 2021, Salamat et al., 2024) lumbar ES EMG activity during

lumbar extension or functional tasks in individuals with CLBP compared to asymptomatic controls.

Alterations in abdominal muscles, particularly inhibition of deeper muscles, such as the TrA, have been consistently documented (Hodges and Richardson, 1998, Massé-Alarie et al., 2015, Massé-Alarie et al., 2012, van Dieën et al., 2019). During walking, increased activation of the RA has been observed, with no significant changes in the activity of the EO muscle, in people with CLBP compared to controls (van der Hulst et al., 2010). However, other studies have observed higher activity of the IO and EO during single leg standing tasks in people with CLBP, with no differences in RA muscle activity (Salamat et al., 2024).

Collectively, these findings show that people CLBP often exhibit alterations in trunk muscle activity, which might not be consistent, particularly for the superficial muscles (van Dieën et al., 2019). A recent narrative review suggested that variability in findings related to trunk muscle activity in CLBP may be due to two distinct motor adaptation phenotypes known as *"tight control"* and *"loose control"* (van Dieën et al., 2019). Initially, these adaptations may protect against tissue strain and spinal compression but could ultimately contribute to the chronicity of symptoms. Therefore, assessing activity of trunk muscles is crucial to understand specific motor adaptations.

1.3.5 Regional Activation Adaptations in LBP

Earlier studies on trunk muscle activity have primarily used bipolar surface EMG, which involves placing a pair of electrodes on the muscle surface to assess muscle activity in a limited number of separate lumbar areas. In contrast, high-density surface EMG (HDsEMG) as a more advanced non-invasive method that uses a dense grid of electrodes (e.g., 13 × 5, spaced 8mm apart) (Drost et al., 2006), allows the timing but also the spatial or regional (i.e., the specific

regions of lumbar ES that are active) distribution of muscle activity to be captured with greater detail (Falla and Gallina, 2020).

Most HDsEMG studies on the trunk have focused on assessing lumbar ES activity (Matheve et al., 2023). These studies have revealed significant changes in the spatial distribution of lumbar ES activity in individuals with CLBP, especially during high-demand tasks like repeated lifting or endurance tests, where activity tends to be more localised (Abboud et al., 2014, Sanderson et al., 2019a, Sanderson et al., 2019b) and involves more cranial regions of the ES compared to those without pain (Arvanitidis et al., 2021a, Sanderson et al., 2019a, Sanderson et al., 2019b). However, during low-load activities like walking or transitioning from sitting to standing, these differences were not apparent (Serafino et al., 2021).

These findings highlight that variations in ES activity between individuals with and without CLBP are task dependent. While previous studies have assessed lumbar ES activity during isometric or functional fatiguing tasks, the effects of load and contraction type on muscle activity in people with CLBP remain unclear. This gap in understanding extends on how different contraction types (isometric, concentric and eccentric) at various force levels impact muscle activity and the control of trunk muscle force. Additionally, while many studies investigated the activity of deeper abdominal muscles in various scenarios, the activity patterns of more superficial muscles like the RA and EO under similar conditions are not as well understood.

Therefore, this thesis aims to investigate whether differences in trunk muscle activity in individuals with CLBP manifest across both low and moderate-intensity isometric, concentric, and eccentric trunk flexion, and extension contractions. To this end, HDsEMG will be utilised in conjunction with controlled resistance provided by an isokinetic dynamometer. This setup not only records muscle activity but also measures the force output, which is crucial for

understanding how force control is affected in individuals experiencing CLBP (i.e., the underlying neuromuscular mechanisms), by allowing relationships between EMG and force to be explored. Additional details on the equipment are provided in subsequent sections (**Section 1.4** & **1.5.3**).

1.4 Isokinetic dynamometry

1.4.1 Definition and Usage

"Isokinetics" refers to dynamic muscular contractions at a constant velocity, controlled by an isokinetic dynamometer (Thistle et al., 1967). Isokinetic dynamometers are electromechanical devices that provide accommodating resistance, matching the device's resistance to the applied muscular torque throughout the pre-set range of movement, which allows for optimal muscle loading by accommodating for the length-tension relationship (Baltzopoulos and Brodie, 1989).

Isokinetic dynamometers can measure torque during isometric, concentric, and eccentric contractions, serving both clinical and research purposes (Kannus, 1994). A key parameter extracted from these assessments is peak torque, which is commonly used as a measure of muscle strength (A et al., 2020). This value can be then used to generate submaximal targets, represented as a percentage of maximum peak torque, which individuals can attempt to match, allowing for the assessment of torque steadiness.

1.4.2 Reliability and Validity of Isokinetic Measurements

Over time, various isokinetic dynamometers have been developed, including the Biodex System 3 Pro isokinetic dynamometer (Biodex Medical Systems, New York), which has been

shown to be mechanically reliable and valid for measuring position, torque and velocity (Drouin et al., 2004). This reliability and validity extend to trunk strength measurements in individuals with and without LBP (A et al., 2020, Mueller et al., 2012). Notably, it has been found that low-velocity movements yield more reliable results when measuring trunk muscle strength (A et al., 2020). Therefore, in this thesis, the Biodex System 3 Pro isokinetic dynamometer was exclusively used at slow speeds (5°/s) to ensure reliable measurements of trunk muscle strength during dynamic trunk movements.

While force generation is the ultimate motor output, uncovering the underlying neural mechanisms within muscle tissue necessitates the use of additional methodologies, such as EMG. By integrating these measurements, it becomes possible to not only quantify force produced by the muscles but also gain insights into the neural factors influencing muscle function. These techniques were briefly overviewed earlier. The following section provides further details, focusing on the technical aspects and the reliability of these methods.

1.5 Electromyography

EMG is an electrophysiological technique commonly used to measure electrical activity generated when motor unit action potentials travel along muscle fibres during muscle contraction (Hug and Tucker, 2017). Due to their ability to reflect muscle activity, EMG signals are valuable electrophysiological indicators for studying the human body's responses under both normal conditions and in the presence of pain, shedding light on function of the neuromuscular system (Chowdhury et al., 2013). EMG is typically divided into two categories, (i) the intramuscular and (ii) the surface EMG, as described in the following sections.

1.5.1 Intramuscular Electromyography

Intramuscular EMG involves the direct insertion of fine-wire or needle electrodes into muscle tissue, making it an invasive technique (Besomi et al., 2019). Fine-wire electrodes consist of a thin insulated wire, inserted into the muscle using a hypodermic needle. Once in place, the exposed tip of the wire, which determines the electrode's receptive field, is bent to secure it within the muscle before the needle is removed (Besomi et al., 2019, Merletti and Farina, 2008). Needle electrodes, on the other hand, remain embedded in the muscle with either the shaft or tip serving as the recording interface (Besomi et al., 2019, Merletti and Farina, 2008).

Intramuscular EMG provides highly selective recordings from muscle fibres near the electrode, essential for studying deep muscles like the deep multifidus, while minimising crosstalk, which refers to a signal recorded over a muscle that is actually generated by a nearby muscle and conducted through the intervening volume to the recording electrodes (Besomi et al., 2019, De Luca and Merletti, 1988). Despite these advantages, the technique has several drawbacks, including muscle contraction intensity constraints due to discomfort, reduced suitability for analysing dynamic movements due to motion artifacts, and limited sampling resolution that may not accurately reflect the activity of the entire muscle (Besomi et al., 2019).

Given these limitations, surface EMG is commonly favoured for its non-invasive approach, which is ideal for analysing the timing and intensity of superficial muscle activity during dynamic contractions across a wide range of applications (Chowdhury et al., 2013).

1.5.2 Conventional Surface Electromyography

Surface EMG is widely used to assess muscle activation and neuromuscular control strategies due to the relationship between neural input to muscles and the electrical voltage they produce (Falla and Gallina, 2020). Traditionally, many studies have used bipolar surface EMG with two large electrodes placed 20-30 mm apart on the skin above the muscle to capture overall activation (Besomi et al., 2019, Falla and Gallina, 2020). However, this method's broad detection volume limits the ability to discern activation patterns within specific muscle regions or between adjacent muscles, such as different levels of the lumbar ES (Abboud et al., 2020, Falla and Gallina, 2020). Additionally, this approach is more susceptible to crosstalk and may suffer from poor repeatability of measurements due to the variability in inter-electrode distance (Besomi et al., 2019). These limitations led to the development of more advanced techniques.

1.5.3 High-density Surface Electromyography

HDsEMG involves placing a large number of small surface electrodes in either one-dimensional (1D) or two-dimensional (2D) arrays over the muscle area of interest, enabling the extraction of spatiotemporal features of the muscle (Besomi et al., 2019). HDsEMG is defined as a technique that involves the concurrent recording of at least 4 surface EMG signals with closely spaced (normally 2.5-10 mm), small-diameter (0.5-3 mm) electrodes (Gallina et al., 2022). Specifically for the lumbar ES muscle in individuals with CLBP, 2D electrode grids are often utilised (Martinez-Valdes et al., 2019, Sanderson et al., 2019a, Sanderson et al., 2019b). These grids typically feature 64 electrodes with a small size (usually < 3mm) and close spacing (typically 10 mm or less), enhancing the selectivity of the recordings (Vieira et al., 2017). This

configuration ensures that the signal recorded by each electrode is mainly representative of the activation of the surrounding muscle fibres.

Unlike conventional surface EMG, and intra-muscular EMG, HDsEMG facilitates the recording over a larger muscle area (i.e., capturing the activation of more motor units) and provides a topographical map of EMG amplitude (Falla and Gallina, 2020). This allows for the analysis of relative changes in muscle activation intensity across different regions as described in the following section alongside with the other parameters (Falla and Gallina, 2020).

1.6 High-density Surface Electromyography Outcome Measures

HDsEMG signals are usually captured in monopolar mode, with data from individual electrodes processed offline in software like MATLAB (The MathWorks Inc., USA) to produce bipolar signals. This involves re-referencing the data to measure potential differences between pairs of active electrodes aligned with the direction of the muscle fibres (Merletti et al., 2016).

1.6.1 Root Mean Square and Mean Power Frequency

Subsequently, the RMS for each signal is typically computed, serving as an indicator of EMG amplitude or the magnitude of muscle activation (Farina et al., 2004). Typically, the RMS values across all channels are averaged to yield a single measure representing overall muscle activity. Furthermore, spectral analysis is conducted to determine the mean power frequency (MNF) of each signal, a parameter used to evaluate the myoelectric signs of fatigue, with a decrease in frequency indicating increased myoelectric fatigue (Merletti et al., 1990). It is essential to understand that myoelectric fatigue does not reveal the precise moment of task failure but rather signifies a gradual reduction in a muscle's capacity to produce maximum force

and/or power (Enoka and Duchateau, 2008). These MNF values can also be averaged similarly to RMS, offering an aggregate MNF value for the entire muscle.

1.6.2 Centroid of Muscle Activation and Modified Entropy

In addition to these parameters which can also be extracted from conventional surface EMG, HDsEMG offers insights into the spatial distribution of muscle activity. This is accomplished by topographically mapping the RMS values of all HDsEMG signals according to the electrode grid layout. Such a spatial arrangement facilitates the calculation of the muscle activation centroid, reflecting the weighted central point of activity based on the RMS distribution. The centroid's position, is described along the y-axis (cranio-caudal) and x-axis (medio-lateral) and is expressed in mm (Falla and Gallina, 2020) (**Figure 1.3**). RMS values can be further analysed to compute the modified entropy within an electrode grid or bipolar electrode arrangement, indicating signal uniformity. In this context, more homogeneous activation patterns result in higher entropy values, which are expressed in arbitrary units (AU) (Farina et al., 2008).

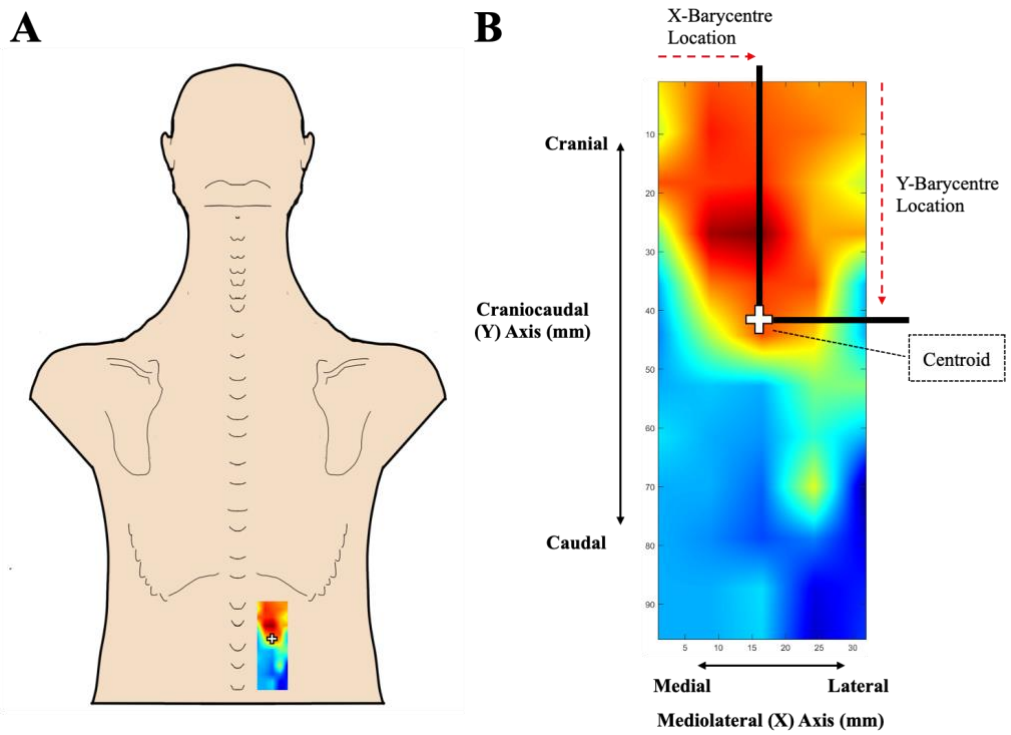


Figure 1.3: **(A) An illustration of the topographical map over the lumbar spine and (B) the axes and measurement characteristics of the EMG amplitude map's centroid, along with separate descriptions of the X- and Y-barycentres on their respective axes.**

1.7 Reliability of High-density Surface Electromyography

Reliability is commonly assessed using the intraclass correlation coefficient (ICC) and its 95% confidence intervals (CIs), with ICC values classified as follows: < 0.5 indicates poor reliability, 0.51-0.75 moderate, 0.76-0.90 good, and 0.91-1.00 excellent (Koo and Li, 2016). This approach is usually preferred because it captures both correlation between assessments and measurement repeatability (Koo and Li, 2016).

Until recently, research on the reliability of HDsEMG procedures, was limited. A recent study aimed to establish the intra- and intersession reliability of HDsEMG parameters recorded from the thoracic ES bilaterally during goal-directed voluntary contractions of the trunk (van Helden et al., 2022). The findings demonstrated good-to-excellent intra-session reliability

across all evaluated parameters and tasks for the thoracic ES (ICC: 0.79-0.99). However, some variability was observed in the inter-session reliability, that was task-dependent, with static movements showing higher reliability across most parameters in comparison to dynamic movements. Absolute RMS and MNF showed the highest overall reliability across tasks (ICC: 0.66-0.98), whereas the spatial distribution of muscle activation (e.g., centroid location) and muscle activation complexity (entropy) displayed variable reliability based on the specific task.

Specifically, for static trunk extension tasks, excellent intra-session reliability was found across parameters (ICC: 0.91 - 0.99). For these tasks, good-to-excellent inter-session reliability was observed for the absolute RMS, x-axis barycentre, y-axis barycentre, and MNF (ICC: 0.84 - 0.98), with entropy showing moderate reliability (ICC: 0.64-0.66). Normalised RMS showed poor-to-moderate inter-session reliability (ICC: 0.21-0.59). For the dynamic movements of trunk flexion, including both phases of the movement (flexion and extension back to neutral) similar intra-session reliability were observed, with all parameters falling within the good-to-excellent range (ICC: 0.87-0.97). Furthermore, inter-session reliability results demonstrated moderate-to-excellent reliability for the absolute RMS, normalised RMS, y-axis barycentre, and MNF (ICC: 0.73-0.93). However, inter-session reliability was poor for the x-axis barycentre and for entropy (ICC: 0.23-0.49).

This body of research collectively indicates that HDsEMG is a reliable method for assessing trunk extensor muscle activity, particularly for intra-session measurements during static contractions and dynamic flexion-extension movements. However, caution is recommended for inter-session measurements, particularly for dynamic contractions, where calculations related to the x-axis centroid and entropy have shown poor reliability. Nonetheless, the intra- and inter-session reliability for of centroid calculations along the y-axis, where typically differences are observed between people with and without CLBP, demonstrated

moderate-to-excellent reliability. However, it is essential to note that the demonstrated reliability of HDsEMG has been established primarily in asymptomatic individuals. HDsEMG's reliability in people with CLBP and for the assessment of abdominal muscle activity, has not been examined.

A previous study (Dankaerts et al., 2004) has demonstrated that the reliability of conventional EMG measurements for trunk extensor (i.e., lumbar multifidus, iliocostalis lumborum pars thoracis and thoracic ES) and flexor (i.e., RA, EO and IO) muscles during maximal and sub-maximal voluntary isometric contractions (MVC) showed excellent intra-day reliability in both healthy controls and CLBP patients (ICC mean 0.91; range 0.75-0.98). Sub-MVC for both groups between-days showed excellent reliability (ICC mean 0.88; range 0.78-0.97). The between-days MVC for both groups showed trends towards lower levels of reliability (ICC mean 0.70; range 0.19-0.99) when compared to sub-MVC. Even though that this provides some evidence that the conventional EMG is reliable at least for muscle activity measurements of the trunk extensor and flexor muscles in both individuals with and without CLBP, the reliability of HDsEMG in this population and for abdominal muscles has not been established and thus should be interpreted with caution. Except from the reliability of the HDsEMG, when EMG is used, we always need to consider various factors that can influence the EMG signal.

1.8 Factors Influencing the Electromyographic Signal

Surface EMG is a cutaneous technique used to measure muscle activity from subcutaneous muscle tissue. Therefore, the EMG signal, on its way from the muscle membrane the electrode is susceptible to numerous factors which can distort its shape and characteristics through the introduction of electrical noise, or other physiological and non-physiological factors (Chowdhury et al., 2013, Farina et al., 2004, Raez et al., 2006).

1.8.1 Electrical Noise and Movement Artifacts

Electrical noise in EMG signals stems from several sources: (i) inherent noise from electronic equipment, which can be mitigated using high-quality components like silver/silver chloride electrodes that provide stable electrical properties and good signal-to-noise ratio; (ii) ambient noise, mainly from electromagnetic radiation, with the human body, acting as an antenna (Raez et al., 2006). A significant source of ambient noise is the 50 Hz radiation in Europe (or 60 Hz in America) from power sources, known as powerline interference which can be minimised with ground electrodes (Chowdhury et al., 2013); (iii) motion artifacts, arising from cable movement or the interaction between the electrode's detection surface and the skin (Chowdhury et al., 2013). Reducing these artifacts involves securing cables and electrodes with tape, using recessed electrodes with a conductive gel at the electrode-skin interface, and proper skin preparation to reduce impedance (Chowdhury et al., 2013). In HDsEMG applications, where electrodes with small contact areas (5-10 mm^2) are common, skin preparation is crucial to minimise impedance, as smaller electrodes can increase electrical resistance and potentially amplify noise (Piervirgili et al., 2014). Achieving high-quality HDsEMG signals requires managing high impedance at the electrode-skin interface to maintain high signal-to-noise and signal-to-interference ratios. Research has shown that skin preparation with abrasive conductive paste significantly reduces impedance and noise more effectively than other methods like rubbing with ethyl alcohol or using adhesive tape (Piervirgili et al., 2014). Consequently, this approach has been adopted in all original studies in this thesis to minimise electrical noise and enhance the quality of EMG recordings.

1.8.2 Physiological and Non-Physiological factors

Physiological factors include muscle fibre membrane properties like average conduction velocity and action potential shape, as well as motor unit characteristics such as the number of units recruited and their firing rates (Farina et al., 2004). Another physiological factor that may contaminate the EMG recordings, is the electrical activity of the heart, often termed *"electrocardiogram (ECG) artifact"*, predominantly observed during evaluations of the shoulder girdle and trunk (Chowdhury et al., 2013). However, this artifact, typically arising during contractions below 25% of an individual's MVC and mainly during isometric contractions, can be reduced through signal differentiation (common-mode rejection) (Chowdhury et al., 2013).

Non-physiological factors affecting EMG signals fall into two categories: modifiable factors, like physical aspects and detection system components, and more fixed factors, such as anatomical and geometrical ones. Regarding the detection system, issues like skin-electrode contact, including impedance and noise, have been addressed in the previous section. An important consideration within this context is the choice of electrode, the distance between electrodes, and the positioning of the electrode relative to the muscle, which should ideally follow the direction of the muscle fibres (Chowdhury et al., 2013, Gallina et al., 2022, Raez et al., 2006). Recent guidelines have recommended specific electrode types and proper placement on targeted muscles (Barbero et al., 2012, Gallina et al., 2022). Crosstalk from adjacent muscles represents another crucial physical factor. While complete elimination of crosstalk is impossible with surface electrodes, employing HDsEMG and smaller electrodes with minimal inter-electrode distance, coupled with signal differentiation in post-processing, can significantly reduce its influence (Chowdhury et al., 2013).

From the factors that cannot really be modified or controlled, the anatomic factors are related to the muscle architecture (e.g., distribution of motor units, innervation zones etc.) and the surrounding tissues (e.g., thickness of subcutaneous tissue) and geometrical. With regards to the anatomical factors, it is important to acknowledge their significant influence on EMG signal amplitude, considering for example that excess body fat acts as internal noise for EMG by increasing the distance between the active muscle fibres and the detection sites (Chowdhury et al., 2013). Additionally, the EMG amplitude can vary significantly depending on whether the electrode is positioned over an innervation zone or not (Barbero et al., 2012). On the other hand, the geometrical factors are related to the movement (shortening or lengthening) of the muscle under investigation relative to the detection system (i.e., electrode) (Farina et al., 2004). These factors can be partially mitigated by assessing muscle activity during isometric contractions; however, this remains a limitation, particularly, for dynamic contractions.

In summary, despite the numerous challenges and factors affecting EMG signal acquisition, acknowledging these as limitations is crucial. However, surface EMG still remains a valuable tool, especially when experimental designs aim to mitigate these factors (Farina et al., 2004). In all original studies in this thesis, HDsEMG was utilised, and practices were implemented to minimise these limitations as much as possible.

1.9 Motor units and Force Control

An additional advantage of HDsEMG is its precise identification of motor unit discharge rates via decomposition algorithms (Del Vecchio et al., 2020). Previous studies have demonstrated that the low-frequency (< 10 Hz) component of the neural command (i.e., the effective neural drive) is mainly responsible for generating muscle force because it reflects the

common synaptic input received by the motor unit population (Farina et al., 2014b, Negro et al., 2009).

Alterations in force steadiness may be linked to changes in motor unit pool behaviour, including variations in motor unit recruitment and firing rates. Therefore, the most direct approach to understand the neuromuscular mechanisms responsible for poorer muscle force control when people have CLBP could be to assess the correlation between the motor unit discharge times and force. However, HDsEMG decomposition is currently challenging on signals collected from the lumbar ES likely due to anatomical factors (**Section 1.8.2**), such as, the complexity of lumbar anatomy (i.e., existence of many different layers of muscles and thoracolumbar fascia) (Christophy et al., 2012), and the volume conductor properties of the lower lumbar area (i.e., thicker subcutaneous layer) (Del Vecchio et al., 2020). These factors can reduce the discriminative information in the action potential waveforms of different motor units, and thus limit the applicability of decomposition algorithms (Del Vecchio et al., 2020).

To overcome this limitation and to understand the relationship between muscle activity and the force that a muscle generates, surface EMG/force relationships have been extensively examined. Such investigations (Moon et al., 2014, Yoshitake and Shinohara, 2013b) have identified an association between low-frequency force fluctuations and the corresponding low-frequency component of the rectified interference surface EMG both in time and frequency domains. This approach might be considered an alternative option when HDsEMG signal decomposition is challenging for muscles like the lumbar ES and assessing the correlation between motor unit discharge times and force (gold standard) is not feasible. Therefore, this type of analysis in original studies of this thesis was based on assessing the relationship surface EMG/force relationships based on the rectified interference surface EMG signal. Additionally,

this approach was combined with the high spatial sampling of HDsEMG, which can further improve the assessment of EMG-torque relationships as explained in the subsequent sections.

1.10 Signal Analysis Techniques

1.10.1 Principal Component Analysis

Due to the high dimensionality of the HDsEMG data, the recordings might contain redundant and correlated information (e.g. noise, artefacts, and channels with low level of muscle activity) which challenges the interpretation of data and can be problematic when assessing surface EMG/force relationships (Naik et al., 2016). An effective way of dealing with the high dimensionality of HDsEMG data is by using principal component analysis (PCA).

PCA is a statistical technique that simplifies the complexity in high-dimensional data while retaining as much variance as possible and thereby revealing trends and patterns in the dataset, without losing any important information (Bai et al., 2019). As previously shown, by using HDsEMG, which provides high spatial sampling resolution, and by applying PCA, surface EMG-based force estimations can be improved (Staudenmann et al., 2006, Staudenmann et al., 2005). Therefore, this technique was used in all original studies of this thesis to improve these estimations.

PCA accomplishes this by decomposing the covariance structure of a set of dependent variables (e.g., HDsEMG channels) into orthogonal (uncorrelated) components by calculating the eigenvalues and eigenvectors of the data's covariance matrix. These two algebraic formulations are always computed as a pair. Eigenvalues represent the percentage of the total variance that is informed by each eigenvector. Eigenvectors, also known as principal components (PCs), represent the weight of each original dependent variable in explaining the portion of the variability defined by the eigenvalue (Johnson, 1998). PCA sorts the PCs in

descending order of variances, meaning that as much activity as possible is accumulated in the first PCs (Naeem et al., 2009). Therefore, the first PCs are expected to contain most of the relevant information, and removing the remaining PCs, simply implies enhancing the signal-to-noise ratio (Naeem et al., 2009). This can also be observed in (**Figure 1.4**), where the first PC (PC_1) is the linear combination of the variables that accounts for the greatest possible variance, while the subsequent second PC (PC_2) is the linear combination of the data that has the greatest possible variance but is uncorrelated with PC_1. This uncorrelated nature of PCs ensures that each component provides new and unique information about the data's structure. Thus, by removing the less significant PCs, that is, those with smaller eigenvalues, PCA effectively enhances the signal-to-noise ratio, allowing the focus of the analysis on the most informative aspects of the HDsEMG data.

Ultimately, the output of the PCA is a *"cleaner"* EMG signal that is composed from the first few PCs that explain most of the variance (pre-set threshold of variance) in the dataset and thus explain most of the variance in the exerted torque. The processing steps needed before and after the application of the PCA, alongside with further information on this approach are provided in the method sections of the following chapters of this thesis.

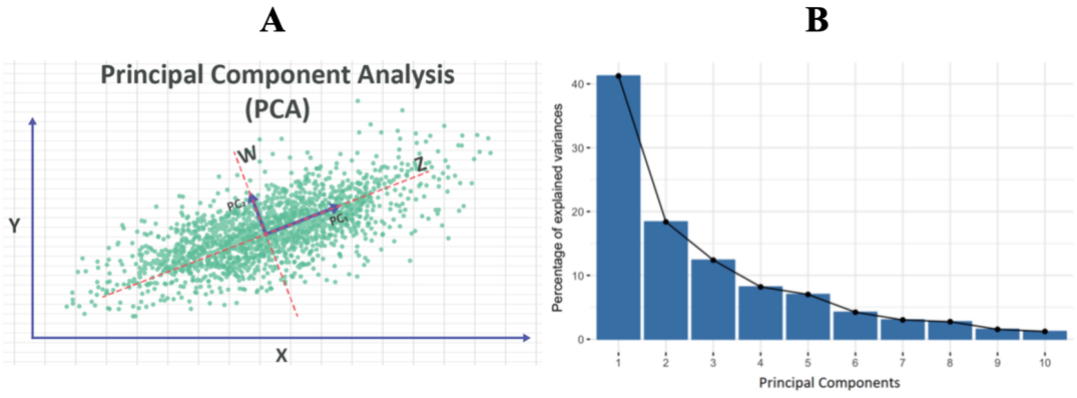


Figure 1.4: **Illustration of the application of PCA on a dataset. (A) displays a scatter plot representing the first two PCs that are derived from the dataset, providing a simplified view while still capturing the most significant variance within the data. (B) shows a scree plot, detailing the proportion of the total variance explained by each of the PCs. The steep**

decline from the first few components indicates their importance compared to the latter ones, which contribute less to the total variance. This visualisation aids in understanding the dimensionality reduction aspect of PCA and highlights which components capture the most information.

1.10.2 Cross-correlation Analysis

Cross-correlation is a time-domain measure commonly used in signal processing to quantify the similarity between two data sets or signals by evaluating the shift of one in relation to the other (Derrick and Thomas, 2004). Cross-correlation values can range between -1 and 1, where 1 represents perfect correlation in phase and -1 perfect correlation but in antiphase. Values around zero represent null correlation between signals. Typically, from the cross-correlation values the maximum peak is identified along with its time lag value.

In the context of this thesis, the PCA-based EMG signal (**Section 1.10.1**) was used to quantify the relationship between surface EMG and torque signals. Similarly to previous studies (Yoshitake and Shinohara, 2013b, Yoshitake and Shinohara, 2013a), cross-correlation was used to quantify the degree of correlation between fluctuations in surface EMG and torque signals in the time domain. This approach can provide information related to the contribution of the muscle to the resultant torque and can be useful in explaining the underlying neuromuscular mechanisms related to alterations in force control in people with CLBP. Other related methodologies like auto-correlation, which measures self-similarity overtime shifts, and convolution, which combines two signals to produce a third, were not suitable for the analyses purposes of this thesis (Derrick and Thomas, 2004).

1.10.3 Coherence Analysis

Correlation between signals can also be explored through spectral analysis methods such as coherence (El-Gohary et al., 2006). EMG signals consist of many frequency components that create complex patterns. Spectral analysis transforms these signals into their frequency spectra, detailing each component's contribution. This transformation allows for a more nuanced understanding of the underlying physiological processes, as it separates the signal into its constituent frequencies. These frequencies are often categorised into bands, each providing different insights about physiological processes.

Coherence extends spectral analysis by measuring the frequency-dependent correlation between signal pairs. The coherence function, often represented by the magnitude-squared coherence (MSC), quantifies how well two signals are linearly related at each frequency (Malekpour et al., 2018). More simply put, it is a measure of the similarity in the frequency content of two signals. MSC coefficients range from 0 (indicating no correlation) to 1 (indicating perfect correlation) (Shaw, 1984). This method is particularly useful in understanding the synchronisation and shared activity between different muscles or between muscle activity and external forces.

In this thesis, the computation of MSC was performed using Welch's method (Welch, 1967), a widely used technique in signal processing. Welch's method involves segmenting the signal into overlapping windows (e.g., Hamming) (Harris, 1978), computing a periodogram (i..e, estimate of the spectral density of a signal) for each segment, and then averaging these periodograms to reduce variance and produce a more stable spectral estimate. This method was chosen due to its effectiveness in reducing spectral leakage and variance, providing robust and reliable estimates for HDsEMG-torque coherence analysis. Similarly to the cross-correlation analysis, coherence analysis was employed using the PCA-based EMG signal, specifically on

the δ band (0-5 Hz), since it is the most relevant band for the generation of force (Farina and Negro, 2015). This approach was used to indirectly estimate the strength and frequency of common rhythmic synaptic inputs across the motor unit pool and establish their relationship with torque (Hansen et al., 2005).

1.11 Thesis Aims and Objectives

The main aim of this thesis was to enhance the understanding of motor adaptations in people with CLBP, focusing on changes in the control of trunk muscle force (torque steadiness) and the potential underlying neuromuscular mechanisms. This was achieved by examining alterations in trunk muscle force control, investigating muscle activation patterns, and studying the EMG-torque relationships using HDsEMG and isokinetic dynamometry. Additionally, the thesis assessed clinical characteristics to uncover potential associations with changes in torque steadiness.

1.11.1 Specific Objectives

The specific objectives of this thesis are summarised below:

1) To explore control of trunk muscle force and assess differences in HDsEMG parameters of the lumbar ES, alongside surface EMG-force relationships, during isometric trunk extension contractions in people with and without CLBP.
2) To examine control of trunk muscle force and assess differences in HDsEMG parameters of the thoracolumbar ES, EO and RA, alongside surface EMG-force relationships, during dynamic eccentric/concentric trunk extension and trunk flexion contractions in people with and without CLBP.

3) To explore motor adaptations and changes in trunk muscle recruitment strategies in the presence of delayed onset of muscle soreness (DOMS) in the trunk extensors of pain-free individuals and compare the findings with those observed in people with CLBP assessed via objectives one and two and previous literature. Specifically, to evaluate the influence of DOMS on various motor performance measures, including control of trunk muscle force, HDsEMG parameters measured from the thoracolumbar ES alongside surface EMG-torque relationships and associated kinematic data during both concentric and eccentric trunk extension contractions.
4) To synthesise the available evidence to understand if musculoskeletal pain, whether it be clinical or experimental, influences control of muscle force during isometric and dynamic voluntary contractions and provide guidance for future research in this field.

1.12 Thesis Chapters Overview

This thesis presents a series of studies, each detailed in its own chapter (**Figure 1.5**). The results shared in this document are designed to aid both researchers and healthcare professionals in expanding their understanding of motor adaptations in individuals with CLBP, with a particular focus on the control of trunk muscle force. The insights acquired from these findings aim to improve both the assessment and potentially aid in the development of novel targeted treatment strategies for people suffering from CLBP.

Chapter 1*,* laid the foundation for understanding motor adaptations to CLBP, and highlighted the need for further research on trunk muscle force control in this population. It addressed how these adaptations are quantified, discussed the limitations of the selected techniques and signal processing methods, explained the rationale for their choice, and provided details on the equipment used.

Chapter 2*,* reports the results of an observational study focused on trunk torque steadiness in people with CLBP compared to asymptomatic controls during isometric trunk extension contractions, aiming to address objective one of this thesis.

Chapter 3*,* after assessing control of trunk muscle force during isometric contractions in *Chapter Two*, this chapter is a continuation and reports the results of an observational study focused on both trunk extensor and trunk flexor muscle torque steadiness in people with CLBP compared to asymptomatic individuals while performing dynamic contractions, aiming to address objective two of this thesis.

Chapter 4*,* reports the results of an experimental study focused on trunk extensor torque steadiness in healthy individuals in the presence of trunk extensor DOMS to answer objective three of the thesis.

Chapter 5*,* a systematic review, and meta-analysis, focuses on alterations in control of muscle force in people with clinical or experimentally induced musculoskeletal pain, to answer objective four of the thesis.

Chapter 6*,* provides a summary of the key research results of the thesis, including a general discussion of the collective research, the strengths and limitations of the work, the implications for clinical practice, and suggestions for future research endeavours.

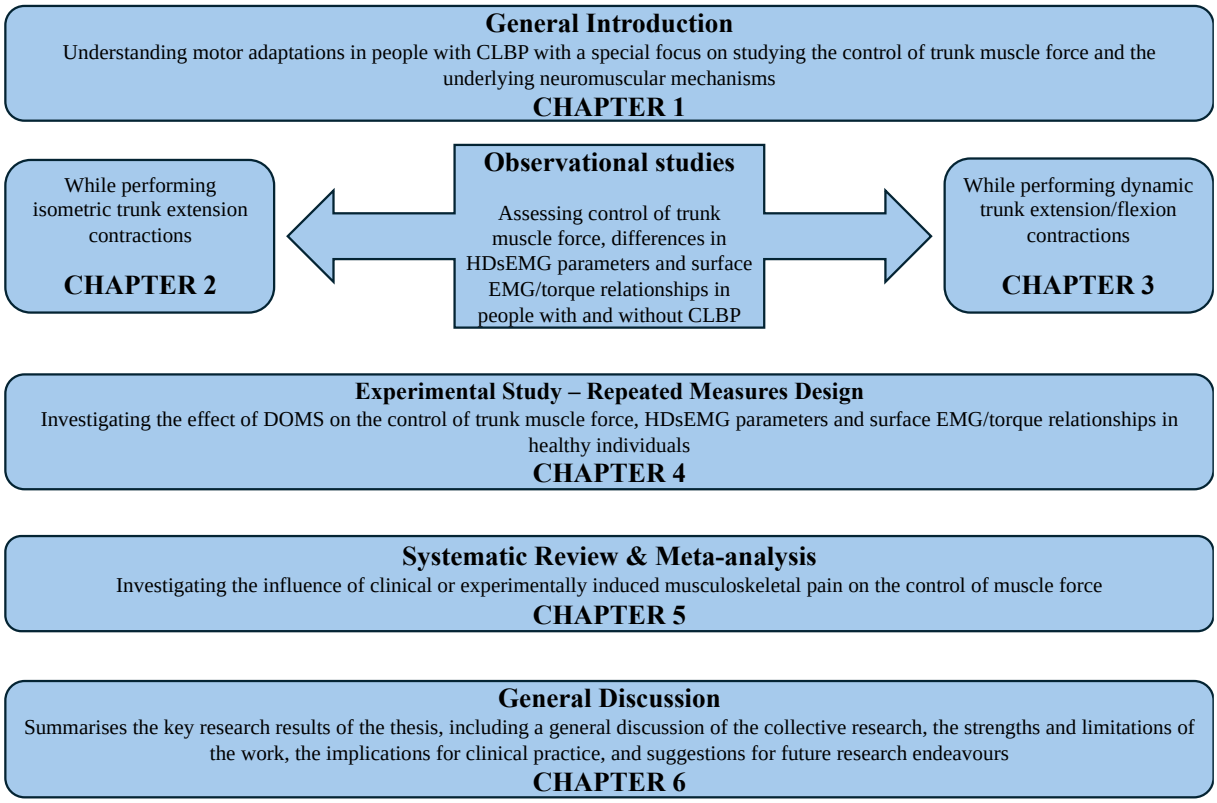


Figure 1.5: **A schematic representation illustrating the structure of the thesis and the key research topics addressed within each chapter.**

Chapter 2

PEOPLE WITH CHRONIC LOW BACK PAIN DISPLAY SPATIAL ALTERATIONS IN HIGH-DENSITY SURFACE EMG-TORQUE OSCILLATIONS

This chapter presents the complete details of a manuscript published by the thesis author (**Appendix 1**) (Arvanitidis et al., 2022). It contains direct passages from the published work, with certain adjustments made to the Abstract, Introduction and Method sections. These modifications enhance the flow between chapters of this thesis and minimise redundancy, particularly concerning background and methodological details already covered in ***Chapter 1***.

Publications and Presentations:

1. **Arvanitidis M**, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. People with chronic low back pain display spatial alterations in high-density surface EMG-torque oscillations. *Sci Rep*. 2022;12(1):15178.
2. **Arvanitidis M**, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Lumbar extensor muscle isometric torque steadiness and torque-HDsEMG coherence is altered in individuals with chronic low back pain. XXVIII Congress of the International Society of Biomechanics (ISB). Digital Congress, July 25 - 29, 2021.

2.1 Abstract

In ***Chapter 1***, the context for addressing the literature gap concerning torque steadiness in individuals with CLBP has been established. Additionally, the methods and equipment that will be used to achieve the aims of the thesis have been introduced. In this first study of the thesis, the relationship between spatial oscillations in surface EMG activity and trunk-extension torque was quantified in individuals with and without CLBP during two submaximal isometric lumbar extension tasks at 20% and 50% of their maximal voluntary torque.

HDsEMG signals were recorded from the lumbar ES with a 64-electrode grid, and torque signals were recorded with an isokinetic dynamometer. Coherence and cross-correlation analyses were applied between the filtered interference HDsEMG and torque signals for each submaximal contraction. PCA was used to reduce dimensionality of HDsEMG data and improve the HDsEMG-based torque estimation. Surface EMG-torque coherence was quantified in the δ (0-5Hz) frequency bandwidth. Regional differences in surface EMG-torque coherence were also evaluated by creating topographical coherence maps.

Surface EMG-torque coherence in the δ band and surface EMG-torque cross-correlation increased with the increase in torque in the controls but not in the CLBP group ($p=0.018$, $p=0.030$ respectively). As torque increased, the CLBP group increased surface EMG-torque coherence in more cranial ES regions, while the opposite was observed for the controls ($p=0.043$). Individuals with CLBP show reductions in surface EMG-torque relationships possibly due to the use of compensatory strategies and regional adjustments of ES-surface EMG oscillatory activity.

2.2 Introduction

When executing a steady submaximal isometric contraction, the applied force or torque is not perfectly accurate but rather, small oscillations occur around the target torque value (Farina et al., 2016). The neural origin of torque fluctuations has been a topic of interest for many years (Farina et al., 2016). Previous studies have proposed that the variability in the times that motoneurons discharge action potentials could be a potential determinant for the accurate control of muscle force (Laidlaw et al., 2000). This variability could be determined by independent and common synaptic inputs received by motor units and/or by the nonlinear input-output properties of individual motoneurons (Farina et al., 2016). However, recent studies have shown that the neural drive to the muscle (i.e., the neural activation signal that the muscles receive from the pool of innervating motoneurons) in low frequencies (<10 Hz) is mainly relevant for torque generation as it reflects the common synaptic input received by the motor unit pool (Farina and Negro, 2015, Farina et al., 2014b, Negro et al., 2009). This happens because a group of activated motoneurons can act as a very selective filter, which eliminates all the independent components, partly linearizes the input-output motoneuron behaviour and amplifies the common component (Farina et al., 2014b). Thus, the control of muscle force depends mainly on the amplitude of the low-frequency oscillations that reflect shared (common) synaptic input (Farina et al., 2016).

As briefly discussed in (**Section 1.3.3**), smooth force production depends highly on our proprioceptive senses of effort and force, with the first being generated centrally (via corollary discharges of the descending motor command), and the latter derived from peripheral sensory receptors (i.e., muscle spindles and tendon organs; reafference activity) (Proske and Allen, 2019). These central and peripheral signals are sent to the somatosensory cortex via spinal, subcortical and cortical neural pathways, where they are integrated along with other

somatosensory, visual, and vestibular information, resulting in the perception of applied forces (Proske and Allen, 2019, Röijezon et al., 2015). A descending motor command is then sent to the tissues involved, resulting in an appropriate action (Ager et al., 2020). The proprioceptive system ensures smooth force production through this interactive process, that requires constant monitoring and modulation of ascending and descending information based on the proprioceptive input, motor output, perception, and the resulting action (Ager et al., 2020). Therefore, any perturbation to these systems, can affect the control of muscle force.

Pain can affect the ability to control muscle force, possibly due to altered afferent input from the painful area and/or neuroplastic changes in the CNS (e.g., changes in the organisation of the sensory and motor cortices) (Ager et al., 2020, Brumagne et al., 2019). For example, studies have shown that people with subacromial impingement syndrome (Bandholm et al., 2006), knee osteoarthritis (OA) (Hortobágyi et al., 2004), neck pain (Muceli et al., 2011) and CLBP (Alsubaie et al., 2021, Pranata et al., 2017, Willigenburg et al., 2013) display reduced force steadiness. Impaired lumbar sensorimotor control could possibly lead to suboptimal tissue loading (i.e., a disturbed body image could lead to unexpected high forces in suboptimal positions during movement, resulting in abnormal mechanical tissue loading, and ultimately stimulation of nociceptors and/or tissue strain) which can induce further pain/injury and/or perpetuation of symptoms (Brumagne et al., 2019). However, the neuromuscular mechanisms responsible for poorer muscle force control when people have pain have not been fully established.

Many studies have attempted to assess the neural origin of fluctuations in muscle force by assessing surface EMG and torque/force relationships. For instance, Yoshitake and Shinohara, (2013) previously demonstrated that the temporal characteristics of force fluctuations at low frequencies (< 5Hz) are not only correlated with the motor unit discharge

times (common drive), but also with the low frequency component of the rectified interference surface EMG (Yoshitake and Shinohara, 2013b). Taking this a step further, Moon et al., (2014) showed that the low frequency component of the rectified interference surface EMG is also coherent with the oscillations in force at low frequencies which contributes to force variability (Moon et al., 2014). Nevertheless, conventional surface EMG recordings present numerous limitations since factors such as those mentioned in (**Section 1.8**) can affect the relationship between surface EMG and torque. Hence, it is not surprising that only weak correlations have been observed between force and surface EMG (Negro et al., 2009).

Recent studies have shown that HDsEMG can improve our understanding of the mechanisms responsible for the control of muscle force with HDsEMG motor unit decomposition. Indeed, HDsEMG recordings allow the identification of a large number of motor units and their discharge characteristics enable an accurate prediction of the resultant torque (Negro et al., 2009). Nevertheless, the applicability of HDsEMG decomposition is limited to certain experimental conditions and can be only achieved for certain muscles (Del Vecchio et al., 2020). For example, the identification of motor units from trunk muscles (i.e., ES) is not currently possible with HDsEMG. Although intramuscular recordings could be potentially used to assess motor unit firing patterns from trunk muscles, their selectivity does not allow identification of a sample of motor units that is large enough to obtain an accurate representation of the exerted torque. One alternative to overcome these issues is taking advantage of HDsEMG's high spatial sampling resolution. Staudenmann et al., (2005) previously showed that HDsEMG can improve surface EMG-based force estimations by 25% (Staudenmann et al., 2005). This improved estimation is enabled by employing dimensionality reduction techniques such as PCA which reflects the common variability between the multiple surface EMG signals recorded with HDsEMG, providing a unique signal which can explain

most of the variance in exerted torque (Staudenmann et al., 2006). In addition to PCA, HDsEMG has the possibility, not yet exploited, of generating a topographical map assessing relationships between torque and surface EMG from the regions covered by the electrode grid. This would allow to determine whether certain muscle regions contribute more to the exerted torque than others. In the case of CLBP, several studies have revealed variations in lumbar ES amplitude distribution (Arvanitidis et al., 2021a, Falla et al., 2014, Martinez-Valdes et al., 2019, Sanderson et al., 2019a, Sanderson et al., 2019b), and in particular, studies have shown that people with CLBP often display less activity in the more caudal regions of the lumbar ES during static-fatiguing and dynamic lumbar extension tasks (Arvanitidis et al., 2021a, Falla et al., 2014, Sanderson et al., 2019a, Sanderson et al., 2019b). It is possible that regional variations in surface EMG-torque relationships are responsible for poorer control of force during visuomotor torque-matching tasks, yet this has never been examined.

Therefore, the study presented within this chapter addressed the first objective of this thesis and aimed to (i) quantify the relationship between HDsEMG oscillations and isometric trunk-extension torque oscillations in both time (i.e., cross-correlation) and frequency domains (i.e., coherence) and (ii) examine and compare regional differences in surface EMG-torque coherence of the ES muscle in individuals with CLBP and asymptomatic controls. It was hypothesised that individuals with CLBP will show a weaker correlation between HDsEMG and torque and a more focalised distribution of HDsEMG-torque coherence of the lumbar ES muscle.

2.3 Methods

2.3.1 Design and setting

This case-control, cross-sectional study was approved by the Ethics Committee of the University of Birmingham (approval number: ERN 19-1148; **Appendix 2**) and work is reported in accordance with the STROBE guidelines (von Elm et al., 2007). Additionally, the Consensus for Experimental Design in Electromyography (CEDE)-Check checklist was used for thorough reporting of the EMG methods (Besomi et al., 2024). All experimental procedures were conducted according to the Declaration of Helsinki. Data collection was performed between April 2019 – January 2020 at a laboratory within the Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), University of Birmingham, UK. All participants attended one laboratory session and their written informed consent was obtained prior to their participation. All participants were encouraged to address any concerns or questions related to the study before signing the informed consent.

2.3.2 Participants

Fifteen individuals with CLBP (seven males, eight females) and 15 asymptomatic controls (eight males, seven females) from the University of Birmingham student and staff community were recruited for this study, by means of information leaflets posted around the University of Birmingham and posts on social media. The sample size was calculated based on an α of 0.05, a power of 0.8, a moderate effect size of (f) 0.28 [calculated based on the results from a previous study (Hadizadeh et al., 2014), from mean (SD) variable error values of individuals with CLBP and asymptomatic controls during a multidirectional isometric tracking

task at 90º and at 20-40% of MVC], and a potential 5% loss of data due to signal quality or participant withdrawal.

2.3.3 Inclusion and exclusion criteria

Inclusion criteria for the CLBP group were men or women aged 18-55 years old, experiencing non-specific CLBP for a minimum of three months over the last six-months (Dionne et al., 2008). Inclusion criteria for the asymptomatic control group were men or women aged 18-55 years old, without current or previous symptoms of back and/or lower limb pain which warranted attention from a health care professional. Due to the higher prevalence of age-related changes in the musculoskeletal system with increasing age, the upper age limit was set at 55, as applied previously (Petry, 2002). The exclusion criteria for both groups were as follows: lumbar radiculopathy and/or radicular pain, spinal deformity and/or surgery, pregnancy, history of cardiovascular diseases, history of neurological and/or chronic respiratory problems and systemic or inflammatory conditions, including rheumatic and neuromuscular disorders. People with CLBP that sought treatment for their LBP in the last six months before enrolment were also excluded.

2.3.4 Questionnaires

At the beginning of the session, the 11-point Numerical Pain Rating Scale (NPRS) was verbally administered to all participants to obtain information about their current level of pain intensity. All participants were asked to indicate the numeric value that best described their pain intensity on a scale from 0 to 10, with 0 = *"no pain"* and 10 = *"worst possible pain"* (Jensen and McFarland, 1993). All participants were also asked to report if they experienced any

increase in their level of pain intensity after performing each of the contractions. The Oswestry Disability Index (ODI) was used to evaluate all participants' perceived level of back disability during everyday activities of daily living (Fairbank et al., 1980). All participants' general health status was assessed with the RAND (research and development)-36-Item Health Survey (Brazier et al., 1992) and fear-avoidance beliefs and fear-avoidance behaviour was assessed with the Tampa Scale for Kinesiophobia (TSK) (Miller et al., 1991).

2.3.5 Electromyography

Surface HDsEMG signals were recorded in monopolar mode from the lumbar ES unilaterally, using a 13-row and 5-column semi-disposable grid of equally spaced electrodes (OT Bioelettronica, Italy). One electrode was missing from the right bottom corner of the grid, to provide directional reference (Sanderson et al., 2019b). Thus, each grid consisted of 64 electrodes of 1-mm diameter that were 8-mm apart. Prior to electrode placement, the HDsEMG grid was prepared by attaching a double-side adhesive foam to the electrode surface (SPES Medica, Genoa, Italy) and by filling the electrode cavities with a highly conductive-adhesive paste which provided electrode-skin contact (AC-CREAM, SPES Medica, Genoa, Italy). Participants' skin preparation procedures were also performed prior to electrode placement, including shaving (if necessary), gentle local skin abrasion and cleaning with water. Then, the HDsEMG grid was placed unilaterally over the lumbar ES, 2cm lateral to the L5 spinous process (AS controls: right side, CLBP group: most painful side) (**Figure 2.1**) (Arvanitidis et al., 2021a, Falla et al., 2014, Sanderson et al., 2019a, Varrecchia et al., 2021). The electrode was placed on the most painful side for the CLBP group as it was expected that this side would show greater changes in myoelectric activity (Martinez-Valdes et al., 2019). The portions of the ES which are likely to be muscular in the region of the electrode grid include the iliocostalis

lumborum pars lumborum and the iliocostalis lumborum pars thoracis (Sanderson et al., 2019b). The anatomy of these muscles has been described in (**Section 1.2.2**).

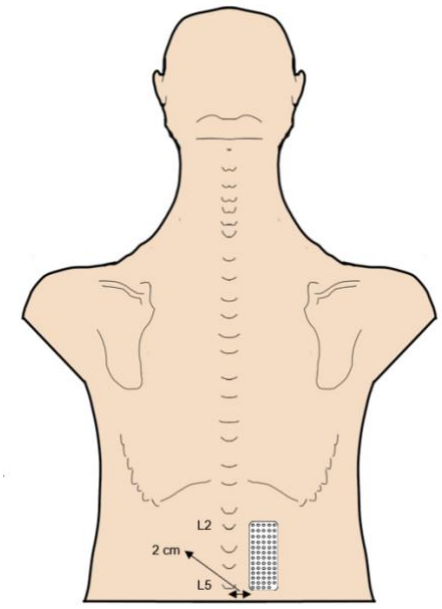


Figure 2.1: **Representation of the position of the HDsEMG electrode grid that was placed over participants' lumbar ES.**

One pair of bipolar electrodes (WhiteSensor WS, Ambu A/S, Ballerup, Denmark; total size: 36 × 40 mm, electrode size: 4mm, centre-to-centre distance ≈3.6 cm) was mounted over the RA muscle as described previously (Silva et al., 2015) in order to be able to quantify the level of co-activation between the trunk flexors and extensors. The bipolar electrodes were placed on the same side as the HDsEMG grid, and the bipolar signals were recorded in differential mode. Ground electrodes (WhiteSensor WS, Ambu A/S, Ballerup, Denmark) were placed over the sacrum, anterior superior iliac spine (ASIS) and wrist of all participants.

The surface EMG signals were synchronised with the torque signals acquired from the isokinetic dynamometer through the auxiliary input of the surface EMG amplifier (Quattrocento- OT- Bioelettronica, Torino, Italy). All surface EMG and torque signals were

amplified by a factor of 150, sampled at 2048Hz, automatically filtered with a band-pass filter (bandwidth: 10-500Hz, first order, -3dB) and digitised with a 16-bit A/D converter.

2.3.6 Dynamometer setup and positioning

The torque exerted by the participants during isometric MVCs and during isometric submaximal torque steadiness tasks was evaluated with an isokinetic dynamometer (System 3 Pro, Biodex Medical Systems, New York). All contractions were performed on the Biodex Dual Position Back Extension/Flexion Attachment.

The participants were seated on the trunk attachment with their hips and knees in 90^{o} of flexion, and their feet parallel to the floor at a distance equal to the distance of the two acromia (**Figure 2.2**). The dynamometer was aligned bilaterally with the ASISs, while the front of the seat was tilted clockwise ≈15^{o}. This position is referred to as *"compressed isolated lumbar position"* and was used to focus on the lumbar region (Moreno Catalá et al., 2018). In this position, the main contributor to trunk extension torque is the lumbar ES (Morini et al., 2008). Additionally, the participants' thighs, pelvis and upper trunk were strapped to minimize compensatory movements and a specific attachment was also used to block any knee movements.

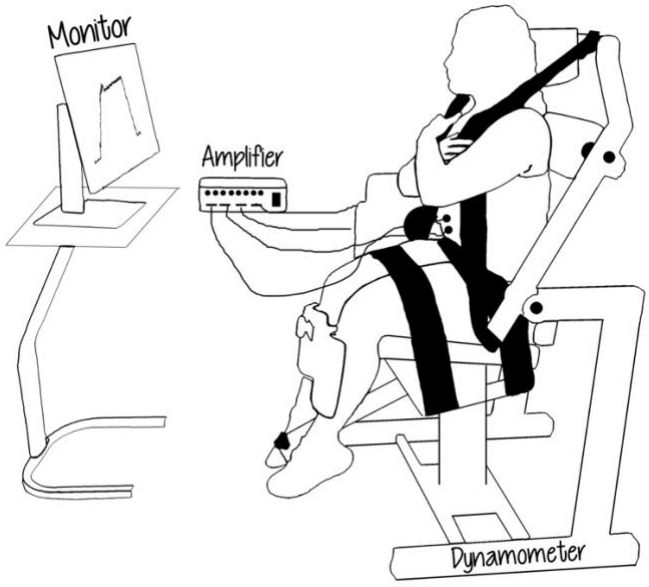


Figure 2.2: **Representation of the testing procedure. A participant is seated on the Biodex chair with the electrodes attached to her and connected to the amplifier, and she performs isometric back extension at one of the two torque levels, while visual feedback of the torque output is provided to her via a monitor.**

For all participants and for both isometric back extension measurements (i.e., maximal, and sub-maximal), the dynamometer was locked with a hip-to-trunk angle of 90°. To achieve this hip-to-trunk angle, the dynamometer was locked at 50° according to the dynamometer's goniometer for all participants.

2.3.7 Testing protocol

After completing the questionnaires and electrode placement, the participants performed three submaximal isometric back extensions on the isokinetic dynamometer as a warm-up. After a brief rest, they were asked to perform three isometric back extension MVCs. Each of these trials lasted 5s and they were separated by 1 min of rest. The highest MVC value was used as a reference to define the submaximal torque level. After the MVC measurement, the participants rested for 5min. Then, after completing a few practice trials, they were asked

to perform one non-fatiguing sustained isometric back extension at 20% (2-s ramp-up and ramp-down contraction with 20s hold phase) and one at 50% (5-s ramp-up and ramp-down contraction with 15s hold phase) of the MVC, respectively. These submaximal torque levels were selected in order to replicate lumbar extensor contraction intensities utilised during activities of daily living (Pranata et al., 2017). The order of the contractions was randomised, and they were separated by a 2min rest period. Real-time visual feedback of the trunk extensors torque output to the dynamometer, and a line indicating the target level of contraction (%MVC) was provided to all participants, via a computer monitor located 1.5m in front of them (**Figure 2.2**). During the submaximal contractions, the participants were first asked to match the %MVC target as accurately as possible, and once the requested target level was achieved (i.e., either 20 or 50%MVC), they were asked to try and maintain their torque as steady as possible for the full duration of the task. The instructions were given to all participants prior to the contractions. All participants were verbally motivated to exert their maximum torque during the MVCs. No verbal encouragement was provided during the two submaximal isometric lumbar extension tasks and the environment was kept silent.

2.3.8 Torque signal analysis

The highest peak torque exerted during the MVCs (SI: Newton-meters) was used as a measure of maximal trunk extension strength for each participant. The absolute peak torque values were normalised to participants body mass ($N \cdot m \cdot kg^{-1}$) to allow statistical comparisons between groups relative to body mass. The amplitude of the torque fluctuations was evaluated in both absolute and relative terms as the SD of the torque signal and as the CoV (CoV= SD/mean × 100) over time respectively. SD and CoV of torque were computed in the same time range used for the surface EMG analysis during the two torque levels (i.e., steady part of the

contraction). A custom-made MATLAB script was used to plot the torque exerted by each participant, visually identify the steady part of the contraction, and select the starting and ending point of the time window needed for our analysis.

2.3.9 Surface EMG signal pre-processing

Prior to coherence and cross-correlation calculations, the 59 differential surface EMG signals (formed by differentiating the 64 monopolar signals in the presumed direction of the muscle fibres) were processed as described previously (Staudenmann et al., 2006): (i) high-pass filtering (10Hz) (PCA-input signals), (ii) selection of the most informative subset of PCs by applying PCA to the 59 differential HDsEMG signals in the time domain (PCA-selected PCs) (iii) full-wave rectification and averaging of the selected PCs to get one time signal (Averaged PCA-selected signal), (iv) low-pass filtering (10Hz), which allows to identify slow frequency fluctuations in motor unit firing rate/recruitment (Negro et al., 2009), (v) smoothing with a 1st order Savitzky-Golay filter and (vi) DC (i.e., zero-frequency) components removal (Final Signal Envelope).

As explained in detail in (***Chapter One*, Section 1.10.1**) due to the high dimensionality of the HDsEMG data, the recordings might contain redundant and correlated information (e.g. noise, artefacts and channels with low level of muscle activity) which challenges the interpretation of data (Naik et al., 2016). In recent surface EMG-related studies, PCA has been used as a pre-filter of highly correlated data for muscle estimation (Staudenmann et al., 2006, Staudenmann et al., 2005). In this study we implemented PCA as a nonlinear dimensionality reduction technique over HDsEMG channels for each participant individually, to reduce a large set of correlated surface EMG signals into a smaller subset of PCs. In this way noise and redundant information is reduced, and the dataset is simplified, allowing the identification of

meaningful patterns. According to Naik et al., (2016), it is reasonable to retain PCs that cover more than 80% of the data variance to reduce the dimensionality of the HDsEMG data (Naik et al., 2016). In the current study, the acceptable percentage of total variance was set to 85%. After organising the PCs in descending order of variance and maintaining those that cumulatively explained 85% of the variance, a new matrix with the PCs eigenvectors was generated. Notably, this was the first step towards dimensionality reduction, as by leaving out some PCs, the final dataset had less dimensions than the original (i.e., <59). Given that in the previous steps no changes have been made to the original data, the last step of the PCA was to derive the new dataset (i.e., original data solely in terms of the vectors we chose). This was done, by using the PCs matrix formed by the eigenvectors of the covariance matrix to reorient the data from the original axes to the ones represented by the PCs. This was simply done by multiplying the transpose of the original dataset by the transpose of the PCs matrix. This led to a reduced dimensionality of the original dataset and allowed us to obtain a subset of HDsEMG channels.

After extracting the relevant force-related information (i.e., low frequency component) from the HDsEMG grid by applying PCA, coherence and cross-correlation analyses were conducted to quantify the degree of similarity between the Final Signal Envelope (i.e., the low pass filtered Averaged PCA- selected signal resulting from the first PCs that explained 85% of the variance, provided by the HDsEMG grid) and torque signals for each submaximal contraction. More specifically, as we also describe later in the cross-correlation and coherence analyses sections, the PCA-selected PCs were averaged to generate one signal (Averaged PCA-selected signal). Then, the surface EMG envelope obtained from this signal (Final Signal Envelope) was correlated with the torque signal in the time and frequency domains.

For the surface EMG amplitude calculation, the monopolar HDsEMG signals were also differentiated in the presumed vertical direction of the muscle fibres (i.e., in the direction of the

electrode columns) to form 59 adjacent bipolar channels, as mentioned earlier (Falla et al., 2014). This resulted in 12 longitudinal bipolar channels in each column, except from the far right which had 11 electrode pairs (due to the missing electrode). Firstly, surface EMG signals were bandpass filtered (10-350Hz, second order, zero lag Butterworth) (Martinez-Valdes et al., 2019). Then, bipolar channels with low signal-to-noise ratio due to poor skin-electrode contact or movement artifacts were removed after visual inspection of their quality. In the current study, the removal rate was < 15%.

2.3.10 Cross-correlation analysis

As also mentioned in ***Chapter One*****, Section 1.10.2**, cross-correlation was used to quantify the degree of correlation between fluctuations in surface EMG and torque signals in the time domain. More specifically, once the PCs which represented 85% of the variability were selected, the input data (PCA-input signals) was reoriented from its original axes to the PCs' axes. In this way, a compressed representation of the HDsEMG signals was obtained which contained the maximum variance (PCA-selected PCs). Then, the recast HDsEMG data obtained from PCA was averaged to get a single signal HDsEMG signal which explained most of the variance in surface EMG activity (Averaged PCA-selected signal). The surface EMG envelope of this signal (Final Signal Envelope) was then correlated with torque. From the cross-correlation values the maximum peak was identified along with its time lag value.

2.3.11 Coherence analysis

Coherence analysis, also briefly described in ***Chapter One*****, Section 1.10.3**, was carried out to indirectly estimate the strength and frequency of common rhythmic synaptic inputs across

the motor unit pool and establish their relationship with torque (Hansen et al., 2005). Coherence between surface EMG and force signals were computed by employing magnitude squared coherence (MSC) with a 50% overlapping Hamming window of 1-s, as done previously (Bai et al., 2019, Castronovo et al., 2015, Laine et al., 2021). Similarly to the cross-correlation analysis, the same surface EMG envelope (obtained from PCA analysis; Final Signal Envelope) was then correlated with the torque signal in the frequency domain. The MSC approach has been previously used in many areas of signal processing (Malekpour et al., 2018). It is a measure that estimates the extent to which one signal can be predicted from another signal using a linear model (Malekpour et al., 2018). The MSC is a real number between zero and one at each frequency. If the MSC value is zero, this indicates that those signals are linearly independent at that frequency (no correlation), and if it is one, that they are perfectly correlated (Halliday et al., 1995). MSC calculations were performed by using the *mscohere* function of the Signal Processing Toolbox of MATLAB, which estimates MSC using Welch's overlapped averaged periodogram method (i.e., N sub-windows with 50% overlap). As described previously (Jiménez-Grande et al., 2021), the MSC between two signals x(t) and y(t) can be computed as follows:

$$MSC_{xy}(f) = \frac{\left|P_{xy}(f)\right|^2}{P_{xx}(f)P_{yy}(f)}$$

where $P_{xy}(f)$ is the cross-power spectral density between the two time-domain signals x(t) and y(t), and $P_{xx}(f)$ and $P_{yy}(f)$ are the auto-power spectral densities of x(t) and y(t) respectively. The magnitude of the spectral density is denoted as |P|. It should be also noted that cross-power spectral density represents the cross-correlation of two different signals on the frequency domain and auto-power density the correlation of one signal with itself (Jiménez-Grande et al., 2021).

To enable statistical comparison of coherence values (C), they were converted to Fisher's values (FZ) and the bias was then removed as shown in the equation below (Laine and Valero-Cuevas, 2017, Laine et al., 2014). As it is possible that the surface EMG recordings may be contaminated by some level of crosstalk, the coherence estimation may also be affected by this. Therefore, we applied the bias which is calculated empirically as the maximum value of coherence at 250Hz, in which range is expected to find no correlation between the signals (Castronovo et al., 2015, Laine and Valero-Cuevas, 2017, Laine et al., 2014).

$$FZ = \operatorname{atanh}\left(\sqrt{C}\right) - bias$$

Since the Savitzky-Golay polynomial filter tends to preserve rapid fluctuations in surface EMG signals (Staudenmann et al., 2006), we also analysed coherence at alpha (5-15Hz) and beta bands (15-30Hz). However, since none of these bandwidths showed significant coherence, we mainly focused on the analysis of the δ band (0-5Hz) which is the most relevant for the generation of force (Farina and Negro, 2015). The δ band coherence values were transformed to z-scores to allow statistical comparisons. Please note that the low frequency components < 5 Hz were filtered out during pre-processing, however, the subsequent full-wave rectification allows the analysis of the low-frequency modulation of the signal amplitude (Suzuki et al., 2021).

Additionally, we created topographical maps of coherence (described below). In these maps, each of the 59 bipolar recordings was correlated with the torque signal in the frequency domain to provide one value. Then all the values were normalised to the maximum coherence value observed at each torque level respectively (i.e., 20% and 50%MVC). This map enabled the identification of areas of higher and lower coherence with torque, respectively. Finally, the

centroid of coherence was calculated. This measure can provide an estimate of where the centroid of coherence is along the x- (medial-lateral) and y-axis (cranial-caudal). These maps follow the same approach as described for the surface EMG amplitude maps in (**Figure 1.3**) This allowed us to examine whether certain muscle regions contribute more to the exerted torque than others, by statistically comparing the x- and y-axis centroid values between groups.

2.3.12 Surface EMG amplitude calculation

RMS values were computed for each bipolar recording (i.e., 59 from ES and one from RA) and for each of the lumbar extension tasks (i.e., MVCs and two torque levels). The 59 RMS values were then averaged to form one value which was used as a global measure of the ES myoelectric activity (HDsEMG amplitude; ES RMSmean) during each task. Please note that this analysis was not the same as the one used for the coherence and cross-correlation analysis (i.e., rectification of the surface EMG signal) mentioned earlier. RMS is commonly used to measure the level of muscle activation as described in (***Chapter One*, Section 1.6.1**). Having one RMS value for each of the RA and ES muscles, enabled us to quantify co-activation (unilaterally) between the trunk flexors and trunk extensors during the isometric lumbar extension at the two different torque levels. The level of co-activation was calculated based on the non-normalised RMS values, as follows: antagonist muscle activity (RA RMS)/agonist muscle activity (ES RMSmean) × 100. To allow between group comparisons, the ES RMSmean values obtained during the two torque levels, were expressed as a percentage of the ES RMS value calculated during the maximal (baseline) MVC. The ES MVC RMS value was extracted separately for each participant. More specifically, from around the peak of the highest isometric MVC, 1s of the contraction was cut and a non-overlapping 0.25s sliding averaging window was

used. In other words, one RMS value was produced each 0.25s (i.e., 4 values in total) and then the average of those was used to calculate the max ES MVC RMS value.

Similarly, to others, all the aforementioned variables (except RMS value during MVC), were determined from the steady torque part of the contraction using a non-overlapping 0.5s sliding averaging window (i.e., one average value was calculated for each variable, every 0.5s) (Farina et al., 2008). The length of the time windows used for the analysis was approximately 18s and 13s for the 20%MVC and 50%MVC torque levels respectively. This was performed to exclude the first and last second of the steady part of the contraction from our analysis, which were the time-instants that participants over or underestimated the requested torque level.

All HDsEMG and torque signals were analysed offline, using a custom script on MATLAB 2020b (The MathWorks Inc., USA).

2.3.13 Statistical analysis

All data analyses were performed on SPSS Statistics, version 27 (IBM, USA). The Shapiro-Wilk test was used to test the normality of the data and the assumption of homogeneity of variance was assessed with a Levene test. These assumptions were met, and thus parametric tests were applied. Descriptive statistics were used to analyse the data and the results are expressed as means and SDs. Anthropometrics, NPRS scores, questionnaire scores and isometric back extension MVC between groups were compared with independent t-tests. Statistical comparison for surface EMG and torque variables between groups (RMS, $Torque_{mean}$, CoV of torque, SD of torque, surface EMG-torque coherence in the δ band, surface EMG-torque cross-correlation, surface EMG-torque coherence y- and x-axis centroid) was performed using a two-way mixed (i.e., with one within- and one between-subjects factor) analysis of variance (ANOVA), using torque target (20%MVC, 50%MVC) and group (CLBP,

control) as within-subject and between-subject factors respectively. The level of co-activation between the ES and RA muscles was also evaluated with the same analysis. When significant interactions were revealed from the ANOVA, the Bonferroni method was used to allow pairwise comparisons. Pearson's correlations evaluated associations between the surface EMG parameters [variations (i.e., 20%MVC to 50%MVC change) in surface EMG-torque coherence in the δ band, variations in surface EMG-torque cross-correlation, variations in surface EMG-torque coherence (δ band) y- and x-axis centroid and variations in the level of RA-ES co-activation and ES RMS amplitude)], the motor performance characteristics (variations in CoV and SD of torque) and the self-reported outcome measures (pain intensity, level of disability, general health and kinesiophobia). The level of statistical significance was set to $p=0.05$.

2.4 Results

2.4.1 Participants

All 30 participants (15 CLBP, 15 controls) successfully completed the study, and their characteristics are reported in **Table 2.1**. The two groups did not differ in terms of demographic characteristics. However, as expected the individuals with CLBP presented with higher levels of disability and lower general health compared to the control group. The individuals with CLBP reported a current level of pain intensity of 2.5 (2.2) which is characterised as mild pain (Breivik et al., 2008). As anticipated, the controls did not report LBP. None of the participants reported an increase in their level of pain intensity after performing the contractions.

Table 2.1: **Characteristics of all participants separated by group. Data are presented as mean ± SD. Asterisks represent significant differences between groups. CLBP: chronic low back pain. BMI: body mass index. NPRS: numerical pain rating scale. ODI: Oswestry Disability Index. RAND: Research and Development. TSK: Tampa Scale for Kinesiophobia. MVC: maximal voluntary contraction. The asterisk (*) indicates statistically significant differences between groups.**

Characteristic	Controls (15)	CLBP (15)	p-value
Gender (%males)	53.3	46.7	–
Age (years)	27.4 (4.9)	27.1 (9.3)	0.931
Height (cm)	171.3 (5.4)	169.9 (5.7)	0.501
Weight (kg)	73.7 (10.4)	69.3 (10.1)	0.264
BMI (kg/m^2)	25.2 (3.5)	23.8 (2.7)	0.271
Average Pain Intensity (NPRS)*	0.0 (0.0)	2.5 (2.2)	< 0.001
ODI (%)*	0.0 (0.0)	14.9 (7.5)	< 0.001
RAND 36-item health survey*	89.6 (6.8)	64.1 (19.6)	< 0.001
TSK*	28.1 (6.0)	34.7 (5.2)	0.004
Isometric back extension MVC ($N \cdot m \cdot kg^{-1}$)	3.7 (1.0)	3.2 (1.6)	0.258

2.4.2 Torque

Both groups exerted similar levels of isometric peak torque during the MVC of isometric back extension (**Table 2.1**). The mean submaximal torque exerted during the two torque levels was similar for both groups ($F=0.904$, $p=0.350$, $\eta p^2= 0.031$). Overall, individuals with CLBP had significantly higher CoV and SD of torque than the asymptomatic controls during the two torque levels (main effect of group: $F=5.327$, $p=0.029$, $\eta p^2= 0.160$ and $F=4.368$, $p=0.046$, $\eta p^2=0.135$ respectively; **Figure 2.3a, b**).

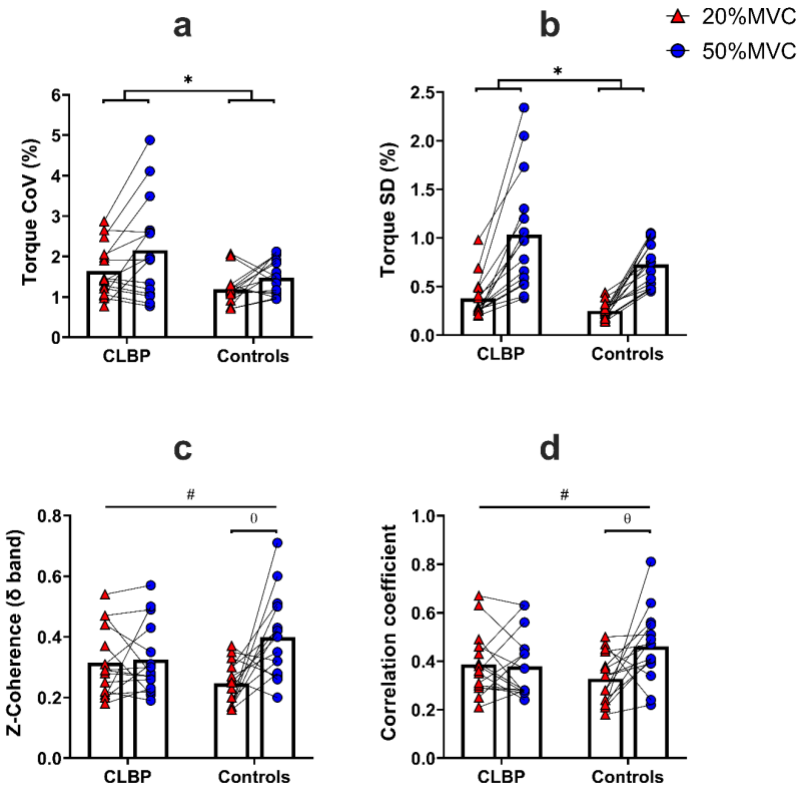


Figure 2.3: **Torque CoV (a), torque SD (b), δ-band Z-coherence (i.e., δ band coherence values that have been transformed to z-scores) (c) and cross-correlation (d) values (mean ± SD) of the CLBP group and AS controls at 20% and 50%MVC respectively (*main effect of group, #interaction effect: group*torque, θ: post hoc tests).**

2.4.3 Electromyographic activity

The normalised spatial mean of the RMS values for the lumbar ES did not differ between groups during the two torque levels (group effect: F=3.850, p=0.060, ηp^2=0.121). The mean values for both groups and torque levels were as follows, controls at 20%, 50%MVC: 37.8(19.9)% and 60.5(17.9)% respectively, CLBP at 20%, 50%MVC: 52.1(15.9)%, 76.1(29.9)% respectively. Both groups presented similar levels of RA-ES co-activation during the submaximal contractions (group effect: F=0.010, p=0.922, ηp^2=<0.001). The average RA-ES co-activation values for both groups and torque levels were as follows, controls at 20%,

50%MVC: 130.4(128.3)% and 84.9(62.5)% respectively, CLBP at 20%, 50%MVC: 114.9(89.9)%, 100.5(70.2)% respectively.

2.4.4 Cross-correlation and coherence

The cross-correlation increased with the increase in torque for the asymptomatic controls, but this was not the case for the CLBP group (interaction: group × force, F=5.234, p=0.030, ηp^2=0.157; **Figure 2.3d**).

Coherence in the δ band increased with the increase in torque for the asymptomatic controls but not in the CLBP group (interaction: group × force, F=6.346, p=0.018, ηp^2=0.185; **Figure 2.3c**). The centroid of coherence along the y-axis differed significantly between the two groups at 50%MVC, with higher coherence being observed in the more cranial region of the lumbar ES for the CLBP group (interaction: group × force, F= 4.511, p=0.043, ηp^2=0.139; **Figure 2.4**). With the increase in torque, a higher coherence in the more caudal region of the lumbar ES was observed in the asymptomatic controls (interaction: group × force, F= 4.511, p=0.043, ηp^2=0.139; **Figure 2.5**).

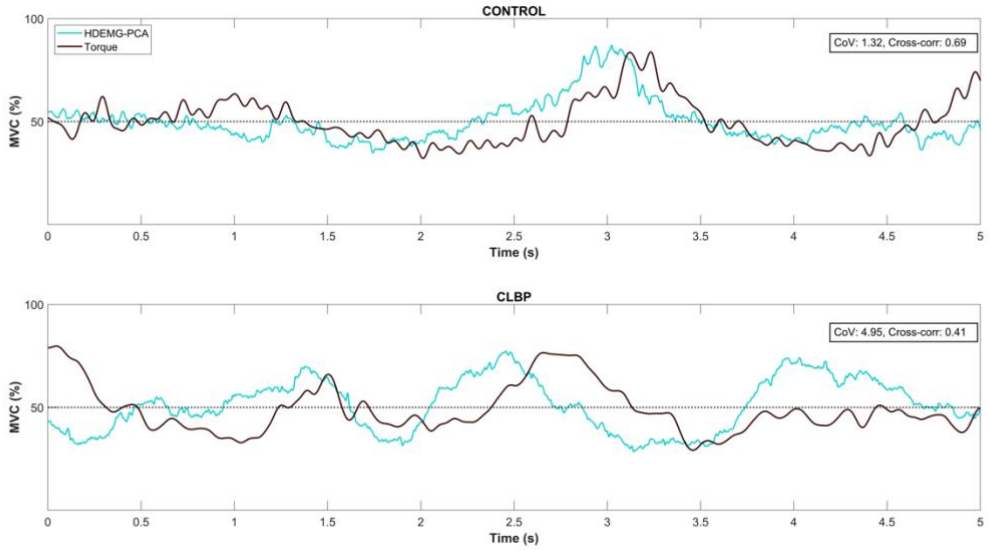


Figure 2.4: **A sample outcome of lumbar extensor muscle torque steadiness assessment (5s window from the steady part of the contraction) for a control and a CLBP participant during the 50%MVC isometric back extension task. The black line represents the oscillations in torque for each participant, while the turquoise line represents the oscillations in the HDsEMG signal (i.e., the PCA-processed sEMG signal envelope). Note that the control participant has greater torque steadiness and at the same time a higher sEMG-torque cross-correlation, while the CLBP participant presents with lower torque steadiness performance and has a lower sEMG-torque cross-correlation at the same time.**

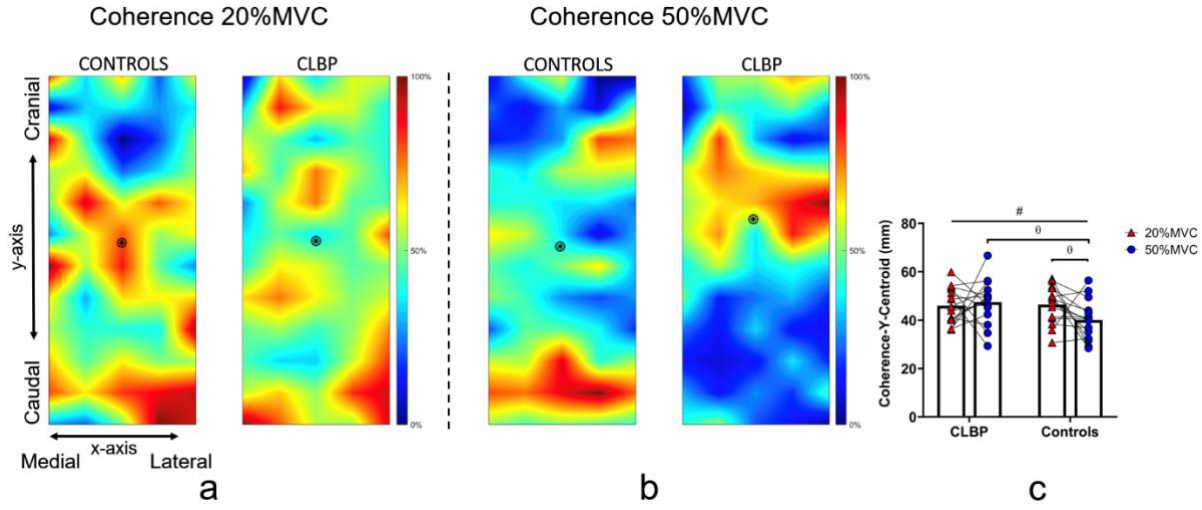


Figure 2.5: **Topographical maps of averaged normalised (to the maximum coherence value) coherence across participants at (a) 20% and at (b) 50%MVC. The black circle in the topographical maps (a, b) represents the centroid of coherence, which was calculated from the bottom of the electrode grid. The spine is located towards the medial side of the x-axis. Figure c depicts the position of the y-axis centroid for both groups at 20% and**

50%MVC (#interaction effect: group*torque, θ: post hoc tests). Hotter/red colours represent higher coherence, while blue/cold colours represent lower coherence.

2.4.5 Associations between outcome variables

No significant correlation (Pearson's *r*) was observed between any of the surface EMG, motor output (torque production) and self-reported (pain and function) parameters ($p>0.05$ in all possible comparisons).

2.5 Discussion

In this study we aimed to (i) measure the relationship between HDsEMG oscillations and isometric trunk-extension torque in both time and frequency domains, using cross-correlation and coherence analysis respectively, and (ii) identify and compare regional differences in surface EMG-torque coherence of the lumbar ES in individuals with CLBP and asymptomatic controls. Surface EMG-torque coherence in the δ band and surface EMG-torque cross-correlation increased with the increase in torque for the asymptomatic controls, but this was not observed for the CLBP group. Additionally, the CLBP group had higher surface EMG-torque coherence in more cranial regions of the lumbar ES at 50%MVC, while the opposite was observed for the asymptomatic controls (i.e., higher surface EMG-torque coherence in more caudal regions of the lumbar ES). Interestingly, the level of lumbar ES activity (HDsEMG amplitude), and the co-activation levels did not differ between groups during the tasks.

2.5.1 Surface EMG-torque coherence and cross-correlation alterations

We quantified the relative power only in the δ (0-5Hz) frequency bandwidth from the interference surface EMG and torque signal since torque fluctuations during isometric contractions are mainly explained by the effective neural drive to the muscle, i.e., low-frequency component (< 10Hz) of the neural drive to the muscle (Enoka and Farina, 2021).

Interestingly, even though an increase in torque is commonly accompanied with an increase in δ band coherence (Castronovo et al., 2015), as seen in the asymptomatic group, the CLBP group failed to increase surface EMG-torque coherence with the increase in torque. This finding is also supported by the cross-correlation results, showing that in the CLBP group, the net increase in torque was not accompanied by an increase in the contribution of the lumbar ES muscle to the resultant torque fluctuations. Given that the low-frequency component of the rectified surface EMG is associated with the variability in motor unit firing rate and hence torque oscillations (Yoshitake and Shinohara, 2013a), correlation and coherence between surface EMG and torque, should have been higher in the CLBP as they had higher variability in torque fluctuations compared to the asymptomatic controls. However, this was not observed, as at both torque levels, cross-correlation and coherence was similar for the CLBP group. Additionally, given that both groups exerted a similar amount of torque during the task, the individuals with CLBP could have compensated by activating synergistic muscles. Under the influence of pain, the CNS can find a new motor strategy to achieve a specific task (e.g., perform an MVC and/or an isometric torque steadiness task in our case) and due to the redundancy of the trunk motor control system, people with CLBP often display substantial reorganisation of their motor control strategies (Hodges and Tucker, 2011). This can allow people with CLBP to adopt different muscle recruitment solutions to achieve a specific outcome and possibly avoid pain. Importantly, these changes can be explained by alterations of the descending drive to the

muscles, but also by changes in motor planning (i.e., modulated by cognitive/emotional factors) (Tucker et al., 2012). In the present study, individuals with CLBP had higher levels of Kinesiophobia (higher scores in TSK) compared to the asymptomatic controls. Thus, it is possible that the CLBP group experienced more fear as the torque increased, leading to the use of compensatory strategies, which likely involved the hip extensors, and this would explain why we did not observe an increase in the surface EMG-torque coherence and cross-correlation values in the δ band (i.e., no increase in the common synaptic input and the contribution of the lumbar ES muscle to the net torque). This is also further supported by a previous observation, showing that initially pain-free individuals with high pain-related fear adopt avoidant strategies during common reaching movements shortly after the induction of delayed-onset muscle soreness (Trost et al., 2012). However, it should be noted that this is speculative, more so considering that the average TSK score of 34.7 for the CLBP group is still considered low. Future studies could investigate this further. Interestingly, the levels of lumbar ES activation and ES-RA co-activation were similar between the two groups. This shows that RMS amplitude alone (i.e., using a simple estimate of muscle activation) could not explain any differences between the two groups in the execution of the torque steadiness task, but the proposed coherence analysis gave us better insight into the actual contribution of the trunk extensor muscles to the resultant torque.

2.5.2 Regional variations in HDsEMG-torque coherence

Moreover, given that regional differences in myoelectric activity of lumbar ES is a common finding in people with CLBP (Arvanitidis et al., 2021a, Falla and Gallina, 2020, Falla et al., 2014, Martinez-Valdes et al., 2019, Sanderson et al., 2019a, Sanderson et al., 2019b) and that altered distribution of input to the motoneurons can change motor unit recruitment patterns

during pain (Sanderson et al., 2021), we investigated whether regional differences in surface EMG-torque coherence also existed between people with CLBP and asymptomatic controls. Differences in topographical representation of coherence were observed at 50%MVC, since the lumbar ES coherence centroid in the CLBP group was displaced more cranially (suggesting higher coherence in the upper region of the muscle), while in the asymptomatic controls, the centroid of coherence was displaced towards more middle-caudal regions of the lumbar ES. This finding likely suggests that that torque is less represented in the caudal region of the muscle in individuals with CLBP at 50%MVC, since the correlation between surface EMG and torque is the lowest in this region. Since common synaptic input is reflected by δ band coherence, this could suggest that individuals with CLBP show reductions in surface EMG-torque relationships due to a more focalized distribution of common synaptic input (HDsEMG-torque coherence) of the lumbar ES and possibly a higher influence of independent synaptic inputs on the lumbar ES motor unit pool, at least when they exert higher forces. However, these findings should be confirmed with surface EMG-torque coherence, based on surface EMG decomposition analysis, as the interference surface EMG signal is influenced by several factors (Farina et al., 2014a). From a clinical perspective, it should be also noted that this more focalised contribution of muscle fibres to the resultant torque, imply that those specific muscles fibres (mainly located in the cranial region of ES) will be the main contributors to the resultant torque during extension. This could possibly lead to an uneven distribution of load, thus, overloading of those specific muscle fibres (Falla and Gallina, 2020). Such motor behaviour could possibly play an important role in the perpetuation of CLBP symptoms.

2.5.3 Impaired torque control in people with CLBP

As anticipated, people with CLBP had reduced trunk extensor muscle torque steadiness, compared to asymptomatic controls (**Figure 2.4**). These findings are in line with those from previous studies (Pranata et al., 2017, Willigenburg et al., 2013) and further support the notion that the control of muscle force (measured either as force accuracy and/or force steadiness/variability) is impaired in individuals with CLBP. Trunk muscle function impairments are common in people with CLBP, and these can be more pronounced when motor control is challenged by tasks that require high precision, such as the one used in the current study (Willigenburg et al., 2013). These impairments, including reduced torque steadiness, are likely attributed to the numerous functional and structural neuroplastic changes that can occur at multiple levels of the nervous system (i.e., periphery, spinal and/or supraspinal centers) when people have pain (Brumagne et al., 2019). For example, proprioceptive acuity is reduced in people with CLBP (Brumagne et al., 2019), and this can be related to suppression of proprioceptive input by nociceptive afference and/or altered afferent input due to changes in the mechanical properties of passive structures (e.g., ligaments and IVDs) (Ager et al., 2020, Röijezon et al., 2015). Additionally, it could be related to structural changes, such as the reduction of white matter integrity of the superior cerebellar peduncle, which is an important brain area for the transmission of proprioceptive input to higher centers (Pijnenburg et al., 2014). Importantly, previous studies have also shown that regions of the motor cortex that are related with the control of specific trunk muscles are also reorganised in people with CLBP (overlap between muscle cortical representations), and this is likely related to a loss of discrete control of paraspinal muscle fascicles (Schabrun et al., 2017, Tsao et al., 2011). Collectively, these neuroplastic changes observed in people with CLBP could explain their impaired capacity to control trunk muscle force accurately. Compensations for proprioceptive deficits and/or other

neuroplastic changes can be reflected as alterations in the efferent motor response (i.e., motor recruitment strategy). Therefore, it is relevant to unravel the motor control strategy that the CLBP group utilized to exert the requested amount of torque during the torque steadiness and MVC tasks.

2.5.4 Trunk muscle strength

Trunk extensor isometric muscle strength did not differ between groups, which is consistent with the results of some previous studies (Arvanitidis et al., 2021a, da Silva et al., 2005, Pranata et al., 2017). Previous research has shown that pain decreases the ability to exert maximal forces (Graven-Nielsen et al., 1997, Khan et al., 2011), due to nociceptive-induced inhibition to agonist muscles (Graven-Nielsen et al., 2002). However, these findings are mainly observed in upper or lower-limb muscles, which produce torque around a single joint (i.e., tibialis anterior; TA) (Graven-Nielsen et al., 1997) or across two joints (i.e., biceps bracchii) (Khan et al., 2011). On the contrary, trunk extension is a multi-joint movement that involves concurrent movement of the lumbar spine, pelvis and hips (San Juan et al., 2005). Therefore, people with CLBP could have performed the MVC by compensating with the large hip extensor muscles (e.g., gluteus maximus and hamstrings), which can influence both the hip and pelvis, thereby minimizing the activation of their lumbar extensors. Although, the thighs and pelvis were stabilised with straps, it is not possible to completely prevent such compensatory strategies. These factors could have allowed the participants to perform the MVC with a higher contribution of their hip extensors, compared to their lumbar extensors (possibly due to pain and/or fear). As previously shown, when the thigh is stabilised, the hamstrings and the gluteus maximus rotate the pelvis posteriorly which likely *"disengages"* and counteracts lumbar extension (Bakkum, 2014). Thus, during the MVC, people with CLBP could have exerted

torque by extending their hips with their pelvis tilted posteriorly (i.e., with higher contribution of the gluteal and hamstring muscles). It could be also argued that people with CLBP managed to exert a similar amount of torque during the MVC by greater activation of deeper lumbar extensor muscles, such as the multifidus muscle, however, this is unlikely as this muscle's main function is to stabilize the lumbar spine and is more commonly inhibited in people with CLBP (van Dieën et al., 2019).

2.5.5 Lack of associations between outcome variables

Lastly, it should be noted that there was no significant correlation between the surface EMG parameters, the motor output (torque production) parameters and the self-reported measures of pain and function. This makes it difficult to explain the observed changes in the surface EMG parameters and means that the neuromuscular mechanisms responsible for the poorer trunk muscle torque steadiness observed in individuals with CLBP, warrant further investigation. However, this is not a surprising finding, as many studies do not report any significant correlation between motor output and self-reported measures of pain/function (Maenhout et al., 2012, Magni et al., 2021, Overbeek et al., 2020) and/or surface EMG parameters (Bandholm et al., 2008, Willigenburg et al., 2013) in people with musculoskeletal pain. Some possible reasons for the lack of correlation between these parameters are the following: (i) the fact that people with CLBP present a wide variety of neuromuscular responses and that there is substantial variability even considering one type of neuromuscular adaptation, (ii) the characteristics of the individuals with CLBP recruited for this study (i.e., mild symptoms), and (iii) the variability in the questionnaire data due to their subjective nature. It is likely that each participant with CLBP used a different strategy to maintain a steady force during the task regardless of the level of pain and/or changes in function (Hodges et al., 2009).

However, this should be confirmed in future studies which incorporate recordings from multiple muscles during similar tasks in order to obtain greater insight of the potential compensatory strategies utilized by people with CLBP.

2.5.6 Methodological considerations and limitations

A limitation of this study is that the sample consisted mainly of young, active individuals with low pain intensity and mild disability. This likely limits the generalisability of the results. However, even with relatively low levels of disability and pain intensity we were still able to identify impairments in this group, although it should be noted that there was variability between individuals with CLBP, as has been commonly observed previously (Falla et al., 2014). It is likely that a sample of people with more severe CLBP would present with even higher deficits, or other neuromuscular adaptations which could negatively impact on the ability to control torque output in a steady way. Additionally, this study did not measure possible compensatory patterns by using kinematic markers and/or recording surface EMG activity of synergist muscles. Another limitation that should be considered is that the rectified interference surface EMG is only a rough estimator of the neural drive to the muscles, as it is influenced by several factors, including amplitude cancellation (i.e., the overlapping of motor unit action potentials) (Dideriksen and Farina, 2019). Based on the findings of a simulation study, amplitude cancellation can distort the spectrum of the rectified surface EMG signal and thus have an influence on the results (Dideriksen and Farina, 2019). This problem is commonly solved by basing the analysis on the identification of motor unit spike trains (i.e., by using surface EMG decomposition), rather than on surface EMG. However, HDsEMG decomposition is currently challenging on signals collected from the lumbar ES likely due to factors such as the (i) complexity of lumbar anatomy (i.e., existence of many different layers of muscles and

thoracolumbar fascia) (Christophy et al., 2012), and (ii) the volume conductor properties of the lower lumbar area (i.e., thicker subcutaneous layer) (Del Vecchio et al., 2020). These factors can reduce the discriminative information in the action potential waveforms of different motor units, and thus limit the applicability of decomposition algorithms (Del Vecchio et al., 2020). Therefore, we based our analysis on the rectified surface EMG signal. Nevertheless, the correlation between the surface EMG signal (i.e., PCA-processed surface EMG signal envelope) and torque was ≈ 0.4 for both groups and torque levels, likely suggesting a moderate correlation between surface EMG and torque oscillations. Studies employing motor unit recordings usually report higher discharge rate vs torque cross-correlation values (approximately 0.75-0.80) (Negro et al., 2009). However, this is usually seen in smaller, single-joint muscles (i.e., TA). It is likely that these correlations would be reduced in larger muscles like ES, however, this is yet to be determined. Lastly, another limitation that needs to be addressed is the calculation of co-activation based on non-normalised RA and ES RMS values, which might have provided less reliable co-activation estimates due to inter-subject anatomical differences (e.g., differences in sub-cutaneous tissue thickness between the abdominal and paraspinal regions). Nevertheless, in our previous study, co-activation was calculated based on normalised RA and ES RMS values during a dynamic isokinetic fatiguing task and again we did not observe differences in co-activation between people with CLBP and asymptomatic controls (Arvanitidis et al., 2021a). On top of this, whether absolute or normalised surface EMG-RMS amplitudes are favourable in the interpretation of co-activation index remains unclear (Gagnat et al., 2020). Thus, we believe that similar findings would have been observed, even if the RMS values were normalised during the calculation of co-activation ratios.

2.6 Conclusion

This study uniquely demonstrates that individuals with CLBP fail to increase the common fluctuations in torque and HDsEMG activity, when exerting higher lumbar extension forces. This reduced ability to alter the surface EMG-torque relationship, is likely due to regional adjustments of ES-surface EMG oscillatory activity (torque was not represented in the caudal region of the lumbar ES in individuals with CLBP) and the use of compensatory trunk extension patterns during this task. The current study contributes to the existing body of knowledge and further supports the notion that individuals with CLBP have poorer control of their trunk extensor muscles compared to asymptomatic individuals. However, it remains unclear whether these impairments are also present during dynamic trunk movements. This research question is addressed in the subsequent study presented in this thesis.

Chapter 3

LOW-BACK PAIN-INDUCED DYNAMIC TRUNK MUSCLE CONTROL IMPAIREMENTS ARE ASSOCIATED WITH ALTERED SPATIAL EMG-TORQUE RELATIONSHIPS

In ***Chapter 2***, we observed that individuals with CLBP have reduced isometric lumbar extensor torque steadiness, that they fail to increase the common fluctuations in torque and HDsEMG activity, when exerting higher lumbar extension forces. We discussed that this reduced ability to alter the surface EMG-torque relationship, is likely due to regional adjustments of ES-surface EMG oscillatory activity and the use of compensatory trunk extension patterns during this task.

In this chapter, we will investigate whether similar impairments are present during dynamic movements, specifically trunk flexion and extension, in this population. We will also explore the surface EMG-torque relationships during these tasks. This chapter also presents the complete details of a manuscript published by the thesis author (**Appendix 3**) (Arvanitidis et al., 2024c). It contains direct passages from the published work, with certain adjustments made in the Abstract, Introduction and Method sections to improve the flow between the chapters of this thesis and minimise redundancy. Specifically, most of the major changes were related to removing information related to the background from the introduction and signal processing methods utilised in the methods part of this study, which were already stated in ***Chapter 1*** and ***Chapter 2***.

Publications and Presentations:

1. **Arvanitidis M**, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Low Back Pain-Induced Dynamic Trunk Muscle Control Impairments Are Associated with Altered Spatial EMG-Torque Relationships. Med Sci Sports Exerc. 2024;56(2):193-208.
2. **Arvanitidis** M, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Associations between impaired dynamic trunk muscle control in people with chronic low back pain and altered spatial EMG-torque correlations. XXIV Congress of the International Society of Electrophysiology and Kinesiology (ISEK). Poster presentation, Nagoya, Japan, June 26 - 29, 2024. (Accepted)

3.1 Abstract

To extend our understanding related to changes in force control in the presence of CLBP, observed in ***Chapter 2***, in this chapter, we quantified the relationship between HDsEMG oscillations (in both time and frequency domains) and torque steadiness during submaximal concentric/eccentric trunk extension/flexion contractions, in individuals with and without CLBP.

Comparisons were made between regional differences in HDsEMG amplitude and HDsEMG-torque cross-correlation and coherence of the thoracolumbar ES, RA and EO muscles between the two groups. HDsEMG signals were recorded from the thoracolumbar ES with two 64-electrode grids and from the RA and EO muscles with a single 64-electrode grid placed over each muscle. Torque signals were recorded with an isokinetic dynamometer. Coherence (δ band (0-5 Hz)) and cross-correlation analyses were used to examine the relationship between HDsEMG and torque signals. For this purpose, we employed PCA analysis to reduce data dimensionality and improve HDsEMG-based torque estimation.

We found that people with CLBP had poorer control during both concentric and eccentric trunk flexion and extension. Specifically, during trunk extension, they exhibited a higher HDsEMG-torque coherence in more cranial regions of the thoracolumbar ES and a higher HDsEMG-cross-correlation compared to asymptomatic controls. During trunk flexion movements, they demonstrated higher HDsEMG amplitude of the abdominal muscles, with the centre of activation being more cranial and a higher contribution of this musculature to the resultant torque (particularly the EO muscle).

Our findings underscore the importance of evaluating torque steadiness in individuals with CLBP. Future research should consider the value of torque steadiness training and

HDsEMG-based biofeedback for modifying trunk muscle recruitment strategies and improving torque steadiness performance in individuals with CLBP.

3.2 Introduction

As recently shown, and mentioned in ***Chapter 1*** and ***Chapter 2***, the low-frequency (< 10Hz) component of the neural command (i.e., the effective neural drive) is mainly responsible for generating muscle force since it reflects the common synaptic input received by the motor unit population (Farina and Negro, 2015, Negro et al., 2009). Hence, the genesis of force fluctuations and the control of muscle force depend mainly on the amplitude of these low-frequency oscillations that reflect common synaptic input (Farina and Negro, 2015). Measuring the amplitude of the force fluctuations (Enoka and Farina, 2021) can provide a measure of force (torque) steadiness, that is, a measure of an individual's ability to maintain a constant level of force during a submaximal contraction (Tracy and Enoka, 2006).

Executing contractions with minimal variations in force is important for normal physical function. Any impairment in this ability can negatively affect the precision of voluntary movements, resulting in alterations in dynamic joint stability/coordination and potentially leading to changes in joint movement patterns. Musculoskeletal pain can significantly impact movement and the ability to control muscle force (Ager et al., 2020), and this has been observed in various painful musculoskeletal conditions discussed in (***Chapter Two*****, Section 2.2**), including in people with CLBP as we observed in the first study of this thesis (Arvanitidis et al., 2022), (***Chapter 2***), where control of trunk muscle force was reduced in people with CLBP compared to asymptomatic controls.

Specifically, using cross-correlation, coherence and PCA to investigate surface EMG/torque relationships (i.e., understand the relationship between muscle activity and the

force that trunk muscle generate), we previously demonstrated that isometric torque steadiness is reduced in people with CLBP, while at the same time they present with reductions in HDsEMG-torque relationships compared to asymptomatic individuals, possibly due to regional adjustments of ES surface EMG oscillatory activity (***Chapter 2***) (Arvanitidis et al., 2022). Regional adjustments of ES surface EMG oscillatory activity were measured by generating topographical maps that evaluate the relationship between torque and surface EMG signals from the regions covered by the HDsEMG electrode grid. These findings suggested that individuals with CLBP may adopt different muscle recruitment strategies and/or use compensatory movement to achieve a specific motor performance outcome, possibly with the aim of avoiding pain. This, in turn, leads to changes in HDsEMG-torque relationships and differences in the region of the muscle with a higher contribution to torque. Assessing regional HDsEMG-torque relationships is particularly important, considering that people with CLBP commonly display less correlated activity in the more caudal regions of the lumbar ES (i.e., this region contributes less to the resultant torque) during static lumbar extension tasks (Arvanitidis et al., 2022). However, the specific neuromuscular processes contributing to decreased muscle force control in individuals with CLBP pain during dynamic contractions have yet to be fully understood. In addition, most studies assessing force control in individuals with chronic musculoskeletal conditions, including CLBP, have predominantly focused on assessing force control during isometric contractions. Concentric (muscle shortening) and eccentric (muscle lengthening) trunk flexion/extension contractions are more representative of the actions that occur during activities of daily living, thus, assessing these more functional contractions could provide a more comprehensive understanding of an individual's ability to control force.

The study within this chapter addressed the second objective of this thesis and aimed to (i) quantify the relationship between HDsEMG oscillations and torque oscillations in both time

and frequency domains while individuals with and without CLBP perform concentric/eccentric trunk extension/flexion contractions and (ii) assess and compare regional differences in HDsEMG amplitude and HDsEMG-torque cross-correlation and coherence of the ES, RA and EO muscles. It was hypothesized that individuals with CLBP would show a weaker correlation between HDsEMG and torque, and a more focalized distribution of HDsEMG amplitude and HDsEMG-torque cross-correlation and coherence of the thoracolumbar ES and the EO muscle during the contractions.

3.3 Materials and Methods

3.3.1 Study design and setting

All procedures of this case-control, cross-sectional study were approved by the Science, Technology, Engineering and Mathematics Ethical Review Committee of the University of Birmingham (approval number: ERN 19-1148; **Appendix 2**) and were conducted in accordance with the Declaration of Helsinki. This study is observational and primarily exploratory in nature, nevertheless, multiple a priori hypotheses were made based on the findings of previous studies from our group and others. This manuscript is reported in line with the STROBE guidelines. The CEDE-Check checklist was used for the reporting of EMG methods (Besomi et al., 2024). Data was collected between April 2019 and July 2022 at a laboratory within the CPR Spine, University of Birmingham, UK. All participants attended the laboratory on one occasion and gave written, informed consent before participating.

3.3.2 Participants

Twenty individuals with CLBP and 20 asymptomatic controls participated. All participants were recruited from the local Birmingham and University of Birmingham student and staff communities through social media posts and posted information leaflets. The sample size calculation for this study was based on a large effect size of f = 0.4, an alpha (α) error probability of 0.001, a beta (β) power of 0.85 and a potential 10% loss of data due to signal quality or participant withdrawal. The choice of this effect size was based on our previous two-way mixed repeated measures ANOVA results, related explicitly to CLBP and asymptomatic control differences in torque CoV, SD, and centroid of coherence (along the y-axis) in the δ band during isometric lumbar extension contractions (Arvanitidis et al., 2022) (***Chapter Two*, Section 2.4.4**).

3.3.3 Inclusion and exclusion criteria

To be included in the CLBP group, participants had to be men or women aged 18-55 years, experiencing non-specific CLBP for at least three months over the last six months. To be included in the asymptomatic control group, participants had to be men or women aged 18-55 years, without current or previous symptoms of back and/or lower limb pain, which led them to seek help from a health care professional. The upper age limit was set at 55 as applied and explained previously (Arvanitidis et al., 2022). The exclusion criteria for both groups were: lumbar radiculopathy, radicular pain, spinal deformity and/or surgery, pregnancy, history of cardiovascular diseases, neurological diseases and/or chronic respiratory problems and systemic or inflammatory conditions. A further exclusion criterion for people with CLBP was seeking treatment for their LBP in the last six months before enrolment. Participants with CLBP

were also advised to refrain from taking any medication with analgesic effects on the day of the experimental session, to avoid potential confounding effects that could interfere with the accurate assessment of the experimental interventions and outcomes.

3.3.4 Questionnaires

At the beginning of the session, participants with CLBP were asked to report their average pain intensity over the last week, in the preceding 24 hours, and their current pain intensity. All participants were also asked to report their level of pain intensity after performing the contractions. Pain intensity was rated on an 11-item NPRS, with *"0"* signifying no pain and *"10"* the worst pain imaginable (Jensen and McFarland, 1993). All participants were asked to report their perceived disability related to back pain using the ODI (Fairbank et al., 1980). Additionally, for all participants, general health and fear-avoidance beliefs and fear-avoidance behaviour were assessed with the RAND-36-Item Health Survey (Brazier et al., 1992) and the TSK (Miller et al., 1991), respectively.

3.3.5 Pressure Pain Thresholds

Pressure pain threshold (PPT) testing, frequently employed to investigate local and widespread hyperalgesia, serves as a measure of pain sensitivity using electronic or mechanical pressure algometry. This tool aids in evaluating pain sensitivity, highlighting differences between individuals with CLBP and asymptomatic individuals. Participants were asked to lie on a plinth in a prone position to measure PPTs (defined as the minimum pressure applied which induces pain). After familiarisation, PPTs were measured with an electronic algometer (probe tip: 1 cm^2, 30kPa/s; NOD, OT Bioelettronica, Italy). Participants were instructed to inform the

researcher when the sensation of pressure had turned to one of pain (i.e., first perception of pain). At that point, the application of pressure was terminated. PPTs were tested on the right side in the asymptomatic group and on the most painful side in the CLBP. The right side was assessed if individuals with CLBP experienced bilateral and symmetrical pain. Ten testing locations were assessed over the thoracolumbar area to explore differences in sensitivity between the two groups over a large area. Specifically, two vertical rows were marked, each consisting of 5 PPT sites (starting from L5 vertebra, distance between vertical points: 3.6 cm). The medial row started directly next to the spinous processes over the ES muscles, and the other was more lateral (3.2 cm distance). Two consecutive PPT measurements were performed at each site in a randomised order. The mean value of the 2 PPT measures at each pressure point was calculated and used for further analysis. Previous studies have established excellent reliability of PPT testing for assessing the lumbar spine in both individuals with CLBP (de Oliveira et al., 2023) and asymptomatic individuals (Mailloux et al., 2021), typically recommending two to three measurements at each site.

3.3.6 Electromyography

Surface HDsEMG signals were recorded in monopolar derivation with four 2D grids of 13 × 5 equally spaced electrodes (diameter: 1mm, inter-electrode distance: 8mm; GR08MM1305, OT Bioelettronica, Italy) with one electrode absent from the upper left corner. Before electrode placement, all HDsEMG electrodes were prepared by attaching a double-sided adhesive foam to the electrode surface (FOA08MM1305, OT Bioelettronica, Italy). Then, the electrodes and participants' skin were prepared before electrode placement, as described earlier in ***Chapter 2*, Section 2.3.5**. To measure activity of the thoracolumbar ES, two HDsEMG grids were placed unilaterally one on top of each other, as shown in **Figure 3.1A** (Arvanitidis et al.,

2021a, Falla et al., 2014, Sanderson et al., 2019a, Varrecchia et al., 2021). The other two HDsEMG grids were placed on the same side, one over the RA (Arvanitidis et al., 2021a) and one over the EO (Boccia and Rainoldi, 2014) (**Figure 3.1B**). Reference electrodes (WhiteSensor WS, Ambu A/S, Ballerup, Denmark) were also mounted over the participants' sacrum, ASIS, and wrist.

Torque and HDsEMG signals were sampled at 2048Hz and converted to digital data by a 16-bit analogue to digital converter (Quattrocento, 400-channel EMG amplifier, OT Bioelettronica, Torino, Italy, gain: 150, bandwidth 10-500Hz, first order, 3dB). All recordings were performed by using the OTBiolab+ software.

3.3.7 Isokinetic dynamometry

The same isokinetic dynamometer (***Chapter 2*, Section 2.3.6**) were used to evaluate the torque exerted by the participants during the isometric, concentric and eccentric trunk flexion and extension MVCs, as well as during the concentric and eccentric submaximal torque steadiness tasks. To focus the contractions on the lumbar region, participants were seated on the Biodex Dual Position Back Extension/Flexion Attachment and their upper trunk, thighs and pelvis were strapped to minimise compensatory movements during the contractions as described in ***Chapter 2*, Section 2.3.6** (Arvanitidis et al., 2021a, Arvanitidis et al., 2022). The positioning of the participant is depicted in **Figure 3.1C**.

The isometric flexion and extension MVCs were only performed to allow HDsEMG signal normalisation during the dynamic contractions and enable comparisons between the eccentric and concentric contractions. For the isometric contractions, the isokinetic device was locked with a hip-to-trunk angle of 90^{o}. All dynamic contractions (concentric and eccentric) were tested in isokinetic mode. The total ROM for the flexion concentric/eccentric and

extension concentric/eccentric contractions was 50º (20º of extension to 30º of flexion) to isolate lumbar motion and minimise compensatory movements from the lower extremities (Arvanitidis et al., 2021a). The angular velocity was set at 5º/s. The contraction mode towards the other direction, i.e., for the person to return to the starting position, was always concentric, and the angular velocity was set at 90º/s. However, the participant's return to the starting position was performed passively by the researcher, who moved the chair back to the starting point during each repetition.

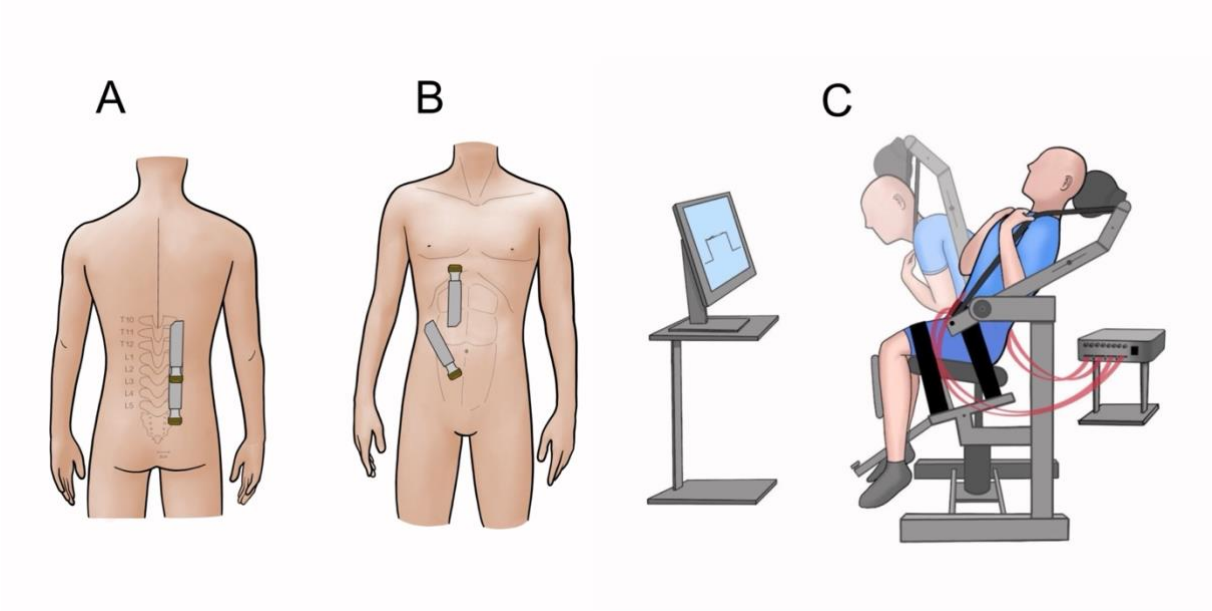


Figure 3.1: **Representation of the HDsEMG electrode placement over participants' thoracolumbar ES, starting 2 cm lateral to the spinous process of the 5th lumbar vertebra and extending up to approximately the 10th thoracic vertebra (asymptomatic controls: right side, CLBP group: most painful side) (A), RA and EO muscles (B). The HDsEMG electrode over the RA was placed as follows: the middle electrode of the medial 1st column of the HDsEMG grid was placed 3 cm lateral to the umbilicus and halfway between the xiphoid process-umbilicus distance parallel to the muscle fibres. For the EO muscle, the middle part of the HDsEMG electrode was placed 14 cm from the median line, lower than 1 cm above the umbilicus, parallel to the line extending from the most inferior point of the costal margin to the opposite pubic tubercle. Representation of the testing setup. An individual seated on the Biodex chair, with the electrodes attached to him and connected to the amplifier. The individuals were able to perform trunk flexion and extension movements through a total range of trunk motion of 50º. At the same time, visual feedback on his trunk muscle torque is provided via a computer monitor located 1.5 m in front of him (C).**

3.3.8 Task

The participants were given some time to familiarise themselves with the dynamometer, practice all contractions and warm up their trunk flexor/extensor muscles. This consisted of sustained and dynamic submaximal contractions. After a brief rest, the participants were asked to perform two isometric MVCs of trunk flexion and two isometric MVCs of trunk extension, respectively (randomized order), with 1 min rest between repetitions. For the isometric MVCs, the isometric mode was used, and the ROM of the isokinetic device was locked at 90^{o} (50^{o} according to the attachment's goniometer) for all participants. After completing the isometric MVCs, the participants rested for 5 mins. Participants were then asked to perform two concentric MVCs of trunk flexion and two of trunk extension (randomized order), moving through a ROM of 50^{o}. For the concentric trunk flexion MVC, the starting position was 20^{o} of trunk extension; for the concentric trunk extension MVC, the starting position was the 30^{o} of trunk flexion. Participants rested for 1 min between repetitions. After performing the concentric MVC in one direction (e.g., trunk flexion), the participants rested for 5 minutes. Then after a few familiarisation trials, they were instructed to perform submaximal trunk contractions towards the same direction, four times at 25% and three times at 50%MVC in a randomized order. During these contractions, participants were instructed to match a line at a target torque of 25%MVC and 50%MVC, respectively, and maintain the contraction for 10s. The highest instantaneous torque recorded during any MVC was used as a reference to define the submaximal torque levels. The participants were then asked to perform the same concentric contraction towards the other direction (i.e., two MVCs, and four and three submaximal contractions at 25% and 50 %MVC, respectively). After completing all concentric muscle actions, participants rested for 5 minutes. Then the same procedures were repeated for the eccentric flexion and extension trunk contractions. **Figure 3.2** schematically depicts the study

procedures. For the eccentric trunk extension contractions, the starting point was 20º of trunk extension, and for the eccentric trunk flexion contractions, it was 30º of trunk flexion.

During all submaximal contractions, real-time visual feedback of trunk extensor and flexor torque output to the dynamometer and a line indicating the target level of contraction (%MVC) was provided on a computer monitor located 1.5 m in front of them (**Figure 3.1C**). The real-time torque output was superimposed on the template for visual feedback. The participants were asked to rapidly match the %MVC target as precisely as possible. Once the requested target level was achieved (i.e., either 25 or 50%MVC), they were asked to try and maintain their torque as steady as possible for the entire task duration. In other words, they were asked to exert the same 25 or 50%MVC torque output throughout the total 50º ROM.

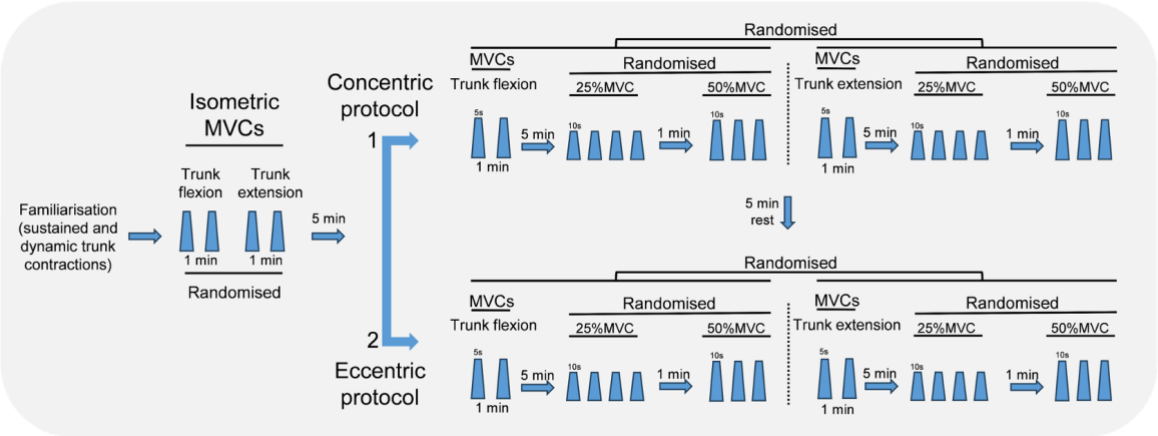


Figure 3.2: **Schematic illustration on the overall study procedure. MVCs: Maximal voluntary contractions.**

3.3.9 Analysis of the torque signal

The highest peak torque during the two MVC trials was used to measure each individual's maximal trunk extension/flexion eccentric, isometric and concentric strength. All absolute peak torque values were then normalised to each individual's body mass ($N \cdot m \cdot kg^{-1}$). Torque steadiness was quantified with the absolute and the normalised amplitude of the torque

fluctuations using the SD and the CoV of the torque signal over time, respectively (Enoka and Farina, 2021). Using a custom-made MATLAB script, the SD and CoV of torque were computed in the same time range used for the HDsEMG analysis during the two torque levels (i.e., the steady part of the contraction). SD and CoV were computed for each repetition separately and then averaged to generate one value for each torque level.

3.3.10 EMG amplitude and topographical map computations

The 64-monopolar HDsEMG channels of each of the electrodes placed over the RA and EO muscles and the 128-monopolar HDsEMG channels of the merged electrodes placed over the thoracolumbar ES were processed offline to form 59 and 124 bipolar derivations, respectively (Arvanitidis et al., 2021a, Arvanitidis et al., 2022, Falla et al., 2014, Martinez-Valdes et al., 2019, van Helden et al., 2022). Before any RMS amplitude calculations took place, the signals were filtered (bandpass zero lag Butterworth: 10-350Hz, 2nd order) and visually inspected to remove any channels with low signal-to-noise ratios (due to electrical interference and/or artefacts). The removal rate was < 15%. The RMS values were calculated for each of the 59 bipolar recordings, for each of the abdominal muscles (i.e., EO and RA), and for each of the trunk flexion tasks. Similarly, RMS values were also calculated for each of the 124 bipolar recordings for the thoracolumbar ES muscle and for each trunk extension task. Calculating an RMS value for each bipolar channel enabled us to generate a topographical map of surface EMG amplitude for each muscle, compute the x-, y- axes coordinates of the centroid of the surface EMG amplitude map during all contractions. This allows changes in the regional activation within a muscle to be examined. Additionally, the RMS values of all bipolar channels were averaged for each muscle to form one value which represented a global measure of

myoelectric activity (HDsEMG amplitude; RMSmean). These calculations were performed for each muscle when it was acting as an agonist.

Co-activation between the trunk flexors and extensors was also quantified during all types of contractions and torque levels. The level of co-activation was calculated based on the normalised RMS_{mean} values, as follows: antagonist muscle activity/agonist muscle activity × 100. For this calculation, the RMS_{mean} values of the abdominal muscles were summed (i.e., RMS_{mean} RA + RMS_{mean} EO). To normalise the surface EMG signals and express them as a percentage of each muscle's RMS value calculated during the maximal (baseline) MVC, the RMS max value was extracted from the isometric MVC signal for each muscle separately using a window of approximately 1s around the peak of the highest isometric MVC (using a non-overlapping sliding averaging 0.25s window). Then the average of the produced values was used as the maximum RMS_{max} value for each muscle. A custom script was developed, and all HDsEMG and torque signals were analysed offline using MATLAB 2020b (The MathWorks Inc., USA). The analysis generated one value for each variable, for each repetition (i.e., four and three values for the 25% and 50%MVC torque levels, respectively). These values were then averaged to generate one value for each variable per torque level.

3.3.11 Pre-processing of HDsEMG data - PCA

To reduce the dimensionality of the HDsEMG data, the acceptable percentage of the total variance was set to 85% (Arvanitidis et al., 2022, Naik et al., 2016). This allowed us to remove a few PCs and resulted in the original dataset having less dimensions (i.e., < 59 and < 128 dimensions, respectively). For additional information about the PCA approach, the reader is referred to ***Chapter Two*, Section 2.3.9** (Arvanitidis et al., 2022).

Before the cross-correlation and coherence computations, the previously offline re-referenced 59 (from the RA and EO muscles, respectively) and the 124 (from the merged electrodes over ES) bipolar HDsEMG channels were processed for PCA calculation with the same steps described in ***Chapter Two*****, Section 2.3.9**. This pre-processing was performed for the thoracolumbar ES, only during the extension movement and for each abdominal muscle, only during the flexion movement (concentric and eccentric).

The Final Signal Envelope that was extracted from the HDsEMG grid by applying PCA contained the relevant force-related information (i.e., low-frequency component). Coherence and cross-correlation analyses were then applied to quantify the similarity of the Final EMG Signal Envelope and the torque signals. This analysis was performed for all submaximal contractions, and the similarity was assessed for each repetition separately and then averaged to produce one value of coherence and cross-correlation, respectively.

3.3.12 Cross-correlation and coherence analyses

Cross-correlation and coherence analysis were used to quantify the similarity of the Final Signal Envelope (i.e., the low pass filtered Averaged PCA-selected signal stemming from the first PCs that explained 85% of the variance) and torque signals for each submaximal contraction. The same exact approach was used for both cross-correlation and coherence analysis methods as in ***Chapter Two*****, Section 2.3.10** and **2.3.11**, while additional information on these methods is provided in ***Chapter Two*****, Sections 1.10.2** and **1.10.3**.

Topographical maps of coherence were also generated as done previously to explore the regional association between torque and EMG in the δ band (0-5Hz) (Arvanitidis et al., 2022) (***Chapter Two*****, Section 2.3.11**). In these maps, the 59 (for RA and EO) or the 124 (for ES) bipolar recordings were correlated with the filtered torque signal in time to provide one

coherence value (δ band). Then all the values were normalised to the maximum coherence value observed at each torque level respectively. The centroid of coherence was also computed, providing an estimate of the centroid of coherence along the medial-lateral (x-axis) and cranial-caudal (y-axis) directions. This information allowed us to investigate whether specific muscle regions have a greater impact on the generated torque when compared to others through statistical comparisons of the x- and y-axis centroid values across the two groups. All calculations were performed for each repetition/contraction and then averaged to generate one value.

3.3.13 Statistical analysis

The Shapiro-Wilk test was used to determine the normality of the data, and the Levene test was used to evaluate the assumption of homogeneity of variance. As these assumptions were met, parametric statistical tests were deemed appropriate. Descriptive results are reported as means and SDs. The anthropometric measurements, scores related to pain intensity, questionnaire scores, PPT values, and trunk extension/flexion MVCs (measured during isometric/concentric/eccentric contractions) were compared between groups using independent t-tests. To assess pre-, and post-contraction between-group differences in pain intensity, a two-way mixed repeated measures ANOVA was applied, using group (CLBP, control) and time (pre, post) as between- and within-subject factors, respectively. The relationship between the outcome variables (self-reported measures and EMG data) was also assessed using Pearson's *r*. These analyses were performed in SPSS Statistics, version 27 (IBM, USA).

All statistical analyses for the HDsEMG and torque data were performed using R (version 4.2.1, R Development Core Team, 2023). A generalised linear mixed-effects model (GLMM) analysis was performed through the R package lme4 (version 1.1.31). GLMM was

deemed particularly suitable for this study because i) of the complexity of the experimental design, ii) it avoids the assumption of conditional independence in observations, and iii) it accounts for unbalanced datasets and handles sporadic missing data (Boccia et al., 2019). The GLMM analysis was performed separately for each movement direction due to the differences in the number of muscles assessed (i.e., one model was used for extension and one for flexion). The following model was used for flexion *"variable of interest ~ condition * contraction * muscle * force * (1| subject)"*. The same model was also used for extension, but *"muscle"* was excluded from the fixed factors since only ES was assessed during extension. This model is read as a *"variable of interest predicted by each of the factors"*. The variable of interest (on the left) is the dependent variable. The ones on the right (except the subject) are the independent (explanatory) variables, or *"fixed effects"*, condition (CLBP, control), contraction (eccentric, concentric, muscle (RA, EO) and force (25%, 50%MVC). The 1|subject in both models is the *"random effect"*, which characterises the variation that is due to individual differences. Considering that this was a repeated measures design, and we had multiple observations for the same individual that could not be regarded as independent from each other (due to individual variations in physiology), the random effect was added to resolve this non-independence in the dataset.

Similar to others (Boccia et al., 2019), the normality of residuals was assessed using the Shapiro-Wilk test after running the model. Residual outliers were removed using Cook's distance method (considering as threshold, a distance of 4 times the SD) when the normality assumption was not met. Post-hoc pairwise comparisons were conducted using Tukey correction and least-squares contrasts, as implemented in the R package *emmeans* (version 1.8.8). The post hoc tests were evaluated based on the interactions identified on the continuous

dependent variables. Post hoc results are reported as mean difference estimates (MD) and 95% CIs. Statistical significance for all statistical analyses was set at $P < 0.05$.

3.4 Results

3.4.1 Participants

All 40 participants (20 CLBP, 20 asymptomatic controls) completed the study. Their characteristics are reported in **Table 3.1**. No differences in demographic characteristics were observed between the two groups. The individuals with CLBP presented with higher levels of disability, kinesiophobia and lower general health, physical functioning, emotional wellbeing, and RAND-36 pain scores compared to the control group. The individuals with CLBP reported a current level of pain intensity of 3.8 (1.6), which is characterized as moderate pain (Breivik et al., 2008). Additionally, greater sensitivity over the lumbar region was observed in this group, as revealed by the lower average PPT values. Neither group experienced an increase in pain intensity after performing all contractions (condition × time interaction: F=0.193, P=0.663). Both groups exerted similar peak torques for all types of contractions.

Table 3.1: **Characteristics of all participants separated by group.**

Characteristic	Controls (20)	CLBP (20)	P-value
Sex (%males)	50	50	–
Age (years)	28.6 (3.9)	31.1 (6.9)	0.198
Height (cm)	171.9 (7.4)	170.6 (9.9)	0.661
Weight (kg)	70.6 (13.4)	75.3 (18.4)	0.374
BMI	23.9 (4.2)	25.5 (4.2)	0.233
Pain Intensity (NPRS) at the beginning of the session*	0.0 (0.0) [0.0 – 0.0]	3.8 (1.6) [1.0 – 6.0]	< 0.001
Average Pain Intensity in the last 24h (VAS) before the session*	0.0 (0.0) [0.0 – 0.0]	44.5 (20.0) [10.0 – 77.0]	< 0.001

Average Pain Intensity (NPRS) over the previous week*	0.0 (0.0) [0.0 – 0.0]	5.0 (1.6) [1.0 – 7.0]	< 0.001
Duration of symptoms (months)*	0.0 (0.0) [0.0 – 0.0]	110.5 (87.1) [3.0 – 294.0]	<0.001
PPTs (average of 10 points; kPa)*	397.8 (95.0) [198.7 – 546.4]	328.7 (119.2) [86.6 – 484.7]	0.024
ODI (%)*	0.0 (0.0) [0.0 – 0.0]	21.5 (13.4) [6.0 – 69.0]	< 0.001
RAND 36-General health*	81.5 (9.8) [65.0 – 100.0]	58.0 (19.2) [25.0 – 85.0]	< 0.001
RAND 36-Physical functioning*	98.0 (5.6) [75.0 – 100.0]	77.8 (15.4) [50.0 – 100.0]	< 0.001
RAND 36-Emotional wellbeing*	80.80 (14.1) [40.0 – 92.0]	61.0 (16.0) [28.0 – 88.0]	< 0.001
RAND 36-Pain*	91.63 (14.4) [35.0 – 100.0]	56.6 (15.2) [12.5 – 80.0]	< 0.001
TSK*	24.8 (4.4) [17.0 – 35.0]	36.6 (7.4) [25.0 – 52.0]	<0.001
Eccentric trunk extension MVC ($N \cdot m \cdot kg^{-1}$)	2.9 (0.7)	2.7 (0.7)	0.376
Concentric trunk extension MVC ($N \cdot m \cdot kg^{-1}$)	3.0 (0.7)	2.7 (0.8)	0.219
Eccentric trunk flexion MVC ($N \cdot m \cdot kg^{-1}$)	1.8 (0.3)	1.7 (0.4)	0.736
Concentric trunk flexion MVC ($N \cdot m \cdot kg^{-1}$)	1.9 (0.4)	1.7 (0.4)	0.114
Pain Intensity (NPRS) at the end of the session*	0.6 (0.8) [0.0 – 3.0]	4.6 (1.7) [0.0 – 7.0]	< 0.001

Data are presented as mean ± SD. For the clinical questionnaires, the range is also displayed as [minimum - maximum].
*Asterisks represent significant differences between groups.

3.4.2 Trunk extension

Torque. Overall, a significantly higher CoV and SD of torque was observed for the individuals with CLBP (condition effect, MD=2.05%, 95% CI [1.39, 2.70], F=40.01; MD=0.60%, 95% CI [0.36, 0.84], F=25.31, respectively, P<0.0001 for both). Importantly, as indicated by the condition × contraction × torque interaction for the CoV of torque variable (F=4.2, P=0.043), the torque steadiness performance of the CLBP group was worse compared to the asymptomatic control group during both the eccentric and concentric contractions, and

at both low and high torque levels (eccentric low: MD=3.09%, 95% CI [1.70, 4.50]; eccentric high: MD=1.35%, 95% CI [0.06, 2.63]; concentric low: MD=2.10%, 95% CI [0.82, 3.39]; concentric high: MD: 1.64%, 95% CI [0.39, 2.91]). The results are depicted in **Figure 3.3A, B, C and D**.

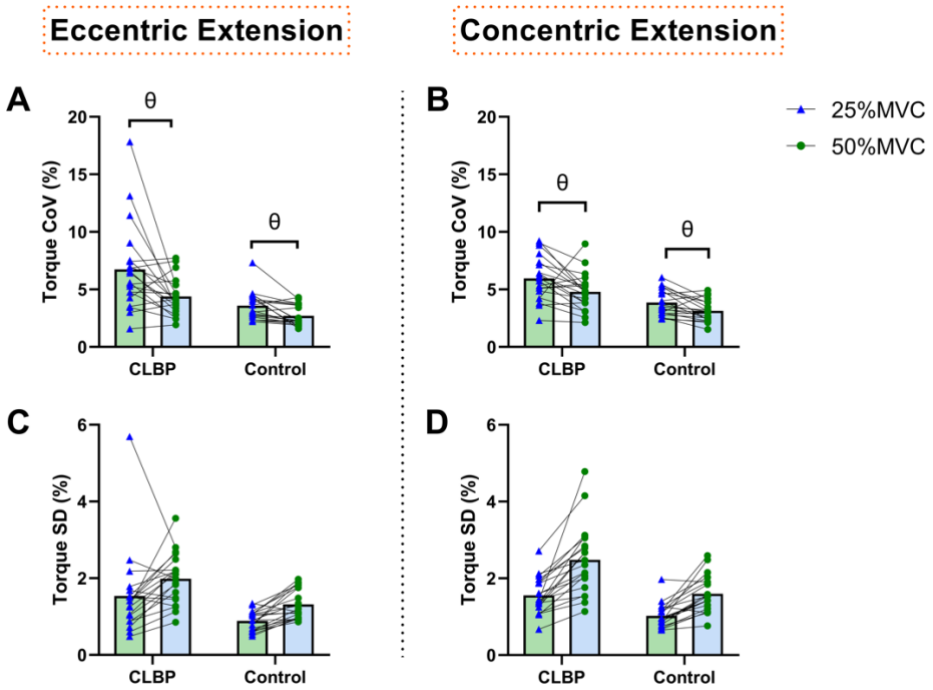


Figure 3.3: **Torque CoV and SD during eccentric contraction (A, C), and concentric (B, D), contractions at 25% and 50%MVC for the CLBP and the asymptomatic controls (mean and individual values). Individuals with CLBP had poorer torque steadiness during both contraction types and torque levels compared to the controls. The condition × contraction × torque interaction (torque CoV variable) revealed significant differences in post hoc comparisons, θ: for eccentric contractions, P-values were <0.0001 (low forces) and 0.0324 (high forces); for concentric contractions, P-values were 0.0001 (low forces) and 0.0028 (high forces).**

Electromyographic activity. Overall, the normalised ES HDsEMG amplitude did not differ between the two groups (condition effect: F=3.62, P=0.064). As expected, a contraction effect was observed (F=5.62, P=0.019), suggesting that overall, ES activity was higher during the concentric muscle contractions, compared to eccentric (MD=3.12%, 95% CI [0.51, 5.74]).

No regional differences in ES muscle activation were observed between the two groups along the y-axis (condition effect: F=2.88, P=0.098) or x-axis (condition effect: F=0.0009, P=0.098). Both groups presented similar RA, EO and ES co-activation levels across contractions and torque levels (condition effect: F=0.02, P=0.887).

Measures of EMG-torque cross-correlation. Overall, the magnitude of coherence in the δ band was similar between the two groups (condition effect: F=0.058, P=0.810). However, the centroid of δ band coherence along the y-axis differed significantly between the two groups, with higher coherence being observed in the more cranial region of the ES for the CLBP group (condition effect: F=4.20, P=0.047, MD= -2.43 mm, 95% CI [-4.83, -0.03]). A condition × torque interaction was also observed for this variable (F=4.51, P=0.036), suggesting that this difference in the centroid of δ band coherence that was more cranially located in the CLBP group, was more pronounced during the 25%MVC (low) level of contraction (MD=-3.40 mm, 95% CI [-6.76, -0.03]. Additionally, a condition × contraction interaction was also observed, showing that (i) the centroid of δ band coherence along the y-axis in the asymptomatic controls was more caudally located compared to the CLBP group during both eccentric and concentric muscle actions and (ii) the centroid of δ band coherence along the y-axis was located in a more cranial region of the ES during the eccentric contraction compared to the concentric contraction in the asymptomatic controls, while for the CLBP group, the centroid of δ band coherence did not differ between the two types of contractions (F=5.56, P=0.020, MD=-3.50 mm, 95% CI [91.8, 96.5]; MD=2.30 mm, 95% CI [0.67, 3.92], respectively). The results are depicted in **Figure 3.4A, B and C**.

Overall, the cross-correlation was higher for the CLBP group (condition effect: F=10.32, P=0.002, MD=0.04, 95% CI [0.02, 0.07]). These differences in cross-correlation are

largely dominated by an increased cross-correlation during the eccentric contractions, observed for the CLBP group (**Figure 3.4D and E**).

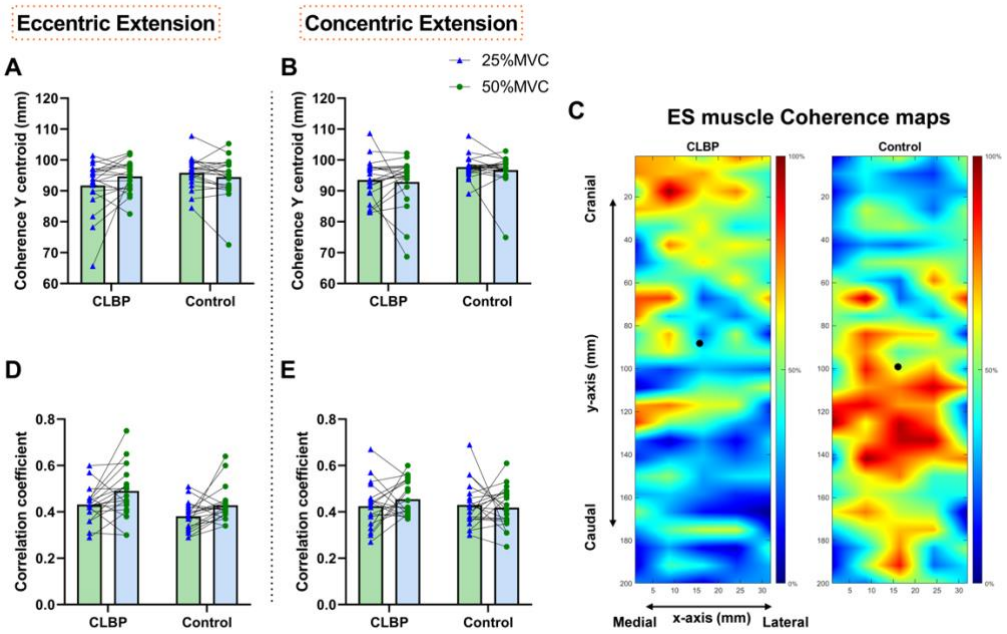


Figure 3.4: **Y-axis centroid of δ band coherence during the eccentric (A) and concentric (B) trunk extension contractions, magnitude of EMG-torque cross-correlation during the eccentric (D) and concentric (E) trunk extension contraction at 25% and 50%MVC for the CLBP group and the asymptomatic controls (mean and individual values) in thoracolumbar ES muscle. Figure C shows representative topographical thoracolumbar ES coherence maps for a CLBP individual and an asymptomatic person during concentric contraction at 25%MVC. Black dot in (C) indicates the centroid of coherence, with spine towards the medial side of the x-axis. Red represents higher coherence, blue represents lower coherence, and maps are normalised to the maximum coherence values. Results suggest that overall, the centroid of δ band coherence (y-axis) in thoracolumbar ES was more cranial in the CLBP group compared to the asymptomatic controls (condition effect), with a condition × torque interaction showing between-group differences only at 25%MVC (post hoc, P=0.047). This is also depicted in Figure C. Asymptomatic controls had more caudally located centroid of δ band coherence during the concentric contractions compared to this of the CLBP group during both eccentric and concentric muscle actions (condition × contraction interaction; post hoc, P=0.0283 and P=0.04, respectively). In asymptomatic controls, the centroid of δ band coherence (y-axis) was more cranially located during the eccentric contractions compared to the concentric ones, CLBP group centroids of δ band coherence did not differ between contraction types (post hoc, P=0.0022 and P=0.9952, respectively). Lastly, EMG-torque cross-correlation was higher overall in the CLBP group (condition effect: P=0.002).**

3.4.3 Associations between outcome variables – trunk extension

The relationship between outcome variables that differed significantly between the two groups was assessed only in the CLBP group, and the associations are reported for the extension movement below.

Torque. The CoV of torque during the eccentric extension contractions at low forces was significantly correlated with the duration of symptoms (r=0.464, P=0.039). The SD of torque was negatively correlated with the centroid of δ band coherence, suggesting that a more caudally located centroid of δ band coherence was associated with better torque steadiness performance (r=-0.460, P=0.041). Both the CoV and SD of torque during the eccentric contractions at 25%MVC were positively correlated with both the HDsEMG-torque cross-correlation, suggesting that a higher HDsEMG-torque cross-correlation was associated with worse torque steadiness in the CLBP group (r=0.645, P=0.002; r=0.601, P=0.005, respectively).

Coherence. The position of the centroid of δ band coherence along the y-axis during the concentric extension contractions was negatively correlated with the duration of symptoms (r= -0.445, P=0.049) at low forces. During the concentric extension contractions at high forces, this variable was also positively correlated with the pain intensity level after the contractions (r=0.611, P=0.004). Pooling these values for the two torque levels (average of 25% and 50%MVC y-axis centroid δ band coherence) revealed a significant correlation between the pooled variable, ODI and the level of pain intensity after performing the concentric contractions (r=0.490, P=0.028; r=0.488, P=0.029, respectively).

3.4.4 Trunk flexion

Torque. Individuals with CLBP demonstrated a significantly higher CoV and SD of torque in comparison to the asymptomatic controls (condition effect, F=41.11, MD=3.36%, 95% CI [2.30, 4.42]; F=53.31, MD=1.31%, 95% CI [0.95, 1.67], respectively, P<0.0001 for both). Additionally, a condition × contraction × torque interaction was observed for the SD of torque, indicating that people with CLBP had worse control during both eccentric and concentric contractions at both 25% and 50%MVC torque levels compared to the asymptomatic controls (F=14.83, P<0.0001; eccentric low: MD=0.94%, 95% CI [0.20, 1.68]; eccentric high: MD=0.85%, 95% CI [0.13,1.57]; concentric low: MD=1.08%, 95% CI [0.38,1.79], concentric high: MD=2.37%, 95% CI [1.60, 3.15]). Importantly, this interaction also revealed that at higher forces, people with CLBP had worse trunk control (SD of torque) during the concentric contractions compared to the eccentric ones (MD=-1.70%, 95% CI [-2.33, -1.08]). On the other hand, the asymptomatic controls had similar torque steadiness performance across contractions and torque levels. The results are depicted in **Figure 3.5A, B, C and D**.

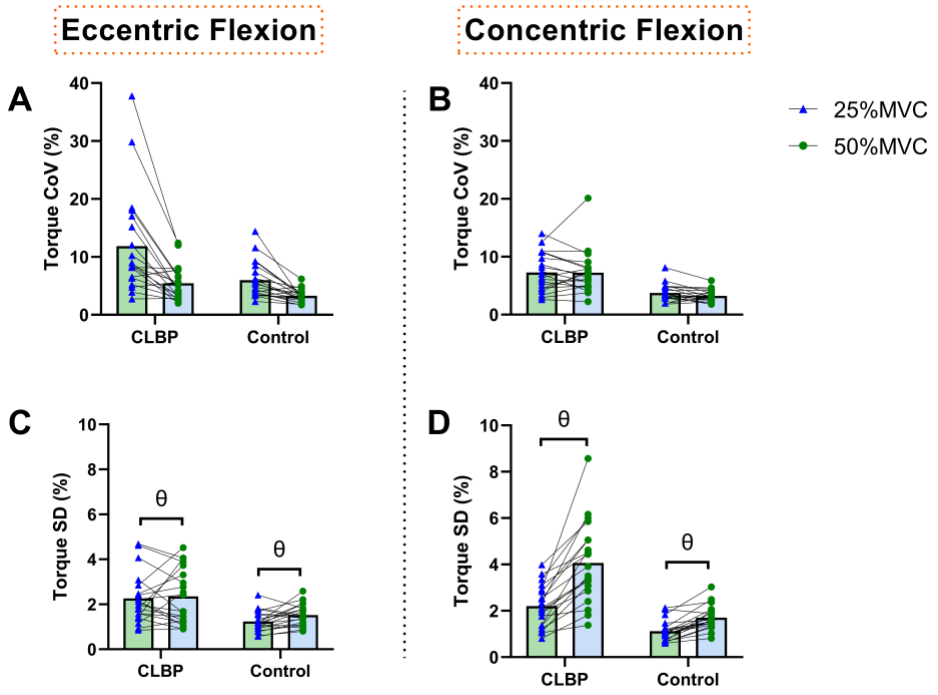


Figure 3.5: **Torque CoV and SD during eccentric (A, C) and concentric (B, D) contractions at 25% and 50%MVC for the CLBP group and the asymptomatic controls (mean and individual values). Results show that the CLBP group had overall worse torque steadiness (higher CoV and SD; condition effect). People with CLBP had poorer torque steadiness (SD of torque) during both contraction types and torque levels compared to controls. The condition × contraction × torque interaction for this variable revealed significant differences in post hoc comparisons, θ: for eccentric contractions, p-values were P=0.0039 (low forces) and P=0.0095 (high forces); for concentric contractions, p-values were P=0.0002 (low forces) and P<0.0001 (high forces). The CLBP group exhibited worse torque steadiness at high forces during concentric compared to eccentric contractions, with no differences observed in the controls (P<0.0001).**

Electromyographic activity. Overall, the individuals with CLBP performed the contractions with higher activation of their abdominal muscles (normalised RMS_{mean}; condition effect: F= 7.81, P=0.009, MD=12.7%, 95% CI [3.48, 21.9]. A condition × muscle interaction was also observed, suggesting that overall, people with CLBP performed the contractions by activating their EO muscle to a greater extent than the asymptomatic controls (F=9.34, P=0.002, MD=16.31%, 95% CI [3.73, 28.90]). In terms of the topographical surface EMG amplitude differences, overall, the centre of abdominal muscle activity along the y-axis was located in

more cranial regions of the EO and RA muscles in the CLBP group, compared to the asymptomatic controls (condition effect: F=9.90, P=0.003, MD=-2.27 mm, 95% CI [-3.74, -0.81]). In addition, a condition × muscle interaction revealed a regional difference in EO muscle activation between the two groups, with this of the CLBP group being more cranially located along the y-axis (F=12.44, P<0.0001, MD=-3.56 mm, 95% CI [-5.75, -1.44]). No regional differences in abdominal muscle activation were observed between the two groups along the x-axis (condition effect: F=1.09, P=0.303). The level of co-activation during the contractions was similar between the two groups (condition effect: F=0.47, P=0.498). The EO RMS amplitude and y-axis centroid results are depicted in **Figure 3.6A, B, C and D**.

Measures of EMG-torque cross-correlation. A condition × contraction interaction was observed for the magnitude of δ band coherence, showing that overall δ band coherence during the concentric contractions was lower in the CLBP group compared to the eccentric contractions (F=5.71, P=0.018, MD=-0.07, 95% CI [-0.14, -0.01]). In terms of differences in the topographical representation of δ band coherence, a condition × muscle interaction was observed (F=4.98, P=0.027). This revealed that the centroid of δ band coherence along the y-axis differed significantly between the EO and RA muscles in the asymptomatic control group only and was located more cranially for the RA muscle (MD=1.14 mm, 95% CI [0.34, 1.94]).

A condition × muscle × torque interaction was observed for the magnitude of HDsEMG-torque cross-correlation, indicating that at low forces, the contribution of the EO muscle to the resultant torque was higher compared to the contribution of the RA muscle in the control group (F=6.95, P=0.009, MD=0.03, 95% CI [0.00, 0.06]). A condition × contraction × torque interaction was also observed, showing that in people with CLBP, (i) at high forces, abdominal muscle HDsEMG-torque cross-correlation was higher during concentric contractions compared to the eccentric ones and (ii) that the contribution of the abdominal muscles increased with the

increase in force during the concentric contractions (F=4.09, P=0.044, MD=0.05, 95% CI [0.03, 0.08]; MD=0.036, 95% CI [0.01, 0.08], respectively). This increase in cross-correlation in the CLBP group might be mainly related to an increase of cross-correlation in EO muscle only during the concentric contractions, as revealed by the condition × contraction × muscle × torque interaction (F=5.80, P=0.017, MD=0.065, 95% CI [0.02, 0.11]). Another interesting finding revealed by this interaction was that at high forces, the contribution of EO muscle to the resultant torque in the CLBP group was higher during the concentric contractions (MD=0.068, 95% CI [0.02,0.11]). The cross-correlation results for the EO muscle are depicted in **Figure 3.6F and G**.

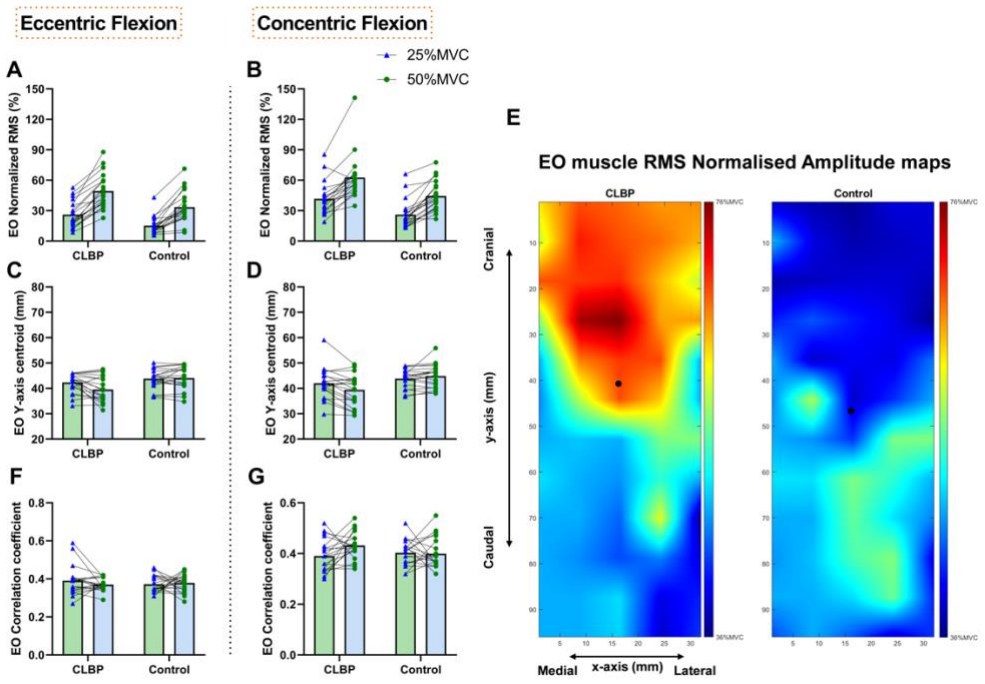


Figure 3.6: **EO RMS normalised amplitude, EO RMS amplitude y-centroid, and cross-correlation EO values during eccentric (A, C, F) and concentric (B, D, G) contractions at 25% and 50% MVC for CLBP group and asymptomatic controls (mean and individual values). Figure E shows representative EO RMS normalised amplitude topographical maps at 25% MVC for one CLBP and one control individual. Black dot: centroid of EO muscle activation. Red colours: higher EO muscle RMS amplitude; blue colours: lower EO muscle RMS amplitude. Overall, individuals with CLBP had higher abdominal muscle activation and greater EO muscle activation compared to controls (condition**

effect; condition × muscle interaction; post hoc, P=0.0066). The centre of abdominal muscle activity was more cranially located in CLBP group, particularly for EO muscle compared to the asymptomatic controls (condition effect; condition × muscle interaction; post hoc, P=0.0003).The centre of abdominal muscle activation in the CLBP group at 50%MVC was more cranially located from that of the asymptomatic controls at both low and high forces (condition × torque interaction; post hoc, P=0.0014 and P=0.0007). CLBP individuals shifted the centre of abdominal muscle activation to more cranial regions at 50%MVC (condition × torque interaction; post hoc, P=0.0015). The between-group difference in magnitude and regional activation of the EO muscle is evident in Figure E, showing a CLBP individual and an asymptomatic control during a concentric contraction at 50% MVC. At low forces, the contribution of the EO muscle to the resultant torque was higher compared to the contribution of the RA muscle in the control group (i.e., the magnitude of HDsEMG-torque cross-correlation was higher for the EO muscle) (condition × muscle × torque interaction; post hoc, P=0.0484). In people with CLBP at high forces, abdominal muscle HDsEMG-torque cross-correlation was higher during concentric compared to eccentric contractions, and cross-correlation increased with the increase in force during the concentric contractions (condition × contraction × torque interaction; post hoc, P<0.0001 and P=0.0081). This increase in cross-correlation in the CLBP group might may be mainly attributed to an increase of cross-correlation in EO muscle only during the concentric contractions (condition × contraction × muscle × torque interaction; post hoc, P=0.0008). At high forces, the contribution of EO muscle to the resultant torque in the CLBP group was higher during concentric than eccentric contractions (condition × contraction × muscle × torque interaction; post hoc, P=0.0001).

3.4.5 Associations between outcome variables – trunk flexion

The relationship between the outcome variables that the two groups differed significantly was assessed only in the CLBP group, and the associations are reported for the flexion movement below.

Electromyographic activity. The HDsEMG amplitude of the EO muscle during the concentric contractions at high forces was correlated with the duration of symptoms (r=0.464, P=0.039).

Cross-correlation. The magnitude of cross-correlation of the EO muscle during concentric contractions at high forces was correlated with the CoV and SD of torque (r=0.575, P=0.008; r=0.573, P=0.008, respectively), suggesting that there was an association with the

higher amount of contribution of this muscle and the worse steadiness performance in the CLBP group.

3.5 Discussion

In this study, we aimed to i) quantify the relationship between HDsEMG oscillations and concentric/eccentric trunk extension/flexion torque oscillations in both time and frequency domains, employing cross-correlation and coherence analysis, respectively; and ii) assess and compare regional differences in surface EMG amplitude and HDsEMG-torque cross-correlation and coherence of the ES, RA, and EO muscles in individuals with CLBP and asymptomatic controls.

During trunk extension concentric and eccentric contractions, people with CLBP i) exhibited poorer trunk extensor muscle torque steadiness (CoV of torque) at both low and high forces, ii) had (overall) higher HDsEMG-torque coherence (δ band) in more cranial regions of the thoracolumbar ES, and iii) showed (overall) a higher thoracolumbar ES surface EMG-cross-correlation. These findings are in line with those reported in ***Chapter 2*** .

On the other hand, the CLBP group exhibited the following during trunk flexion contractions, i) poorer trunk flexor muscle control and higher activation of abdominal muscles, particularly of the EO muscle, ii) regional differences in abdominal muscle activation, with the centre of activation, particularly that of the EO muscle, being more cranial compared to the asymptomatic controls, iii) lower coherence in the δ band during concentric compared to eccentric contractions , and iv) a higher contribution of the abdominal muscles, especially of the EO muscle, to the resultant torque during concentric contractions (HDsEMG-torque cross-correlation).

3.5.1 Impaired torque steadiness in people with CLBP

Our findings align with previous studies (Arvanitidis et al., 2022, Pranata et al., 2017), which show that the control of trunk extensor muscle force is impaired in individuals with CLBP. In the current study, we expanded our understanding of impaired torque control in people with CLBP by assessing not only trunk extension but also trunk flexion, as well as dynamic concentric and eccentric contractions. We uniquely showed that individuals with CLBP exhibit poorer control of their trunk extensors during both concentric and eccentric contractions, at both low and high forces, compared to asymptomatic controls. As described previously (Arvanitidis et al., 2021b, Arvanitidis et al., 2022), the torque steadiness deficits observed in people with CLBP can be due to several possible reasons, including but not limited to i) functional and structural neuroplastic changes in the nervous system caused by pain (Brumagne et al., 2019), ii) reduced proprioceptive acuity, which can be attributed to suppressed proprioceptive input by nociceptive afference or altered afferent input from changes in passive and active structures (e.g., ligaments, IVDs and muscles) (Ager et al., 2020, Brumagne et al., 2019), iii) fatty infiltration of the lumbar paraspinal muscles (e.g., ES and multifidus) (Mengiardi et al., 2006, Parkkola et al., 1993), and iv) structural brain changes, such as reduced white matter integrity in the superior cerebellar peduncle (Pijnenburg et al., 2014), and reorganisation of motor cortex regions related to trunk muscle control, leading to a loss of discrete control of paraspinal muscle fascicles (Schabrun et al., 2017). These factors contribute to altered motor responses, which manifest as changes in recruitment strategies and movement patterns, as individuals with CLBP attempt to compensate for proprioceptive deficits and other neuroplastic changes. Additionally, other factors such as fear-avoidance beliefs may also have an influence on these altered motor responses observed in individuals with CLBP (Rainville et al., 2011). Interestingly, the CoV of torque during the eccentric extension contractions at low forces was moderately correlated with

the duration of symptoms (*r=0.464*), likely suggesting that people who experience CLBP for a longer period (more likely to have such structural alterations) (Hodges and Danneels, 2019) had worse torque steadiness performance.

Moreover, we also revealed for the first time that these individuals exhibit worse trunk flexor muscle control compared to asymptomatic controls, with the deficits likely being more pronounced during concentric contractions, as indicated by the increased SD of torque. This greater impairment in trunk flexor muscle control during concentric contractions compared to eccentric contractions in individuals with CLBP could be explained by, i) altered muscle activation, since concentric contractions rely more on motor unit recruitment and may require greater neural drive (e.g., higher discharge rate) (Duchateau and Baudry, 2014, Duchateau and Enoka, 2016), as well as increased energy expenditure (Herzog et al., 2016) (due to the inherent physiological disparities between concentric and eccentric contractions, including the contributions of passive components as the muscle lengthens), ii) the muscle force-velocity relationship, which inherently results in lower force production during concentric contractions compared to eccentric contractions (Herzog et al., 2016), and iii) proprioceptive deficits that might make it more challenging for people with CLBP to perceive and regulate muscle length changes during concentric contractions, considering that eccentric contractions generate more afferent input through muscle spindles due to the muscle stretch associated with the movement, leading to heightened spindle activity (Burke et al., 1978).

3.5.2 Differences in electromyographic activity

Both groups showed similar thoracolumbar ES activity (HDsEMG amplitude) and co-activation during trunk extension contractions, consistent with prior findings (Arvanitidis et al., 2022) implying that RMS amplitude was insufficient to explain the differences between the two

groups during the execution of the trunk extension contractions. However, coherence/cross-correlation analyses better demonstrated (at least) the trunk extensor muscles' contribution to the resultant torque, as described below.

CLBP individuals activated their abdominal muscles, particularly the EO muscle, more than controls to achieve equivalent force during concentric and eccentric trunk flexions. This implies a less efficient neuromuscular system. Indeed, the CLBP group demonstrated altered muscle recruitment patterns compared to controls, with abdominal muscle activity, particularly in EO and RA muscles, centred more cranially and shifting further cranially with an increase in force. These findings suggest that individuals with CLBP, are not activating their muscles to the same extent, and rather are relying on specific muscle fibres repeatedly. This uneven distribution of load across the muscle may lead to faster fatigue (Falla and Gallina, 2020, Falla et al., 2014), which could explain the worse torque steadiness performance observed in the CLBP group compared to the asymptomatic controls. Additionally, people with CLBP might require greater muscle activation to produce the same amount of force, leading to faster fatigue and likely to a reduced capacity to maintain steady torque output. Interestingly, a positive moderate correlation was observed between the HDsEMG amplitude of the EO muscle during the concentric contractions at high forces and the duration of symptoms ($r=0.464$). The degree of co-activation during flexion contractions was comparable between both groups, indicating compensation may stem from alterations in specific abdominal muscle regional activation and magnitude, rather than changes in overall co-activation patterns.

3.5.3 Measures of EMG-torque cross-correlation

We aimed to elucidate possible mechanisms underlying the greater deficits in trunk flexor/extensor muscle force control during concentric and eccentric contractions in individuals

with CLBP, by assessing i) the relationship between the low-frequency component (< 10Hz) of the neural drive to the muscle (effective neural drive) (Enoka and Farina, 2021) and torque fluctuations in both time and frequency domains (δ band, 0-5Hz), and ii) whether regional differences in HDsEMG-torque coherence also exist between people with CLBP and asymptomatic controls. The findings revealed that during trunk extension concentric and eccentric contractions, people with CLBP displayed higher HDsEMG-torque coherence (δ band) in more cranial regions of the thoracolumbar ES compared to asymptomatic controls. This aligns with our previous study suggesting that the similar neuromuscular strategy (i.e., higher coherence in more cranial region of the lumbar ES) was used by people with CLBP during an isometric lumbar extension torque steadiness task at 50%MVC. These findings provide new insights into the altered neuromuscular strategies employed by individuals with CLBP during concentric and eccentric trunk extension contractions, which could potentially contribute to their reduced torque steadiness performance. This is because common synaptic input is reflected by δ band coherence, and variations in the centroid location of δ band coherence indicate differences in common synaptic input distribution. This suggests that in individuals with CLBP, common synaptic input is likely more focalised and unevenly spread throughout the thoracolumbar ES. Common synaptic input, which refers to the shared neural drive from the CNS to motor neurons controlling specific muscles or muscle groups, is crucial for coordinating motor unit recruitment and firing patterns, ultimately affecting force production and torque steadiness (Farina and Negro, 2015). A more evenly distributed common synaptic input across motor units could potentially enhance torque steadiness. Nonetheless, it is important to validate these findings using HDsEMG-torque coherence derived from sEMG decomposition analysis, as the interference surface EMG signal can be affected by multiple factors (Farina et al., 2014a). Importantly, the more focused contribution of muscle fibers to the

resultant torque, predominantly located in the cranial region of the thoracolumbar ES, implies that these specific muscle fibers serve as the primary contributors to the torque during concentric/eccentric trunk extension. Notably, the position of the centroid of δ band coherence along the y-axis during the concentric extension contractions at low forces was negatively correlated with the duration of symptoms (*r=-0.445*). Additionally, during the concentric extension contractions, this variable was also positively correlated with the pain intensity level after performing the concentric contractions (*r=0.488*), suggesting that higher contribution to the torque from the more cranial regions of the thoracolumbar ES resulted to increased pain levels after the contractions. Lastly, during the eccentric contractions at high forces, the location of the centroid of the δ band coherence was negatively correlated with the SD of torque (*r=-0.460*), implying that a more caudally located centroid of δ band coherence was associated with better torque steadiness performance.

Another interesting observation was the overall higher thoracolumbar ES HDsEMG-torque cross-correlation in the CLBP group during trunk extension contractions. This may be due to the low-frequency component of rectified surface EMG, which is related to motor unit firing rate fluctuations and torque oscillations. As the CLBP group demonstrated increased torque variability compared to the controls, this may account for their elevated cross-correlation. A positive correlation between thoracolumbar ES HDsEMG-torque cross-correlation with CoV and SD of torque during eccentric contractions at low forces further supports this statement, suggesting that a higher cross-correlation was associated with torque steadiness performance in the CLBP group (*r=0.645* and *r=0.601*). Interestingly though, these differences were primarily driven by increased cross-correlation during the eccentric contractions in the CLBP group. This is unexpected since the control strategies employed by the nervous system during eccentric contractions typically involve less muscle

contribution/activation and greater passive muscle structure contribution (elastic energy storage) (Herzog et al., 2016). This could suggest a reduced contribution of the passive muscle elastic structural elements to the resultant torque in people with CLBP. However, this hypothesis needs to be confirmed by integrating sEMG and ultrasound imaging measures similarly to others (Martinez-Valdes et al., 2022).

During the trunk flexion contractions people with CLBP showed overall lower coherence in the δ band during concentric compared to eccentric contractions. This was unexpected since the contribution of the abdominal muscles should have been higher during the concentric than the eccentric contractions and suggests again that the neuromuscular control strategies employed by individuals with CLBP are altered between contraction types. Given that people with CLBP had more pronounced torque control deficits during concentric contractions, it also shows that this might be related to the lower coherence in the δ band which reflects less coordinated motor unit recruitment/firing and could contribute to less smooth and steady force output. Additionally, individuals with CLBP exhibited a greater involvement of the abdominal muscles, particularly the EO, in generating torque during concentric contractions at high forces compared to eccentric contractions. Moreover, the contribution of the abdominal muscles, mainly the EO, to the resultant torque during concentric contractions increased with the increase in force.

The disparity in torque steadiness performance between concentric and eccentric contractions in individuals with CLBP may be influenced by their perceived control during these movements. Eccentric contractions, which involve resisting an external force, could create a greater sense of control (heightened muscle spindle activity) (Burke et al., 1978) resulting in more efficient muscle activation patterns and improved torque steadiness. Conversely, concentric contractions involve the initiation of movement by the person, which

may generate a heightened sense of vulnerability, especially if they are experiencing pain or fear of movement related to injury, as in the current study [NPRS: 3.8 (1.6), TSK: 36.6 (7.4)]. This apprehension could result in overcontribution of the abdominal muscles during concentric contractions, as the individual attempts to protect their back from potential harm. However, this overactivation might inadvertently disrupt optimal motor control strategies, leading to worse torque steadiness performance during concentric contractions compared to eccentric contractions in people with CLBP. This altered strategy could be an attempt to compensate for pain. The higher contribution of the abdominal muscles, and especially of the EO muscle during concentric contractions in more challenging conditions (higher forces) might be an unconscious effort to protect the back from potential pain or injury, but it could inadvertently result in less efficient force production and reduced torque steadiness. This is further supported by the fact that the magnitude of HDsEMG-torque cross-correlation for the EO muscle during concentric contractions at high forces correlated with the CoV and SD of torque, indicating a relationship between the increased contribution of this muscle and the reduced steadiness performance observed in the CLBP group ($r=0.575$, $r=0.573$).

3.5.4 Clinical relevance and future directions

Consistent with previous studies (Alsubaie et al., 2021, Arvanitidis et al., 2022, Pranata et al., 2017), the findings underscore that individuals with CLBP manifest altered muscle recruitment patterns and torque steadiness deficits. Despite this evidence, particularly regarding torque steadiness deficits, such insights have yet to be incorporated into CLBP management. Assessing torque steadiness deficits and neuromuscular disparities in the thoracolumbar ES and abdominal muscles and then trying to alter them with the methodology used in the current study (torque steadiness with/without HDsEMG biofeedback) could potentially offer a more

comprehensive approach to CLBP management strategies. Nonetheless, before adopting these interventions, rigorous studies are essential to determine how this type of training impacts individual symptoms and to identify if it leads to physiological changes (i.e., changes in muscle recruitment behaviour). Given that CLBP remains a leading cause of disability globally (Ferreira et al., 2023), the findings suggest the need to refine and expand therapeutic strategies for CLBP, integrating innovative assessment methods and interventions.

3.5.5 Methodological considerations

A possible limitation of this study is related to the MVC assessment in individuals with CLBP. These individuals might not have performed a true maximum contraction due to pain or discomfort, which can impact the RMS normalised amplitude calculations (Besomi et al., 2020). This is because observed differences in surface EMG amplitude may be mistakenly attributed to alterations in muscle activation rather than the confounding influence of pain on MVC performance. To minimize the impact of this limitation, we allowed participants with CLBP to perform familiarization contractions before performing the actual MVC contractions. This aimed to warm up their muscles and reduce their movement-related fear. Nevertheless, the only significant differences in RMS amplitude observed in this study were related to the abdominal muscles RMS amplitude which were also confirmed by the HDsEMG-torque cross-correlation results showing a higher contribution of those muscles to the torque during trunk flexion contractions. Therefore, we are confident about these observations.

Another important consideration is the use of the rectified surface EMG to estimate neural drive to muscles. Indeed, surface EMG signals can be affected by several factors, such as amplitude cancellation, crosstalk and changes in skin-electrode interface impedance, which can limit their accuracy in reflecting the underlying neural activity. Although surface EMG

decomposition techniques can help to identify motor unit action potentials and provide a more accurate assessment of neural drive to muscles, this approach remains challenging for trunk muscles due to the complexity of trunk muscle anatomy and/or the properties of the surrounding tissues, which can reduce the discriminative information in the action potential waveforms of different motor units. Consequently, similarly to others (Moon et al., 2014, Yoshitake and Shinohara, 2013b), the analysis was based on the rectified surface EMG signal, as it approximates the motor unit firing rates. A key challenge with raw interference EMG is the standard high-pass filtering at 10–20 Hz during either recording or post-processing, which causes a notable reduction of the low-frequency content (Moon et al., 2014, Yoshitake and Shinohara, 2013b). This filtering is widely recognised as essential for removing movement-related artefacts from the EMG data (Moon et al., 2014, Yoshitake and Shinohara, 2013b). Herein lies the utility of rectified surface EMG: it induces nonlinear alterations in the EMG's frequency profile (Farina et al., 2004), revealing out the existing low-frequency modulations and facilitating in their clearer representation and analysis (Moon et al., 2014). Even though this approach was used, the results showed a moderate correlation (approximately cross-correlation values of 0.4) between the surface EMG signal and torque in both groups and torque levels. Studies that used motor unit recordings have reported higher cross-correlation values (approximately 0.75-0.80), however, in smaller, single-joint muscles such as the TA (Martinez-Valdes et al., 2021, Martinez-Valdes et al., 2022). Future studies should explore such correlations when decomposition of trunk musculature (e.g., thoracolumbar ES) is feasible. Moreover, the study's limited generalisability due to the CLBP group's low to moderate levels of pain, disability, and fear is acknowledged. Nevertheless, significant differences between the two groups were observed, indicating evident altered motor responses within this range of symptoms and suggesting potentially even greater differences in individuals with more severe

symptoms (Mannion et al., 2000). Furthermore, another limitation of the study is the presentation of the findings, which may have appeared as being derived from a confirmatory research model with an a priori hypothesis, rather than an exploratory one. We would like to clarify that this study was observational and primarily exploratory in nature. Nevertheless, multiple a priori hypotheses were made based on the findings of previous studies from our group and others (Alsubaie et al., 2021, Arvanitidis et al., 2022, Pranata et al., 2017). Lastly, considering that the reliability of HDsEMG had been previously demonstrated by van Helden et al., (2022) in asymptomatic controls (***Chapter One*, Section 1.7**), we decided not to have participants perform the same test on consecutive days (van Helden et al., 2022). However, we acknowledge that including such a session could have further enhanced the findings.

3.6 Conclusions

This study has revealed notable differences in muscle activation patterns, particularly in the thoracolumbar ES and EO between individuals with CLBP and asymptomatic controls during trunk extension and flexion contractions. Individuals with CLBP demonstrated poorer trunk muscle force control during both concentric/eccentric flexion and extension contractions, underlining the significance of evaluating torque steadiness deficits in this population.

Chapter 4

ECCENTRIC EXERCISE-INDUCED DELAYED ONSET TRUNK MUSCLE SORENESS ALTERS HIGH-DENSITY SURFACE EMG-TORQUE RELATIONSHIPS AND LUMBAR KINEMATICS

The findings of the studies presented in ***Chapter 2*** and ***Chapter 3*** revealed that pain significantly impairs isometric and dynamic trunk muscle torque steadiness in individuals with CLBP. Additionally, these studies showed that people with CLBP display alterations in surface EMG-torque relationships and muscle recruitment strategies compared to asymptomatic controls during these contractions. These impairments reflected long-term motor adaptations to chronic pain.

To better understand these neuromuscular adaptations, we investigated whether lumbar DOMS could serve as a viable model for replicating the motor impairments observed in CLBP. Specifically, we assessed whether low back DOMS in healthy individuals could mimic the reductions in trunk force control and changes in muscle recruitment seen in CLBP, providing insight into the early motor adaptations that occur in response to acute pain.

By tracking these adaptations over the soreness period, we aimed to explore how initial protective strategies may evolve and contribute to motor performance deficits, trunk muscle recruitment alterations, and movement pattern changes. Understanding these early responses to acute pain offers valuable insights into the mechanisms that could lead to long-term

maladaptive motor behaviours and the progression from acute to chronic pain-related impairments.

This chapter reports in full a manuscript which has been published by the thesis author (**Appendix 4**) (Arvanitidis et al., 2024b). Changes have been made in the text of this chapter for the purposes of a thesis, specifically:

- A sentence has been added to the Abstract to link this work with the previous two chapters.
- The Introduction has been revised to align with the content from earlier chapters of this thesis and minimise repetition.
- Where there is overlap, sections of the methodology have been condensed and the reader is referred to the sections of the previous chapters that this information has already been reported.

Publication:

1. **Arvanitidis M,** Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Eccentric exercise-induced delayed onset trunk muscle soreness alters high-density surface EMG-torque relationships and lumbar kinematics. *Sci Rep*. 2024;14(1):18589.

Presentation:

1. **Arvanitidis M**, Jiménez-Grande D, Haouidji-Javaux N, Falla D, Martinez-Valdes E. Associations between delayed onset trunk muscle soreness, altered EMG-torque relationships, and lumbar kinematics in dynamic contractions. XXIV Congress of the

International Society of Electrophysiology and Kinesiology (ISEK). Oral presentation, Nagoya, Japan, June 26 - 29, 2024.

4.1 Abstract

After observing that individuals with CLBP have reduced trunk muscle torque steadiness and display alterations in surface EMG/torque relationships, we sought to determine if similar behaviour is observed in acute, experimentally induced LBP. To this end, we aimed to assess HDsEMG-torque relationships in the presence of trunk DOMS and the effect of these relationships on torque steadiness and lumbar movement during concentric/eccentric submaximal trunk extension contractions.

Twenty healthy individuals attended three laboratory sessions (24 hours apart). HDsEMG signals were recorded unilaterally from the thoracolumbar ES with two 64-electrode grids. HDsEMG-torque signal relationships were explored via coherence (0-5Hz) and cross-correlation analyses. PCA was used for HDsEMG-data dimensionality reduction and improvement of HDsEMG-torque-based estimations.

Thoracolumbar muscle soreness and pressure pain sensitivity, assessed using a visual analogue scale (VAS) and PPTs respectively, both increased 24h and 48h in the presence of DOMS. DOMS did not reduce either concentric or eccentric trunk extensor muscle strength. However, in the presence of DOMS, improved TS, alongside an altered HDsEMG-torque relationship and kinematic changes were observed, in a contraction-dependent manner. For eccentric trunk extension, improved TS was observed, with greater lumbar flexion movement and a reduction in δ-band HDsEMG-torque coherence and cross-correlation. For concentric trunk extensions, TS improvements were observed alongside reduced thoracolumbar sagittal movement.

DOMS does not seem to impair the ability to control trunk muscle force, however, perceived soreness induced changes in lumbar movement and muscle recruitment strategies, which could alter motor performance if the exposure to pain is maintained in the long term.

4.2 Introduction

The findings of the studies presented in ***Chapter 2*** and ***Chapter 3*** demonstrated that people with CLBP exhibit reduced torque steadiness during isometric and dynamic movements of the trunk (Arvanitidis et al., 2022, Arvanitidis et al., 2024c). In this chapter, we will explore how these parameters are altered in the presence of trunk extensor DOMS.

DOMS represents a form of ultrastructural muscle injury that typically emerges following intense, unfamiliar exercises, particularly those emphasizing eccentric contractions (Hotfiel et al., 2018, Houle et al., 2020). Clinical signs of DOMS, include reduced force production, painful movement limitations, stiffness, swelling, and dysfunction in adjacent joints (Hotfiel et al., 2018). These symptoms can persistently impair muscle function (Semmler, 2014). Although considered a mild form of injury, DOMS frequently undermines athletic performance (Hotfiel et al., 2018) and may disrupt daily activities (Semmler, 2014), likely due to alterations in EMG-force relationships, during muscle contractions (Semmler, 2014). Evaluating the relationship between EMG and force/torque provides valuable insights into neuromuscular function (Hof, 1997). EMG measures the electrical activity of muscle fibres, indicating the efficiency of neuromuscular transmission, which is the process by which the nervous system activates muscles to generate force (De Luca, 1997, Hof, 1997). This electrical activity must be efficiently translated into mechanical output for effective muscle function. During DOMS, neuromuscular function may be compromised, potentially affecting this translation process. Assessing EMG-torque relationships can help us uncover the underlying mechanisms responsible for alterations in motor function.

Numerous studies have investigated the effect of DOMS on the neuromuscular function of peripheral muscles, such as the elbow flexors and hamstrings (Brockett et al., 2001, Chapman et al., 2006, Chen et al., 2019, Lavender and Nosaka, 2006, Nosaka and Newton, 2002, Nosaka

et al., 2002, Semmler, 2014). In contrast, research focusing on trunk muscles is less extensive, with only a few studies inducing DOMS to assess its influence on trunk muscle function. For example, some of these investigations have revealed altered activation patterns (Abboud et al., 2021, Larsen et al., 2017) and decreased force accuracy (Houle et al., 2020). Given these findings and considering that people often move differently when experiencing pain (Hodges and Tucker, 2011), it is hypothesized that DOMS may also lead to changes in trunk movement patterns, yet this aspect remains poorly understood. Additionally, it remains to be investigated whether DOMS alters trunk extensor muscle torque steadiness.

Performing contractions with minimal force fluctuations is crucial in everyday life activities, as reduced torque steadiness can affect the precision of voluntary movements and functional ability. During a voluntary contraction, the output from the activated motor unit population leads to force generation, which is not constant but rather fluctuates around an average value (Enoka and Farina, 2021). Years of investigation into the neural mechanisms causing variations in muscle force during voluntary contractions have revealed that the neural command's low-frequency component (<10Hz) is the most relevant for force generation (Negro et al., 2009). This component mirrors the common synaptic input received by the motor unit population (Farina and Negro, 2015). It has previously been demonstrated that eccentric exercise can cause increased elbow flexor muscle force fluctuations, likely due to an increased common neural drive to the muscles (Ye et al., 2014). Given these findings, it is relevant to explore the effect of DOMS on torque steadiness, trunk muscle activation, and spine kinematics during dynamic contractions.

To understand the relationship between muscle activity and the force output, in ***Chapter 2*** and ***Chapter 3***, where we employed HDsEMG combined with PCA as a methodological approach, we evaluated both magnitude and regional alterations in HDsEMG-torque

relationships in individuals with and without CLBP during isometric (Arvanitidis et al., 2022) and dynamic trunk extension (Arvanitidis et al., 2024c). However, how these relationships are altered in the presence of thoracolumbar ES DOMS remains unclear. Given the frequent use of trunk muscles in daily activities involving eccentric contractions, understanding the effects of DOMS on these muscles is crucial. Specifically, changes in trunk neuromuscular function, such as increased force fluctuations and altered recruitment strategies, may predispose individuals to more severe muscle injuries under certain conditions (Proske et al., 2004). Additionally, studying trunk muscle adaptations in the presence of DOMS could enhance our understanding of whether adaptations in trunk muscle function or movement patterns similarly to those seen in people with CLBP, are likely to occur shortly after the onset of pain or back soreness.

This study addressed the third objective of this thesis and aimed explore motor adaptations and changes in recruitment strategies due to DOMS by evaluating its influence on various motor performance measures and HDsEMG parameters measured from the thoracolumbar ES during both concentric and eccentric trunk extension contractions. Specifically, the primary objectives were to (i) quantify changes in the relationship between HDsEMG oscillations and torque oscillations in both time and frequency domains, (ii) assess and compare regional differences in HDsEMG amplitude and HDsEMG–torque cross-correlation and coherence of the ES, and (iii) investigate differences in torque steadiness and associated kinematic data from the lumbar spine following the induction of DOMS in asymptomatic individuals. It was hypothesized that individuals would exhibit reduced torque steadiness under the influence of DOMS, accompanied by alterations in EMG-torque relationships and lumbar kinematics. Secondary objectives also included assessing changes in muscle soreness, thoracolumbar sensitivity measured as PPTs, and muscle strength measured as peak torque over three days to confirm the presence and progression of DOMS.

4.3 Materials and Methods

4.3.1 Study design and setting

This experimental study with a repeated measures design received approval from the Ethical Review Committee at the University of Birmingham, United Kingdom (approval number: ERN 19-1148) and adhered to the Declaration of Helsinki. The CEDE-Check checklist was used for the reporting of EMG methods (Besomi et al., 2024). Data collection spanned from April 2019 to July 2022 at a laboratory within the Centre of Precision Rehabilitation for Spinal Pain, University of Birmingham, United Kingdom. The study was conducted over three sessions on consecutive days, and each were separated by approximately 24 h (baseline, post 24h, post 48h). These time points were selected similarly to previous research (Semmler, 2014) to capture the progression of DOMS, considering that its onset typically occurs at 24 hours and peaks within 72 hours (Byrnes and Clarkson, 1986, Ebbeling and Clarkson, 1989). At baseline, the measurements taken immediately after the eccentric exercise protocol (described later) were conducted to confirm that the protocol was effective in inducting immediate muscle soreness (Lewis et al., 2012). All participants gave their written consent before involvement.

4.3.2 Participants

Twenty asymptomatic controls (ten males, ten females) were recruited from the local Birmingham community, including the University of Birmingham's student and staff populations, through social media announcements and distributed information leaflets. The sample size was based on previous studies (Abboud et al., 2021, Larsen et al., 2017) that used a similar number of participants but also on a moderate effect size of $f = 0.36$, an α of 0.05, a β

power of 0.9 and a 10% data loss due to signal quality of participant withdrawal, for a repeated measures ANOVA using a within factors design consisting of three measurement points. The effect size was calculated from the mean ± SD of lumbar ES HDsEMG reflex amplitude values before and after the induction of DOMS (averaged effect sizes for both sides and first and last trials) reported by Abboud et al., (2021) (Abboud et al., 2021).

Participants were eligible for the study if they were men or women aged 18 to 55 years, asymptomatic, with no prior back or lower limb pain requiring medical attention. Exclusion criteria included cardiovascular diseases, pregnancy, spinal deformities or surgeries, systemic or inflammatory conditions, rheumatic and neuromuscular disorders, neurological conditions, and lumbar radiculopathy. During the three days, as well as the day preceding the experiment, participants were advised against engaging in any high-intensity or atypical exercises and refraining from taking medications intended to alleviate pain or soreness (Arvanitidis et al., 2024c).

4.3.3 Questionnaires

At the start of the session, to assess the level of physical activity, participants were asked to complete the full version of the International Physical Activity Questionnaire (IPAQ). The reliability and validity of the complete IPAQ have been previously established (Craig et al., 2003). Lumbar muscle soreness was also verbally assessed at the beginning and end (i.e., immediately after the eccentric exercise protocol) of the first session. Subsequent evaluations were made at the beginning of the following sessions at 24 and 48 hours, respectively. Participants were instructed to evaluate the subjective intensity of movement-related lumbar muscle soreness using an adapted 0-10 VAS, where 0 represented *"no soreness at all"* and 10 signified *"extreme soreness"* (Chen et al., 2019, Hjortskov et al., 2005). During the eccentric

exercise protocol (detailed below), participants were prompted to indicate their perceived exertion levels (after each set of 5 repetitions) using a modified Borg scale (Category-Ratio-10 Scale; Borg, 1998). The scale spans from *"0"* (no perceived exertion) to *"10"* (extreme exertion).

4.3.4 Pain sensitivity assessment

PPT testing was performed to quantitatively assess changes in thoracolumbar ES sensitivity across consecutive days after the induction of DOMS and confirm local sensitisation as described in ***Chapter Three*****, Section 3.3.5** (Arvanitidis et al., 2024c). Briefly, PPTs were performed only on the right side for all participants over ten testing sites (spanning approximately from L5 to T10). Specifically, two vertical rows were marked, each consisting of 5 PPT sites. These rows started from the L5 vertebra and extended vertically to approximately the T10 vertebra, covering a total distance of approximately 20 cm. The five PPT sites were spaced equally along this distance (approximately 4.8 cm apart). The medial row was positioned 2 cm lateral from the spinous processes over the ES muscles, while the other row was placed 3.2 cm further lateral. At each location, two PPT measurements were performed (randomised order), and the average of the two measurements at each site was used for subsequent analysis (mean thoracolumbar ES sensitivity). PPTs were assessed at the beginning and end of session 1 (immediately after the eccentric exercise protocol), as well as at the start of session 2 (24h later) and session 3 (48h later). Topographical maps of PPTs were also generated using the mean values of all 10 PPT sites across all participants. The centroid (x-axis and y-axis coordinates) was computed to identify the region of increased sensitivity (i.e., areas with the lowest PPTs). This approach facilitated comparisons of sensitivity areas across different days and was also useful to understand if the location of pain was related to

regional changes in HDsEMG-based parameters (e.g., muscle activity, coherence) mentioned below. The same researcher performed all PPT measurements, ensuring the reduction of inter-experimenter variability.

4.3.5 Electromyography

Surface HDsEMG recordings were acquired in monopolar configuration using two 2D (13 × 5) electrode grids. To ensure consistent electrode placement across the three days, the electrode placement area was marked with a surgical skin marker. Additionally, room temperature was controlled to maintain a stable environment. To monitor thoracolumbar ES activity, the two HDsEMG grids were placed vertically on the right side, starting 2 cm lateral to the spinous process of the 5th lumbar vertebra and extending up to approximately the 10th thoracic vertebra, for all participants (Arvanitidis et al., 2024c, Falla et al., 2014). Reference electrodes were also affixed to the participant's sacrum, the ASIS, and wrist. For a comprehensive description and visual representation of the HDsEMG electrode placement related procedures, we direct readers to ***Chapter Three*****, Section 3.3.6 and Figure 3.1** (Arvanitidis et al., 2024c).

Both torque and HDsEMG signals were sampled at a rate of 2048Hz. These signals were digitised using a 16-bit A/D converter (Quattrocento, 400-channel EMG amplifier, OT Bioelettronica, Torino, Italy, amplification: 150, frequency range 10-500Hz, 1st order, 3dB). The OTBiolab+ software platform was used for data acquisition.

4.3.6 Lumbar kinematics

Lumbar movements during the contractions were quantified using Noraxon's myoMOTION system and two wearable Inertial Measurement Units (Research PRO IMUs, Noraxon USA) with a sampling rate of 100 Hz. The sensors were attached via double-sided tape on the lower thoracic and lumbar spine (T12 and L5, respectively). Using Noraxon's myoRESEARCH software (version 3.14), custom angles were created based on the difference between these two sensors. This allowed lumbar flexion/extension, lateral flexion and rotation angles to be captured during all contractions. Before any measurement commenced, participants were asked to adopt a natural upright position while sitting on the dynamometer's chair, and the sensors were calibrated. The myoMOTION software and hardware allowed the synchronization of the myoMOTION receiver with other systems.

4.3.7 Isokinetic dynamometry

The same isokinetic dynamometer and participants' position (***Chapter Two*, Section 2.3.6**) was utilised to assess the torque produced by participants during concentric and eccentric trunk extension MVCs and the torque steadiness tasks performed at submaximal levels.

For all contractions, the dynamometer operated in isokinetic mode. The ROM for both concentric/eccentric extension contractions was 50°, spanning from 20° extension to 30° flexion, emphasising lumbar movement and minimising compensatory actions from the legs (Arvanitidis et al., 2021a). It should be noted that these angles refer to the attachment angles rather than thoracolumbar angles. Therefore, participants had some freedom of movement and could alter their lumbar kinematics by utilising a more stooped position, performing pelvic tilts, or lateral bending and slight rotation, which could be captured with kinematic analysis. A

consistent angular speed of 5°/s was maintained. When returning to the starting position, the concentric contraction mode was consistently set at an angular velocity of 90°/s. For the eccentric mode, the return velocity was adjusted to 20°/s to ensure optimised comfort for the participant. Nonetheless, participants were assisted back to the initial position by the researcher, who manually readjusted the chair for every repetition.

4.3.8 Eccentric exercise protocol (DOMS)

The eccentric exercise protocol consisted of three sets of 15 eccentric contractions of the trunk extensors, moving from 20° of trunk extension to 30° of trunk flexion. The protocol was performed only at the end of session 1. Resistance was set at 50% of their MVC (the %MVC was chosen after pilot testing to induce mild-moderate muscle soreness), with an angular speed of 5°/s. Participants were given a 30-second rest between each set. Participants were asked to perform an MVC immediately after the eccentric contractions to further assess the trunk extensors and validate the effectiveness of the eccentric exercise to induce fatigue (i.e., reduction in maximal torque output).

4.3.9 Experimental protocol

Participants were given time to familiarise themselves with the dynamometer, by practising all contractions and warming up their trunk extensor muscles via sustained and dynamic submaximal contractions.

After a brief rest, they were asked to perform two concentric trunk extension MVCs, moving through a 50° ROM. The starting position for the concentric trunk extension, MVC, was 30° of trunk flexion, and the final position was 20° of trunk extension. Between these

contractions, 1-minute rest was provided. After a 5-minute rest, participants were instructed to perform submaximal concentric trunk contractions, four times at 25% and three times at 50% MVC, in a randomised order. During these contractions, they were asked to match the target torque lines at 25% and 50% MVC, keeping the contraction for 10 seconds. They were allowed to practice each submaximal contraction once before the actual recordings. The highest peak torque observed during the MVC was used to set the submaximal torque targets. After these, participants repeated the same procedures for the eccentric trunk contractions (i.e., the concentric and eccentric contractions were performed separately). The only difference for the eccentric trunk extension contractions was that the starting position was at 20° of trunk extension, and the final position at 30°of trunk flexion (i.e., the opposite from the concentric contractions).

Throughout all submaximal contractions, real-time visual feedback of their torque output and a line representing the desired contraction level (%MVC) was visible on a computer screen positioned 1.5 meters in front of them. This real-time torque data was superimposed over the template for visual feedback. Participants aimed to swiftly and accurately match the %MVC target. Once they achieved the set target (either 25% or 50% MVC), they were advised to keep their torque output as steady as possible for the whole contraction. Essentially, they were asked to produce consistent torque output (25% or 50%MVC) across the entire 50° ROM. The overall study procedure is depicted schematically in **Figure 4.1**.

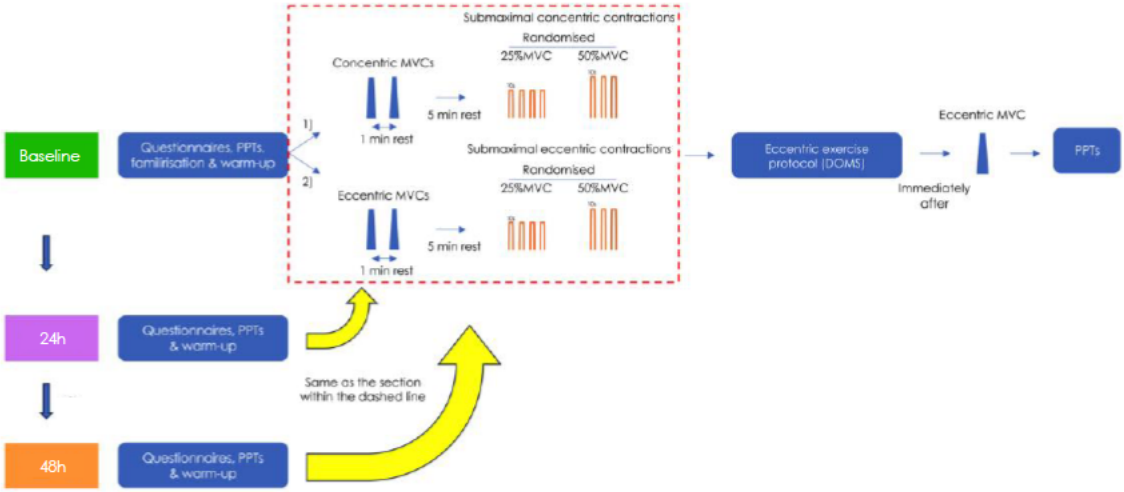


Figure 4.1: **Schematic representation of the overall study procedure. Participants performed the same concentric and eccentric contractions during sessions two and three (part within the red dashed line).**

4.3.10 Analysis of the torque signal

The highest peak torque during the MVCs was used to assess each individual's maximum trunk extension concentric and eccentric strength. Torque steadiness was evaluated by calculating the absolute and relative amplitude of the torque fluctuations, determined by the SD and the CoV of torque, respectively (Enoka and Farina, 2021). A custom MATLAB script was employed to allow the computation of the SD and CoV of torque within the same time window used for the HDsEMG analysis, during the steady phase of the contraction. These values were determined for each repetition and then averaged to provide a single value for each torque level for each contraction. The time windows selected for the analysis were approximately 8 seconds for both submaximal torque levels. This approach aimed to exclude the first and last second of the steady part of the contraction, periods during which participants typically overestimated or underestimated the requested torque level.

4.3.11 EMG amplitude and topographical map computations

During the offline analysis, the 128-monopolar channels from the merged electrodes over the thoracolumbar ES, were processed to 124 bipolar channels, as also done in ***Chapter Three*****, Section 3.3.10**. Before the RMS amplitude calculations, the HDsEMG signals were filtered with a bandpass zero-lag Butterworth filter (10-350Hz, 2nd order) and visually inspected, to exclude channels with low-quality signals due to electrical interference and/or artifacts. Less than 15% of the channels were discarded.

One RMS value was calculated for each of the 124 bipolar channels for the thoracolumbar ES during all trunk eccentric/concentric extension contractions. By determining the RMS for each channel, a HDsEMG amplitude map was generated for the (agonist) thoracolumbar ES and the centroid (x-,y- coordinates) of this map was calculated using all channels, during all muscle contractions. This allowed us monitor regional changes in thoracolumbar ES activation. Additionally, a global measure of myoelectric activity was calculated by calculating the average of RMS values from all 124 channels, which formed a single value (HDsEMG amplitude; RMS_{mean}). In this study, EMG signals were not normalised due to the established reliability of HDsEMG-derived measures in within-subject designs, particularly during voluntary trunk movements (van Helden et al., 2022).

All HDsEMG and torque data was assessed offline using a custom MATLAB 2020b script (The MathWorks Inc., USA). Concentric and eccentric muscle contractions were recorded separately.

4.3.12 HDsEMG data pre-processing for PCA analysis

As mentioned in previous chapters, PCA is a dimensionality reduction technique that effectively identifies redundant information in HDsEMG data and can also enhance the accuracy of HDsEMG-based force estimations (Staudenmann et al., 2006, Staudenmann et al., 2005). This approach was also used in this study. For further information on PCA readers are referred to ***Chapter One*****, Section 1.10.1** and ***Chapter Two*****, Section 2.3.9**.

Before performing the cross-correlation and coherence analyses, the formerly offline-referenced 124 bipolar HDsEMG channels (from the combined electrodes placed over ES) underwent the exactly the same pre-processing for PCA computations as described in ***Chapter Two*****, Section 2.3.9** to obtain a final signal envelope that was obtained by applying PCA to the HDsEMG grid and contained the low-frequency components of the HDsEMG data.

Coherence and cross-correlation analyses were then conducted to estimate the similarity between this final EMG signal envelope and torque signals. Please note that the PCA and subsequent coherence and cross-correlation analyses were exclusively conducted for the thoracolumbar ES, which functioned as the primary agonist muscle during the eccentric and concentric contractions.

4.3.13 Cross-correlation and coherence analyses

Cross-correlation and coherence analyses have been described previously and exactly the same methodology was used in this study (***Chapter One*****, Sections 1.10.2** and **1.10.3** and ***Chapter Two*****, Sections 2.3.10** and **2.3.11**.

Similarly to ***Chapter Three*****, Section 3.3.12**, this study's coherence analysis focused on the δ band (0-5Hz). Except of coherence magnitude measurements, topographical coherence

maps were also generated. In this process, each of the 124 HDsEMG signals from the thoracolumbar ES was individually assessed for coherence in frequency with the filtered torque signal. This analysis resulted in 124 distinct coherence values, one for each HDsEMG signal. These values were then utilized to construct topographical coherence maps. The maps were then normalised to the maximum coherence value at each torque level. The coherence's centroid provided an estimate of the centre of ES muscle δ-band coherence along both medial-lateral (x-axis) and cranial-caudal (y-axis) directions. This analysis enabled us to examine if certain areas of the thoracolumbar ES have greater influence on torque generation and to determine whether the regions with predominant influence shifted across days due to muscle soreness, by statistically comparing x- and y-axis centroid values across days. In ***Chapter 2*** and ***Chapter 3*** we demonstrated that individuals with CLBP exhibit regional differences in HDsEMG-torque coherence compared to pain-free individuals. Therefore, this analysis was used again to determine if similar regional differences occur in the presence of DOMS.

For all maps (i.e., RMS amplitude, coherence and PPT) the origin of the coordinates was at the top left corner of the grid, as depicted in the PPT maps in **Figure 4.2**.

4.3.14 Analysis of lumbar kinematics

Custom anatomical angles (flexion/extension, rotation, and lateral flexion) were generated based on the differences between the two IMU sensors (T12 and L5). The raw data of custom angles was exported in MATLAB (R2020b, MathWorks) for further offline analysis. A low-pass Butterworth filter with a cut-off frequency of 10Hz was applied to all kinematic data (Devecchi et al., 2022). Kinematic angles were calculated for all contractions, for all days, during each repetition (25%: 4 repetitions, 50%: 3 repetitions) and then averaged. Based on the averaged data (average of all repetitions), eight epochs were created. The eight epochs were

normalised by subtracting epoch 1 from all epochs and were converted to positive (absolute) values. This was necessary to allow the calculation of the area under the curve (AUC) for all movement planes (i.e., sagittal, frontal and transverse), which was used to assess differences in the magnitude of movement across days.

Please note that HDsEMG, torque, cross-correlation, coherence and kinematic analyses were performed separately for each type of contraction (concentric, eccentric). Additionally, for every repetition, a single value was computed, i.e., four values for 25%MVC and three values for 50%MVC. These were then averaged to form one value for each submaximal level. This analysis was consistently applied to the data from all three sessions and was used for the statistical analysis.

4.3.15 Statistical procedures

Statistical analyses were performed on SPSS Statistics, version 29 (IBM, USA). The Shapiro–Wilk and the Levene tests were used to confirm data normality and ensure homogeneity of variance, respectively. Given that these conditions were satisfied, parametric tests were used. Data are presented as mean and SD, unless otherwise specified. For the pre-and-post assessments of muscle soreness, PPTs and MVCs, paired samples t-Tests were employed.

For HDsEMG, torque and kinematic variables (i.e., RMS, centroid values of the RMS amplitude map in both axes, level of co-activation between the ES and abdominal muscles, δ band surface EMG-torque coherence, surface EMG-torque cross-correlation, centroid values for surface EMG-torque coherence in both axes mean torque, torque CoV, torque SD, AUC), a two-way repeated measures ANOVA was performed separately for each type of contraction (eccentric, concentric). The torque target (20%MVC and 50%MVC) and session (baseline, 24h,

48h) were used as within-subject factors. One-way repeated measures ANOVA was also used to monitor changes in muscle soreness, PPTs and MVCs across the three testing days.

In instances where the ANOVA indicated significant interactions, a Bonferroni correction was applied for detailed pairwise comparisons. The threshold for statistical significance was set at p=0.05.

4.4 Results

4.4.1 Muscle soreness

All 20 participants (10 males, 10 females) completed the study, with their characteristics detailed in **Table 4.1**. The eccentric exercise protocol performed at the end of session one induced a moderate level of movement-related back muscle soreness immediately post-exercise (4.1/10) ($t=-8.305$, $p<0.001$). Participants reported mild muscle soreness 24h and 48h compared to baseline (session effect: $F=28.222$, $p<0.001$, $\eta p^2=0.744$). Muscle soreness immediately post-exercise was higher compared to that observed at 24h and was similar to that observed at 48h (session effect: $F=5.760$, $p=0.012$, $\eta p^2=0.233$).

Table 4.1: **Demographic characteristics and descriptive data of all 20 asymptomatic individuals that participated in the study. Data are presented across different time points (baseline, after the eccentric exercise protocol, after 24 and 48h respectively).**

Characteristic	Mean ± SD
Age (years)	28.7 ± 3.9
Height (cm)	171.9 ± 7.4
Body mass (Kg)	70.6 ± 13.4
Body mass Index (kg/m^2)	23.9 ± 4.2
PPT Session 1 – Baseline (kPa)	397.8 ± 95.0

PPT Session 1 – Post	370 ± 110.74
PPT 24h	361.0 ± 113.7
PPT 48h	357.9 ± 106.6
VAS Session 1 – Baseline (0-10)	0.0 ± 0.0
VAS Session 1 – Post	4.1 ± 2.2
VAS 24h	2.6 ± 2.1
VAS 48h	2.9 ± 1.8
IPAQ (Total METs score)	4325.1 ± 3578.2
ECC MVC Session 1 – Baseline (N·m)	203.4 ± 48.9
ECC MVC Session 1 – Post	174.2 ± 53.3
ECC MVC 24h	194.8 ± 51.6
ECC MVC 48h	191.4 ± 54.9
CON MVC Session 1 (N·m)	211.8 ± 58.7
CON MVC 24h	200.2 ± 43.1
CON MVC 48h	197.0 ± 48.1

Abbreviations: Pressure pain threshold (PPT), visual analogue scale (VAS) and International Physical Activity Questionnaire (IPAQ), eccentric (ECC), maximum voluntary contractions (MVC), metabolic equivalents (METs), concentric (CON).

4.4.2 Mean thoracolumbar PPTs

During the first session, after the eccentric exercise protocol, PPTs assessed over the lumbar region decreased significantly ($t=2.195$, $p=0.041$). This heightened mean thoracolumbar sensitivity (i.e., lower values of PPTs) persisted 24h and 48h post-baseline (session effect: $F= 6.355$, $p=0.004$). No significant differences in thoracolumbar sensitivity were observed between measurements taken immediately after the eccentric exercise protocol, and those taken at 24 hours and 48 hours later ($F=0.744$, $p=0.482$). Mean ± SD PPT values are reported in **Table 4.1**.

4.4.3 PPT maps

PPT maps were generated to determine if regional pain sensitivity at 24h and 48h differed significantly from baseline in specific thoracolumbar areas due to the eccentric exercise protocol. There were no differences for both the y- and x-axes compared to baseline (session effect: $F=1.054$, $p=0.358$, $\eta p^2=0.053$ and $F=1.340$, $p=0.274$, $\eta p^2=0.066$ respectively). The PPT maps are illustrated in **Figure 4.2**.

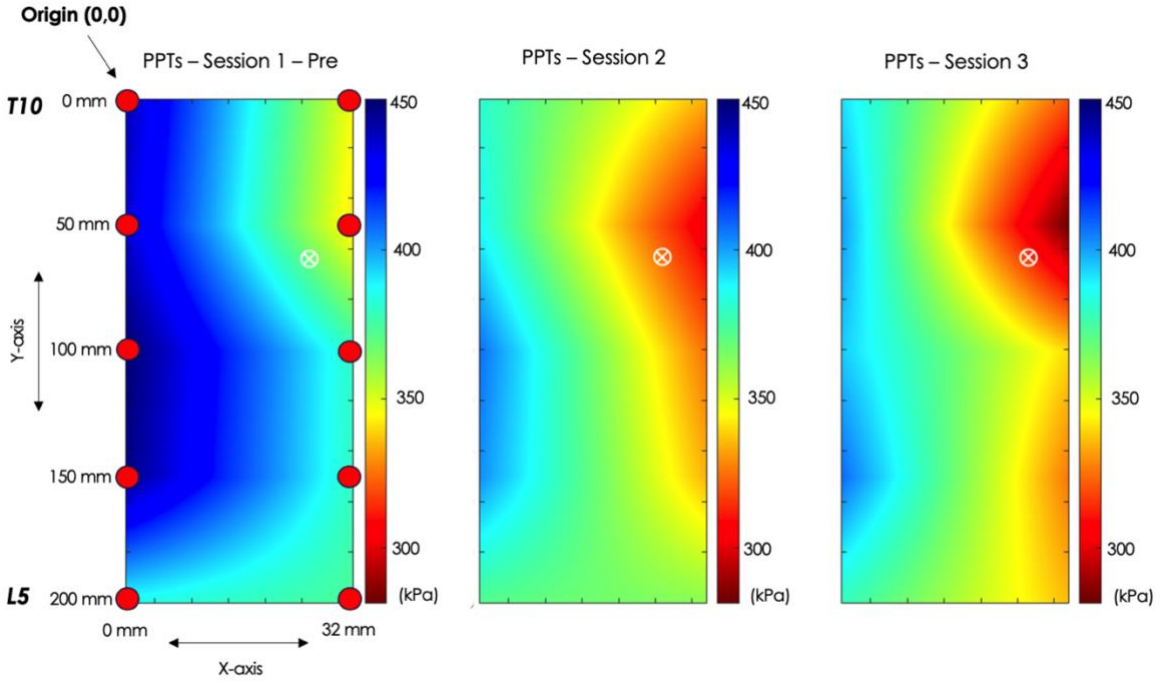


Figure 4.2: **Topographical maps of PPTs are presented across three consecutive days: baseline (Session 1 - Pre), after 24 hours (Session 2), and after 48 hours (Session 3). The red coloration indicates areas of heightened sensitivity, while blue colours represent areas of less sensitivity, denoting higher PPT values. Notably, there is increased sensitivity observed at 24h and 48h compared to baseline. All PPT maps utilise the same scale and have been normalised according to the maximum and minimum of all values. The red circles show the PPT sites over the thoracolumbar area that spanned from T10 to L5 vertebrae, with the medial part of all maps being close to the spine. A white circle with an "X" inside represents the centre of sensitivity, indicating the location of overall heightened sensitivity, which was similar during all days. The distances along the x and y axis are the coordinates of the centre of sensitivity and could also help understand the distance between the PPT points along the two axes. The origin for these coordinates is at the top left corner.**

4.4.4 Rate of perceived exertion

At the end of session 1, during the eccentric exercise protocol, the participants were asked to report their rate of perceived exertion on a modified Borg scale (10 point scale), every 5 repetitions. An increase in the rate of perceived exertion was observed, with the average Borg value at the end of the protocol being 7.4/10, suggesting that the task was interpreted as *"very hard"* by the individuals (time effect: $F=44.082$, $p<0.001$, $\eta p^2=0.699$).

The results presented below are reported per outcome variable for the eccentric and concentric contractions respectively.

4.4.5 Muscle strength

In session one, following the eccentric exercise protocol, there was a decrease in peak eccentric torque (i.e., MVC), equivalent to a 29.2 N·m or 14.35% decrease ($t=3.032$, $p=0.007$; **Figure 4.3A**). No decline in peak eccentric torque was observed 24h and 48h compared to baseline at the beginning of the session (session effect: $F=0.939$, $p=0.379$, $\eta p^2=0.047$; **Figure 4.3B**).

No decline in peak concentric torque was observed 24h and 48h compared to baseline, suggesting that individuals were able to produce the same amount of peak torque during all three sessions irrespective of their muscle soreness and increased mean thoracolumbar muscle sensitivity (i.e., reduced PTT values) (session effect: $F=1.896$, $p=0.164$, $\eta p^2=0.091$; **Figure 4.4A**). Mean ± SD peak torque values for both contractions are reported in **Table 4.1**.

4.4.6 Torque steadiness

Eccentric contractions. A significant lower torque SD was observed 24h and 48h compared to baseline, suggesting that individuals had better torque steadiness in sessions two and three (session effect: F=5.952, p=0.006, ηp^2=0.239; **Figure 4.3C**; baseline: 1.1 ± 0.3%; 24h: 0.9 ± 0.2%; 48h: 0.9 ± 0.2%). No differences were observed across sessions for torque CoV (session effect: F=1.295, p=0.280, ηp^2=0.263; baseline: 3.2 ± 0.9%; 24h: 2.6 ± 0.7%; 48h: 3.0 ± 1.6%).

Concentric contractions. The torque steadiness performance of the participants was better during session 3 compared to baseline as shown from both the torque CoV and SD variables (session effect: F=4.327, p=0.020, ηp^2=0.185; baseline: 3.5 ± 0.9%; 24h: 3.2 ± 0.9%; 48h: 3.0 ± 0.5% and F=5.452, p=0.008, ηp^2=0.223; baseline: 1.3 ± 0.3%; 24h: 1.1 ± 0.3%; 48h: 1.1 ± 0.2%, respectively; **Figure 4.4B, C**).

4.4.7 Electromyographic activity

Eccentric contractions. No differences in the level of activation of the thoracolumbar ES were observed across the three sessions (session effect: F=1.250, p=0.289, ηp^2=0.062; baseline: 41.8 ± 21.5 μV; 24h: 40.6 ± 21.7 μV; 48h: 38.6 ± 19.7 μV). The regional activation of the thoracolumbar ES along the y- and x-axes was similar during all sessions (session effect: F=0.479, p=0.539, ηp^2=0.025; baseline: 93.7 ± 11.1 mm; 24h: 95.9 ± 5.5 mm; 48h: 95.6 ± 6.8 mm and F=1.945, p=0.157, ηp^2=0.093; baseline: 16.2 ± 1.2 mm; 24h: 16.2 ± 0.9 mm; 48h: 15.8 ± 1.0 mm). The level of co-activation between the RA, EO and ES was similar across days (session effect: F=0.649, p=0.491, ηp^2=0.033; baseline: 151.7 ± 123.2 %; 24h: 153.3 ± 117.2 %; 48h: 142.3 ± 101.0 %).

Concentric contractions. No differences in the level of thoracolumbar ES activity were observed across days (F=0.021, p=0.923, ηp^2=0.001; baseline: 44.7 ± 25.1 μV; 24h: 44.2 ± 21.8 μV; 48h: 44.2 ± 21.2 μV). The regional activation of the thoracolumbar ES along the y- and x-axes was similar for all three days (F=0.281, p=0.656, ηp^2=0.015; baseline: 96.4 ± 9.5 mm; 24h: 97.1 ± 8.1 mm; 48h: 95.2 ± 9.1 mm and F=1.120, p=0.337, ηp^2=0.056; baseline: 16.3 ± 1.0 mm; 24h: 16.1 ± 0.8 mm; 48h: 15.9 ± 0.8 mm). The level of co-activation between the abdominal (RA, EO) and lumbar ES was similar during all three sessions (F=1.474, p=0.243, ηp^2=0.076; baseline: 153.3 ± 99.2 %; 24h: 136.8 ± 93.5 %; 48h: 132.0 ± 114.9 %).

4.4.8 EMG-torque relationships

Eccentric contractions. A session effect was observed for the magnitude of δ band coherence, showing that δ band coherence at 48h was lower compared to baseline (session 1) and 24h (session 2) (F=6.685, p=0.003, ηp^2=0.260; Z-coherence in the δ band, baseline: 0.8 ± 0.2; 24h: 0.7 ± 0.1; 48h: 0.7 ± 0.1; **Figure 4.3D**). In terms of differences in the topographical representation of δ band coherence along the y- and x-axes, no differences were observed (session effect: F=1.306, p=0.276, ηp^2=0.064; baseline: 94.2 ± 8.1 mm; 24h: 96.6 ± 2.3 mm; 48h: 96.1 ± 3.0 mm and F=0.958, p=0.393, ηp^2=0.048; baseline: 16.7 ± 0.5 mm; 24h: 16.6 ± 0.4 mm; 48h: 16.5 ± 0.3 mm).

Similarly, a session effect was observed for the magnitude of HDsEMG-torque cross-correlation, showing a reduction in the contribution of the thoracolumbar ES at session 3, compared to the other two sessions (F=7.416, p=0.002, ηp^2=0.281; cross-correlation coefficient, baseline: 0.4 ± 0.0; 24h: 0.4 ± 0.1; 48h: 0.37 ± 0.0; **Figure 4.3E**). No differences in the topographical representation of HDsEMG-torque cross-correlation along the y- and x-axes, were observed (session effect: F=0.096, p=0.847, ηp^2=0.005; baseline: 94.3 ± 7.9 mm; 24h:

94.8 ± 3.2 mm; 48h: 95.0 ± 4.2 mm and F=1.541, p=0.227, ηp^2=0.075; baseline: 16.7 ± 0.5 mm; 24h: 16.6 ± 0.4 mm; 48h: 16.5 ± 0.3 mm).

Concentric contractions. No differences were observed for the magnitude of δ band coherence, across days (F=0.373, p=0.691, ηp^2=0.019; Z-coherence in the δ band, baseline: 0.8 ± 0.1; 24h: 0.8 ± 0.1; 48h: 0.8 ± 0.1). Similarly, no differences in the topographical representation of δ band coherence along the y- and x-axes, were observed (session effect: F=1.216, p=0.297, ηp^2=0.060; baseline: 94.7 ± 10.4 mm; 24h: 98.3 ± 5.7 mm; 48h: 96.8 ± 3.2 mm and F=0.270, p=0.765, ηp^2=0.014; baseline: 16.6 ± 0.4 mm; 24h: 16.6 ± 0.3 mm; 48h: 16.5 ± 0.3 mm).

The magnitude of HDsEMG-torque cross-correlation was similar across sessions (F=0.343, p=0.712, ηp^2=0.018; cross-correlation coefficient, baseline: 0.4 ± 0.1; 24h: 0.4 ± 0.1; 48h: 0.4 ± 0.1). No differences in the topographical representation of HDsEMG-torque cross-correlation along the y- and x-axes, were observed (session effect: F=1.461, p=0.245, ηp^2=0.071; baseline: 93.7 ± 10.1 mm; 24h: 97.1 ± 4.8 mm; 48h: 96.5 ± 3.1 mm and F=0.742, p=0.483, ηp^2=0.038; baseline: 16.6 ± 0.4 mm; 24h: 16.6 ± 0.3 mm; 48h: 16.5 ± 0.4 mm).

4.4.9 Thoracolumbar kinematics

Eccentric contractions. A session × torque interaction was observed for the AUC variable in the sagittal plane, suggesting that in sessions two and three, as the task was more demanding (i.e., higher %MVC), individuals increased their trunk flexion ROM (F=6.479, p=0.004, ηp^2=0.254; 25%MVC-24h: 50.6 ± 28.3 º·epoch, 50%MVC-24h: 69.8 ± 32.2 º·epoch; 25%MVC-48h: 46.7 ± 18.8 º·epoch, 50%MVC-48h: 65.1 ± 25.9 º·epoch ; **Figure 4.3F**). Additionally, this interaction showed that at high forces there was a significant difference between sessions one and two for this variable (50%MVC-baseline: 54.0 ± 22.9 º·epoch,

50%MVC-24h: 69.8 ± 32.2 º·epoch). No significant differences were observed for this kinematic variable nor for the frontal or transverse planes ($p>0.05$).

Concentric contractions. At 48h there was a reduction in the AUC in the sagittal plane compared to the baseline, suggesting decreased thoracolumbar ROM (session effect: $F=5.723$, $p=0.007$, $\eta p^2=0.23$; baseline: 48.7 ± 20.0 º·epoch; 24h: 36.4 ± 18.7 º·epoch; 48h: 33.4 ± 16.7 º·epoch; **Figure 4.4D**). This might indicate that participants were aiming to maintain a more neutral or stable lumbar spine position. No significant differences were observed for movement in the frontal or transverse planes ($p>0.05$).

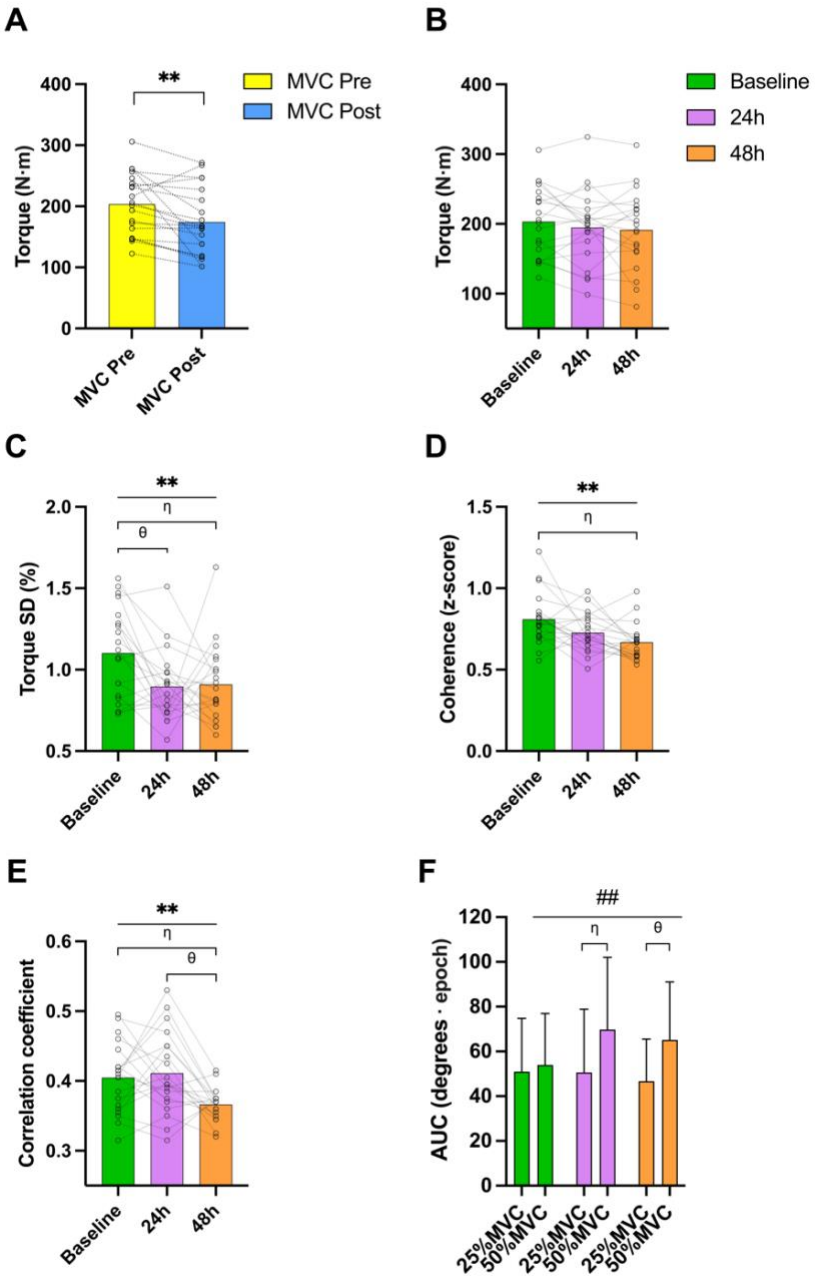


Figure 4.3: **A visual representation of the key results obtained from the eccentric trunk extensions. Eccentric strength during the first session, before and after the exercise protocol to induce delayed onset of trunk muscle soreness (A), eccentric strength (B), torque SD (C), coherence z-scores in the δ band (D), HDsEMG-torque cross correlation (E) across all three measurement points, AUC in the sagittal plane across all measurement points and for both force levels (F). The results for graph F are presented as mean ± SD and for the rest as mean and individual values. For graphs B, C, D and E data is pooled and presented across force levels (i.e., 25% and 50%). Main effect of session, p<0.01: **; session × torque interaction, p<0.01: ##; η, θ: post hoc pairwise comparisons with Bonferroni correction.**

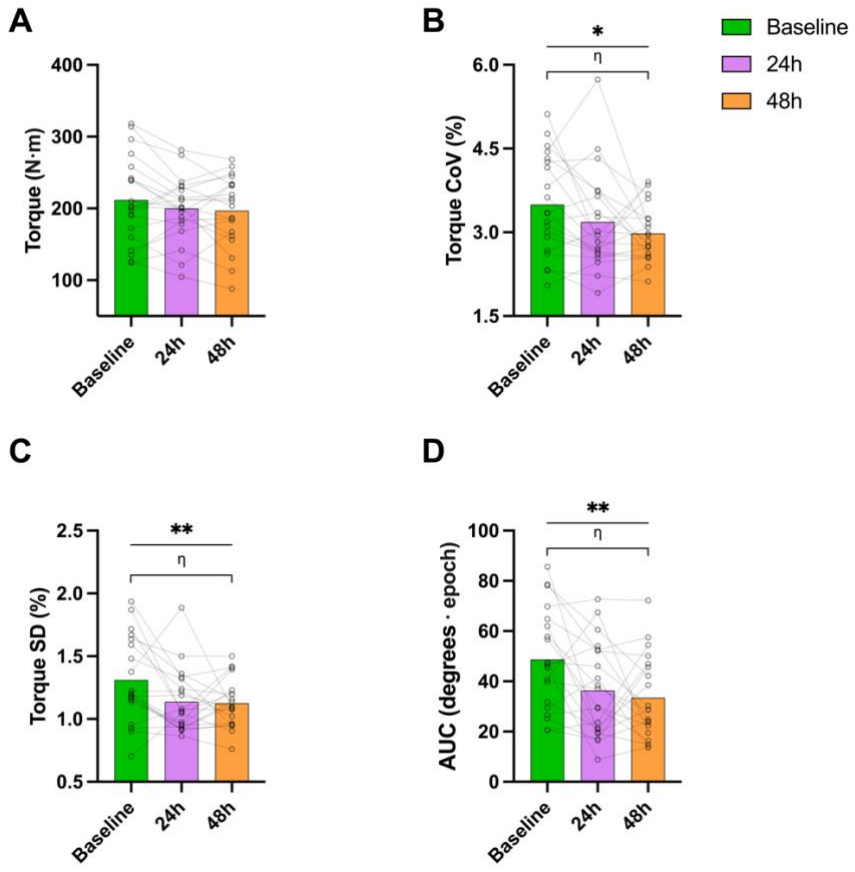


Figure 4.4: **A visual representation of the key results obtained from the concentric trunk extension contractions. Concentric strength (A), torque CoV (B), torque SD (C) over the three measurement points, AUC in the sagittal plane across all measurement points and for both force levels (D). The results for all graphs are presented as mean and individual values. For all graphs data is pooled and presented across force levels (i.e., 25% and 50%). Main effect of session, $p<0.05$: *, $p<0.01$: **; η: post hoc pairwise comparisons with Bonferroni correction.**

4.5 Discussion

This study examined the influence of DOMS on torque steadiness, HDsEMG-torque relationships from the thoracolumbar ES, and kinematic data from the thoracolumbar spine in asymptomatic individuals during submaximal concentric and eccentric trunk extension contractions at 25% and 50%MVC. No significant changes were observed for eccentric and concentric trunk extension muscle strength across sessions. The participants demonstrated

improved torque steadiness during submaximal concentric and eccentric trunk extension contractions in the presence of DOMS. However, HDsEMG-torque relationships and kinematics were altered in a contraction-dependent manner. During eccentric contractions, a decrease in the thoracolumbar ES contribution to the resultant torque was observed, and individuals showed increased lumbar flexion during the more demanding contractions (50%MVC). During concentric contractions, a reduction in thoracolumbar ROM in the sagittal plane was observed, suggesting the maintenance of a more neutral lumbar spine posture, but no alterations in HDsEMG-torque relationships were observed in the presence of DOMS.

4.5.1 Muscle soreness and sensitivity

The increased soreness and mean thoracolumbar pressure pain sensitivity observed after 24h and 48h support the occurrence of DOMS following the eccentric exercise protocol. This aligns with the observations of previous studies (Abboud et al., 2021, Abboud et al., 2019, Larsen et al., 2017). Notably, the mild soreness levels we observed at 24h and 48h (VAS scores of 2.6 ± 2.1 and 2.9 ± 1.8, respectively) fall within the range of peak soreness levels (2 to 2.9/10 on the VAS) documented in similar timeframes by other researchers (Abboud et al., 2021). The observed decrease in mean PPT values aligns with findings from Abboud et al., (2019), who also reported reduced PPT values over the L2-L5 region with the presence of DOMS, suggesting a link to peripheral sensitization driven by inflammatory processes or tissue damage associated with DOMS (Abboud et al., 2019).

The mechanisms behind DOMS are multifaceted and not fully understood (Hyldahl and Hubal, 2014). Traditionally, eccentric exercise-induced microstructural muscle damage was believed to trigger inflammation followed by biochemical, thermal, and mechanical changes, sensitizing muscle afferents and causing soreness and mechanical hyperalgesia (Hyldahl and

Hubal, 2014). However, recent studies highlight bradykinin, nerve growth factor (NGF), and COX-2-glial cell line-derived neurotrophic factor (GDNF) as key contributors, suggesting that myofiber micro-damage may not be necessary for initiating inflammation or DOMS (Hody et al., 2019, Hyldahl and Hubal, 2014, Mizumura and Taguchi, 2016). These molecules could stimulate muscle nociceptors or extracellular receptor binding, indicating their role in mechanical hyperalgesia and inflammation in the extracellular matrix, even without apparent muscle damage (Peake et al., 2016). Interestingly, an ultrasound study also suggested an involvement of the paraspinal extramuscular connective tissue (ECT) of trunk extensors in the genesis of DOMS (Brandl et al., 2023). However, it is important to note that research on these mechanisms has predominantly focused on limb muscles, leaving other areas, such as the trunk, less explored.

4.5.2 Trunk muscle strength

DOMS typically induces a temporary decrease in muscle force. As expected, following the eccentric exercise protocol, we observed an immediate reduction in eccentric extension trunk strength, which can most likely be attributed to acute muscular fatigue. However, contrary to some prior studies (Abboud et al., 2021, Abboud et al., 2019, Chen et al., 2019, Hjortskov et al., 2005), this decrease in trunk extension MVC was not observed at 24h and 48h post-exercise. Reductions in muscle force following eccentric exercise are well-documented for upper and lower limb muscles (Chen et al., 2019), however, this trend does not appear to apply as consistently to trunk muscles, particularly in the context of dynamic trunk MVCs. This could be because trunk extension is a multi-joint movement of the lumbar spine, pelvis, and hips, where potential compensation by lower limb muscles, such as the gluteus maximus and hamstrings, can play a significant role. These muscles can influence both the hip and pelvis,

thereby minimizing the engagement of the thoracolumbar extensors. Despite stabilization efforts, such as using straps to secure the thighs and pelvis, it is challenging to prevent these compensatory strategies completely. This suggests that participants might have executed the MVCs by compensating with their hip extensor muscles, particularly if DOMS influenced the use of the thoracolumbar extensors. Furthermore, it is important to consider that participants could also have compensated with upper thoracic muscles of the erector spinae group, whose activity could not be captured with the current electrode placement (e.g., longissimus thoracis and iliocostalis thoracis) (Cramer and Darby, 2014). Additionally, contrasting findings may result from protocol differences: (i) previous studies focused on isometric strength, whereas we assessed eccentric/concentric strength, which could increase the likelihood of compensatory torque exertion as mentioned above, (ii) variations in exercise protocol speed (to induce DOMS), load and the use of an isokinetic dynamometer, considering that fast velocity eccentric exercise causes more muscle fibre damage than slow contractions (Chapman et al., 2006) and because muscle loading level impacts damage extent and recovery rates (Nosaka and Newton, 2002). Lastly, as mentioned above, individuals might exhibit DOMS without damaging contractile structures, suggesting the involvement of neurotrophic factors and/or connective tissue damage in the increased soreness experienced after exercise (Hody et al., 2019, Mizumura and Taguchi, 2016). These factors likely explain how individuals' trunk strength was maintained 24h and 48h post-exercise.

4.5.3 Torque steadiness

Considering that trunk extensor torque steadiness is commonly reduced in individuals with CLBP as we observed in ***Chapter 2*** and ***Chapter 3*** (Arvanitidis et al., 2022, Arvanitidis et al., 2024c), we anticipated a reduction in both eccentric and concentric trunk extension torque

steadiness due to DOMS. However, contrary to our hypothesis, torque steadiness improved in both concentric and eccentric contractions 48h after the eccentric exercise protocol that was used to induce DOMS.

According to previous studies there is conflicting evidence on how DOMS influences the control of muscle force. Some studies (Houle et al., 2020, Koutris et al., 2018, Vila-Chã et al., 2012) have observed worse motor control in the presence of DOMS, while others have observed no changes (Look et al., 2021). However, no previous study has assessed trunk extensor torque steadiness in the presence of DOMS. To date, only one study has investigated this aspect using an alternative model of acute experimental pain. Specifically, this study found no significant changes in trunk extensor force variability following intramuscular injection of hypertonic saline into the longissimus muscle (Hirata et al., 2015). In contrast, investigations into lower/upper limb muscles (Lavender and Nosaka, 2006), observed significant increases in force fluctuations, but only immediately and 1h after eccentric exercise, with no differences observed at 24h and 48h. Similarly, a study investigating the knee extensors (Vila-Chã et al., 2012) observed that force steadiness deficits were more pronounced immediately post-exercise and primarily at lower %MVC levels (2.5, 5 and 10%), with less impact at 20 or 30% MVC, and no data available for periods beyond 24h or for higher loads.

Collectively, the findings from these studies support our observation that DOMS does not necessarily lead to reduced force steadiness. Additionally, it is important to consider that immediate reductions in force steadiness, observed by some studies (Lavender and Nosaka, 2006, Vila-Chã et al., 2012), are mainly attributed to acute muscular fatigue following eccentric exercise rather than DOMS which occurs later. The lack of reductions in force steadiness in the presence of trunk extensor DOMS can be attributed to some factors, including: (i) compensatory mechanisms inherent in multi-joint movements, such as trunk extension, which allow for

significant compensatory strategies when experiencing DOMS. The activation of the hamstrings, gluteals and the not recorded parts of the thoracic ES to compensate for decreased functionality in the sore thoracolumbar ES and (ii) a learning effect, possibly linked to the improved force steadiness after 48h. This effect, likely arising from frequent task repetition with visual feedback during the eccentric exercise protocol, demonstrates that despite the presence of DOMS or acute discomfort, individuals can enhance their performance, suggesting this sensation does not necessarily hinder the learning and adaptation process. This notion is further supported by a previous study (Salomoni et al., 2019) using an experimental pain model, where individuals with acute shoulder pain showed an improvement level in movement accuracy during fast arm-reaching movements and force field perturbations comparable to that of pain-free controls. Furthermore, this improvement in force steadiness may also be understood as a strategy for individuals to maintain a more consistent force output, thereby avoiding increases in the sensation of discomfort that may result from a less steady force output with sudden alterations. Additionally, the use of HDsEMG and kinematic data in the current study helped explore these improvements further.

4.5.4 HDsEMG amplitude and HDsEMG regional activation

During both eccentric and concentric contractions, we observed no changes in the magnitude of thoracolumbar ES activation or regional activity in the presence of DOMS. These findings align with similar previous research on the trunk extensors (Abboud et al., 2021, Hjortskov et al., 2005) and medial gastrocnemius (GM) (Pincheira et al., 2021), further supporting the theory related to the involvement of muscle-associated connective tissue (Hyldahl and Hubal, 2014, Wilke and Behringer, 2021) instead of changes in the muscle itself. A review (Semmler, 2014) has previously aimed to examine the course of EMG changes and

alterations at the motor unit level. However, the most common muscle assessed was the biceps brachii (BIC), and most differences were reported immediately after an eccentric exercise protocol, 2h and 24h. Importantly, it highlighted an inconsistency of change in agonistic and antagonistic EMG amplitude at 24h, and no data were presented at 48h. Interestingly, many changes can happen at the motor unit level. However, capturing these changes using HDsEMG in the thoracolumbar ES poses significant challenges. By examining the HDsEMG-torque relationship, we gained additional insights into why individuals show improved torque steadiness in the presence of DOMS. Nevertheless, it is important to note that DOMS is not always indicative of muscle damage, which might explain some of the inconsistency in the findings and the absence of differences in EMG variables when DOMS is present. It is important to mention that most of these changes at a motor unit level were reported immediately after eccentric exercise, thereby not excluding, or underestimating the confounding factor of fatigue in these observations.

4.5.5 HDsEMG-torque relationships

The magnitude of HDsEMG cross-correlation and δ band coherence at 48h post-exercise was reduced during eccentric trunk extensions when compared to the previous two sessions. However, no regional changes in δ band coherence maps were observed during either eccentric or concentric contractions at 24h and 48h post-exercise. This uniformity in δ band coherence, reinforced by the PPT maps, which revealed no regional sensitivity differences in the thoracolumbar area, suggests that the changes were primarily in magnitude and indicates a highly localised nature of DOMS. Another noteworthy observation was the absence of differences in the magnitude of these variables during concentric trunk extension contractions across days. This is not surprising, considering the inherent differences between eccentric and

concentric contractions. Eccentric contractions involve greater passive muscle element contribution, distinct neural control, higher force production with lower metabolic energy consumption, and increased mechanical stress, resulting in more microtrauma (Herzog, 2018, Herzog et al., 2016, Hody et al., 2019). Consequently, due to the increased stress on connective tissue and muscle fibres during DOMS, we can anticipate more pronounced changes in these patterns, aiding in task adaptation and performance enhancement. Furthermore, during eccentric contractions, individuals are likely to leverage this additional component effectively for torque production. These insights could be further elucidated by examining thoracolumbar kinematics, as detailed in the following section.

4.5.6 Thoracolumbar kinematics

Distinct differences were observed in the sagittal plane during both eccentric and concentric contractions. Notably, in the presence of DOMS, individuals demonstrated increased lumbar flexion during eccentric contractions at both 24h and 48h, particularly at higher loads (i.e., 50%MVC). This pattern was not observed at baseline, suggesting that the individuals had to alter their movement pattern to be able to perform the more demanding trunk extension eccentric contractions. In contrast, during the concentric contractions, different adaptations were observed. At 48h, individuals used a more neutral or stable lumbar spine position during the concentric contractions compared to baseline. The lack of notable differences in other planes of movement could be attributed to the individual's position on the chair, which was stabilised by straps, and the attachment system that limits movements to the frontal and transverse planes.

Even though distinct, the adaptations observed in movement patterns during both eccentric and concentric contractions could likely serve two functions. Firstly, these adaptations might be a self-protective mechanism for the tissues involved, potentially reducing the risk of

further damage. Secondly, they may be related to a learning effect, particularly considering the exercise protocol's similarity with the torque steadiness tasks, enabling more efficient and effective task performance. For example, in the case of eccentric extension, an increased lumbar flexion can be explained in two ways, (i) it might be related to a more efficient utilisation of the passive muscle elements or of the ECT and/or (ii) it could represent a protective strategy to reduce strain on these tissues by engaging compensatory muscle groups such as the hamstrings, gluteals and/or other parts of the thoracic ES. This explanation is supported by recent findings showing that eccentric exercise can lead to increases in lumbar ECT thickness (Brandl et al., 2023) and immediate changes in the optimum length for force generation in the hamstring muscles (Brockett et al., 2001).

Conversely, the controlled back extension observed during concentric movements could contribute to minimising unnecessary thoracolumbar motions. This controlled motion might optimise the length-tension relationship in the trunk extensor muscles, avoiding overly stretched or contracted positions. Consequently, this approach could reduce the risk of further damage to the connective or muscle tissue and likely enhance force steadiness by maintaining muscle efficiency and stability.

4.5.7 Methodological considerations

A potential limitation of the study relates to the generalisability of the results, considering the sample primarily consisted of young and highly active individuals. Such a group may exhibit a faster recovery from DOMS compared to older individuals or those with lower levels of physical activity. Despite this, the presence of mechanical hyperalgesia and mild muscle soreness did confirm the presence of DOMS in our sample. Moreover, while the positioning of individuals could have allowed for compensation using hip, gluteal and/or other

parts of the thoracic ES muscles during the task, we aimed to minimise such compensatory movements in our protocol. This was achieved by restricting movement with straps over the pelvis and thighs and by instructing participants to rely mainly on their trunk extensor muscles as they performed the task. Another limitation of the study is the use of rectified surface EMG to estimate neural drive to muscles. While surface EMG signals can be influenced by various factors, the rationale behind choosing this method has been previously detailed (Arvanitidis et al., 2024c). It is also important to acknowledge that factors such as skin temperature, hydration, and electrolyte balances, which can affect surface EMG signals, were not controlled in this study. However, the reliability of HDsEMG for these muscles has been previously established (van Helden et al., 2022), supporting the robustness of the findings.

Another important consideration is the specific load, speed, and measurement time points chosen for this study. Although changes were observed and DOMS was induced by the eccentric exercise protocol, employing an eccentric protocol with maximal effort and faster contractions, along with incorporating immediate and 2-hour post-task measurements, might have revealed additional insights, particularly in terms of HDsEMG measures related to thoracolumbar ES activity, as indicated in previous research for limb muscles (Semmler, 2014). Lastly, it would be beneficial to confirm our speculation regarding the contribution of lower limb musculature to the resultant torque and gain insights into the behaviour of synergistic muscles. The positioning of the electrodes, coupled with the seated posture of the participants, restricted our ability to place additional electrodes on these lower limb muscles.

4.6 Conclusion

This study uniquely demonstrates that in the presence of DOMS, individuals exhibit improved torque steadiness during trunk concentric and eccentric extension contractions, likely

due to adaptations of movement and muscle recruitment strategies, influenced by a learning effect from initial training exposure. This also shows that contrary to individuals with CLBP who may lack the motor resources to compensate for motor control impairments, resulting in reduced torque steadiness, pain-free individuals can make adjustments that lead to improvements in torque steadiness. Importantly, the study also reveals that movement patterns differ significantly between contractions in the presence of DOMS. Increased lumbar flexion was observed in the more challenging eccentric contractions, whereas in concentric contractions, there was a noticeable reduction in thoracolumbar (sagittal) movement. This variation in behaviour could suggest a strategy of protecting the involved tissues and learned efficiency to optimise torque steadiness performance. Collectively, the findings of this work underscore the significance of adaptive strategies in response to DOMS and their influence on muscular performance.

Chapter 5

DOES PAIN INFLUENCE CONTROL OF MUSCLE FORCE? A SYSTEMATIC REVIEW AND META-ANALYSIS

After observing in ***Chapter 2*** and ***Chapter 3*** that control of trunk muscle force is impaired in individuals with CLBP, we sought in ***Chapter 4*** to determine whether DOMS would induce similar motor impairments in healthy individuals, an aspect previously underexplored. Given our findings related to CLBP, the investigation within this chapter extends the exploration of the effects of musculoskeletal pain across various clinical and experimental conditions. Importantly, we strategically excluded DOMS from this review to focus on pain models that more directly simulate clinical conditions. This decision was aimed at minimising the confounding effects associated with DOMS's complex pathophysiology, which includes structural changes alongside nociceptor activation. Instead, we utilised more controlled experimental models that specifically sensitise nociceptors and are less prone to confounding factors, providing clearer insights into the mechanisms of pain and muscle force control.

The protocol for this systematic review and meta-analysis has been published (**Appendix *5***) (Arvanitidis et al., 2021b). This chapter reports in full the manuscript of the actual systematic review and meta-analysis which has been published by the thesis author (**Appendix *5***) (Arvanitidis et al., 2024a).

Publications:

1. **Arvanitidis M,** Falla D, Sanderson A, Martinez-Valdes E. Does pain influence control of muscle force? A systematic review and meta-analysis. *Eur J Pain*. 2024.

2. **Arvanitidis M**, Falla D, Sanderson A, Martinez-Valdes E. Does pain influence force steadiness? A protocol for a systematic review. BMJ Open. 2021;11(1):e042525.

5.1 Abstract

In the presence of pain, whether clinical or experimentally induced, individuals may have impairments in the control of muscle force (commonly known as force steadiness). In this systematic review and meta-analysis, we synthesized the available evidence on the influence of clinical and experimental pain on force steadiness. The focus on clinical and experimental musculoskeletal pain in general, rather than just CLBP as in the previous chapters, was chosen to gain a broader understanding of how different pain presentations influence force steadiness. This approach was used to draw more generalisable conclusions about the influence of pain on force steadiness and identify which populations show impairments and could potentially benefit from targeted interventions.

MEDLINE, EMBASE, PubMed, CINAHL Plus, and Web of Science databases were searched from their inception to December 19, 2023, using Medical Subject Headings (MeSH) terms and preselected keywords related to pain and force steadiness. Two independent reviewers screened studies for inclusion and assessed their methodological quality using a modified Newcastle-Ottawa risk of bias tool (NOS).

In total, 32 studies (19 clinical pain, 13 experimental pain) were included. Meta-analyses revealed reduced force steadiness in the presence of clinical pain as measured by the CoV and SD of force (standardised MD; SMD = 0.80, 95% CI = 0.31-1.28 and SMD = 0.61, 95% CI = 0.11-1.11). These findings were supported by moderate and low strength of evidence, respectively. In the presence of experimental pain, meta-analyses revealed reductions in force steadiness when measured by the CoV of force but not by the SD of force (SMD = 0.50, 95% CI = 0.01-0.99 and SMD = 0.44, 95% CI = -0.04-0.92), each supported by very low strength of evidence.

This work demonstrates that pain, particularly clinical pain, impairs force steadiness. Such impairments likely have clinical relevance and could become targets for treatment when managing people experiencing musculoskeletal pain.

5.2 Introduction

During voluntary submaximal movements, the force exerted by individuals inherently varies, fluctuating around an average value (Enoka et al., 2003). Such force variability stems from neuromuscular noise and other external factors (Oomen and van Dieën, 2017). As defined in previous chapters, the ability to generate steady force output during submaximal voluntary contractions is termed force steadiness (Tracy and Enoka, 2002). Minimising these force fluctuations is vital for maintaining physical functionality, and its deterioration could compromise the precision of voluntary actions, affecting joint stability, coordination, and overall movement (Deering et al., 2017, Maenhout et al., 2012).

The smooth generation of force relies heavily on the perception of force, a component of proprioception (Ager et al., 2020). Proprioception is commonly compromised in the presence of acute, chronic, or experimentally induced pain, likely due to altered afferent information from the affected area and/or central changes (Ager et al., 2020, Lee et al., 2010, Röijezon et al., 2015, Salahzadeh et al., 2013, Sjölander et al., 2008, Treleaven, 2008). Proprioceptive and nociceptive inputs share a complex neurological pathway and may interfere with each other at different levels of processing (Ager et al., 2020). Moreover, musculoskeletal injuries can further impair proprioception by structural damage of tissue (Röijezon et al., 2015). Therefore, pain-induced proprioceptive alterations could potentially degrade our ability to control muscle force.

Assessment of force steadiness typically involves measuring the variability of the force output, quantified by the SD or CoV of the force or torque signal over time, which serve as

indicators of absolute and relative neuromuscular control (Fiogbé et al., 2019), where higher SD and CoV values denote less force steadiness. Additionally, measures such as approximate and sample entropy are sometimes used (SampEn, ApEn), as they offer insights into the complexity and regularity of the force signal. Lower entropy values suggest a more predictable and regular force output, while higher values indicate greater complexity and potential instability in motor control (Smith et al., 2021).

The current literature offers inconsistent findings on the effect of pain, be it clinical or experimental, on force steadiness. Some studies suggest that conditions such as CLBP (Arvanitidis et al., 2022, Miura and Sakuraba, 2014), chronic neck pain (CNP) (Muceli et al., 2011) or patellofemoral pain syndrome (PFP) (Ferreira et al., 2021) are associated with decreased force steadiness in specific isometric tasks, while others report no such changes (Camargo et al., 2009, Crowley et al., 2022, Hirata et al., 2015, Martinez-Valdes et al., 2020). Similarly, studies have shown that experimentally induced pain is associated with reductions in isometric fifth finger abduction (Farina et al., 2012) and knee extension (Poortvliet et al., 2019) force steadiness, while others did not observe changes in dorsiflexion steadiness in the presence of experimental induced pain (Martinez-Valdes et al., 2021, Martinez-Valdes et al., 2020). Given this variability, the aim of this systematic review is to synthesise the available evidence to understand if pain, whether it be clinical or experimental, influences force steadiness during isometric and dynamic voluntary contractions.

5.3 Methods

This review was conducted in line with the 2020 guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021) as evidenced in **Appendix 6 – Supplemental File 1**. The protocol for this review was pre-registered on the

International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42020196479 on July 21, 2020, and has been published (Arvanitidis et al., 2021b). While adherence to the published protocol was rigorous, minor deviations were necessary during data synthesis. Specifically, it was not possible to subgroup data based on the muscle/joint assessed or the implementation of visual feedback. To address the variability among studies, additional heterogeneity measures were evaluated. Furthermore, the standardised mean difference (SMD) was utilized for all studies instead of odds ratios, as it was considered more appropriate for the analysis.

5.3.1 Eligibility criteria

The inclusion criteria for this systematic review were defined by using a modified version of the PICOS framework, which included Population, Indicator, Comparison, Outcomes, and Study Design (Smith et al., 2021). Due the nature of the studies, the original term *"Intervention"* was replaced with *"Indicator"*, in line with previous adaptations for observational studies (Devecchi et al., 2019, Devecchi et al., 2021).

5.3.2 Population

Studies were eligible for inclusion if they focused on adults (≥ 18 years) with musculoskeletal pain (clinical), defined as *"pain experienced in muscles, tendons, bones or joints that arises from an underlying disease classified elsewhere"* — chronic secondary musculoskeletal pain (Perrot et al., 2019) or *"pain that is characterised by significant emotional distress or functional disability, and cannot be attributed directly to a known disease or damage process"* — chronic primary musculoskeletal pain (Nicholas et al., 2019, Perrot et al., 2019).

Additionally, studies investigating experimentally induced musculoskeletal pain, i.e., pain arising from the sensitization of nociceptors in subcutaneous tissues through electrical or chemical stimulation of the muscle and/or joint (Reddy et al., 2012), were also included. These models were specifically chosen because they can induce deep tissue pain, closely mirroring the characteristics of clinical musculoskeletal pain (Graven-Nielsen et al., 1997). A requirement for inclusion was a control group of asymptomatic individuals or a crossover design where the same participants serve as their controls in a pain-free state. There were no restrictions based on gender or ethnicity. The exclusion criteria applied to studies involving pain from exercise-induced muscle soreness (DOMS) or fatigue, or thermal models, as well as participants with neuromuscular and neurological disorders, systemic inflammatory diseases, or a history of surgery/fracture in the area of interest, to eliminate confounding factors.

5.3.3 Indicator

Studies selected included those using dynamometers or similar instruments, such as force or torque sensors, to assess steadiness of force or torque or related measures of variability. Studies employing force platforms for assessing postural steadiness, such as during standing, were not considered. Inclusion was not limited by the provision of visual feedback during trials; studies with and without visual feedback on the force or torque output were eligible for inclusion. All forms of contractions, whether measured at an absolute level or relative to the individual's MVC, were considered and there was no restriction for the side of the body assessed (i.e., dominant or non-dominant).

5.3.4 Comparison

Studies that were selected included those that compared force or torque steadiness in voluntary contractions between painful and non-painful states. Comparisons were conducted either within participants, as in studies of experimentally induced pain, or between groups, such as between pain-affected participants and a control group. Additionally, comparisons encompassed multiple assessments and measurements taken both pre- and post-task.

5.3.5 Outcomes

The primary outcome assessed was the measurement of force or torque steadiness. For this purpose, the following force steadiness measures were considered: the CoV and SD of force or torque, as well as the RMS of the force or torque signal during force-template matching tasks. Studies that evaluated torque complexity through measures such as SampEn or ApEn were also included. The inclusion was restricted to quantitative studies that measured force or torque steadiness or variability. Studies that investigated other aspects of muscle force control, such as force accuracy (i.e., the ability of an individual to produce a force that matches a specified target force as closely as possible; force reproduction tasks etc.) (Pranata et al., 2017) were excluded.

5.3.6 Study design

Scoping searches indicated that observational studies primarily explore the research question of this systematic review. Consequently, only observational studies employing quantitative methods, specifically cross-sectional, case-control, and cohort studies, were included. Non-original works such as systematic and narrative reviews, as well as other study types, were excluded. To reduce potential bias, the search encompassed studies in all languages.

However, due to constraints of time and resources, studies not written in English were excluded. Details of any excluded studies are documented in the PRISMA flow diagram (**Figure *5.1***).

5.3.7 Information sources

Electronic databases were searched from their inception to December 19, 2023, and included MEDLINE (Ovid Interface), EMBASE (Ovid Interface), PubMed, CINAHL Plus (EBSCO Interface), and Web of Science (Clarivate Analytics). While the ZETOC database was initially considered for the search, it was ultimately not accessed as the database was closed as of August 1, 2022. Tailored search strategies were formulated for each database, incorporating MeSH where applicable to refine and optimise the search (Richter and Austin, 2012).

In parallel with the electronic database search, hand searches of select journals were also performed. These journals encompassed PAIN, Journal of Physiology, Journal of Neurophysiology, Acta Physiologica, Journal of Electromyography and Kinesiology, Clinical Biomechanics, Muscle & Nerve, Journal of Orthopaedic & Sports Physical Therapy, Journal of Science and Medicine in Sport, Isokinetics and Exercise Science, and Journal of Applied Physiology. Efforts were made to identify any unpublished but relevant studies by directly contacting subject-matter experts in the field. To mitigate the risk of publication bias, grey literature was also reviewed, accessed through the British National Bibliography for Report Literature, OpenGrey database, ProQuest Dissertations & Theses Global, and EThOS.

Additionally, proceedings from the World Congress of Biomechanics, the International Society of Biomechanics, the International Society of Electrophysiology and Kinesiology, and the World Confederation for Physical Therapy were scrutinized, covering the years 2016 to 2023. Authors of studies that appeared to be eligible were contacted to confirm the publication status of their work. To further reduce the chance of publication bias, the reference lists of all

included studies were manually reviewed to identify any relevant studies that might have been missed during the initial search.

5.3.8 Search strategy

The lead author (MA) conducted the search without imposing limitations on date, format, design, geographical area, or language. To guarantee both comprehensiveness and reproducibility of the search, it was crafted following initial scoping searches and with guidance from a skilled Health Sciences Librarian, a member of the University of Birmingham's Research Skills Team. The full electronic search approach for the MEDLINE (Ovid Interface) database is detailed in **Appendix 6 – Supplemental File 2**. This approach combined MeSH terms and keyword searches to optimize the search yield. The search was slightly adapted for different databases, but consistency was ensured. These changes involved alterations in MeSH terms and syntax. For example, the *"ADJ"* operator was switched to *"NEAR"* in the Web of Science database and to *"N"* in the CINAHL Plus (EBSCO Interface) database. The search strategies for all databases are detailed in **Appendix 6 – Supplemental File 2**.

5.3.9 Selection process

All search results were imported into EndNote Version 20 (Clarivate Analytics) by one reviewer (MA) for data management. Duplicates were automatically removed by the software. For screening, the search results were also made available in separate folders for each independent reviewer (MA and AS) and were assessed using a pre-tested screening form. Titles and abstracts were initially screened by two independent reviewers (MA and AS) to categorize studies as definitely eligible, ineligible, or doubtful. Any disagreements or doubtful studies were

discussed between reviewers and in cases of disagreement or uncertainty, a third reviewer (EM-V) was consulted.

The two reviewers independently conducted both stages of the selection process, including the screening of titles/abstracts and full-text evaluation. Any disagreement between reviewers was resolved by the third reviewer (EM-V). The level of agreement between reviewers was evaluated using the kappa (κ) statistic.

5.3.10 Data collection process and data items

Data extraction was conducted by one reviewer (MA) using a tested extraction form, designed to gather essential elements aligned with the review's objectives. The accuracy of the extracted data was verified by a second reviewer (AS). When additional clarification was needed for ambiguous or incomplete data, authors were contacted with a two-week reply window. Failure to respond, led to the study's exclusion for ambiguity.

As detailed earlier, data relevant to each element of our inclusion criteria were extracted. When studies included additional groups not relevant to our review, only data relevant to our specific interest groups were extracted.

5.3.11 Risk of bias assessment

Two independent reviewers (MA and AS) employed two adapted versions of the NOS to assess risk of bias; one version for clinical pain studies adapted from the case-control version and another for experimental pain studies adapted from the cohort version. It is important to note that the experimental pain studies had a repeated measures or cross-over design and were experimental in nature. We selected to use the adapted cohort version of the NOS for these

studies to ensure consistency within the manuscript, to adhere to our previously published protocol (Arvanitidis et al., 2021b), and because it was considered to be more appropriate to the case-control version. The changes and justifications for each are included in **Appendix 6 – Supplemental File 3**. Briefly, in both versions of the tool the *"exposure"* domain in the original NOS was specifically modified to an *"outcome"* domain to fit the nature of our studies better while maintaining the essence of the questions. Scoring ranged from 0 to 9, with higher scores indicating lower risk of bias. Quality categorization for each study was then done as *"good"*, *"fair"*, or *"poor"*, according to established thresholds. Further information on our rationale for selecting the NOS tool for the risk of bias can be found in our published protocol (Arvanitidis et al., 2021b).

5.3.12 Synthesis methods

Both narrative and meta-analyses methods were used to synthesise the data from the included studies, to explore the influence of pain on force steadiness (Deeks et al., 2019, McKenzie et al., 2019). Studies were grouped by the type of pain (clinical or experimental) for methodological consistency, and the narrative synthesis included the outline and tabulation of study characteristics (McKenzie et al., 2019). This allowed studies, not included in the meta-analysis, to be interpreted and the influence of their findings to be considered, alongside other clinical or methodological-related information from each study.

In preparation for the meta-analysis, studies were further subgrouped based on the outcome investigated (e.g., CoV or SD of force/torque). Considering our research question and the limited number of studies per muscle/joint, subgroup analysis by muscle/body region or type of contraction was not performed. Only studies with available or retrievable mean ± SD data on force steadiness were included for meta-analysis. Before conducting the meta-analysis,

descriptive statistics were used to appropriately format the data. For example, if a study reported the standard error (SE) instead of the SD, this was calculated by using the following formula.

$$SD = SE \times \sqrt{N}$$

Additionally, for within-study calculations where multiple observations per group were reported, a weighted average was employed to adjust for any differences in sample size across these observations. A pooled SD was used to pool the individual variances of these observations into a cohesive measure of dispersion. The formulas used are reported below:

$$\bar{x}_w = \frac{\sum_{i=1}^{k}(x_i \cdot n_i)}{\sum_{i=1}^{k} n_i}, SD_{pooled} = \sqrt{\frac{\sum_{i=1}^{k}\left((n_i - 1) \cdot SD_i^2\right)}{\sum_{i=1}^{k}(n_i - 1)}}$$

where for the formula for the weighted mean ($\bar{x}_w$), x_i is the mean of observation i, n_i is the sample size associated with observation i, and k the total number of observations. For the SD pooled formula (SD_{pooled}), SD_i is the SD of observation i, n_i is the sample size for observation i and k is the number of observations. All meta-analysis procedures and forest plot generation were performed using the R software (4.2.1) (Team, 2022) and the *"meta"* package (Balduzzi et al., 2019) by selecting a multi-level random-effects model to adequately accommodate the anticipated heterogeneity across the included studies and adjust the weight of studies that were included more than one time in the model (Deeks et al., 2019). Data pooling was performed using the SMD and the *"metacont"* function within the *"meta"* package which is designed for continuous outcomes using 95% CIs in line with others (Devecchi et al., 2021, Pethick et al., 2022) and guidelines (Deeks et al., 2019). The Knapp-Hartung adjustment (Knapp and Hartung, 2003) was also used to calculate the 95% CI around the pooled effect estimate (Jackson et al., 2017).

Even though we implemented a random-effects model to address heterogeneity statistically, it is important to recognise that this approach does not eliminate heterogeneity; it

merely accounts for it (Deeks et al., 2019). Therefore, as recommended (Deeks et al., 2019, IntHout et al., 2016) we further explored heterogeneity within the data, by calculating and reporting additional measures. Rather than relying solely on the I^2 statistic, which has some limitations in providing insights into the nature of heterogeneity, we also incorporated tau^2 (τ^2). τ^2, which is a quantitative estimate of the extent to which the true effects vary across studies (Deeks et al., 2019). As recommended (Deeks et al., 2019, IntHout et al., 2016, Jackson et al., 2017, Teichert et al., 2023), the between-study variance (τ^2) was estimated using the restricted maximum likelihood estimator. In accordance with recent recommendations (IntHout et al., 2016), we also incorporated the calculation of the prediction interval for the pooled effect size into the analysis. This approach offers a broader perspective on the potential range of true effects within comparable studies (Deeks et al., 2019, IntHout et al., 2016). By including the prediction interval alongside the summary estimate and CI, our reporting illustrates the expected range of true effects in future studies and can simplify its clinical interpretation (Deeks et al., 2019, IntHout et al., 2016).

5.3.13 Sensitivity Analyses

Due to the expected high heterogeneity commonly seen in pain studies, we also conducted a sensitivity analysis (Deeks et al., 2019). This involved excluding each study in turn to check the consistency of the meta-analysis results, as detailed in **Appendix 6 – Supplemental File 4**. This step confirmed the findings' robustness and assessed the impact of excluding each study on overall heterogeneity.

Additionally, considering that the presence of outliers and influential cases may affect the validity and robustness of the conclusions from a meta-analysis, we quantitatively explored potential outliers using deletion diagnostics known from linear regression (i.e., externally

standardised residuals, DFFITS values, Cook's distances, covariance ratios, DFBETAS values, estimates of τ^2 and Q when each study is removed in turn, diagonal elements of the hat matrix, and the weights (%) given to the observed outcomes during model fitting) that can also be adapted to the context of meta-analysis as described previously (Viechtbauer, 2010, Viechtbauer and Cheung, 2010). This was performed using the *"influence"* function from the *"metafor"* package in R (Viechtbauer, 2010). Sensitivity analyses were also performed by removing studies that did not use visual feedback during the contractions, as it could have been a confounding factor, and by removing studies of poor quality to see their influence on the overall result. Using this comprehensive approach to identify influential cases and conducting sensitivity analyses, we aimed to ensure the robustness of the meta-analysis results.

5.3.14 Certainty of evidence

The cumulative evidence from the meta-analyses (for each outcome and type of pain) was also appraised by the two independent reviewers (MA and AS) using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method, assessing cumulative strength and quality. This process involved five steps, as described previously (Goldet and Howick, 2013), with the final evidence quality classified as *"high"*, *"moderate"*, *"low"*, or *"very low"*. Observational studies initially received a low-quality rating, which was then adjusted based on certain criteria. Evidence was upgraded for substantial effect sizes and clear dose-response trends. Conversely, risk of bias, study inconsistencies, imprecision, indirectness, and publication bias led to downgrades (Balshem et al., 2011). Publication bias was assessed by generating funnel plots and visually inspecting their symmetry, as well as using Egger's regression test to quantify the presence of publication bias (Egger et al., 1997, Sterne and Egger, 2001). We applied this quality assessment across all studies and subgroups in our

review, leading to tailored evidence interpretation recommendations in line with guidelines for observational studies (Dekkers et al., 2019, Mueller et al., 2012).

5.4 Results

5.4.1 Search results and study selection

The results of the search and selection process are outlined in **Figure *5.1***. The database searches initially resulted in 5,301 records, with nine additional records/abstracts identified through targeted handsearching of conferences. After removing duplicates, 3,230 records from databases and nine from conference handsearching underwent title and abstract screening, with the inter-reviewer agreement reflected by a high kappa coefficient $\kappa = 0.9$. Full-text screening was then applied to 78 records from the databases/journal search, excluding the other nine records for reasons specified in **Figure *5.1***. The inter-reviewer agreement for the full-text screening was perfect, with $\kappa = 1.00$. The review ultimately included 32 studies.

Some studies that may seem relevant for this review were excluded. Specifically, seven studies (Hollman et al., 2021, Maenhout et al., 2012, Ross et al., 2015, Saccol et al., 2014, Ward et al., 2019, Zanca et al., 2010, Zanca et al., 2013) were excluded because the patient groups did not experience or report pain during the assessment. Moreover, one study (Dinsdale et al., 2023) was excluded because the assessment of force steadiness was performed during an endurance contraction, and muscle fatigue could have been a confounding factor. Lastly, another study was excluded due to its randomised controlled trial design, which was outside the methodological scope of this review (Mista et al., 2016). Furthermore, this study was quite different from the others included, as it consisted of two groups that attended three experimental sessions (day 0, day 2, and day 4), with one group receiving NGF and the other isotonic saline.

The only usable data would have been from day 2, but even the control group (i.e., the individuals that received the isotonic saline injection) experienced some minimal pain, and a learning effect could not be excluded, considering that the individuals had already performed the task twice on day 0.

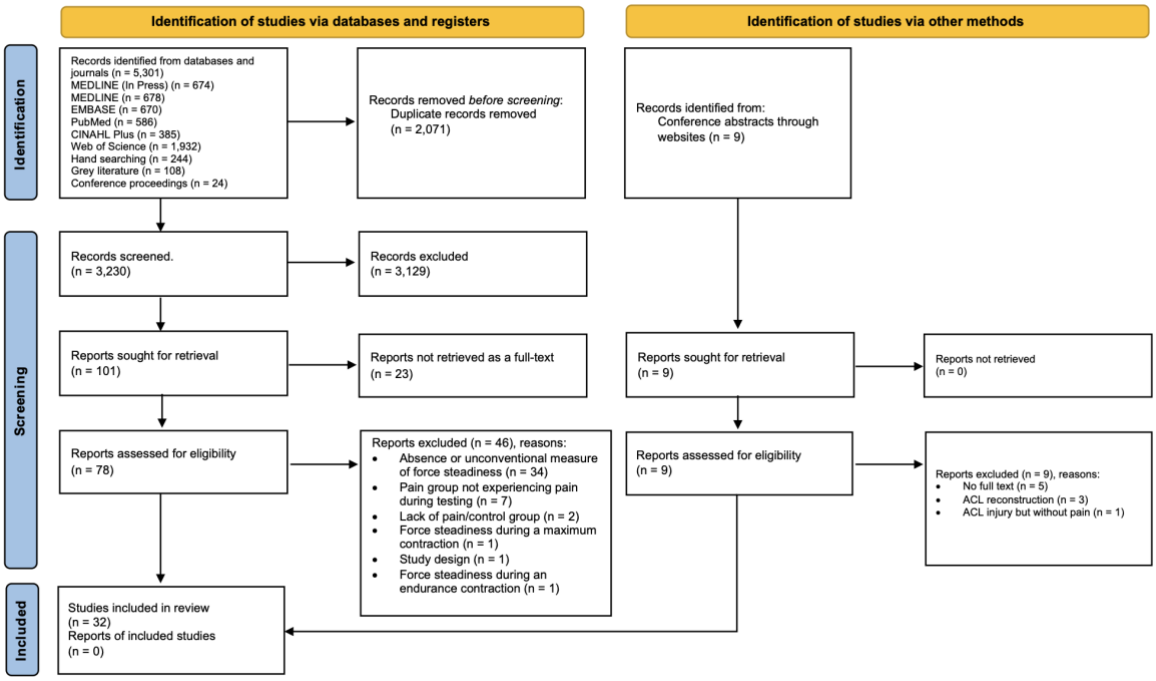


Figure 5.1: ***PRISMA flow diagram, adapted from (Page et al., 2021).***

5.4.2 Characteristics of included studies

This review included 32 studies (19 clinical pain, 13 experimental pain), and their characteristics are summarised in **Table *5.1*** and **Table *5.2***. Most studies used CoV and/or SD of force to quantify force steadiness, while only a few used other measures such as SampEn and ApEn for force complexity and RMS for force steadiness.

Clinical pain studies. Nineteen studies investigated the impact of clinical pain on force steadiness. These involved a total of 756 participants, of whom 402 were experiencing

musculoskeletal pain and the rest being asymptomatic controls. Specifically, from these nineteen studies, five assessed force steadiness at the jaw (n=69; CNP, chronic jaw pain, and temporomandibular disorders; TMDs) (Testa et al., 2017, Testa et al., 2015, Testa et al., 2018, Wang et al., 2020, Wang et al., 2018), three at the shoulder (n=76; subacromial impingement syndrome (Bandholm et al., 2006, Camargo et al., 2009, Overbeek et al., 2020) and another three for the lower back (n=49, CLBP) (Arvanitidis et al., 2022, Arvanitidis et al., 2024c, Miura and Sakuraba, 2014). Additionally, two studies assessed force steadiness at the neck (n=28; CNP) (Falla et al., 2010, Muceli et al., 2011), another two at the knee (n=50, OA) (Ferreira et al., 2021, Hortobágyi et al., 2004) and another two at the hand or wrist (n= 81; OA) (Magni et al., 2021, Mista et al., 2018). Finally, one study focused on the ankle (n=34; insertional Achilles tendinopathy, IAT) (Crowley et al., 2022) and another one on the elbow (n=15; chronic lateral epicondylitis; CLE) (Chen et al., 2023). The average age of participants ranged from 21 to 70 years, while the pain intensity scores reported by the patients ranged from 0.8 to 7.1 out of 10 (NPRS or VAS).

Thirteen of these studies reported a significant decline in force steadiness in the presence of pain (Arvanitidis et al., 2022, Arvanitidis et al., 2024c, Bandholm et al., 2006, Chen et al., 2023, Falla et al., 2010, Ferreira et al., 2021, Hortobágyi et al., 2004, Magni et al., 2021, Miura and Sakuraba, 2014, Muceli et al., 2011, Testa et al., 2018, Wang et al., 2020, Wang et al., 2018). However, five studies observed no significant differences between those with and without pain (Camargo et al., 2009, Crowley et al., 2022, Mista et al., 2018, Testa et al., 2017, Testa et al., 2015), and one study (Overbeek et al., 2020) observed greater force steadiness in those with shoulder pain during shoulder abduction contractions, whereas no significant difference was observed during shoulder adduction. Notably, two of the five studies (Testa et al., 2017, Testa et al., 2015) which found no significant differences, specifically investigated jaw clenching

steadiness in individuals with neck pain, however, when the same research group specifically assessed jaw clenching force steadiness in a cohort of individuals with TMDs, i.e., where the pain was task-specific, a significant difference was observed.

Experimental pain studies. Thirteen studies involving a total of 174 participants were evaluated to investigate the effect of experimental pain on force steadiness. For 12 studies, hypertonic saline was the experimental pain model used, and one further study (Del Santo et al., 2007) used ascorbic acid. Four studies assessed the effect of experimental pain on knee force steadiness (n=61) (Poortvliet et al., 2019, Rice et al., 2015, Salomoni et al., 2013, Smith et al., 2021) and two on the ankle (n=30) (Martinez-Valdes et al., 2021, Martinez-Valdes et al., 2020). One study assessed the low back (n=12) (Hirata et al., 2015), one the shoulder (n=9) (Bandholm et al., 2008), one the elbow (n=12) (Mista et al., 2015) and one the fifth finger (n=11) (Farina et al., 2012). Additionally, three of these studies investigated the effect of experimentally induced pain on force steadiness in various regions. One study evaluated this at the elbow and fifth finger (n=8) (Del Santo et al., 2007), another one at the ankle, elbow and knee (n=15) (Salomoni and Graven-Nielsen, 2012), and a third one at the fifth finger and ankle (n=16) (Yavuz et al., 2015). Most of these studies (10 out of the 13) (Bandholm et al., 2008, Del Santo et al., 2007, Farina et al., 2012, Martinez-Valdes et al., 2021, Mista et al., 2015, Poortvliet et al., 2019, Rice et al., 2015, Salomoni et al., 2013, Salomoni and Graven-Nielsen, 2012, Yavuz et al., 2015) observed reductions in force steadiness when experimental pain was induced. In contrast, three studies found no differences in force steadiness (Hirata et al., 2015, Martinez-Valdes et al., 2020) or torque complexity (Smith et al., 2021) between conditions with or without pain for the same individuals. However, the SD of torque data provided by (Smith et al., 2021), which was included in the meta-analysis, revealed that force steadiness is reduced in the presence of experimental pain when quantified with this variable. The average age of

participants ranged from 22 to 53 years, while the peak pain intensity scores reported by the patients during the task ranged from 2.6 to 6.3 out of 10 (NPRS or VAS scales).

Table 5.1: ***Characteristics of studies examining whether people with clinical pain show differences in force steadiness with respect to asymptomatic controls.***

Study	Patient population characteristics & self-reported measures	Control population characteristics & self-reported measures	Force steadiness task and contraction intensity	Outcome Measure	Results
1. Arvanitidis et al., 2022	**15 CLBP participants** (7M, 8F, 27.1 ± 9.3 years, 69.3 ± 10.1 kg, 169.9 ± 5.7 cm); **Average pain intensity (NPRS, 0-10):** 2.5 ± 2.2; **ODI (%):** 14.9 ± 7.5; **SF-36 (general health score):** 64.1 ± 19.6; **TSK:** 34.7 ± 5.2	**15 asymptomatic controls** (8M, 7F, 27.4 ± 4.9 years, 73.7 ± 10.4 kg, 171.3 ± 5.4 cm); **Average pain intensity (NPRS, 0-10):** 0.0 ± 0.0; **ODI (%):** 0.0 ± 0.0; **SF-36 (general health score):** 89.6 ± 6.8; **TSK:** 28.1 ± 6.0	Isometric trunk extension contractions (90º) at **20%MVC** and **50%MVC**, with visual feedback provided by a monitor placed 1.5 m in front of the participants. Participants seated on an isokinetic dynamometer (Biodex System 3 Pro).	**SD (%), CoV (%)**	↓ torque steadiness in people with CLBP (CoV and SD of torque, main effect of group: *F = 5.327, P = 0.029, ηp^2 = 0.160 and F = 4.368, P = 0.046, ηp^2 = 0.135* respectively).
2. Arvanitidis et al., 2024c	**20 CLBP participants** (10M, 10F, 31.1 ± 6.9 years, 75.3 ± 18.4 kg, 170.6 ± 9.9 cm); **Average pain intensity (NPRS, 0-10):** 3.8 ± 1.6; **ODI (%):** 21.5 ± 13.4; **SF-36 (general health score):** 58.0 ± 19.2; **TSK:** 36.6 ± 7.4	**20 asymptomatic controls** (10M, 10F, 28.6 ± 3.9 years, 70.6 ± 13.4 kg, 171.9 ± 7.4 cm); **Average pain intensity (NPRS, 0-10):** 0.0 ± 0.0; **ODI (%):** 0.0 ± 0.0; **SF-36 (general health score):** 81.5 ± 9.8; **TSK:** 24.8 ± 4.4	Concentric and eccentric trunk flexion and extension contractions on an isokinetic dynamometer (Biodex System 3 Pro). Total ROM: 50º. Four contractions at **25%MVC** and three at **50%MVC**, with visual feedback provided by a monitor placed 1.5 m in front of the participants.	**SD (%), CoV (%)**	↓ **trunk extension** torque steadiness in people with CLBP (CoV and SD of torque, condition effect: *MD = 2.05%, F = 40.01; MD = 0.60%, F = 25.31*, respectively; *P < 0.0001* for both). This was evident during both the eccentric and concentric contractions, and at both low and high torque levels. ↓ **trunk flexion** torque steadiness in people with CLBP (CoV and SD of torque, condition effect, *F = 41.11, MD = 3.36%; F = 53.31, MD = 1.31%*, respectively; *P < 0.0001* for both). This was evident during both the eccentric and concentric contractions, and at both low and high torque levels.
3. Bandholm et al., 2006	**Nine participants with SIS** (28.2 ± 5.3 years; range, 21–38 years; physically active despite shoulder pain); **Mean duration of symptoms:** 27.6± 27.7 (range, 5–72 months); **Pain intensity during contractions (VAS, 0-10): ISO TF20:** 1.8 ± 1.3, **ISO TF27.5:** 2.1 ± 1.4, **ISO TF35:** 2.4 ± 2.1; **DYN TF20:** 2.5 ± 1.2, **DYN TF27.5:** 2.9 ± 2.0, **DYN TF35:** 3.6 ± 2.3.	**Nine asymptomatic controls** (27.7 ± 4.2 years; range, 22–37 years)	Isometric (90º), isokinetic (DYN, 30-120 at 15 /s) shoulder abduction contractions on an isokinetic dynamometer (Kin-Com) with an oscilloscope placed 1 m away from their seat. Seated, with dominant arm at 90 elbow flexion, neutral lower arm. TFs: **20, 27.5, 35%MVC**.	**SD(N), CoV (%)**	↓ reduced force steadiness in people with SIS at 35%MVC during concentric contractions for both SD and CoV of force (*P<0.05* and *P=0.03*). No differences during isometric contractions.
4. Camargo et al., 2009	**27 participants with unilateral SIS** (33.48 ± 9.94 years; 9F, 18M); Dominant involved side (**N**=17), Nondominant involved side (**N**=10); **Duration** of shoulder pain (self-reported): 31.31 ± 33.09 months; **DASH questionnaires: SIS (Dominant side):** 22.64 ± 17.53 (1.66–50.83); **SIS**	**23 asymptomatic controls** (32.26 ± 9.04 years; 8F, 15M); **DASH questionnaire:** 0.98 ± 1.79 (0.00–5.83)	Isometric shoulder abduction (80º) on an isokinetic dynamometer from a seated position. Torque steadiness was assessed at **35% MVC**. Visual feedback was provided via a monitor. The SIS group was divided into two groups: (1) SIS with the dominant	**SD (N), CoV (%)**	No changes in shoulder abduction torque steadiness in individuals with SIS (SD, CoV; *P>0.05*).

	(Nondominant involved): 18.00 ± 12.47 (6.66–44.16)		involved side and (2) the nondominant involved side		
5. Chen et al., 2023	**15 people with CLE** (10M, 5F, 46.5 ± 6.3 years, 75.7 ± 13.1 kg, 168.3 ± 8.2 cm); **Pain intensity (VAS, 0-10):** 7.1 ± 1.8; **DASH score:** 35.1 ± 16.1.	**15 asymptomatic controls** (10M, 5F, 45.3 ± 2.5 years, 75.1 ± 14.9 kg, 169.1 ± 6.1 cm); **Pain intensity (VAS, 0-10):** N/A; **DASH score:** N/A.	Isometric wrist extension against a force sensor (Model: MB-100, Interface Inc., Scottsdale, AZ, United States). Visual feedback provided by a monitor. TF: up to **75%MVC** (8s ramp-up and 8s ramp-down). Each participant performed three trials.	**SampEn, RMS**	↓ reduced force steadiness (RMS, ramp-up phase), in people with CLE RMS (*P = 0.001*). No differences when measured as SampEn during the ramp-up phase (*P = 0.226*).
6. Crowely et al., 2022	**34 men with IAT** (age 43.7 ±10.02 years, weight 89.6 ± 16.3 kg); **VISA-A (0-100):** 54.1 ± 16.6; **Pain catastrophizing scale:** 12.6 ± 11.2; **TSK:** 36.4 ± 6.6; **Single leg calf raise pain (NPRS):** 2.8 ± 2.3	**34 healthy men** (age 42.8 ± 8.9 years, weight 87.2 ± 9.7 kg)**; VISA-A (0-100):** 97.7 ± 0.5; **Pain catastrophizing scale:** 5.2 ± 6.8; **TSK:** 29.7 ± 7.2;	Isometric plantar flexion (0º dorsiflexion; knee flexed to 50◦) on a custom designed chair with foot plates. Isometric plantar flexion contractions at **10%MVC.** Real-time force output displayed on a monitor.	**CoV (%)**	No between group differences were found for plantarflexor force steadiness (*P=0.09, d = 0.44*).
7. Falla et al., 2010	**Nine women** (age, mean ± SD: 40.4 ± 3.5 years; height: 170.8 ± 5.5 cm; weight: 73.7 ± 10.1 kg) with **chronic, non-traumatic neck pain** greater than 3 months (years, mean ± SD: 12.3 ± 11.1; range: 1–33); **NDI (0-50):** 16.5 ± 8.8 (range: 5–31); **Average pain intensity rated on VAS (0-10):** 4.3 ± 1.5 (range: 2.0–6.9).	**Nine women** were recruited as **controls** (age, mean ± SD: 35.4 ± 7.5 years; height: 164.8 ± 7.7 cm; weight: 65.0 ± 12.3 kg).	Isometric neck contractions (seated) in 8 different angles and circular neck contractions (45 intervals) 0-360º with a load of **15 and 30N**. Circular contractions in the horizontal plane at **15 and 30 N** force, from 0 to 360 were also performed (clockwise, and counterclockwise). Real-time visual feedback was provided via an oscilloscope.	**CoV (%)**	↓ reduced force steadiness in people with neck pain (CoV) during brief constant force contractions and circular contractions performed at 30 N *(P = 0.03; SNK P = 0.002*).
8. Ferreira et al., 2021	**30 people with PFP** **Age(years):** 21.26 ± 3.06; **Body mass (kg):** 62.66 ± 10.61; **Height (m):** 1.62 ± 0.05; **BMI:** 23.80 ± 3.86; **Worst pain level in the last month, VAS (0-100):** 51.67 ± 16.15; **Pain level during knee extension - VAS (0-100):** 28.00 ± 19.93; **Pain level during hip abduction, VAS (0-100):** 23.66 ± 26.45; **Symptoms duration (months):** 60.53 ± 54.01	**30 asymptomatic controls** **Age(years):** 22.10 ± 2.78 **Body mass (kg):** 57.66 ± 8.76 **Height (m):** 1.61 ± 0.06 **BMI:** 22.15 ± 3.07	Knee extensor and hip abductor force steadiness on an isokinetic dynamometer (Biodex System 4 Pro). **Knee extension:** seated, with the hip and untested knee stabilized at 90 flexion. Knee joint angle of 60 flexion during testing. **Hip abduction:** side-lying, with untested hip and knee flexed and fixed. Hip abductor testing was done at 20 hip abduction. Submaximal isometric force target set at **10%MVC.** Real-time visual feedback provided via a monitor.	**CoV (%)**	↓ reduced knee extensor and hip abductor isometric force steadiness in women with PFP (*Cohen's d=2.04; 95% CI=[5.25, 8.82]* and *Cohen's d=2.35; 95% CI [10.98, 17.18]*, respectively).
9. Hortobagyi et al., 2004	**20 Participants with OA** (**N**= 15F, 5M), **Age (years):** 57.5 ± 7.3 (43-68), **Mass (kg):** 86.8 ± 18.3 (62-110), **Height (m):** 1.64 ± 0.09 (1.50-1.82), **BMI (kg/m^2):** 29.3 ± 3.2 (24-35); Level of pain for the week before testing (mean ± SD: 1.87 ± 0.32), immediately before (1.96 ± 0.38), and immediately after (1.86 ± 0.29) the testing session (0-4 scale, where 0= no pain, 4 = excruciatingly painful).**Level walking:** 17.6 ± 2.1 s; **Stair descent:** 10.2 ± 2.3 s; **Stair ascent:** 12.8 ± 3.2 s; **Get-up-and-go:** 9.3 ± 1.1s; **Mean:** 12.5 ± 2.2 s	**20 asymptomatic controls** (**N**= 15F, 5M), **Age (years):** 56.8 ± 5.0 (45-66), **Mass (kg):** 81.2 ± 12.5 (60-96), **Height (m):** 1.67 ± 0.07 (1.52-1.83), **BMI (kg/m^2):** 28.3 ± 3.0 (23-33) No knee pain. **Level walking:** 11.5 ± 1.1 s; **Stair descent:** 5.8 ± 0.9 s; **Stair ascent:** 7.2 ± 0.8 s; **Get-up-and-go:** 5.7 ± 0.7 s; **Mean:** 7.6 ± 0.9 s;	Knee extension steadiness tasks on an isokinetic dynamometer (KinCom). Three types of contractions: eccentric, concentric and isometric. Seated position, the dominant leg was tested. Steadiness tasks using TFs of 50N and 100N. During testing, real-time visual feedback for the force output was provided to all participants on a computer monitor.	**SD (N)**	↓ quadriceps force steadiness in people with knee OA during DYN contractions. OA patients were unsteady at both 50-N and 100-N TFs. No reductions observed during isometric contractions.
10. Magni et al., 2021	**62 participants with symptomatic hand OA**	**26 asymptomatic controls**	Grip and pinch isometric force steadiness tasks from a seated position using a digital	**SD (%), CoV (%)**	↓ **grip** force steadiness **(SD and CoV of force**; group main effects, *F1,85 =*

	Age (years): 70 ± 8.5, **Mass (kg):** 69.5 ± 15.3, Height (m): 1.65 ± 0.1, **BMI (kg/m^2):** 25.4 ± 4.9; **DASH:** 28.4 ± 15.9; **FIHOA:** 8.3 ± 5.6; **Bilateral hand pain, n (%):** 13 ± 21.0; **Number of painful joints, n:** 5.1 ± 3.9; **Average hand pain, NPRS (0-10):** 4.2 ± 2.2; **Duration of pain, years:** 9.5 ± 9.1	**Age (years):** 70 ± 11.5, **Mass (kg):** 70.8 ± 15.2, **Height (cm):** 1.66 ± 0.08, **BMI (kg/m^2):** 25.4 ± 4.4	hand and pinchmeter dynamometer (Biometric Ltd). The TF was set at **50%MVC**.		*20.4; P < 0.0001* and *F1,85 = 12.8; P < 0.01*, respectively). ↓ **pinch** force steadiness **(SD and CoV of force**; group main effects, *F1,85 = 6.4; P < 0.05* and F1,85 = 6.4; *P < 0.05*, respectively).
11. Mista et al., 2018	**19 Chronic elbow pain patients,** 57 % women, **Age:** 41 ± 11 years, **Weight:** 70.0 ± 16.4 kg, **Height:** 166.3 ± 2.3 cm; **Epicondyle PPT, N:** 15.8 ± 8.7, **TA PPT, N:** 57.4 (20.2), **DASH (0-100):** 25.0 (15.6); **Mean (SD) VAS scores (0-10) after isometric wrist extension: 5%MVC:** 0.8 ± 0.2; **30%MVC:** 1.7 ± 0.4; **50%MVC:** 4.7 ± 0.4; **70%MVC:** 6.2 ± 0.4.	**21 asymptomatic controls,** 55 % women, **Age:** 37 ± 13 years, **Weight:** 68.9 ± 12.5 kg, **Height:** 161.5 ± 8.3; **Epicondyle PPT, N:** 35.8 ± 11.5, **TA PPT, N:** 71.5 ± 18.8; **DASH (0-100):** 0.7 ± 2.4; **Mean (SD) VAS scores (0-10) after isometric wrist extension: 5%MVC:** 0.0 ± 0.2; **30%MVC:** 0.0 ± 0.4; **50%MVC:** 0.0 (0.4); **70%MVC:** 0.2 (0.4)	Isometric wrist extension using a six-axis load cell transducer. Seated upright in a chair with their back resting against a backrest and the shoulder at 90^o, participants performed two sets of isometric wrist extension at **5, 30, 50, and 70% MVC**. Force was presented in real-time on a computer screen.	**SD (N)**	No significant differences in force steadiness, between patients and controls.
12. Miura et al., 2014	**14 individuals with NSLBP** **Age (year):** 21.1 ± 1.1, **Height (cm):** 172.2 ± 5.5, **Weight (kg):** 62.2 ± 4.4 **BMI:** 21:0 ± 1.9 **VAS scale pain intensity** > 3/10.	**14 asymptomatic controls** **Age (year):** 21.6 ± 2.3 **Height (cm):** 173.8 ± 5.3 **Weight (kg):** 65.5 ± 5.6 **BMI:** 21:7 ± 2.0	Isometric trunk extension using a force transducer (TU-BR, TEAC). The TFs were performed in a random order with three trials at each of **2, 5, 10, 15, 20, 30, 50, 70, 80 and 90% of MVC** force. A visual display was positioned 50 cm away from the face of the participants.	**SD (N)** **CoV (%),**	↓ isometric trunk extension force steadiness in NSLBP (**CoV of force**; main effect of group, *F1,26=4.698, P<0.05*). Specifically, CoV of the NSLBP group was higher than that of the controls at 30% and 50%MVC. No between- group differences for **force SD** (*F1,26=0.787, P=0.383*).
13. Muceli et al., 2011	**19 people with CNP** ***Exp 1 included nine women*** (age, mean ± SD: 40.4 ± 3.5 years; height, 171.1 ± 10.6 cm; body mass, 73.4 ± 10.6 kg); ***Exp 2 included 10 women*** (age, mean ± SD: 35.3 ± 7.5 years; height, 169.7 ± 7.4 cm; body mass, 72.2 ± 8.5 kg), Different individuals for each experiment. ***Exp1:*** **Onset (idiopathic trauma %trauma:** 33.3%; **Length of history (years):** 13.6 (10.2); **NDI (0-50):** 14.8 ± 8.6; **Average pain (VAS, 0-10):** 4.4 ± 1.7; ***Exp2:*** **Onset (idiopathic trauma %trauma:** 80.0%; **Length of history (years):** 7.6 ± 5.3; **NDI (0-50):** 24.8 ± 7.2; **Average pain (VAS, 0-10):** 6.0 ± 1.4; Values are reported as **mean ± SD.**	**19 asymptomatic controls** ***Exp 1 included nine healthy women*** (age, mean ± SD: 38.9 ± 10.5 years; height, 165.4 ± 8.2 cm; body mass, 63.6 ± 10.7 kg) ***Exp 2 included 10 healthy women*** (age, mean ± SD: 35.4 ± 8.9 years; height, 168.1 ± 5.1 cm; body mass, 66.5 ± 11.8 kg) as controls. Different individuals for each experiment. No history of pain.	Participants underwent isometric cervical flexion with their head secured in a device that provided resistance through a force transducer. Seated with supported backs, knees, and hips at 90 degrees, and torsos strapped to the seat, participants executed isometric neck contractions at either **15 N** (***Exp 1***) or **25%MVC** (***Exp 2***) for 10 seconds. The desired force output was shown on an oscilloscope placed 80 cm in front of them.	**CoV (%)**	In ***Exp 1***, ↓ cervical flexion force steadiness (**CoV**, main effect of group, *P<0.05*). In ***Exp 2***, the CoV of force depended on the interaction between group and time (*P<0.05*). People with CNP displayed ↓ force steadiness during submaximal sustained contractions compared to the control participants.
14. Overbeek et al., 2020	**40 people with SAPS** **Age, years (mean ± SD):** 50 ± 6.38 **Female (N, %):** 23 (58%), **Right side dominance (N, %):** 35(88%), **Dominant side measured/affected (N, %):** 25(63%), **Duration of complaints (median, IQR):** 18 (12-29) **Clinical scores:** **VAS (0-100) for pain in rest:** 19 ± 20 **VAS (0-100) for pain during movement:** 39 ± 24 **Constant Score:** 70 ± 13	**30 asymptomatic controls** **Age, years (mean, SD):** 51 ± 5.71, **Female (N, %):** 17 (57%), **Right side dominance (N, %):** 25(83%), **Dominant side measured/affected (N, %):** 17(57%); **Duration of complaints (median, IQR):** N/A; **VAS for pain in rest:** 2.1 ± 1.7; **VAS for pain during movement (0-100):** 2.0 ± 1.6	Isometric shoulder abduction and adduction using a 1D force transducer at the wrist. Isometric shoulder ab- and adduction contractions from a standing position, facing a computer for force feedback, with the target arm in external rotation at the side attached to a 1D force transducer at the wrist. The TF was similar for both abduction and adduction and equal to **60%MVC**	**CoV (%), SD (N)** and **ApEn**	Better shoulder abduction force steadiness in people with SAPS **SD of force** (group-difference: *-0.006 N (CI [−0.011; −0.001], P=0.013*) and CV (group-difference: *-0.51 (CI [−0.93; −0.10], P=0.016*). No differences in magnitude of variability were observed during adduction. Patients with SAPS had lower ApEn-values during the abduction task *(−0.16, 95%*

		Constant Score: 94 ± 4.1 Controls were recruited under a separate protocol.	(defined as the lowest absolute value of the MVC in abduction or adduction).		*CI [−0.33; −0.00], P=0.048)* and adduction task *(−0.20, 95% CI [−0.37; −0.03], P=0.024*).
15. Testa et al., 2017	**12 people with neck pain** **Age(years):** 28.2 ± 6.2, **Sex(%female):** 75, **Weight:** 64.8 ± 7.7, **Height:** 174 ± 11.6, **Duration of pain (months):** 60.8 ± 63.7, **Current Pain Intensity (NPRS, 0-10):** 5.1 ± 1.6, **NDI: (%):** 21.9 ± 7.5; ***SF-36:*** **Physical:** 47.4 ± 5.5, **Mental:** 47.8 ± 10.8; **TSK:** 30 ± 5, **STAI:** 47 ± 6	**12 controls** **Age(years):** 27.2 ± 6.5 **Sex(%female):** 75 **Weight:** 63.4 ± 11.9 **Height:** 169.3 ± 7.2	Submaximal isometric bilateral jaw clenching contractions using two force transducers. Participants were seated, hips and knees in 90 of flexion and their feet flat on the floor. Bilateral bite force was displayed in real time on the PC monitor. Contraction level: **10, 30, 50, and 70% MVC**. Contractions were performed both with and without visual feedback (total: 32 submaximal contractions).	**SD (%), CoV (%)**	No differences in force steadiness between the two groups were observed for the **SD and CoV of force**.
16. Testa et al., 2015	**10 people with neck pain** **Age(years):** 28.9 ± 6.0, **Sex(%female):** 70, **Weight:** 64.8 ± 7.9, **Height:** 175.2 ± 11.4, **Duration of pain (months):** 67 ± 64.5, **Current Pain Intensity (NPRS, 0-10):** 5.2 ± 1.5, **NDI (%):** 22.5 ± 7.1; ***SF-36:*** **Physical:** 46.5 ± 5.3, **Mental:** 47.6 ± 11.0; **TSK:** 29.2 ± 5.0; **STAI:** 48.7 ± 5.8	**10 controls** **Age(years):** 27.2 ± 5.8 **Sex(%female):** 70, **Weight:** 63.9 ± 11.6, **Height:** 170.0 ± 7.0	Submaximal isometric unilateral jaw clenching contractions. The experimental setup was same as in the study above (study 13). The experimental procedure then involved matching four force targets, representing **10%, 30%, 50%, and 70% of MVC**. Participants performed these four contractions on both the right and left sides.	**SD (%)**	No differences in force steadiness between groups (*P>0.05*).
17. Testa et al., 2018	**12 individuals with TMD** **Age(years):** 30.9 ± 7.4, **Sex(%female):** 75, **Weight:** 62.9 ± 10.5, **Height:** 169.1 ± 8.7; **Duration of pain (months):** 69.6 ± 37.6; **Current pain intensity (NPRS, 0-10):** 1.6 ± 1.5; **Side of the greatest pain (Right, Left, %):** 58.4, 41.6; **Bilateral pain (%):** 75; **JPF (%):** 13.4 ± 5.4; **NDI (%):** 17.6 ± 7.0; **TSK:** 28.0 ± 530; **PCS:** 9.3 ± 11.1	**12 asymptomatic controls** **Age(years):** 31.4 ± 7.9 **Sex(%female):** 75 **Weight:** 66.0 ± 9.2 **Height:** 171.9 ± 9.1	Submaximal isometric unilateral jaw clenching contractions. A flexible piezoresistive force transducer was used. For the patient group, the painful and non-painful side were considered and in the case of bilateral symptoms, the side with the greatest pain intensity was considered as the painful side (i.e., both sides were assessed). Same experimental set-up as in the studies above (13 and 14). Participants performed contractions to match force targets representing **10, 30, 50 and 70% of MVC**. All participants performed the contractions with and without visual feedback (four contractions for feedback, no feedback conditions and both sides).	**SD (%)**	↓ force steadiness was observed in people with myogenic TMD. The SD of force was dependent on the interaction between group and matched side *($\chi^2(1)=4.21$, P=0.04)*. The multiple comparisons revealed that the SD of the most painful side of the patient group *(SD=4.89, 95% CI=3.48–6.90)* was significantly higher than the matched side (response ratio=*0.66*, *t ratio=−3.28, P<0.01*) and the unmatched side (*response ratio=1.34*, *t ratio=2.69, P<0.05*) of the control group.
18. Wang et al., 2020	**18 people with jaw pain** **Age:** 32.78 ± 10.84, **Gender:** 5M, 13F; **Duration of pain (months):** 84.83 ± 71.94, *P=0.00*; ***JFLS-20:*** **Mastication (0–60):** 15.06 ± 8.23, *P=0.00*; **Jaw mobility (0–40):** 9.56 ± 5.90, *P=0.*00; **Emotional and verbal expression (0–80):** 6.44 ± 7.23, *P=0.00*; ***GCPS:*** **Disability days (last 6 months):** 109.61 ± 66.64, *P=0.00*; **Characteristic pain intensity (0–100):** 44.63 ± 18.81, *P=0.*00; **Disability score (0–100):** 17.41 ± 19.35, *P=0.00*;	**16 asymptomatic controls** **Age:** 31.31 (10.85), **Gender:** 6M, 10F; **Duration of pain (months):** 0.0 ± 0.0; ***JFLS-20:*** **Mastication (0–60):** 0.25 ± 1.00; **Jaw mobility (0–40):** 0.0 ± 0.0; **Emotional and verbal expression (0–80):** 0.0 ± 0.0; ***GCPS:*** **Disability days (last 6 months):** 0.0 ± 0.0; **Characteristic pain intensity (0–100):** 0.0 ± 0.0; **Disability score**	Submaximal isometric jaw clenching force steadiness tasks (custom-built force transducer). Sitting position, with the bite plates held between the upper row and lower row of teeth in the mouth with the base of the device mounted on a table. Real-time feedback of the force performance was provided. Two targets: a low force level	**SD (%), CoV (%)**	↓ force steadiness in people with chronic jaw pain (**SD and CoV of force**; main effect of group: *P=0.03* for both).

	OBC (0–100): 27.56 ± 8.79, *P=0.00*; **Pain rating during the tasks (VAS, 0-10) at low force:** 2.84 ± 2.17, **high force:** 4.47 ± 2.37. **Mean ± SD** values.	**(0–100):** 0.0 ± 0.0; **OBC (0–100):** 12.06 ± 9.69; **Pain rating during the tasks (VAS, 0-10) at low force:** 0.23 ± 0.32, **high force:** 0.57 ± 0.86. **Mean ± SD** values.	(**2%MVC,** and moderate force level (**15% MVC**). Trials were split into four blocks of 24 trials. Each block consisted of 12 low force trials and 12 moderate force trials. Each participant therefore completed a total of 48 low force trials and 48 moderate force trials.		
19. Wang et al., 2018	**17 people with jaw pain** **Age:** 33.53 ± 12.65; **Gender:** 5M, 12F; **Duration of pain (years):** 9.56 ± 9.55, *P<0.05*; ***JFLS-20:*** **Mastication (0–10):** 2.26 ± 1.37, *P<0.05*; **Jaw mobility (0–10):** 2.34 ± 1.88, *P<0.05*; **Emotional and verbal expression (0–10):** 0.91 ± 1.65, *P<0.05*; **Global score (0-10):** 1.84 ± 1.48,*P<0.05*;**OBC (0–100):** 31.94 ± 7.49, *P<0.05*; ***GCPS:*** **Disability days (last 6 months):** 86.82 ± 53.09, *P<0.05*; **Characteristic pain intensity (0–100):** 42.84 ± 15.02, *P<0.05 ;***Interference score (0-100):** 14.41 ± 17.02, *P<0.05*; **Low force level pre-task pain intensity:**19.16 ± 15.8 and **high force level:** 17.77 ± 16.6 **(VAS,0-100)**. **Mean ± SD** values.	**19 asymptomatic controls** **Age:** 29.16 ± 10.43, **Gender :** 8M, 11F; **Duration of pain (years):** 0.00 ± 0.00, ***JFLS-20:*****Mastication (0–10):** 0.05 ± 0.17;**Jaw mobility (0–10):** 0.05 ± 0.23; **Emotional and verbal expression (0–10):** 0.00 ± 0.00; **Global score (0-10):** 0.04 ± 0.13; **OBC (0–100):** 15.18 ± 7.90; ***GCPS:*** **Disability days (last 6 months):** 0.05 ± 0.23; **Characteristic pain intensity (0–100):** 1.40 ± 3.35; **Interference score (0-100):** 0.00 ± 0.00; **Pre-task pain intensity at low:** 1.59 ± 3.1, **high:** 1.81 ± 3.0 **force level (VAS, 0-100)**. **Mean ± SD** values.	Submaximal isometric jaw clenching force steadiness tasks. Supine position, with the bite plates held between the upper row and lower row of teeth in the mouth with the base of the force transducer device resting on the chest. A custom-built LabVIEW software sampled the force signal and displayed it as a green bar on a magnetically shielded display, which was visible to the participant via a mirror, providing the participant with real-time feedback of their force performance. Two runs of experimental trials, each consisting of 5 trials with alternating force production at low force level (**2% of MVC**) and at high force level (**15% of MVC)**.	**SD (%), CoV (%)** and **ApEn**	↓ force steadiness in the chronic jaw pain group (**SD and CoV of force**; main effect of group, *P<0.05*). No differences for ApEn between the two groups (*P>0.05*).

ApEn: Approximate Entropy; **CI:** Confidence Interval; **CLBP:** Chronic Low Back Pain; **CLE:** Chronic Lateral Epicondylitis; **CNP:** Chronic Neck Pain; **CoV:** Coefficient of Variation; **DASH:** Disabilities of the Arm, Shoulder and Hand; **DYN:** Dynamic; **F:** Females; **FIHOA:** Functional Index of Hand Osteoarthritis; **GCPS:** Graded Chronic Pain Scale; **IAT:** Insertional Achilles Tendinopathy; **ISO:** Isometric; **IQR:** Inter-quartile Range; **JFLS-20:** Jaw Functional Limitation Scale; **JPF:** Jaw Pain and Function; **M:** Males; **MVC:** Maximal Voluntary Contraction; **N/A:** Not Applicable; **NDI:** Neck Disability Index; **NSLBP:** Non-specific Low Back Pain; **NPRS:** Numeric Rating Scale; **OA:** Osteoarthritis; **OBC:** Oral Behavioural Checklist; **ODI:** Oswestry Disability Index; **PFP:** Patellofemoral Pain Syndrome; **PCS:** Pain Catastrophizing Scale; **PPT:** Pressure Pain Threshold; **RMS:** Root Mean Square; **ROM:** Range of Motion; **SAPS:** Sub-Acromial Pain Syndrome; **SD:** Standard Deviation; **SF-36:** 36-Item Short Form Health Survey; **SIS:** Shoulder Impingement Syndrome; **STAI:** State-Trait Anxiety Inventory; **TMD:** Temporomandibular Disorder; **TSK:** Tampa Scale Of Kinesiophobia; **TF:** Target Force; **VAS:** Visual Analogue Scale.

Table 5.2: ***Characteristics of studies examining the effects of experimental pain on force steadiness.***

Study	Population characteristics	Characteristics of pain	Force steadiness task and contraction intensity	Outcome Measure	Results
1. Bandholm et al., 2008	**Nine healthy individuals** (age range: 22 to 37 years; mean age 27.7 years).	**Hypertonic saline (1ml, 6%)** into the supraspinatus muscle. Shoulder pain **(VAS, 0-10)** during **isometric** shoulder abduction contractions:**TF20:** 3.5 ± 1.5, **TF27.5:** 3.2 ± 1.6, **TF35:** 2.8 ± 1.4. Shoulder pain during DYN shoulder abduction contractions: **TF20:** 2.9 ± 1.5, **TF27.5:** 3.1. ± 1.1, **TF35:** 3.8 ± 2.5.	Shoulder abduction contractions, seated position, pre-, during-, and post-pain (after 15 minutes) on an isokinetic dynamometer (Kin-Com KC 125 AP) and an oscilloscope 1 meter from the seat. Isometric (at 90), concentric, and eccentric. DYN contractions: 30-120 at 15 /s. TF: **20, 27.5, and 35%MVC**. Two isometric and three DYN contractions at each MVC level (isometric, 10s hold).	**SD (%)** **CoV (%)**	↓ isometric shoulder-abduction force steadiness (**SD of force**; *F=6.5, P=0.009*). However, no changes in differences when measured as **CoV** *(F=2.9, P=0.087)*. Experimental pain did not have any effect on shoulder-abduction force steadiness during DYN contractions (*P>0.05*).
2. Del Santo et al., 2007	**Eight asymptomatic volunteers** (5M) right-handed participants (mean age 33.86 ± 11.51 years, range 26–53).	**Ascorbic acid** in the ADM muscle belly and the BIC muscle (40 mg in 0.2 ml and 90 mg in 0.5 ml, respectively). Pain time duration of about 10 min. ADM/ average peak-pain on the **VAS scale (0-10) was** 6.25 ± 2.12 at about 1 min after injection. In BIC chemically induced pain generated a cramp-like, localised sensation at muscle belly. Nociceptive sensation lasted about 10 min and peaked at about 2 min after the end of injection (**average peak-pain** was 5.75 ± 0.71; 0-10).	Fifth finger abduction (ADM) and elbow flexion (BIC) isometric contractions from a seated position. ADM's force was measured using a force transducer, with the fifth finger at 10 horizontal abduction. BIC measurement was done with the arm fixed, forearm supine, and wrist neutral. Contractions: pre-, during-, and post. Force level was set at **30%MVC** for both muscles (force transducer: FGP instrumentation, Les Clayes Sous Bois, France). Visual force feedback was provided on-screen.	**CoV (%)**	↓ in force steadiness of the ADM and BIC muscles. Mean **CoV** of the ADM was significantly higher during pain (14.43%±0.30 SE) than in control (11.30%±0.20 SE) (*t=3.23, P=0.008*). Similarly in the BIC, fluctuations of the force were higher during pain stimulation (**CoV**=22.73% ± 0.52 SE) than in control (**CoV**=19.56% ± 0.41 SE).
3. Farina et al., 2012	**11 asymptomatic men** (age 25.1 ± 2.5 years)	**Hypertonic saline (0.5ml, 5.8%)** into the right ADM muscle. The **NPRS (0-10)** score for pain was 4.1 ± 1.8 at the beginning of the painful set of contractions and decreased, although not significantly, to 3.7 ± 2.2 by the end of the set of contractions.	Isometric fifth finger abduction: baseline, isotonic saline, hypertonic saline, and post pain. Isometric contraction at **10% MVC** for 60 s. The TF output was displayed on a PC monitor located 1 m in front of the participant. Adjustable chair with the right arm extended in a force brace. The fifth finger was fixed in the isometric device for measurement of finger abduction forces.	**CoV (%)**	↓ force steadiness after injection of hypertonic saline (**CoV of force**; *F = 5.6, P<0.01; SNK P <0.05*).
4. Hirata et al., 2015	**12 young asymptomatic volunteers** (7M; age: 25 ± 4 years, height: 172 ± 11 cm; weight: 70 ± 13 kg)	**Hypertonic saline (1ml, 5.8%)** injection into the right m. longissimus to induce low-back pain. **Pain intensity (VAS, 0-10):** 2.6 ± 0.4	Six series of submaximal isometric trunk extensions (before, during, and after a painful or non-painful injection). Each series comprised contractions at **5%, 10%, and 20% of MVC** (each lasting 45 seconds). High-sensitivity 3-dimensional force sensor (MC3A, AMTI, USA). Force feedback was displayed on a computer screen.	**SD (N)**	The variability of task-related force was not altered by pain.
5. Martinez-Valdes et al., 2021	**15 asymptomatic volunteers** participated [age 26 (11) years, 9M, 6F].	**Hypertonic saline (0.5 ml, 5.8%)**, into the TA muscle. Pain lasted for the full set of contractions, reaching a peak intensity (**NPRS scale, 0-10)** of mean (SD) 6.3 (1.6) out of 10, 60 s after the hypertonic	Participants were seated on a Biodex System 3 dynamometer and performed isometric ankle dorsiflexion contractions (90º ankle joint angle). They were asked to track sinusoidal torque trajectories at frequencies of **0.25** or **1 Hz** and	**SD (%)** **CoV (%)**	↓ torque variability during the pain condition at the fastest contraction rates when calculated both in terms of **SD** torque (frequency x condition interaction: *P=0.007, η^2=0.267*) and **CoV** torque

		saline injection, with a range between 4.5 (2.2) and 3.3 (1.5) points after the first and last contraction, respectively. Pain was felt on location of injection (TA muscle) and two participants also experienced referred pain to the lateral malleoli and dorsal region of the foot.	amplitudes **of 5 or 10% MVC**. Under four conditions (baseline, isotonic, pain, and post pain), they performed four sinusoidal contractions. Duration of each contraction: 40 seconds. Real-time torque feedback was provided via a computer monitor.		(frequency x condition interaction: *P<0.001, η^2=0.35*).
6. Martinez-Valdes et al., 2020	**15 asymptomatic volunteers** participated in the experiments (age: mean (SD) 26 (3) years, 9M, 6F).	**Hypertonic saline (0.5ml, 5.8%)** into TA muscle. The painful sensation lasted for the full set of contractions, reaching its peak: 6.3 (1.6) 1min after the injection and ceasing completely within 500 s. Pain was consistently felt under the electrode grid by all participants (mainly under the 2nd, 3rd and 4th columns of the grid); however, three participants also experienced referred pain at the lateral malleoli. **NPRS Peak (0-10):** 6.34 ± 1.67 at 60s.	Seated on the chair of a Biodex System 3, with the back flexed at 30 . The right leg (dominant side for all) was positioned over a support, the knee was flexed to 160 (with 180 representing full knee extension), and the foot was fixed to a footplate (90 ankle joint angle). Participants performed ramp-hold contractions at **20** or **70%MVC**. Two contractions were performed at each MVC level (four contractions in total, 10s hold each). Real-time torque feedback was provided via a computer monitor.	**SD (%)** **CoV (%)**	No differences in torque steadiness (average value across conditions: 2.2 (0.2) % at 20% MVC and 2.4 (0.2) % at 70% MVC, *P=0.76* and *P=0.20*, respectively)
7. Mista et al., 2015	**12 right-handed asymptomatic individuals** (8M, age 25 ± 5 years; height 171 ± 9 cm; weight 67 ± 10 kg, mean ± SD) participated in the study.	**Hypertonic saline (1 ml, 5.8%)** into the long head of the right BIC. **VAS (0-10) mean scores:** 3.5 ± 0.5 cm	Isometric elbow flexion contractions against a 3D force transducer. Contractions were performed using two types of visual feedback: (1) 1D displaying only the task-related force component (i.e. elbow flexion force), and (2) 3D displaying the three force components. Contractions (20 s) using 1D and 3D feedback at **5%, 15%, and 30% MVC** were performed pre, during, and after experimental pain.	**Normalised SD, SampEn**	↓ in task-related and tangential elbow flexion force variability during the 1D feedback (NK: *P<0.033)*. Post hoc analysis also revealed an increased force complexity during muscle pain and post-pain compared with baseline (*NK P<0.012*).
8. Poortvliet et al., 2019	**17 asymptomatic adults** (33 ± 6 years, 14M)	**Hypertonic saline (0.25 ml, 5%)** into the infrapatellar fat pad of the test leg. Overall **pain intensity** reported during the contractions after hypertonic saline injection was: 4.1 ± 1.3/10. (Majority with **NPRS**, 0-10)	Isometric knee extension at **10%MVC**. Participants were in supine, with the knee and hip flexed to 90 . A force gauge attached via an adjustable cable between the ankle and table was used.	**SD (N)**	↓ isometric knee extension force steadiness Fluctuations of force around the target were (no-pain: 1.51 ± 0.49-pain: 1.95 ± 0.66; *t-test P<0.001*).
9. Rice et al., 2015	**15 asymptomatic individuals** (mean age 28 years, range 18–49 years; 8F). One participant had an adverse effect. Data collected from 14.	**Hypertonic saline (1ml, 5.8%)** into the infrapatellar fat pad. The average peak pain rating **(NPRS, 0-10)** following the injection was 5.5 ± 2.1 and lasted 18 ± 4 minutes after needle withdrawal.	Isometric knee extension, eccentric and concentric force steadiness contractions against a dynamometer (Biodex Medical Systems Inc, Shirley, New York, USA). For each contraction, the target was set at 1**0%MVC**. A monitor was used to show the actual knee extensor force to the participants.	**SD (N)**	↓ knee force steadiness (**force SD**) during pain compared with baseline (*P=0.02*) and with post pain (*P<0.001*). The interaction effect between contraction and pain was not significant (*F4,52 = 2.9; P=0.06*).
10. Salomoni et al., 2013	**15 asymptomatic volunteers** (12M, age 27.1 ± 4.6 years, height 175.1 ± 7.9 cm, weight 71.9 ± 13.8 kg, mean ± SD)	**Hypertonic saline (1 ml, 5.8%)** into the medial part of the infrapatellar pad of the dominant leg. Peak in **VAS (0-10)** after 1.26 mins, 4.52 ± 0.54 (SEM).	Isometric knee extension contractions (dominant leg) at **2.5, 5, 20, 50, and 80 % of MVC** force. A total of six series of contractions were performed (pre, during and post pain conditions). 3D forces were recorded using a high sensitivity six-axis force sensor, yielding three force and three moment components (MC3A, AMTI, USA)	**CoV (%)**	↓ knee force steadiness (**CoV)** of the task-related force component compared with non-painful assessments [RM-ANOVA: *F(2,8)>10.8, P<0.0003; NK P<0.0005*].

11. Salomoni et al., 2012	**15 asymptomatic individuals** (12M, age 28.3 ± 6.5 years; height 175 ± 10 cm; weight 72.8 ± 12.7 kg; mean ± SD) with no known musculoskeletal disorder participated in this study	**Hypertonic saline (1ml, 6%)** into one agonist muscle of each muscle group: TA for dorsiflexors, brachioradialis for elbow flexors, VM for knee extensors, and GM for plantarflexors. **Peak pain (VAS, 0-10, mean, SEM): Dorsiflexors (1.73 mins):** 4.19 ± 0.61; **Elbow flexors (1.16 mins):** 4.49 ± 0.56; **Knee extensors (1.22 mins):** 4.16 ± 0.44; **Plantarflexors(1.66 mins):** 4.39 ± 0.5	Submaximal isometric force steadiness contractions of dorsiflexors, elbow flexors, knee extensors and plantar flexors at **2.5, 20, 50, and 70% of MVC** force. Six series of isometric contractions performed before, immediately after the injection, and after the cessation of any painful effects due to the injection. During all contractions, a computer screen provided a ramp-and-hold TF feedback corresponding to 2 s of ramp phase and 11 s of hold phase. A six-axis force sensor was used to record 3D forces (MC3A 250, AMTI, USA)	**SD (N) CoV (%).**	No significant reductions in force steadiness (**SD of force**), except for a ↓ in knee extension force steadiness during the painful condition at 70% MVC *(F6,78 = 2.4428, P = 0.0323; NK P = 0.0001*). ↓ force steadiness (**CoV of force**) (RM-ANOVA: *F2,26–28 > 4.82, P < 0.015; NK P < 0.03*) during pain for all muscle groups and, except for dorsiflexors, also higher than pre and post injection conditions (*NK P < 0.03*).
12. Smith et al., 2021	**14 asymptomatic and recreationally active participants** (13M, 1F; mean ± SD: age: 25.3 ± 4.5 years; height: 1.78 ± 0.1 m; body mass: 73.9 ± 12.3 kg; physical activity: 5.6 ± 2.2h/week) volunteered to participate in the present study.	**Hypertonic saline (1ml, 5.8%)** into the middle third of the VL of the right leg. Pain intensity was measured with the **VAS scale (0-10)**. **VAS mean:** 3.1 ± 1.0 **VAS peak:** 5.7 ± 1.7 **VAS onset:** 1.7 ± 1.3 **VAS time to peak, s:** 71 ± 24 **VAS duration, s:** 233 ± 60 **VAS area:** 759.8 ± 325.6	Participants engaged in isometric knee extension (right side) torque steadiness tasks using a Cybex HUMAC Norm isokinetic dynamometer at 15% and 20% MVC, with trials conducted both with and without force feedback. Target and actual torques were displayed on a computer. The study comprised two sessions: a control session with isotonic saline and an experimental session with hypertonic saline. In each session, participants completed six trials in a sequence of alternating feedback conditions: feedback, no feedback, feedback, no feedback, feedback, no feedback.	**ApEn SampEn**	The presence of pain did not influence torque complexity, measured as ApEn or SampEn (*P>0.05*).
13. Yavuz et al., 2015	**9 of 11 asymptomatic individuals** (9M; age 25.1 (2.5) years) for the ADM muscle and **7 of 12 asymptomatic individuals** (7M; age 24.2 (2.1) years) for the TA muscle. Two participants excluded because of the limited of motor units identified.	**Hypertonic saline (0.5ml, 5.8%)** into the ADM and TA muscles. **ADM (Pain: NPRS, 0-10):** 4.4 (2.1) **TA (Pain: NPRS, 0-10):** 3.5 (1.2)	In **Experiment 1**, participants were seated with the arm and first four digits secured, and the fifth digit attached to a load cell to measure isometric abduction force. They performed a 60-second isometric abduction of the fifth digit at 10% MVC under three conditions: baseline, isotonic saline, and hypertonic saline. In **Experiment 2**, participants, with their foot in an isometric force brace, executed a 4-minute isometric dorsiflexion at 25% MVC. After a 20-minute rest, one leg was treated with hypertonic saline (to induce discomfort) and the other with isotonic saline. Following the infusion, the isometric dorsiflexion was repeated, with visual force feedback provided via an oscilloscope in both experiments.	**CoV (%)**	↓ force steadiness after the injection of hypertonic saline for both muscles (ADM and TA) when measured as SD of force (*P<0.01* for both) and CoV of force (*P<0.05* for both).

ADM: Abductor Digiti Minimi; **BIC:** Biceps Brachii; **CoV:** Coefficient of Variation; **DYN:** Dynamic; **F:** Females; **GM:** Gastrocnemius medialis; **M:** Males; **MVC:** Maximal Voluntary Contraction; **NPRS:** Numeric Pain Rating Scale; **RM-ANOVA:** Repeated Measures Analysis of Variance; **SampEn:** Sample Entropy; **SD:** Standard Deviation; **SE:** Standard Error; **TA:** Tibialis Anterior; **TF:** Target Force; **VAS:** Visual Analogue Scale; **VM:** Vastus medialis; **1D:** One-dimensional; **3D:** Three-dimensional.

5.4.3 Risk of bias

Comprehensive summaries of the risk of bias scores are presented in Tables 3 and 4, respectively. In the assessment of risk of bias across the 19 clinical pain studies, the scores varied from 4 to 9 out of a possible 9. The quality of studies was rated as "poor" for ten, "good" for eight, and "fair" for one (**Table 5.3**). The most common reasons for "poor" ratings were from potential biases introduced by not matching participants on age and/or gender as part of the study methodology, and not reporting full participant recruitment information. The assessment was also performed across 13 experimental pain studies with the scores ranging between 5 and 9 out of 9. The quality was rated as "good" in eight of the studies, "fair" in three and "poor" in two (**Table 5.4**).

Table 5.3: **Risk of Bias of clinical pain studies.**

Study	Selection	Comparability	Exposure	Total	Quality
Arvanitidis 2022	★★★		★★★	6	Poor
Arvanitidis 2024c	★★★		★★★	6	Poor
Bandholm 2006	★	★★	★★★	6	Poor
Camargo 2009	★★	★★	★★★	7	Fair
Chen 2023	★		★★★	4	Poor
Crowely 2022	★★★	★★	★★★	8	Good
Falla 2010	★		★★★	4	Poor
Ferreira 2021	★★★★		★★★	7	Poor
Hortobagyi 2004	★★★★	★★	★★	8	Good
Magni 2021	★★★	★★	★★★	8	Good
Mista 2018		★★	★★★	5	Poor
Miura 2014	★		★★★	4	Poor
Muceli 2011	★★★★		★★★	7	Poor
Overbeek 2020	★★★★	★★	★★	8	Good
Testa 2017	★★★★	★★	★★★	9	Good
Testa 2015	★★★★	★★	★★★	9	Good
Testa 2018	★★★	★★	★★★	8	Good
Wang 2020	★★★★	★	★★★	8	Good
Wang 2018	★★		★★★	5	Poor

Table 5.4: **Risk of Bias of studies of experimental pain studies.**

Study	Selection	Comparability	Exposure	Total	Quality
Bandholm 2008	★★	★	★★★	6	Fair
Del Santo 2007	★★		★★★	5	Poor
Farina 2012	★	★	★★★	5	Poor
Hirata 2015	★★	★★	★★★	7	Fair
Martinez-Valdes 2021	★★★	★★	★★★	8	Good
Martinez-Valdes 2020	★★★	★★	★★★	8	Good
Mista 2015	★★★	★	★★★	7	Good
Poortvliet 2019	★★★	★	★★★	7	Good
Rice 2015	★★	★	★★★	6	Fair
Salomoni 2013	★★★	★★	★★★	8	Good
Salomoni 2012	★★★	★★	★★★	8	Good
Smith 2021	★★★	★★	★★★	8	Good
Yavuz 2015	★★★	★★	★★★	8	Good

5.4.4 Results of syntheses and certainty of evidence

Meta-analyses for both clinical and experimental pain studies were conducted using the CoV and SD of force measures. However, since some studies utilised either the CoV or the SD measure, but not both, it was not feasible to incorporate all studies into both meta-analyses. As a result, some studies could be included in either the CoV-based meta-analysis or the SD-based meta-analysis, but not both.

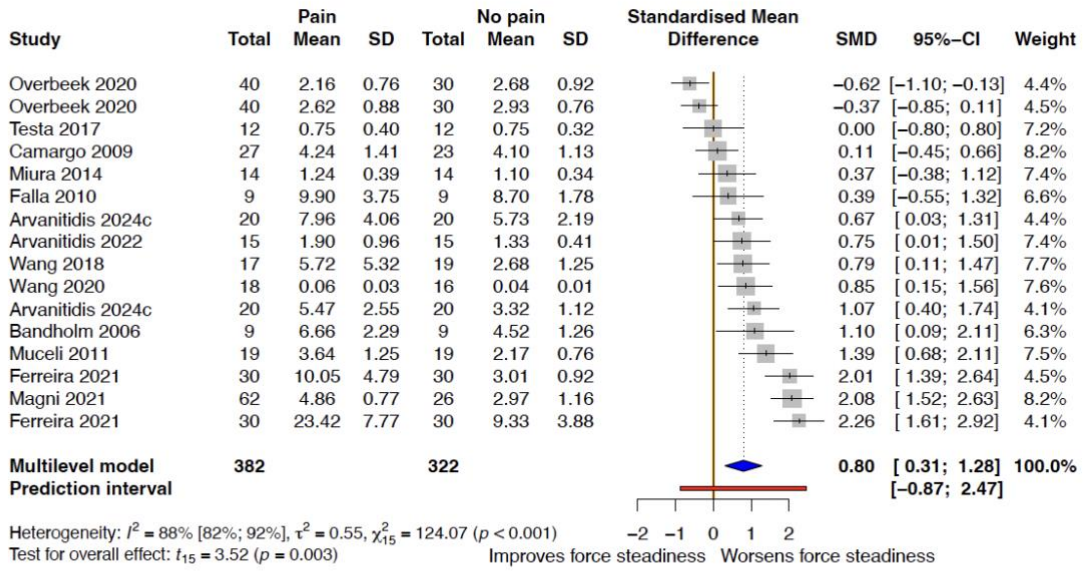
5.4.4.1 Force steadiness in the presence of clinical pain

The results of the meta-analysis that included 13 out of the total 19 studies with clinical pain, involving 382 participants with pain and 322 without, demonstrated that there was a significant overall effect of musculoskeletal pain on the CoV of force, indicating that force steadiness is impaired in the presence of pain (SMD = 0.80 [95% CI, 0.31 to 1.28], I^2 = 88% [95% CI, 82% to 92%], τ^2 = 0.55, Q = 124.07, t_{15} = 3.52, P = 0.003). Similarly, the results of the meta-analysis that included 14 out of the total 19 studies with clinical pain, involving 355

participants with pain and 297 without, demonstrated that there was a significant overall effect of musculoskeletal pain on the SD of force, indicating impaired force steadiness in the presence of pain (SMD = 0.61 [95% CI, 0.11 to 1.11], I^2 = 87% [95% CI, 80% to 91%], τ^2 = 0.66, Q =114.18, t_{15} = 2.60, P = 0.020). The results of the forest plots with meta-analyses are presented in **Figure 5.2**.

One study was excluded from both meta-analyses because related data could not be extracted (Crowley et al., 2022). This study did not observe any differences in plantar flexor steadiness (measured as CoV of force) in people with IAT compared to controls. In the CoV-based meta-analysis, four studies were not included because they quantified force steadiness using the SD of force. Among these, two observed reductions in force steadiness in people with TMD (Testa et al., 2018) and knee OA (Hortobágyi et al., 2004) compared to controls, while the other two found no significant differences in individuals with chronic elbow pain (Mista et al., 2018) or people with CNP (Testa et al., 2015). Conversely, in the SD-based meta-analysis, three studies were excluded because they only used CoV of force as the outcome measure with all observing significant reductions in force steadiness in people with CNP (Falla et al., 2010, Muceli et al., 2011) and PFP (Ferreira et al., 2021), which is in line with the findings of the meta-analysis.

(a) *Force/Torque CoV for studies on clinical pain*



(b) *Force/Torque SD for studies on clinical pain*

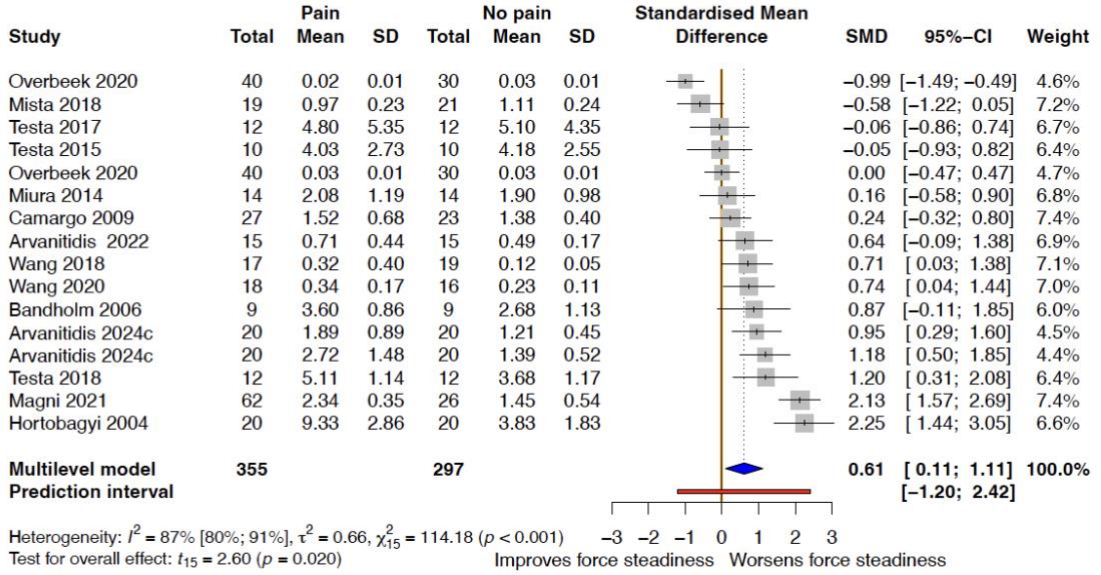


Figure 5.2: **Meta-analyses on the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside with the SMD and 95% CIs. The analysis is divided into two segments, (a) focuses on the CoV of force/torque, while (b) is based on the SD of force/torque. All heterogeneity measures and overall effect size tests are reported below each meta-analysis. The prediction interval is also depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.**

5.4.4.2 Force steadiness in the presence of experimental pain

The results of the meta-analysis that included 10 out of the total 13 studies on experimental pain, involving 188 participants measured under both pain and no pain conditions, demonstrated that there was a significant overall effect of experimental musculoskeletal pain on the CoV of force indicating worse force steadiness in the presence of pain (SMD = 0.50 [95% CI, 0.01 to 0.99], I^2 = 54% [95% CI, 18% to 75%], τ^2 = 0.37, Q = 30.72, t_{14} = 2.19, P = 0.046). However, the results of the meta-analysis that included nine out of the total 13 studies with experimental pain, involving 127 participants measured under both pain and no pain conditions, demonstrated that there was not a significant overall effect of experimental musculoskeletal pain on the SD of force (SMD = 0.44 [95% CI, -0.04 to 0.92], I^2 = 56% [95% CI, 11% to 78%], τ^2 = 0.25, Q = 20.44, t_9 = 2.08, P = 0.067). The results of the forest plots with meta-analyses are presented in **Figure 5.3**.

Since some experimental studies utilised either the CoV or the SD measure, but not both, it was not feasible to incorporate all studies into the respective CoV and SD-based meta-analyses. Three studies were excluded from the CoV-based meta-analysis. Among these, two did not observe any differences in elbow flexion (Mista et al., 2015) and trunk extension (Hirata et al., 2015) force steadiness between the experimental pain and baseline conditions, while the other one showed that knee extension force fluctuations were higher in the presence of experimentally induced knee pain (Poortvliet et al., 2019). Four studies were excluded from the SD-based meta-analysis. Among these studies, three showed that force steadiness is reduced in the presence of experimentally induced knee (Salomoni et al., 2013), fifth finger (Farina et al., 2012) and fifth finger and elbow pain (Del Santo et al., 2007). The last one investigated the effect of experimentally induced pain on the force steadiness of multiple muscles and observed

reductions in force steadiness only for the knee at higher forces (Salomoni and Graven-Nielsen, 2012).

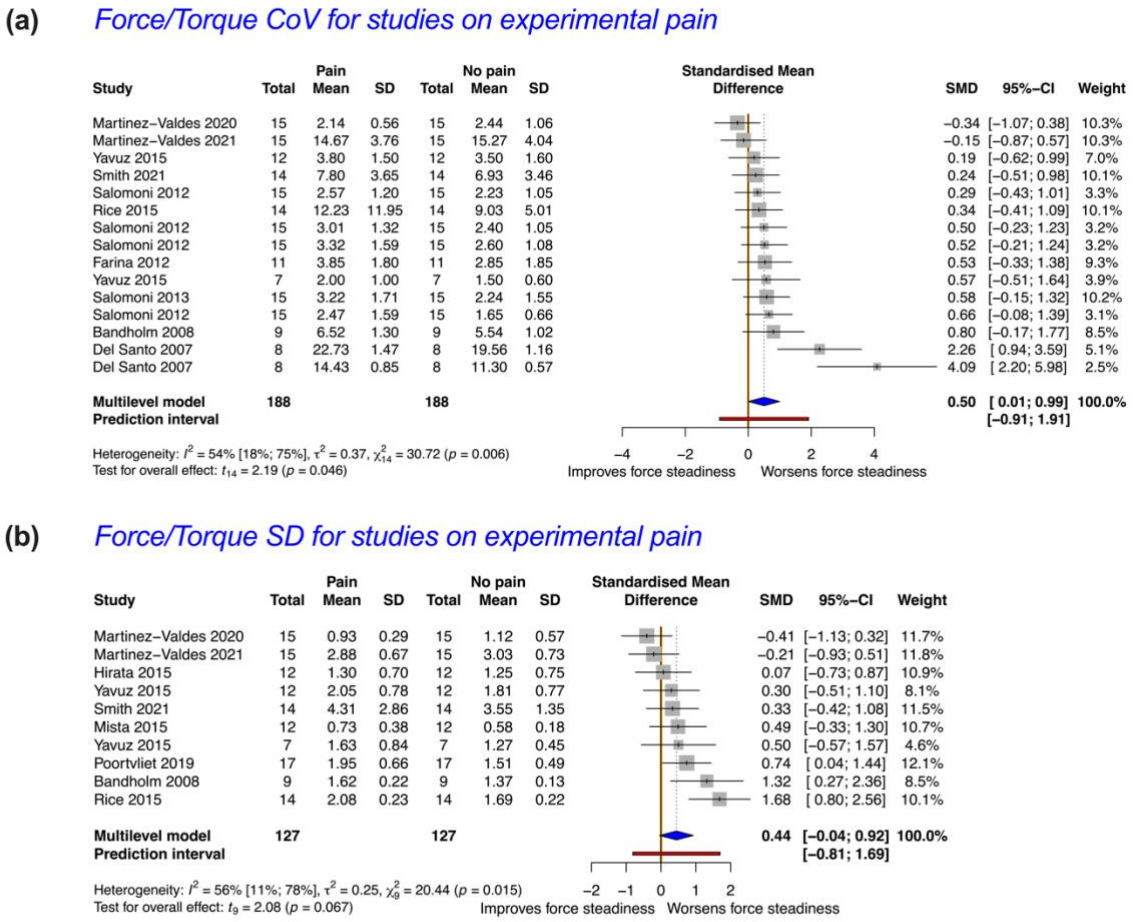


Figure 5.3: **Meta-analyses on the effect of experimental pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside with the SMD and 95% CIs. The analysis is divided into two segments, (a) focuses on the CoV of force/torque, while (b) is based on the SD of force/torque. All heterogeneity measures and overall effect size tests are reported below each meta-analysis. The prediction interval is also depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.**

5.4.4.3 Alternative measures of force control

There was inadequate data to conduct meta-analyses on studies involving other measures of force control. Specifically, in the studies with clinical pain, only two used ApEn as a measure of force complexity with one of them showing that people with SAPS had lower ApEn values during shoulder abduction and adduction tasks (i.e., a smoother force pattern with less variability) compared to the controls (Overbeek et al., 2020), while the other did not observe any differences for ApEn values during a jaw clenching task in people with and without jaw pain (Wang et al., 2018). These studies were included in the meta-analysis as they also assessed steadiness using the CoV or SD of torque. However, another study with clinical pain was not included in any meta-analysis because it only used RMS and SampEn to quantify changes in force control between the two groups. This study showed that RMS was larger in people with CLE, while no differences were observed in terms of the complexity of the force signal (measured using SampEn) (Chen et al., 2023).

From the experimental pain studies only two used alternative measures of force control to assess the effect of experimental pain on force control. One used both ApEn and SampEn to assess changes in isometric knee extension force control (Smith et al., 2021), while the other only the latter during elbow flexion contractions (Mista et al., 2015), with both studies not observing significant differences in these variables during the painful and non-painful states.

5.4.5 Certainty of evidence – Sensitivity Analyses & GRADE

Influence analyses on the main meta-analyses for both clinical and experimental studies, focusing on force/torque CoV and SD, did not identify any potential outliers, except for the SD-based meta-analysis in experimental pain studies, where one study (Rice et al., 2015) was

detected as potentially influential (**Appendix *6* – Supplemental File 4**). This study was removed as part of the sensitivity analysis to explore its influence on the overall result as described below. Additionally, the sensitivity analyses included: i) removal of one study at a time, ii) removal of studies that did not provide visual force feedback, and iii) removal of studies classified as having poor quality.

Clinical pain studies. Sensitivity analyses indicated that the overall results of the meta-analyses for both force/torque CoV and SD were not influenced by the removal of any single study or by excluding data from studies that did not provide force visual feedback (**Appendix *6* – Supplemental File 4**). However, removing studies of poor quality altered the overall result, showing no differences in force steadiness in the presence of clinical pain. This change is likely due to the removal of the majority of studies from the meta-analysis (eight and six studies, respectively). This likely does not provide an accurate representation, as many studies were rated poor, primarily due to a lack of information on the comparability of groups within the methodology, which was only reported in the results section.

Experimental pain studies. Removing the study (Rice et al., 2015) that could potentially influence the SD-based meta-analysis resulted in a similar outcome to the meta-analysis that included all studies. Removing each study one at a time had a significant impact on the CoV-based meta-analysis, usually showing no changes in force steadiness in the presence of experimentally induced pain. For the SD-based meta-analysis, the result of no differences was maintained most of the time, but the overall effect became significant when two studies were removed (Martinez-Valdes et al., 2021, Martinez-Valdes et al., 2020). Excluding force/torque SD data from studies that did not provide visual feedback did not alter the overall result of the main meta-analysis. However, the CoV-based meta-analysis result changed when this data was removed, suggesting that experimentally induced pain does not influence force steadiness.

Further exploration identified one study as potentially influential in the model; when this study was removed, the same result as the main meta-analysis was observed. Lastly, removing two studies of poor quality (Del Santo et al., 2007, Farina et al., 2012) did not alter the overall result for the CoV-based meta-analysis, while no studies could be removed from the SD-based meta-analysis since none were classified as having poor quality.

The evaluation of the certainty of evidence was conducted independently for studies with clinical and experimental pain, based on the outcome used. This assessment was performed on studies using the CoV and SD of force as measures of force steadiness, due to the limited number of studies using alternative metrics. Any sources of publication bias were assessed by visually inspecting funnel plots and using Egger's regression tests, as shown in **Figure 5.4**.

The results showed that for the clinical pain studies, funnel plots were quite symmetrical, and Egger's regression test did not reveal any potential sources of publication bias (*Torque CoV: P = 0.591*, *Intercept = 0.0427*, *t = 0.553*; *Torque SD: P = 0.633*, *Intercept = 0.0563*, *t = 0.491*; **Figure 5.4A** and **Figure 5.4B**, respectively). In contrast, for the experimental pain studies, the funnel plot for Torque CoV (**Figure 5.4C**) suggested potential sources of publication bias, as indicated by the clustering of dots around the 0.4 level of SE and confirmed by Egger's regression test (*P<0.01*, *Intercept = -1.96*, *t = 4.06*). However, the funnel plot for Torque SD (**Figure 5.4D**) did not reveal any significant publication bias (*P = 0.12*, *Intercept = -2.14*, *t = 1.77*).

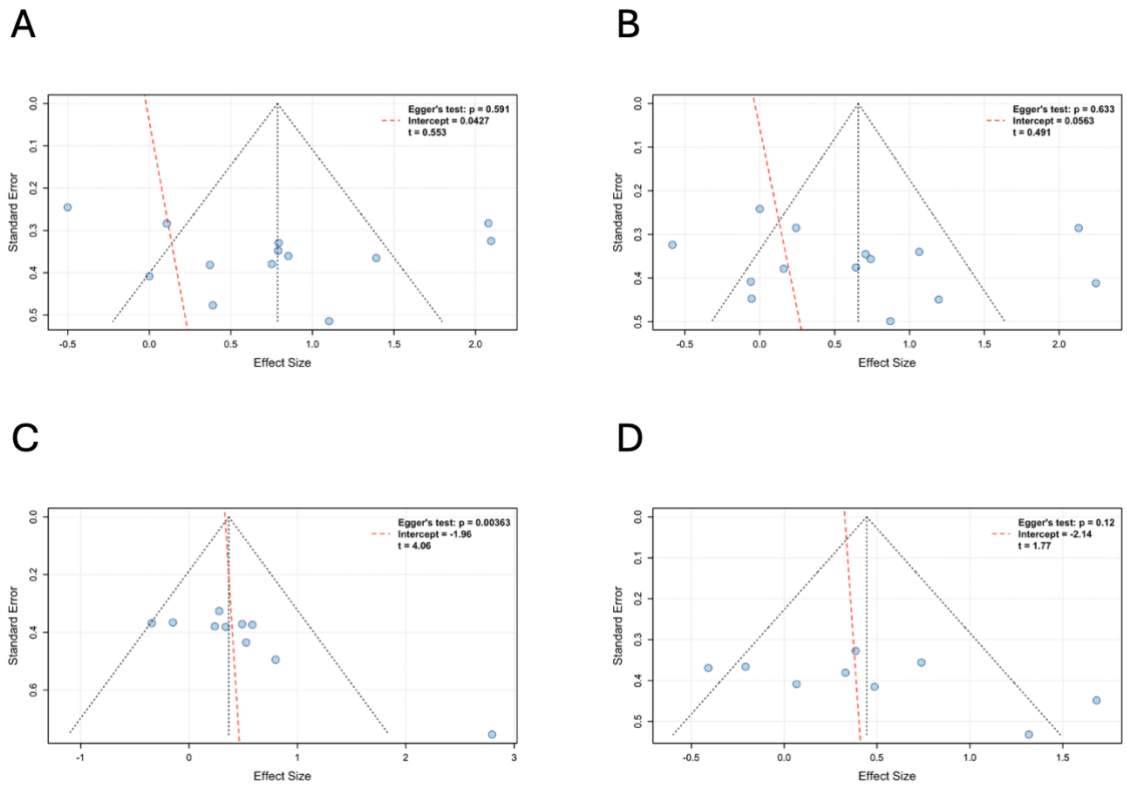


Figure 5.4: **Funnel plots of the four meta-analyses performed alongside the results of the Egger regression test. Funnel plots are presented for (A) Torque CoV for clinical pain studies, (B) Torque SD for clinical pain studies, (C) Torque CoV for experimental pain studies, and (D) Torque SD for experimental pain studies. The blue dots in each scatterplot represent the values from individual studies, with effect size on the x-axis and SE on the y-axis. The middle-dotted line represents the overall effect size, and the side dotted lines form a triangle indicating the 95% CIs for the expected distribution of studies in the absence of publication bias. The dotted red line represents Egger's regression line, used to test for potential sources of publication bias. Egger's test values of $P < 0.05$ indicate potential publication bias.**

Considering the above and the other domains assessed with GRADE, the findings from the meta-analysis indicate, with moderate and low levels of evidence strength, that force steadiness is impaired in the presence of clinical pain when measured using force CoV and SD, respectively. Additionally, it indicates with very low strength of evidence that force steadiness is impaired in the presence of experimental pain when quantified as the CoV of force, but not when quantified using the SD of force. The summary of findings is presented in **Table 5.5**.

Table 5.5: **Summary of the overall certainty of evidence for each outcome, differentiated between clinical and experimental pain studies assessing the influence of pain on force/torque steadiness using the GRADE approach. Studies highlighted in bold were excluded from the meta-analysis for the specified outcome.**

Studies included in each GRADE assessment	Outcome/Finding	Confidence	Reason for downgrade or upgrade
Studies with Clinical Musculoskeletal Pain			
Arvanitidis 2022; Arvanitidis 2024c; Bandholm 2006; Camargo 2009; Falla 2010; Ferreira 2021; Magni 2021; Miura 2014; Muceli 2011; Overbeek 2020; Testa 2017; Wang 2018; Wang 2020; **Crowley 2022**	Reduced force steadiness (force CoV)	Moderate	↓ Study limitations (mainly due to groups comparability) ↑↑ Large magnitude of effect and derived from direct evidence
Arvanitidis 2022; Arvanitidis 2024c; Bandholm 2006; Camargo 2009; Hortobagyi 2004; Magni 2021; Mista 2018; Miura 2014; Overbeek 2020; Testa 2015; Testa 2017; Testa 2018; Wang 2018; Wang 2020	Reduced force steadiness (force SD)	Low	↓ Inconsistency (sensitivity analysis had minimal impact on heterogeneity, with some p-values approaching statistical insignificance) ↑ Moderate magnitude of effect and derived from direct evidence
Studies with Experimental Musculoskeletal Pain			
Bandholm 2008; Del Santo 2007; Farina 2012; Martinez-Valdes 2020; Martinez-Valdes 2021; Rice 2015; Salomoni 2012; Salomoni 2013; Smith 2021; Yavuz 2015	Reduced force steadiness (force CoV)	Very low	↓ Inconsistency, ↓ Imprecision, ↓ Publication bias Significant change of results when sensitivity analysis is performed; Wide CIs and small sample size studies; Asymmetry of funnel plots and Egger's test.
Bandholm 2008; Hirata 2015; Martinez-Valdes 2020; Martinez-Valdes 2021; Mista 2015; Poortvliet 2019; Rice 2015; Smith 2021; Yavuz 2015; **Salomoni 2012**	No changes in force steadiness (force SD)	Very low	↓ Imprecision (wide CIs, a few studies of small sample size)

5.5 Discussion

This systematic review and meta-analysis investigated the influence of clinical and experimentally induced musculoskeletal pain on force steadiness. Integrating data from 32 studies, the analysis indicated that clinical musculoskeletal pain is associated with a decrease in force steadiness, as indicated by large and moderate effects on the CoV and SD of force *(SMD = 0.80 [95% CI, 0.31, 1.28], SMD = 0.61 [95% CI, 0.11, 1.11])*. Experimental pain was associated with a reduction in force steadiness only as measured by the CoV of force *(moderate effect size; SMD = 0.50 [95% CI, 0.01, 0.99)]*, and not in the SD of force *(SMD = 0.44 [95% CI, -0.04, 0.92])*.

5.5.1 Does clinical pain influence force steadiness?

The findings confirm that clinical musculoskeletal pain is associated with reduced force steadiness. This aligns with the findings from a previous systematic review indicating that peripheral musculoskeletal conditions are also associated with increased force CoV (Pethick et al., 2022). For both meta-analyses the heterogeneity observed was quite high, however, this was expected, and this is why a random effects model was used. The observed heterogeneity is likely be attributed to several factors, including differences in participant characteristics, the diverse nature and severity of pain, differences in pain duration, methodological differences, and the wide range of musculoskeletal pain conditions studied. However, the sensitivity analysis further confirms the robustness of the findings showing that the removal of each individual study did not influence the overall result (**Appendix *6* – Supplemental File 4**).

While most studies support that clinical pain is associated with reduced force steadiness, some exceptions were observed. For example, two studies (Testa et al., 2017, Testa et al., 2015) assessing jaw clenching force steadiness in people with CNP found no significant

differences between groups, while in contrast, when the same authors assessed force steadiness in people with TMD, a reduction in force steadiness was observed for the patient group (Testa et al., 2018). This suggests that the presence of pain at the specific location being assessed is crucial for such observations. Additionally, variations in force steadiness could be attributed to the level of force assessed. Many studies explored a broad range of low to high submaximal forces, whereas some examined a single submaximal level. Considering that certain studies (Bandholm et al., 2006, Miura and Sakuraba, 2014) reported deficits at specific force levels, this implies that force steadiness deficits might be force-level specific, an important consideration for future research designs. Moreover, it is worth noting that these deficits may also be present during specific types of muscle contractions. Therefore, for a more comprehensive assessment of force steadiness, future studies should include both isometric and dynamic contractions.

5.5.2 Does experimental pain influence force steadiness?

This review also revealed that experimental musculoskeletal pain is associated with reduced force steadiness when measured as the CoV of force. The meta-analyses showed lower heterogeneity and smaller, more consistent effect sizes. This consistency is likely due to the use of similar pain models and the assessment of comparable anatomical regions in many studies. One study had a notably larger effect size, likely due to its unique use of ascorbic acid to induce pain **Figure 5.3A**. However, the p-values from both the CoV- and SD-based meta-analyses, along with insights from the sensitivity analysis in **Appendix *6* – Supplemental File 4**, suggest that the removal of some of the individual studies significantly influenced the overall effect. Therefore, these findings should be interpreted with caution.

The absence of significant differences in the SD of force could stem from the inherent characteristics of the force steadiness outcome measures. The CoV quantifies variability

relative to the mean force output, thus reflecting proportional changes, while SD, as an absolute measure, is inherently sensitive to individual differences in strength. This distinction becomes particularly noticeable when synthesising data across multiple studies, where variability in baseline strength among participants can substantially influence SD outcomes. Moreover, the heterogeneity in measurement units (e.g., Newtons versus percentages) across studies might confound comparisons, though this issue was mitigated in our analysis by using SMD for meta-analytic calculations. These factors, coupled with the sample sizes and the number of studies included, could explain the observed discrepancies between CoV and SD findings. Interestingly, although in experimental pain the effect size for torque SD was not significant, the effect sizes for both torque SD and CoV were very similar. This similarity suggests that the overall trend towards impaired force steadiness in the presence of experimental pain is consistent across these measures. However, interpreting CoV results necessitates caution; sensitivity analysis indicated that excluding certain studies substantially alters outcomes, underscoring careful result interpretation and advocating for using both CoV and SD to assess force steadiness in people with pain (**Appendix 6 – Supplemental File 4**).

5.5.3 Differences between clinical and experimental pain

The findings of this systematic review suggest that the deficits in force steadiness are less marked during experimental pain than in clinical pain conditions, a disparity likely stemming from the fundamental differences between these two pain types. Clinical pain, characterized by its multidimensional and persistent nature, encompasses physical, psychological, and emotional elements, along with extensive neurophysiological changes. As clinical pain becomes chronic, significant modifications occur across various levels of the nervous system. Notably, alterations in brain structure and function are prevalent, particularly in regions involved in emotional and sensory processing (Sibille et al., 2016). These alterations

include reductions in gray matter volume and white matter integrity, changes in neurotransmitter activity, and reduced descending inhibition (Sibille et al., 2016). Such comprehensive changes across multiple levels of the nervous system in clinical pain, coupled with alterations in muscle structure, such as atrophy, fatty tissue infiltration, and fibre type changes, which have been documented in people with chronic pain, are more likely to alter neuromuscular control than experimental pain (Hodges and Danneels, 2019, Matheve et al., 2023).

Experimentally induced pain more related to the sensitization of nociceptive pathways and is transient. Moreover, participants in experimental settings are aware that the pain is temporary and will dissolve, a psychological factor that might influence their pain perception and response differently compared to the unpredictability and persistence of clinical pain. This is further supported by a systematic review that investigated clinical and experimental pain-induced changes in motor neuron excitability during voluntary contractions in humans, showing that experimental pain models do not create the same changes which are seen in clinical pain conditions across the neuromuscular pathway (Sanderson et al., 2021). Importantly, in the presence of acute experimental pain individuals might employ more strategies to compensate for their pain, including changes in movement and muscle activation patterns, which may be the reason that the deterioration in force is less evident in the experimental pain studies (Devecchi et al., 2023).

5.5.4 Physiological explanation of the observed findings

Pain likely impairs muscle force control through altered sensory input from the affected area and/or central changes (Ager et al., 2020). Structural alterations in brain areas essential for proprioceptive input processing, or muscle composition changes may also contribute (Pijnenburg et al., 2014, Sterling et al., 2001). Additionally, force steadiness changes can also

be linked to adjustments in the descending neural pathways and motor planning, influenced by cognitive and emotional factors (Tucker et al., 2012). These sensory integration changes can alter the efferent response, thereby influencing muscle recruitment strategies employed by individuals to perform muscle contractions.

Alterations in force steadiness may be linked to changes in motor unit behaviour. Reduced modulation in the discharge rates of motor units in the sternocleidomastoid muscle in women with CNP has been observed, indicating a change in neural drive to muscles in the presence of pain (Falla et al., 2010). Additionally, increased motor unit recruitment and firing rates have been observed in early knee OA (Ling et al., 2007) and in women with PFP (Gallina et al., 2018), respectively. Experimentally induced knee pain, influences force steadiness in healthy individuals (Rice et al., 2015), and notably, changes in motor unit discharge patterns have also been reported in the presence of experimental pain within the same region (Poortvliet et al., 2019).

Recent studies have indicated that the effective neural drive predominantly operates in the low-frequency band (<10 Hz), reflecting the common synaptic input to the motor unit pool, essential for force generation (Farina et al., 2014b, Negro et al., 2009). Since, muscle force control relies on the amplitude of these oscillations, increased amplitude fluctuations observed in pain conditions may indicate greater variability in synaptic input to α motor neurons. Given the α motor neuron's role in integrating complex inputs and the interplay between proprioceptive and nociceptive signals, the physiological mechanism by which musculoskeletal pain influences force control may vary among different pain types and individuals (Hug et al., 2023).

5.5.5 Clinical relevance

Impaired force steadiness may lead to suboptimal tissue loading, where a disrupted sense of body position may result to the application of excessive forces in unfavourable positions during movement. This abnormal mechanical stress on tissues can activate nociceptors and cause tissue strain, potentially contributing to the development of additional pain or injuries and the perpetuation of existing symptoms. These impairments likely have clinical relevance and could become targets for treatment for people experiencing musculoskeletal pain.

5.5.6 Limitations

This review's limitations include the predominance of observational studies in the meta-analyses, which hinders causal inference between musculoskeletal pain and decreased force steadiness. Factors such as reduced activity, medication, sleep, and psychological conditions may also influence force steadiness. The relatively small sample sizes of the included studies, particularly in experimental pain studies, also pose a challenge to the robustness of the evidence. Nonetheless, within-participant comparisons mitigate interindividual variability, enhancing statistical power.

5.5.7 Recommendations for future research

Future research should explore force steadiness at various force levels and during isometric and dynamic contractions in people with pain, to understand changes in force control across different conditions. Both the CoV and the SD of force should be used for assessing force steadiness, since they offer unique insights into force variability. Additionally, calculating SD in Newtons based on a submaximal percentage MVC can be problematic due to the non-

linear relationship between force output and MVC percentage, especially when considering inter-individual differences in muscle strength. Thus, studies should express SD as a percentage or ensuring both SD and the target are on the same scale.

Moreover, although most studies use the term force steadiness and report results in Newtons (for the SD), the measurements actually pertain to joint moments rather than muscle forces. Often, force transducers are attached at positions defined relative to anatomical landmarks, which can create differences in moment arms between individuals. These variations in moment arms can influence the calculated SD, as the lever arm length directly affects the torque produced by a given force. However, this variability should not affect the CoV, as it normalises the SD by the mean force, thereby reducing the impact of individual differences in moment arm lengths. It is relevant to acknowledge this issue, as it introduces an additional source of variability that future studies need to account for when measuring and interpreting force steadiness.

5.6 Conclusion

This systematic review demonstrates that individuals with clinical pain exhibit decreased force steadiness, quantified by both the CoV and SD of force. It also reveals that force steadiness, quantified as CoV, is reduced in individuals subjected to experimentally induced pain, primarily induced through hypertonic saline injections. However, the results of the experimental pain studies should be interpreted with some caution. Future studies should explore the relationship between enhancements in force steadiness and improvements in patients' symptoms and functional performance.

Chapter 6

GENERAL DISCUSSION

6.1 Summary of findings

The main aim of this thesis was to enhance the understanding of motor adaptations in people with CLBP, focusing on changes in the control of trunk muscle force and the potential underlying neuromuscular mechanisms. Additionally, this thesis explored the effect of eccentric exercise-induced DOMS in the trunk extensors and of musculoskeletal pain, whether clinical or experimental, on the control of muscle force.

Chapter 1 provided an overview of LBP, emphasising its significance as a major clinical challenge affecting quality of life and leading to disability worldwide (Ferreira et al., 2023). This chapter also highlighted differences in movement patterns between individuals with and without CLBP (Hodges and Tucker, 2011, van Dieën et al., 2019), likely due to various neuromuscular adaptations in response to spinal pain (Devecchi et al., 2021). It also discussed the anatomy of the trunk, focusing on key muscles like the RA, EO, and the thoracolumbar ES, emphasising the importance of investigating these muscles in the presence of CLBP. Within this context, torque steadiness emerged as an area of research that merits further investigation, forming the central focus of this thesis.

Chapter 2 presented a cross-sectional, observational study addressing Objective One (**Section 1.11.1**). This study used HDsEMG to investigate trunk muscle force control and lumbar ES surface EMG/torque relationships during submaximal isometric trunk extension contractions at 20% and 50%MVC in individuals with and without CLBP (Arvanitidis et al., 2022). Results showed that individuals with CLBP exhibited reduced torque steadiness

compared to the controls. Additionally, surface EMG-torque coherence in the δ band and surface EMG-torque cross-correlation did not increase with the increase in torque in individuals with CLBP. In contrast, the control group demonstrated an increase in both surface EMG-torque coherence and cross-correlation with the increase in torque, suggesting an increase in the contribution of the lumbar ES to the resultant torque. Interestingly, as torque increased, the CLBP group showed higher EMG-torque coherence in more cranial ES regions (i.e., higher contribution of these regions to the resultant torque), while the opposite was observed for the controls. These findings, measured on the most painful side in people with CLBP, indicated the presence of reductions in surface EMG/torque relationships likely due to the use of compensatory strategies and regional adjustments of lumbar ES surface EMG oscillatory activity. However, it remained uncertain if individuals with CLBP would also show impairments in the control trunk muscle force during more functional movements, such as dynamic trunk flexion and trunk extension concentric/eccentric contractions.

Chapter 3 addressed Objective Two (**Section 1.11.1**), presenting another cross-sectional observational study exploring torque steadiness and surface EMG/torque relationships during more functional tasks, such as dynamic trunk flexion and extension contractions in people with CLBP. Findings mirrored those of ***Chapter 2***, with CLBP individuals showing reduced torque steadiness during both eccentric and concentric dynamic trunk flexion and trunk extension contractions, alongside altered trunk muscle behaviour. Specifically, during trunk extension, individuals with CLBP exhibited a higher HDsEMG–torque coherence in more cranial regions of the thoracolumbar ES (as also observed in ***Chapter 2***) and a higher HDsEMG cross-correlation compared with asymptomatic controls. During trunk flexion movements, individuals with CLBP demonstrated higher HDsEMG amplitude of the abdominal muscles, with the centre of activation being more cranial and a higher contribution of this musculature to the resultant torque (particularly the EO muscle).

Chapter 4, addressing Objective Three (**Section 1.11.1**), investigated the effects of acute low-back soreness induced by DOMS on trunk muscle function, recruitment behaviour, movement patterns, and underlying neuromuscular mechanisms. Contrary to the findings observed in people with CLBP (***Chapter 2*** and ***Chapter 3***), DOMS did not impair trunk force control. However, HDsEMG-torque relationships and kinematics were altered in a contraction-dependent manner. During eccentric contractions, a decrease in the thoracolumbar ES contribution to the resultant torque was observed, and individuals showed increased lumbar flexion during the more demanding contractions (50%MVC). During concentric contractions, a reduction in thoracolumbar ROM in the sagittal plane was observed, suggesting the maintenance of a more neutral lumbar spine posture, but no alterations in HDsEMG-torque relationships were observed in the presence of DOMS. These findings suggested that pain-free individuals could adapt their motor strategies and maintain muscle performance despite DOMS.

Chapter 5, addressing Objective Four (**Section 1.11.1**), presented a systematic review on the influence of clinical and experimental musculoskeletal pain on control of muscle force. While DOMS was used as an experimental model of pain in ***Chapter 4***, it was not included in this systematic review due to the many confounding factors associated with DOMS, such as muscle damage and inflammation, which could influence the control of muscle force. This review focuses on more controlled experimental pain models (e.g., injections with hypertonic saline) to ensure that the findings are not confounded by these additional factors. This work showed that pain, particularly clinical pain impairs control of muscle force. This suggested that the persistent, multidimensional nature of clinical pain leads to more pronounced force control impairments compared to the temporary nature of experimental pain (particularly for the trunk).

In conclusion, this chapter, ***Chapter 6***, summarises the key findings of this thesis, draws conclusions, outlines the strengths and limitations of the work presented, discusses the clinical implications and provides recommendations for future research.

6.2 Impairments in Control of Trunk Muscle Force in people with LBP

This thesis confirmed that individuals with CLBP exhibit impairments in trunk muscle force control during both static and dynamic tasks. ***Chapter 2*** supported that the control of trunk muscle force is impaired in individuals with CLBP during isometric trunk extension contractions. These results are consistent with those from other studies that investigated the trunk force control during isometric trunk extension contractions of a similar effort (Miura and Sakuraba, 2014, Pranata et al., 2017). ***Chapter 3*** extended these findings to dynamic movements, showing reduced torque steadiness during concentric and eccentric trunk flexion and trunk extension contractions. Although it is not possible to compare these findings with current literature on dynamic trunk muscle force control, neuromuscular deficits and altered trunk muscle activity patterns have also been observed in individuals with CLBP during dynamic movements (Matheve et al., 2023, van Dieën et al., 2019, van Dieën et al., 2003). Such alterations can affect muscle force production and control, suggesting that similar impairments would likely be observed in other studies.

Conversely, ***Chapter 4*** showed that trunk DOMS did not impair force control. This aligns with the findings of a previous study that explored the effect of experimentally induced acute LBP on control of trunk muscle force, observing no impairments either (Hirata et al., 2015). Additionally, other studies on lower and upper limb muscles also did not observe differences in the control of muscle force at 24h and 48h post eccentric exercise (Lavender and Nosaka, 2006, Vila-Chã et al., 2012). Collectively, these findings suggest that the neuromuscular adaptations underlying acute muscle soreness/pain are distinct from those

associated with CLBP. Acute experimental LBP does not appear to elicit the same level of neuromuscular deficits or alterations in motor control strategies seen in CLBP, where persistent pain and long-term adaptations may contribute to impaired force control. Additionally, experimental and chronic clinical pain appear to have differing effects on corticospinal excitability, which may further explain the observed differences (Sanderson et al., 2021). However, we should not underestimate that a learning effect could also explain why no differences in force control were observed.

The meta-analysis in ***Chapter 5*** confirmed that control of muscle force is impaired in people experiencing clinical pain, including CLBP. This is also supported by a previous systematic review (Pethick et al., 2022), showing that control of muscle force is impaired in people with peripheral musculoskeletal conditions. The large effect size observed, suggests a significant influence of clinical pain on control of muscle force. However, experimental pain seemed to alter control of muscle force to a lesser extent, with no alterations observed in the trunk and the findings not being consistent, as demonstrated by the sensitivity analysis. This finding suggests that impairments in control of muscle force less marked during experimental pain than in clinical pain conditions, a disparity likely stemming from the fundamental differences between these two pain types. Clinical pain, characterised by its multidimensional and persistent nature, encompasses physical, psychological, and emotional elements, along with extensive neurophysiological changes. In acute experimental pain, pain is temporary, and individuals are aware that the discomfort will cease, which might allow them to employ more strategies, such as changing movement and muscle patterns, to compensate for pain. This could explain why force deterioration appears less pronounced in experimental studies.

The changes in the control of trunk muscle force observed in our studies were accompanied by changes in the behaviour of the trunk muscles, as described in the following section.

6.3 Physiological Explanation of the Observed Findings

Examining HDsEMG-torque relationships provided insights into the neuromuscular mechanisms underlying trunk muscle force control deficits in CLBP. Even though the observational nature of our studies cannot confirm causality, they provide important information that can help improve our understanding of the motor alterations that co-occur with these motor output deficits. This was necessary considering that the limited number of previous studies investigating control of trunk muscle force in individuals with CLBP either did not find differences in conventional EMG parameters (RMS and MNF) (Miura and Sakuraba, 2014) or did not use EMG to investigate this (Pranata et al., 2017). The specific reasons for the lack of findings in other trunk parameters have been detailed in the respective chapter. Here, we focus on discussing the main findings that co-occurred with the poorer control of trunk muscle force.

In ***Chapter 2***, we observed that people with CLBP show altered HDsEMG-torque relationships. Specifically, they fail to increase HDsEMG-torque coherence and cross-correlation as contractions became more challenging. This essentially means that they do not increase the contribution of the ES muscle to the resultant torque as expected. Importantly, as this happens, people with CLBP demonstrate higher HDsEMG-torque coherence in more cranial regions of the lumbar ES at higher forces, while the opposite was observed in asymptomatic controls. These altered relationships likely occur due to the use of compensatory strategies and regional adjustments of ES-sEMG oscillatory activity. These compensatory strategies could also be aimed at minimising stress on the compromised area and reducing pain (Falla and Gallina, 2020, Falla et al., 2014). By altering muscle recruitment strategies, individuals with CLBP may be attempting to protect the painful region, thereby preventing further injury or discomfort. This suggests that their motor control adjustments, while potentially limiting optimal force production, serve a protective function to manage pain and avoid exacerbation of their symptoms. Similarly, in ***Chapter 3***, notable differences in muscle

activation patterns were observed, particularly in the thoracolumbar ES and EO between individuals with CLBP and asymptomatic controls during trunk extension and flexion contractions. During eccentric contractions, people with CLBP had higher HDsEMG-torque coherence in more cranial regions of the thoracolumbar ES (as observed in ***Chapter 2***) and higher thoracolumbar ES HDsEMG-torque cross-correlation. On the other hand, during the trunk flexion contractions, individuals with CLBP exhibited higher activation of abdominal muscles, particularly the EO muscle. There were also regional differences in abdominal muscle activation, with the centre of activation, particularly that of the EO muscle, being more cranial compared with the asymptomatic controls. Additionally, there was a higher contribution of the abdominal muscles, especially of the EO muscle, to the resultant torque during concentric contractions (HDsEMG-torque cross-correlation). Collectively, these changes could potentially play a role in the poorer control of trunk muscle force seen in individuals with CLBP.

In contrast, ***Chapter 4*** showed altered HDsEMG-torque relationships in terms of magnitude and altered lumbar movement patterns in a task dependent-manner in the presence of DOMS, however, the control of muscle force was not impaired, likely suggesting that pain-free individuals were able to use adaptive motor strategies to maintain their muscular performance despite DOMS.

Chapter 5 discussed that in the presence of clinical or experimental musculoskeletal pain, motor behaviour might be altered (e.g., reduced or increased discharge rate of motor units), affecting the effective neural drive to the muscle and consequently force control (Falla et al., 2010, Gallina et al., 2018, Ling et al., 2007, Poortvliet et al., 2019, Rice et al., 2015). However, these findings are based on muscles other than the trunk, due to the challenges of decomposing HDsEMG signals collected from trunk muscles as described earlier.

These changes are likely related to the poorer control of trunk muscle force often seen in individuals with CLBP. However, it is also important to understand the changes in the afferent pathways that might be linked to alterations in the efferent response. This has been discussed in earlier sections of this thesis. Pain-induced changes in sensory input and central processing, including alterations in brain structure and muscle composition, likely contribute to these impairments. Collectively, these changes can affect the low-frequency component (<10Hz) of the neural command, which is most relevant for force generation (effective neural drive) (Farina et al., 2014b, Negro et al., 2009). Since muscle force control relies on the amplitude of these oscillations, increased amplitude fluctuations observed in pain conditions may indicate greater variability in synaptic input to α motor neurons. Given the role of α motor neurons in integrating complex inputs and the interplay between proprioceptive and nociceptive signals, the physiological mechanisms by which musculoskeletal pain influences force control may vary among different pain types and individuals (Hug et al., 2023). These changes are more pronounced in chronic conditions, explaining the greater impairments observed in CLBP compared to acute pain.

6.4 Integrated Understanding of Pain-Related Adaptations in Low Back Pain

After discussing the findings of each chapter, it is essential to integrate them within the context of existing pain-adaptation theories to better understand motor adaptations in response to LBP. Historically, two main theories have been proposed: the *"vicious cycle"* theory (Roland, 1986) and the *"pain adaptation"* theory (Lund et al., 1991). The vicious cycle theory suggested that pain induces a stereotypical increase in muscle activity in the painful region, leading to ischemia and the accumulation of pain-related metabolites, perpetuating the pain experience. Conversely, the pain adaptation theory proposed that pain reduces the activity of agonist muscles involved in the painful movement, while the antagonist muscles are facilitated,

resulting in altered voluntary movement patterns. While these models have contributed to our understanding, they focus on stereotypical motor changes and do not account for the significant inter-individual variability observed in clinical populations, as seen in this thesis. This highlights the need to consider individual-specific motor responses to pain, which the earlier models fail to explain.

To address these limitations, (Hodges and Tucker, 2011) proposed a more sophisticated theory that acknowledges motor adaptations are highly variable, involving a redistribution of activity within and between muscles, alongside changes in mechanical behaviour (e.g., movement patterns, stiffness). Rather than following the stereotypical response of uniform inhibition of agonists or facilitation of antagonists proposed by earlier models, this theory suggests that individuals search for alternative motor solutions that best suit their unique situation. These adaptations likely aim to reduce nociceptive input and pain while allowing the individual to maintain function, though they may come at the cost of altered motor patterns, reduced movement variability, and potential long-term impairments. Importantly, these adaptations are task-dependent and highly individualised, reflecting the flexible nature of motor control in response to pain. The findings from this thesis align well with the *"moving differently in pain"* theory (Hodges and Tucker, 2011), as described below.

In ***Chapter 2***, individuals with CLBP exhibited worse torque steadiness and altered motor control during more challenging isometric contractions (50% MVC). Notably, large inter-individual variability was observed, highlighting the diverse motor adaptations employed by participants with CLBP to likely manage pain while matching the requested torque. During these contractions, participants utilised a different region of the lumbar ES muscle and likely employed compensatory strategies involving synergistic muscles, rather than following the stereotypical patterns of activation proposed by earlier theories (Lund et al., 1991, Roland, 1986). Similarly, in ***Chapter 3***, dynamic trunk flexion/extension tasks involving both

concentric and eccentric contractions provided an additional challenge to the motor system. Impairments in trunk muscle force control were more pronounced during dynamic tasks compared to isometric ones, as individuals with CLBP exhibited greater deficits in torque steadiness (reflected in higher CoV and SD values) across both lower and higher force levels. During dynamic trunk flexion, participants exhibited worse control of trunk muscle force and more pronounced alterations in recruitment patterns, with differences observed within individual abdominal muscles and between different abdominal muscles (i.e., EO, RA). In contrast, during extension contractions, participants displayed overall a more consistent recruitment strategy similar to that observed during isometric trunk extension at 50% MVC in ***Chapter 2*** (i.e., higher contribution of more cranial parts of the thoracolumbar ES).

The contrast between isometric and dynamic contractions shows that motor adaptations in CLBP are highly task dependent, with dynamic contractions offering more degrees of freedom compared to isometric tasks, giving individuals with CLBP greater potential to use compensatory movement strategies. The increased mechanical demands and neuromuscular coordination required for dynamic movements, especially during trunk flexion, likely contribute to greater impairments in motor control. Additionally, the heightened perceptual threat or fear of movement/reinjury during dynamic movements may further disrupt control, prompting stronger protective strategies that may compromise performance. These findings further support the *"moving differently in pain"* theory (Hodges and Tucker, 2011), showing that motor adaptations observed in people with CLBP are related to the task, including contraction type, movement, and load and the adaptations likely being more pronounced during more challenging tasks, such as those involving higher loads and dynamic movements. While there was significant inter-individual variability in individuals with CLBP, the overall muscle recruitment strategy differed from asymptomatic controls. This strategy may have originally developed as an adaptive response (i.e., to avoid pain), but, due to long-term reliance, has

become rigid and overused. As a result, in the chronic phase, it may now be considered maladaptive, contributing to reduced motor variability (i.e., specific muscle recruitment strategies), increased tissue loading, and the perpetuation of pain. Conversely, in the acute phase, the search for new motor solutions can be beneficial, as demonstrated in ***Chapter 4*** and ***Chapter 5***, detailed below (Hodges and Tucker, 2011, Summers et al., 2019).

The findings from ***Chapter 4*** add further nuance to this understanding, as no significant impairments in control of trunk muscle force were observed in the presence of acute exercise-induced LBP (DOMS). This suggests that motor adaptations in the acute stage of pain or soreness may follow a different pattern than those seen in chronic pain conditions like CLBP. In this case, the short-term adaptations, characterised by increased motor variability, likely represent a protective strategy aimed at optimizing performance while minimising discomfort (Hodges and Tucker, 2011). These acute alterations are not necessarily maladaptive; rather, they may serve as beneficial adjustments, helping individuals maintain function and manage pain more effectively. This is further supported by the findings of ***Chapter 5***, which show that individuals experiencing acute experimental pain, particularly in the low back, do not exhibit impairments in trunk muscle force control but do adopt a different motor strategy compared to the pain-free condition (Hirata et al., 2015).

This distinction between acute and chronic pain responses highlights the importance of context when interpreting motor adaptations. In the case of DOMS, the increased motor variability, such as changes in kinematics and muscle recruitment, may not immediately lead to impaired function, as the motor system is temporarily searching for more effective strategies to cope with transient soreness. However, if these altered motor patterns persist after pain resolves, as seen in chronic pain conditions, they could contribute to long-term issues such as maladaptive motor strategies, increased tissue loading, and the risk of developing persistent or recurrent pain (Hodges and Tucker, 2011, Summers et al., 2019). This aligns with recent

evidence, such as studies using NGF, which suggest that motor control changes can persist even after acute pain subsides, potentially due to lasting alterations in corticomotor excitability (Summers et al., 2019). The inter-individual variability observed across both acute and chronic conditions further reinforces the idea that motor responses to pain are highly individualised and influenced by the nature and duration of pain. However, it remains challenging to discern when these adaptations are beneficial and when they become maladaptive, as they appear to exist on a continuum. Understanding this transition is crucial for developing targeted interventions that prevent the progression from protective strategies to maladaptive patterns.

In summary, control of trunk muscle force appears to be primarily impaired in individuals with CLBP and is not significantly affected in the acute stages of pain. However, when the task becomes more challenging (e.g., higher levels of force and/or dynamic movements), these impairments may become even more pronounced. Both acute and chronic pain can lead to alterations in the recruitment strategies used to perform the task. In the acute stage, these changes may be beneficial, but longitudinal studies are needed to determine whether such adaptations persist in the long term and contribute to reduced motor variability and rigid motor strategies, as seen in individuals with CLBP. Given that these adaptations are highly individualised and often persist even after pain resolution, there is a pressing need for advanced assessment methods to identify the specific motor patterns used by each individual. This will allow for the determination of whether these patterns are maladaptive, enabling the use of advanced technologies to develop tailored interventions aimed at restoring optimal motor function, which will differ based on each person's unique motor adaptations and needs.

6.5 Quality of Evidence for the Conclusions of this Thesis

The quality of the research conducted in this thesis has been assessed using various risk of bias evaluation tools and reporting guidelines to ensure that the conclusions drawn are

meaningful and reliable. All studies conducted in this thesis and reported in ***Chapter*** 2 ***Chapter 3*** and ***Chapter 4*** were carried out in accordance with the Declaration of Helsinki to ensure the ethical treatment of participants (Riis, 2003). Although the Declaration of Helsinki does not directly address bias, it contributes to bias reduction by ensuring that participants have a comprehensive understanding of the study's objectives, procedures, and potential risks through informed consent. Additionally, all empirical studies reported in this thesis adhered to the STROBE guidelines (von Elm et al., 2007). While the STROBE guidelines do not specifically evaluate bias, they provide a framework for assessing the study and ensuring transparency in reporting results. Despite these guidelines not targeting bias explicitly, every potential measure has been implemented to limit bias in the reporting of this thesis's results.

The studies reported in ***Chapter 2*** and ***Chapter 3*** were included in the systematic review that is presented in ***Chapter 5*** where the risk of bias was assessed using an adapted version of the NOS tool. To minimise bias, these studies were assessed by the second reviewer of the systematic review and were rated as of *"poor quality"*. It is important to mention, though, that this was mainly because these two studies did not specify that the matching of participants by age and/or gender was part of the study methodology (even though this was controlled). If this had been reported, both studies would have been rated as high quality. This highlights the importance of correctly reporting this information. The risk of bias of the study reported in ***Chapter 4*** was not initially assessed as it was not included in the systematic review. However, after evaluating it using the same adapted NOS tool for experimental pain studies to ensure consistency across the thesis, it was rated as of good quality. It is important to consider that this assessment was performed by the author of this study, which might introduce a potential source of bias in the evaluation process.

In ***Chapter 5***, the systematic review was evaluated using the AMSTAR-2 guidelines to assess the quality of systematic reviews (Shea et al., 2017). The evaluation showed that most

items on the checklist were met, including a well-defined research question and inclusion criteria incorporating PICOS components, a comprehensive literature search strategy using multiple databases, a list of excluded studies with justifications, the involvement of two independent reviewers for study selection and data extraction and the use of appropriate meta-analytical procedures that included additional analysis (e.g., sensitivity) to understand the influence of individual studies on the overall result (Shea et al., 2017). However, one component that was not met was the reporting of the sources of funding for the studies included in the review. The main reason for this omission was that not all included studies disclosed their funding sources. In cases where funding was mentioned, it was stated that it did not influence the study's conduct or reporting. This highlights the importance of transparent reporting of funding information to allow for a thorough evaluation of potential biases or conflicts of interest.

The protocol of the systematic review was published in advance, registered on PROSPERO, and the review was conducted according to PRISMA guidelines. All these steps were taken to ensure that bias was minimized. All studies included in the systematic review were screened using two adapted versions of the NOS tool. Additionally, the quality of evidence was further assessed using the GRADE approach (Atkins et al., 2004). The overall quality of evidence for clinical pain, which was the main focus of this thesis, was rated as *"moderate"* for CoV and as *"low"* for SD of force. On the other hand, the overall quality of evidence for experimental pain, for both measures, was downgraded to very low, particularly due to inconsistency in effect sizes, imprecision (e.g., wide CIs, a few studies with small sample sizes), necessitating caution in the interpretation of these results.

6.6 Overall Strengths and Methodological Considerations

This thesis has several strengths and some limitations that need to be acknowledged. One of the primary strengths is the comprehensive methodology used in ***Chapter*** 2 ***Chapter 3*** and ***Chapter 4*** which involved dynamometry, HDsEMG, and various advanced signal processing techniques to study the control of trunk muscle force in people with LBP. This multidisciplinary approach provided a detailed understanding of motor adaptations to pain, and in ***Chapter 4***, this also included kinematic changes. Importantly, the research focused on both isometric and dynamic movements, which are more clinically relevant. The inclusion of different studies allowed for a broader understanding of trunk force control mechanisms in both chronic and acute stages of LBP. The meta-analysis further expanded this understanding to musculoskeletal pain in general. A significant strength of this thesis is the identification of additional neuromuscular impairments in individuals with CLBP beyond just muscle strength and endurance. These findings suggest potential targets for future tailored interventions, which could lead to improved treatment outcomes for CLBP. Highlighting these impairments provides a new direction for developing more effective therapeutic strategies.

However, the thesis has some limitations. A major limitation is the small sample size, predominantly consisting of young, active individuals with low to moderate pain intensity and disability, which limits the generalisability of the results. Despite the low levels of disability and pain, impairments were still identifiable, although variability among individuals with CLBP was noted. It is likely that a sample with more severe CLBP would exhibit greater deficits or different neuromuscular adaptations impacting torque control. Another limitation is the lack of measurement of compensatory patterns using kinematic markers or recording surface EMG activity of synergist muscles, particularly in ***Chapter 2*** and ***Chapter 3***. Additionally, another important limitation is that the rectified interference surface EMG is a rough estimator of neural drive to muscles, influenced by factors like amplitude cancellation,

which can distort the EMG signal spectrum and affect results (Dideriksen and Farina, 2019). However, HDsEMG decomposition is currently challenging on signals collected from the lumbar ES due to its anatomical complexity and volume conductor properties, which can reduce the discriminative information in the action potential waveforms of different motor units and this limits the applicability of decomposition algorithms (Del Vecchio et al., 2020). Therefore, the analysis was based on the rectified surface EMG signal. The moderate correlation between surface EMG and torque (≈ 0.4) suggested a valid, albeit less precise, measure compared to motor unit recordings, which show higher correlations in smaller muscles. Moreover, the reliability of HDsEMG for abdominal muscles has not been established, so results should be interpreted cautiously. While statistical differences in trunk muscle force control were observed, the minimal clinically significant difference and its relation to patient symptoms remain to be established. Finally, the observational nature of most studies limits the ability to infer causality.

6.7 Implications for Clinical and Future Research

The findings of this thesis highlight significant clinical implications and pave the way for future research directions. Impaired force steadiness may lead to suboptimal tissue loading, where a disrupted sense of body position results in the application of excessive forces in unfavourable positions during movement. This abnormal mechanical stress on tissues can activate nociceptors and cause tissue strain, potentially contributing to additional pain or injuries and perpetuating existing symptoms. Such impairments are clinically relevant and should be targeted in treatment strategies for individuals experiencing musculoskeletal pain, including CLBP. Consistent with previous studies, our findings underscore that individuals with CLBP exhibit altered muscle recruitment patterns and torque steadiness deficits. Despite

this evidence, particularly regarding torque steadiness deficits, these insights have yet to be incorporated into CLBP management.

Assessing torque steadiness deficits and neuromuscular differences in the thoracolumbar ES and abdominal muscles and attempting to alter them using the methodology employed in this thesis (torque steadiness with/without HDsEMG biofeedback), could potentially offer a more comprehensive approach to CLBP management. However, before these interventions are widely adopted, rigorous studies are essential to determine their impact on individual symptoms and their potential to induce physiological changes, such as modifications in muscle recruitment behaviour. Given that CLBP remains a leading cause of disability globally, the findings of this thesis suggest the necessity to refine and expand therapeutic strategies, integrating innovative assessment methods and interventions.

This is further supported by a narrative review (Falla and Hodges, 2017) suggesting that exercise is the most effective treatment for managing and preventing spinal pain; yet, on average, it delivers small to moderate treatment effects, which are rarely long-lasting. Exercise interventions could potentially be optimised when targeted towards the right patients and tailored to address the neuromuscular impairments of each individual (Falla and Hodges, 2017). Therefore, future research should focus on personalised therapeutic strategies that incorporate these insights to improve long-term outcomes for individuals with CLBP. By targeting specific neuromuscular impairments and tailoring interventions to individual needs, it may be possible to enhance the effectiveness of treatments and provide more sustained relief from symptoms.

6.8 Conclusion

This thesis provides evidence that individuals with CLBP exhibit impairments in the control of trunk muscle force during both isometric and dynamic trunk movements. Notably, it

also reveals significant differences in muscle activation patterns, particularly in the thoracolumbar ES and EO, between individuals with CLBP and asymptomatic controls. Additionally, it demonstrates that impairments in trunk muscle force control are not observed in acute exercise-induced LBP.

Overall, this thesis shows that clinical musculoskeletal pain, including CLBP, has a detrimental effect on the control of muscle force. Considering that suboptimal control of muscle force may lead to suboptimal tissue loading and play a role in the perpetuation of symptoms, our findings underscore the importance of evaluating torque steadiness in individuals with CLBP. Future research should consider the value of torque steadiness training and HDsEMG-based biofeedback for modifying trunk muscle recruitment strategies and improving torque steadiness performance in individuals with CLBP.

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APPENDICES

Appendix 1 – Arvanitidis et al., 2022 (*Chapter 2*)

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People with chronic low back pain display spatial alterations in high-density surface EMG-torque oscillations

Michail Arvanitidis, David Jiménez-Grande, Nadège Haouidji-Javaux, Deborah Falla & Eduardo Martinez-Valdes✉

We quantified the relationship between spatial oscillations in surface electromyographic (sEMG) activity and trunk-extension torque in individuals with and without chronic low back pain (CLBP), during two submaximal isometric lumbar extension tasks at 20% and 50% of their maximal voluntary torque. High-density sEMG (HDsEMG) signals were recorded from the lumbar erector spinae (ES) with a 64-electrode grid, and torque signals were recorded with an isokinetic dynamometer. Coherence and cross-correlation analyses were applied between the filtered interference HDsEMG and torque signals for each submaximal contraction. Principal component analysis was used to reduce dimensionality of HDsEMG data and improve the HDsEMG-based torque estimation. sEMG-torque coherence was quantified in the δ(0–5 Hz) frequency bandwidth. Regional differences in sEMG-torque coherence were also evaluated by creating topographical coherence maps. sEMG-torque coherence in the δ band and sEMG-torque cross-correlation increased with the increase in torque in the controls but not in the CLBP group ($p = 0.018$, $p = 0.030$ respectively). As torque increased, the CLBP group increased sEMG-torque coherence in more cranial ES regions, while the opposite was observed for the controls ($p = 0.043$). Individuals with CLBP show reductions in sEMG-torque relationships possibly due to the use of compensatory strategies and regional adjustments of ES-sEMG oscillatory activity.

When executing a steady submaximal isometric contraction, the applied force or torque is not perfectly accurate but rather, small oscillations occur around the target torque value[1]. The neural origin of torque fluctuations has been a topic of interest for many years[1]. Previous studies have proposed that the variability in the times that motoneurons discharge action potentials could be a potential determinant for the accurate control of muscle force[2]. This variability could be determined by independent and common synaptic inputs received by motor units and/or by the nonlinear input–output properties of individual motoneurons[1]. However, recent studies have shown that the neural drive to the muscle (i.e., the neural activation signal that the muscles receive from the pool of innervating motoneurons) in low frequencies (< 10 Hz) is mainly relevant for torque generation as it reflects the common synaptic input received by the motor unit pool[3–5]. This happens because a group of activated motoneurons can act as a very selective filter, which eliminates all the independent components, partly linearizes the input–output motoneuron behavior and amplifies the common component[4]. Thus, the control of muscle force depends mainly on the amplitude of the low-frequency oscillations that reflect shared (common) synaptic input[1].

Smooth force production depends highly on our proprioceptive senses of effort and force, with the first being generated centrally (via corollary discharges of the descending motor command), and the latter derived from peripheral sensory receptors (i.e., muscle spindles and tendon organs; reafference activity)[6]. These central and peripheral signals are sent to the somatosensory cortex via spinal, subcortical and cortical neural pathways, where they are integrated along with other somatosensory, visual, and vestibular information, resulting in the perception of applied forces[6,7]. A descending motor command is then sent to the tissues involved, resulting in an appropriate action[8]. The proprioceptive system ensures smooth force production through this interactive process, that requires constant monitoring and modulation of ascending and descending information based on the proprioceptive input, motor output, perception, and the resulting action[8]. Therefore, any perturbation to these systems, can affect the control of muscle force.

Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, UK. ✉email: e.a.martinezvaldes@bham.ac.uk

Appendix 2 – Ethics Approval Letter

From: Samantha Waldron (Research Support Group) <[redacted]>
Sent: Monday, November 11, 2019 9:55 AM
To: Eduardo Martinez Valdes (Sport, Exercise and Rehabilitation Sciences) <[redacted]>
Cc: Michail Arvanitidis (PhD School of Sprt+Ex Scie FT) <[redacted]>
Subject: Application for Ethical Review ERN_19-1148

Dear Dr Eduardo Martinez-Valdes,

Re: "Control of trunk muscle force in individuals with and without non-specific low back pain. Can eccentric exercise induced muscle damage be used as a model for low back pain?"
Application for Ethical Review ERN_19-1148

Thank you for your application for ethical review for the above project, which was reviewed by the Science, Technology, Engineering and Mathematics Ethical Review Committee.

On behalf of the Committee, I confirm that this study now has full ethical approval.

I would like to remind you that any substantive changes to the nature of the study as described in the Application for Ethical Review, and/or any adverse events occurring during the study should be promptly brought to the Committee's attention by the Principal Investigator and may necessitate further ethical review.

Please also ensure that the relevant requirements within the University's Code of Practice for Research and the information and guidance provided on the University's ethics webpages (available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Links-and-Resources.aspx) are adhered to and referred to in any future applications for ethical review. It is now a requirement on the revised application form (https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx) to confirm that this guidance has been consulted and is understood, and that it has been taken into account when completing your application for ethical review.

Please be aware that whilst Health and Safety (H&S) issues may be considered during the ethical review process, you are still required to follow the University's guidance on H&S and to ensure that H&S risk assessments have been carried out as appropriate. For further information about this, please contact your School H&S representative or the University's H&S Unit at healthandsafety@contacts.bham.ac.uk.

Kind regards,

Ms Sam Waldron
Research Ethics Officer
Research Support Group
[redacted]

Please remember to submit a new Self-Assessment Form for each new project. Click Ethical Review Process for further details regarding the University's Ethical Review process.

Click Research Governance for further details regarding the University's Research Governance and Clinical Trials Insurance processes, or email researchgovernance@contacts.bham.ac.uk with any queries

Appendix 3 – Arvanitidis et al., 2024 (*Chapter 3*)

CLINICAL SCIENCES

Low Back Pain–Induced Dynamic Trunk Muscle Control Impairments Are Associated with Altered Spatial EMG–Torque Relationships

MICHAIL ARVANITIDIS, DAVID JIMÉNEZ-GRANDE, NADÈGE HAOUIDJI-JAVAUX, DEBORAH FALLA, and EDUARDO MARTINEZ-VALDES

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ABSTRACT

ARVANITIDIS, M., D. JIMÉNEZ-GRANDE, N. HAOUIDJI-JAVAUX, D. FALLA, and E. MARTINEZ-VALDES. Low Back Pain–Induced Dynamic Trunk Muscle Control Impairments Are Associated with Altered Spatial EMG–Torque Relationships. *Med. Sci. Sports Exerc.*, Vol. 56, No. 2, pp. 193–208, 2024. **Purpose:** We quantified the relationship between high-density surface electromyographic (HDsEMG) oscillations (in both time and frequency domains) and torque steadiness during submaximal concentric/eccentric trunk extension/flexion contractions, in individuals with and without chronic low back pain (CLBP). **Methods:** Comparisons were made between regional differences in HDsEMG amplitude and HDsEMG–torque cross-correlation and coherence of the thoracolumbar erector spinae (ES), rectus abdominis (RA), and external oblique (EO) muscles between the two groups. HDsEMG signals were recorded from the thoracolumbar ES with two 64-electrode grids and from the RA and EO muscles with a single 64-electrode grid placed over each muscle. Torque signals were recorded with an isokinetic dynamometer. Coherence (δ band (0–5 Hz)) and cross-correlation analyses were used to examine the relationship between HDsEMG and torque signals. For this purpose, we used principal component analysis to reduce data dimensionality and improve HDsEMG-based torque estimation. **Results:** We found that people with CLBP had poorer control during both concentric and eccentric trunk flexion and extension. Specifically, during trunk extension, they exhibited a higher HDsEMG–torque coherence in more cranial regions of the thoracolumbar ES and a higher HDsEMG cross-correlation compared with asymptomatic controls. During trunk flexion movements, they demonstrated higher HDsEMG amplitude of the abdominal muscles, with the center of activation being more cranial and a higher contribution of this musculature to the resultant torque (particularly the EO muscle). **Conclusions:** Our findings underscore the importance of evaluating torque steadiness in individuals with CLBP. Future research should consider the value of torque steadiness training and HDsEMG-based biofeedback for modifying trunk muscle recruitment strategies and improving torque steadiness performance in individuals with CLBP. **Key Words:** LOW BACK PAIN, HIGH-DENSITY SURFACE EMG, TORQUE STEADINESS, COHERENCE, CROSS-CORRELATION

The force exerted by our muscles depends on the number of motor units activated and their discharge rates (1). The output of the active motor unit population during a voluntary contraction results in the production of force, which is never constant but instead fluctuates about an average value (2). The underlying neural mechanisms contributing to variations in muscle force during voluntary contractions have been a topic of interest for many years. However, as recently shown, the low-frequency (<10 Hz) component of the neural command (i.e., the effective neural drive) is mainly responsible for generating muscle force because it reflects the common synaptic input received by the motor unit population (3,4). Hence, the genesis of these force fluctuations and the control of muscle force depend mainly on the amplitude of these low-frequency oscillations that reflect common synaptic input (3). Measuring the amplitude of the force fluctuations (5) can provide a measure of force (torque) steadiness, that is, a measure of an individual's ability to maintain a constant level of force during a submaximal contraction (2).

Executing contractions with minimal variations in force is important for normal physical function. Any impairment in this ability can negatively affect the precision of voluntary movements, resulting in alterations in dynamic joint stability/coordination and potentially leading to changes in joint movement patterns. Musculoskeletal pain can significantly impact movement and the ability to control muscle force, potentially due to changes in afferent input from the painful area (6) or

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Submitted for publication June 2023.
Accepted for publication September 2023.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

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DOI: 10.1249/MSS.0000000000003314

Appendix 4 – Arvanitidis et al., 2024b (*Chapter 4*)

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Eccentric exercise-induced delayed onset trunk muscle soreness alters high-density surface EMG-torque relationships and lumbar kinematics

Michail Arvanitidis, David Jiménez-Grande, Nadège Haouidji-Javaux, Deborah Falla & Eduardo Martinez-Valdes

We aimed to assess high-density surface electromyography (HDsEMG)-torque relationships in the presence of delayed onset trunk muscle soreness (DOMS) and the effect of these relationships on torque steadiness (TS) and lumbar movement during concentric/eccentric submaximal trunk extension contractions. Twenty healthy individuals attended three laboratory sessions (24 h apart). HDsEMG signals were recorded unilaterally from the thoracolumbar erector spinae with two 64-electrode grids. HDsEMG-torque signal relationships were explored via coherence (0–5 Hz) and cross-correlation analyses. Principal component analysis was used for HDsEMG-data dimensionality reduction and improvement of HDsEMG-torque-based estimations. DOMS did not reduce either concentric or eccentric trunk extensor muscle strength. However, in the presence of DOMS, improved TS, alongside an altered HDsEMG-torque relationship and kinematic changes were observed, in a contraction-dependent manner. For eccentric trunk extension, improved TS was observed, with greater lumbar flexion movement and a reduction in δ-band HDsEMG-torque coherence and cross-correlation. For concentric trunk extensions, TS improvements were observed alongside reduced thoracolumbar sagittal movement. DOMS does not seem to impair the ability to control trunk muscle force, however, perceived soreness induced changes in lumbar movement and muscle recruitment strategies, which could alter motor performance if the exposure to pain is maintained in the long term.

Keywords Delayed onset of muscle soreness, Exercise-induced muscle damage, Eccentric, Concentric, High-density surface EMG, Torque steadiness

Delayed-onset muscle soreness (DOMS) represents a form of ultrastructural muscle injury that typically emerges following intense, unfamiliar exercises, particularly those emphasizing eccentric contractions[1,2]. Clinical signs of DOMS, include reduced force production, painful movement limitations, stiffness, swelling, and dysfunction in adjacent joints[1]. These symptoms can persistently impair muscle function[3]. Although considered a mild form of injury, DOMS frequently undermines athletic performance[1] and may disrupt daily activities[3], likely due to alterations in electromyography (EMG)-force relationships, during muscle contractions[3]. Evaluating the relationship between EMG and force/torque provides valuable insights into neuromuscular function[4]. EMG measures the electrical activity of muscle fibers, indicating the efficiency of neuromuscular transmission, which is the process by which the nervous system activates muscles to generate force[4,5]. This electrical activity must be efficiently translated into mechanical output for effective muscle function. During DOMS, neuromuscular function may be compromised, potentially affecting this translation process. Assessing EMG-torque relationships can help us uncover the underlying mechanisms responsible for alterations in motor function.

Numerous studies have investigated the effect of DOMS on the neuromuscular function of peripheral muscles, such as the elbow flexors and hamstrings[3,6–11]. In contrast, research focusing on trunk muscles is less extensive, with only a few studies inducing DOMS to assess its influence on trunk muscle function. For example some of

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Appendix 5 – Arvanitidis et al., 2024a (*Chapter 5*)

Received: 5 April 2024 | Revised: 30 July 2024 | Accepted: 7 August 2024

DOI: 10.1002/ejp.4716

REVIEW ARTICLE

Does pain influence control of muscle force? A systematic review and meta-analysis

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Abstract

Background and Objective: In the presence of pain, whether clinical or experimentally induced, individuals commonly show impairments in the control of muscle force (commonly known as force steadiness). In this systematic review and meta-analysis, we synthesized the available evidence on the influence of clinical and experimental pain on force steadiness.

Databases and Data Treatment: MEDLINE, EMBASE, PubMed, CINAHL Plus and Web of Science databases were searched from their inception to 19 December 2023, using MeSH terms and pre-selected keywords related to pain and force steadiness. Two independent reviewers screened studies for inclusion and assessed their methodological quality using a modified Newcastle–Ottawa risk of bias tool.

Results: In total, 32 studies (19 clinical pain and 13 experimental pain) were included. Meta-analyses revealed reduced force steadiness in the presence of clinical pain as measured by the coefficient of variation (CoV) and standard deviation (SD) of force (standardized mean difference; SMD = 0.80, 95% CI = 0.31–1.28 and SMD = 0.61, 95% CI = 0.11–1.11). These findings were supported by moderate and low strength of evidence respectively. In the presence of experimental pain, meta-analyses revealed reductions in force steadiness when measured by the CoV of force but not by the SD of force (SMD = 0.50, 95% CI = 0.01–0.99; and SMD = 0.44, 95% CI = −0.04 to 0.92), each supported by very low strength of evidence.

Conclusions: This work demonstrates that pain, particularly clinical pain, impairs force steadiness. Such impairments likely have clinical relevance and could become targets for treatment when managing people experiencing musculoskeletal pain.

Significance Statement: This systematic review and meta-analyses enhances our understanding of motor impairments observed in people experiencing musculoskeletal pain. It underscores the significance of incorporating force steadiness assessment when managing individuals experiencing musculoskeletal pain. Additionally, it suggests that future research should explore the potential benefits

Arvanitidis et al., 2021b (*Protocol*)

Open access Protocol

BMJ Open

Does pain influence force steadiness? A protocol for a systematic review

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To cite: Arvanitidis M, Falla D, Sanderson A, *et al*. Does pain influence force steadiness? A protocol for a systematic review. *BMJ Open* 2021;**11**:e042525. doi:10.1136/bmjopen-2020-042525

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-042525).

Received 07 July 2020
Revised 26 November 2020
Accepted 30 December 2020

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ABSTRACT

Introduction Performing contractions with minimum force fluctuations is essential for everyday life as reduced force steadiness impacts on the precision of voluntary movements and functional ability. Several studies have investigated the effect of experimental or clinical musculoskeletal pain on force steadiness but with conflicting findings. The aim of this systematic review is to summarise the current literature to determine whether pain, whether it be clinical or experimental, influences force steadiness.

Methods and analysis This protocol for a systematic review was informed and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols and the Cochrane Handbook for Systematic Reviews of Interventions. Key databases will be searched from inception to 31 August 2020, including MEDLINE, EMBASE, PubMed, CINAHL Plus, ZETOC and Web of Science. Grey literature and key journals will be also reviewed. Risk of bias will be assessed with the Newcastle-Ottawa tool, and the quality of the cumulative evidence assessed with the Grading of Recommendations, Assessment, Development and Evaluation guidelines. If homogeneity exists between groups of studies, meta-analysis will be conducted. Otherwise, a narrative synthesis approach and a vote-counting method will be used, while the results will be presented as net increases or decreases of force steadiness.

Ethics and dissemination The findings will be presented at conferences and the review will be also submitted for publication in a refereed journal. No ethical approval was required.

PROSPERO registration number CRD42020196479

Strengths and limitations of this study

- This will be the first systematic review to synthesise evidence and examine the effect of experimental and/or clinical pain on force steadiness.
- The effect of experimental or clinical pain on force steadiness will be considered for a wide range of joints and muscles during different contraction types of varying force.
- This protocol was written in accordance with the recommendations provided by the Cochrane Handbook for Systematic Reviews of Interventions.

INTRODUCTION

During a voluntary movement of submaximal effort, the force produced by an individual is not constant, instead, it fluctuates around an average value.[1] This variability of force is the consequence of neuromuscular noise and other environmental influences.[2] The ability of an individual to produce a steady force during a submaximal voluntary contraction is defined as force steadiness (or torque steadiness) and is an important aspect of force control.[3] Being able to perform contractions with minimum force fluctuations is essential for physical function and its impairment could influence the precision of voluntary movements. This could affect the joints' dynamic stability, coordination and potentially result in altered joint kinematics and overall function.[4–8]

Smooth force generation is highly dependent on the sense of force, which is part of proprioception.[9] Multiple neuromuscular receptors, including Golgi tendon organs, muscle spindles (proprioceptors) and pressure-sensitive skin receptors contribute to the perception of force, by detecting mechanical tissue changes and transmitting action potentials to the central nervous system (CNS).[10] The proprioceptive information (afferent inflow) from these receptors enters the spinal cord dorsal horn and then ascends via the dorsal column medial lemniscus pathway to the cerebral cortex (conscious path) or via the spinocerebellar pathways to the cerebellum (unconscious path).[11] Processing of proprioceptive afferent information can occur at all levels of the CNS, while it is consciously appreciated in the primary somatosensory area of the cerebral cortex.[11] In this area, proprioceptive information is integrated with other somatosensory, vestibular and visual information.[11] Then, a descending cerebral (efferent) motor command is sent to the tissues involved, resulting in an appropriate action.[9] For this interactive and complex process, continuous monitoring and modulation of ascending and descending information is required, based on

Appendix 6 – Supplementary Material of *Chapter 5*

Supplementary Material 1 – PRISMA Checklist

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	✓
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	✓
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	1-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	2-3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3-7, 11-14
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7-8
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplemental file 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	9
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	10
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	10
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	10
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	10
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	11-12
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	11-13
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	11-13
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	11-13
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	11-13
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	13
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	14
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	13-14
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	14

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	14-15, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	15
Study characteristics	17	Cite each included study and present its characteristics.	16-29, Tables 1 & 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	19 Tables 3 & 4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 1 & 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	20-23, Tables 3& 4
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	20-23, Figures 2 & 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	25, 27 Supplemental file 4
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Supplemental file 4
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Table 5
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	24, Table 5
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	24-29
	23b	Discuss any limitations of the evidence included in the review.	30
	23c	Discuss any limitations of the review processes used.	30
	23d	Discuss implications of the results for practice, policy, and future research.	30-31
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	3
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	32
Competing interests	26	Declare any competing interests of review authors.	32
Availability of data, code and	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included	32

Section and Topic	Item #	Checklist item	Location where item is reported
other materials		studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary Material 2 – Full search strategies for all databases

Search Strategy (MEDLINE, Ovid Interface)

1. Force.mp
2. Torque.mp
3. Moment.mp
4. 1-3 (OR)
5. Control.mp
6. Steadiness.mp
7. Variab*.mp
8. Modulat*.mp
9. 5-8 (OR)
10. Target.mp
11. Trajectory.mp
12. 10-11 (OR)
13. Coefficient of variation.mp
14. CoV.mp
15. Standard deviation.mp
16. SD.mp
17. Mean squar* error.mp
18. 13-17 (OR)
19. exp Pain/
20. exp Solutions/
21. Pain.mp
22. Acute Pain.mp
23. Chronic Pain.mp
24. Nociceptive pain.mp
25. Musculoskeletal pain.mp
26. Nocicept*.mp
27. Musculoskeletal disease*.mp
28. Hypertonic solution*.mp
29. Isotonic solution*.mp
30. Injections, Intramuscular.mp
31. Injections, Intra-Articular.mp
32. Electric stimulation.mp
33. 19-32 (OR)

34. **4 ADJ5 9**
35. **4 ADJ5 12**
36. **4 ADJ5 18**
37. **34 OR 35 OR 36 AND 33**
38. **Limit 37 to Humans**

Search Strategy (EMBASE, Ovid Interface)

1. Force.mp
2. Torque.mp
3. Moment.mp
4. 1-3 (OR)
5. Control.mp
6. Steadiness.mp
7. Variab*.mp
8. Modulat*.mp
9. 5-8 (OR)
10. Target.mp
11. Trajectory.mp
12. 10-11 (OR)
13. Coefficient of variation.mp
14. CoV.mp
15. Standard deviation.mp
16. SD.mp
17. Mean squar* error.mp
18. 13-17 (OR)
19. exp injection pain/
20. exp injection site pain/
21. exp musculoskeletal pain/
22. exp pain/
23. exp experimental muscle pain/
24. exp experimental pain/
25. exp nociceptive pain/
26. exp isotonic solution/
27. exp hypertonic solution/
28. Pain.mp
29. Acute Pain.mp
30. Chronic Pain.mp
31. Nociceptive pain.mp
32. Musculoskeletal pain.mp
33. Nocicept*.mp
34. Musculoskeletal disease*.mp
35. Hypertonic solution*.mp
36. Isotonic solution*.mp
37. Electric stimulation.mp
38. Intra-articular injection
39. Intramuscular injection
40. Intraarticular injection
41. Intra-muscular injection
42. 19-41 (OR)

43. **4 ADJ5 9**
44. **4 ADJ5 12**
45. **4 ADJ5 18**
46. **43 OR 44 OR 45 AND 42**
47. **Limit 46 to Humans**

Search Strategy (PubMed)

1. "Force control"
2. "Control of force"
3. "Force steadiness"
4. "Torque steadiness"
5. "Force variability"
6. "Torque variability"
7. "Force target"
8. "Torque target"
9. "Coefficient of Variation"
10. "Force SD"
11. "Torque SD"
12. 1-11 (OR)
13. Pain
14. Hypertonic solution*
15. Isotonic solution*
16. Nocicept*
17. Musculoskeletal disease*
18. "Musculoskeletal pain"[MeSH Terms]
19. 13-18 (OR)

20. **12 AND 19**
21. **Limit 20 to Humans**

Search Strategy (CINAHL Plus, EBSCO Interface)

S1 (force) n5 (control or steadiness or variab* or modulat*)
S2 (torque) n5 (control or steadiness or variab* or modulat*)
S3 (moment) n5 (control or steadiness or variab* or modulat*)
S4 (force) n5 (target or trajectory)
S5 (torque) n5 (target or trajectory)
S6 (moment) n5 (target or trajectory)
S7 (force) n5 (Coefficient of variation OR CoV OR Standard deviation OR SD OR Mean squar* error)
S8 (torque) n5 (Coefficient of variation OR CoV OR Standard deviation OR SD OR Mean squar* error)
S9 (moment) n5 (Coefficient of variation OR CoV OR Standard deviation OR SD OR Mean squar* error)

S10 (MH "Pain+" OR
(OR) MH "Nociceptive Pain+" OR
MH "Injections, Intramuscular+" OR
MM "Injections, Intraarticular" OR
MH "Hypertonic Solutions+" OR
MH "Isotonic Solutions+")

S11 (Pain OR
(OR) Acute Pain OR

Chronic Pain OR
Nociceptive pain OR
Musculoskeletal pain OR
Nocicept* OR
Musculoskeletal disease* OR
Hypertonic solution* OR
Isotonic solution* OR
Electric stimulation OR
Injections, Intramuscular OR
Injections, Intraarticular)

S12 **S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9**
S13 **S10 OR S11**
S14 **S12 AND S13**
S15 **Limit S14 to Human**

Search Strategy (Web of Science, Clarivate Analytics)

1. TS=(force near/5 (control or steadiness or variab* or modulat*))
2. TS=(torque near/5 (control or steadiness or variab* or modulat*))
3. TS=(moment near/5 (control or steadiness or variab* or modulat*))
4. TS=(force near/5 (target or trajectory))
5. TS=(torque near/5 (target or trajectory))
6. TS=(moment near/5 (target or trajectory))
7. TS=(force near/5 ("Coefficient of variation" OR CoV OR "Standard deviation" OR SD OR "Mean squar* error"))
8. TS=(torque near/5 ("Coefficient of variation" OR CoV OR "Standard deviation" OR SD OR "Mean squar* error"))
9. TS=(moment near/5 ("Coefficient of variation" OR CoV OR "Standard deviation" OR SD OR "Mean squar* error"))
10. 1-9 (OR)

11. TS=(Pain OR
(OR) Acute Pain OR
Chronic Pain OR
Nociceptive Pain OR
Musculoskeletal pain OR
Nocicept* OR
Musculoskeletal disease* OR
Hypertonic Solution* OR
Isotonic Solution* OR
Electric stimulation OR
Intra-articular injection OR
Intramuscular injection OR
Intraarticular injection OR
Intra-muscular injection OR
Experimental pain)

12. **10 AND 11**

Supplementary Material 3 – Changes in Newcastle Ottawa Quality Assessment Scale

Changes for studies with clinical pain

Newcastle Ottawa Quality Assessment Scale
Cross-Sectional Studies

Adapted from Newcastle Ottawa Quality Assessment Scale for Case-Control Studies based on elements from the STROBE guidelines and the Newcastle Ottowa Scale manual (Wells, Accessed 2018, von Elm et al., 2008)

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) Yes, with independent validation ❋
   b) Yes, e.g. record linkage or based on self-reports
   c) No description

2) Representativeness of the cases
   a) Consecutive or obviously representative cases ❋
   b) Generally representative cases ❋
   c) Potential for selection biases or not stated

3) Selection of Controls
   a) Community Controls ❋
   b) Alternative Control recruitment
   c) No Description

4) Definition of Controls
   a) No history of disease ❋
   b) No mention of history of outcome

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) Study controls for two or more elements of the Population Demographics ❋❋
   b) Study controls for any one element of the population demographics ❋
   c) Study does not control for any factor

Exposure

1) Description of Force/Torque steadiness Exposure
   a) Force/Torque steadiness evaluation, recording equipment and processing are clearly described and standardised ❋
   b) Force/Torque steadiness evaluation, recording equipment and processing are sufficiently described and standardised ❋
   c) Force/Torque steadiness evaluation, recording equipment and processing are poorly described

2) Same Force/Torque steadiness Exposure for cases and controls
   a) yes ❋
   b) no
3) Description of Task Exposure
   a) Task was well described and implemented in a standardised well in both groups ❋
   b) Task was well described but not standardised
   c) Task was poorly described and standardised

Question Number	Changes	Justification
Section 1	**Minor question wording changes**	
1	No Changes made	This inquiry aims to determine the extent to which the symptoms or absence of symptoms in the Clinical-Experimental Pain/Con groups have been confirmed.
2	Addition of a second category	To address this issue, an extra classification has been introduced to acknowledge cases where the sample meets the eligibility criteria and participates but doesn't completely reflect the population under study. For instance, in the context of musculoskeletal pain (clinical or experimental), individuals with relatively low average pain levels (e.g., rated 2/10 on the PNRS) are included. Although these individuals may satisfy the inclusion criteria and exhibit no sampling bias, they do not fully represent the clinical population characterised by persistent high levels of pain and disability.
3	Modification of second category	The original wording assumed recruitment of cases exclusively from hospitals or through structured processes. The objective was to determine if the only distinction between cases and controls was the presence of case symptoms, while both originated from the same community. The second category aimed to identify whether controls were individuals from the hospital without the case, potentially representing a different background or community. The revised phrasing accommodates the likelihood of cases not being recruited solely from a hospital, eliminating the option of hospital controls. Instead, the new classification considers whether cases and controls were sourced from the same population or if different sampling methods were employed for controls, potentially introducing selection bias.
4	Rewording of second category	This question examines whether bias may arise from including individuals who have previously experienced the case symptoms and whether such individuals should be excluded. The original wording of the question focused on the "source" of the case symptom, which is not relevant to the studies under review. The revised phrasing specifically addresses whether controls should have no prior history of the symptoms, ensuring the essence of the question is preserved.
Section 2	**Minor Alterations**	

5	A third category has been included, and specific factors have been included.	The original question evaluates the extent to which cases and controls can be effectively compared and whether matching was incorporated during the design phase. The design allowed individual reviewers to choose the most relevant factors for their specific review. In this case, population demographics were selected as the factor to control for, considering that anthropomorphic features could potentially influence the primary outcome, force/torque steadiness. As per the coding manual, if the specified criteria are not met or if group comparability occurs by chance after the fact, no stars should be assigned for this section. However, the original format did not provide an option for addressing this scenario. In this modification, an additional category has been included to ensure that this question is addressed and intentionally not assigned any stars, avoiding accidental omissions due to oversight.
Section 3	**Major Changes**	**Questions in this section have required the most modifications as the original section sought to ascertain if the cases and controls were exposed to the variable of interest. In studies included here, the variable of interest is the force/torque steadiness and by participating in the experiment, it is known that cases and controls are exposed.**
6	This question has been specifically rewritten for the force/torque steadiness exposure.	The original question aimed to evaluate the potential introduction of bias through the inadvertent inclusion of individuals as cases who have not been exposed to the variable of interest. This consideration is particularly important when tracking the progression of individuals with conditions like vertebral fractures over time, as the process of confirming or disproving the occurrence of a fracture can introduce bias. However, in this systematic review, there are two exposures to be considered: one to musculoskeletal pain and another to force/torque steadiness assessment and a specific task. The exposure to musculoskeletal pain cannot be externally verified due to its nature as an "invisible disability"; thus, all included studies would be categorised as "self-report" (as already considered in Q1). The essence of this question lies in establishing the causality of results based on an individual's exposure to the variable of interest. In the context of assessing force steadiness, it is equally important to examine how the principles of force steadiness assessment are consistently applied across groups, including the choice of the dynamometer, task, position, and other relevant factors. Failure to standardise these aspects could introduce bias, making it challenging to determine if the results are attributable to an individual being a case or control or if the assessment of force steadiness was conducted accurately.

7	Slight change in the question wording	This question inquired whether the response to Q6 was consistent between cases and controls. Due to the modification of Q6, the title of this question has been slightly adjusted to align with this change.
8	This question has been specifically rewritten for the description of the force/torque steadiness exposure.	The original question assessed if reporting bias had been introduced through different numbers of participants in each group not responding to follow-up/the variable of interest. This question is not appropriate for the cross-sectional basis of this cohort as there is no follow-up period, and the outcome of interest is force/torque steadiness which, as a passive measurement technique, all participants will respond to. The revised question evaluates whether the force/torque steadiness task was implemented consistently for all participants by determining if bias might have been introduced through non-standardised task instructions, ensuring uniformity in the assessment of force/torque steadiness across groups.

Changes for studies with experimental pain

Newcastle Ottawa Quality Assessment Scale
Cohort Studies

Adapted from Newcastle Ottawa Quality Assessment Scale for Case-Control and Cohort Studies based on elements from the STROBE guidelines and the Newcastle Ottowa Scale manual (Wells, Accessed 2018, von Elm et al., 2008)

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Selection of Participants
    a) Community Participants ❋
    b) Alternative Participant recruitment
    c) No Description
2) Definition of Participants
    a) No history of disease ❋
    b) No mention of history of outcome
3) Ascertainment of pain exposure
    a) Pain was assessed, reported and it was >2/10 (NRS) ❋
    b) Minimal pain <2/10 (NRS) or no specific information on pain intensity and location
4) Demonstration that pain was not present at baseline
    a) Yes ❋
    b) No

Comparability

1) Comparability Criteria in Within-Subject Design (Pain and No-Pain Conditions):
    a) Randomisation was used for pain/no pain and order of testing ❋❋

b) Partial randomisation (one of the two) ❋
c) No randomisation procedures

Exposure

1) Description of Force/Torque steadiness Exposure

a) Force/Torque steadiness evaluation, recording equipment and processing are clearly described and standardised ❋
b) Force/Torque steadiness evaluation, recording equipment and processing are sufficiently described and standardised ❋
c) Force/Torque steadiness evaluation, recording equipment and processing are poorly described

2) Same Force/Torque steadiness Exposure for controls during pain and no-pain conditions

a) yes ❋
b) no

3) Description of Task Exposure

a) Task was well described and implemented in a standardised well in both conditions❋
b) Task was well described but not standardised
c) Task was poorly described and standardised

Question Number	Changes	Justification
Section 1	**Major changes**	
1	The original question 1 was removed and replaced by question number 3 (*case-control* document)	Considering that there are no cases/clinical pain group this question was completely removed for all the studies that used an experimental pain model and had a within-participant comparison. Question number 3 took its place, and the following changes were made to that question too: The original wording in the document for case-control studies assumed recruitment of cases exclusively from hospitals or through structured processes. The objective was to determine if the only distinction between cases and controls was the presence of case symptoms, while both originated from the same community. The second category aimed to identify whether controls were individuals from the hospital without the case, potentially representing a different background or community. The revised phrasing accommodates the likelihood of cases not being recruited solely from a hospital, eliminating the option of hospital controls. Instead, the new classification considers whether participants were sourced from the community or if different sampling methods were employed, potentially introducing selection bias.

2	The original question 2 was removed and replaced by question number 4 (*case-control* document)	Considering that there are no cases/clinical pain group this section was removed entirely for all the studies that used an experimental pain model and had a within-participant comparison. Question number 4 took its place, and the following changes were made to that question too: This question examines whether bias may arise from including individuals who have previously experienced the case symptoms and whether such individuals should be excluded. The original wording of the question in the case-control document focused on the "source" of the case symptom, which is not relevant to the studies under review. The revised phrasing specifically addresses whether participants should have no prior history of the symptoms, ensuring the essence of the question is preserved.
3	Used from the *cohort-studies* document and heavily modified	The title of this section was revised to explicitly reference exposure to painful stimuli. This modification was necessary to accurately reflect the nature of the studies discussed. To streamline the focus, the subcategories have been condensed into two distinct groups. The first group encompasses studies where participants experienced pain exceeding 2/10 on the Numeric Rating Scale (NRS), ensuring that the stimuli were sufficiently intense to replicate a genuine pain scenario. The second group includes studies where pain was either below this threshold or where specific details about the pain's intensity and location were not provided.
4	Used from the *cohort-studies* document and slightly modified	The title of this section has been updated to clearly indicate that the primary focus is on pain as an outcome. This subcategory specifically examines the methodological rigor of the studies, particularly in terms of testing sequence and overall design. The objective is to ascertain whether appropriate controls were in place to guarantee that participants were not experiencing pain at the start of the study, and this was demonstrated by a measurement of pain level in participants at the point of injection. This assessment is crucial to ensure the validity of the results, as it helps to determine whether any observed pain is a direct consequence of the experimental conditions rather than a pre-existing condition.
Section 2	**Minor Changes**	
5	The wording has changed, and two stars are only given for the first answer	This section has been updated to control for confounding factors and biases, specifically in the context of within-subject designs focusing on pain and no-pain conditions. This revision categorises studies based on the use of randomisation (pain model, order of testing), emphasising its role in enhancing methodological rigor. The first category includes studies that implement full randomisation for both pain/no pain conditions and the order of testing (two stars). The second category

		encompasses studies that apply partial randomisation, either to the pain/no pain conditions or the order of testing. (one star). The final category is reserved for studies that do not employ any randomisation procedures (no stars). These changes aim to provide a more detailed and accurate assessment of each study's approach to managing potential biases and confounding factors, thereby ensuring comparability between painful and non-painful statuses in pain research.
Section 3	**Major Changes**	**Questions in this section have required the most modifications as the original section sought to ascertain if the cases and controls were exposed to the variable of interest. In studies included here, the variable of interest is the force/torque steadiness and by participating in the experiment, it is known that cases and controls are exposed.**
6	This question has been specifically rewritten for the force/torque steadiness exposure.	The original question aimed to evaluate the potential introduction of bias through the inadvertent inclusion of individuals as cases who have not been exposed to the variable of interest. This consideration is particularly important when tracking the progression of individuals with conditions like vertebral fractures over time, as the process of confirming or disproving the occurrence of a fracture can introduce bias. However, in this systematic review, there are two exposures to be considered: one to musculoskeletal pain and another to force/torque steadiness assessment and a specific task. The exposure to musculoskeletal pain cannot be externally verified due to its nature as an "invisible disability"; thus, all included studies would be categorised as "self-report" (as already considered in Q1). The essence of this question lies in establishing the causality of results based on an individual's exposure to the variable of interest. In the context of assessing force steadiness, it is equally important to examine how the principles of force steadiness assessment are consistently applied across conditions (pain, no-pain), including the choice of the dynamometer, task, position, and other relevant factors. Failure to standardise these aspects could introduce bias, making it challenging to determine if the results are attributable to an individual being a case or control or if the assessment of force steadiness was conducted accurately.
7	Slight change in the question wording	This question inquired whether the response to Q6 was consistent between the two conditions (pain, no-pain). Due to the modification of Q6, the title of this question has been slightly adjusted to align with this change.

8	This question has been specifically rewritten for the description of the force/torque steadiness exposure.	The original question assessed if reporting bias had been introduced through different numbers of participants in each group not responding to follow-up/the variable of interest. This question is not appropriate for the cross-sectional basis of this cohort as there is no follow-up period, and the outcome of interest is force/torque steadiness which, as a passive measurement technique, all participants will respond to. The revised question evaluates whether the force/torque steadiness task was implemented consistently for all participants by determining if bias might have been introduced through non-standardised task instructions, ensuring uniformity in the assessment of force/torque steadiness across conditions (pain, no-pain).

Thresholds were used to convert the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.
Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain.

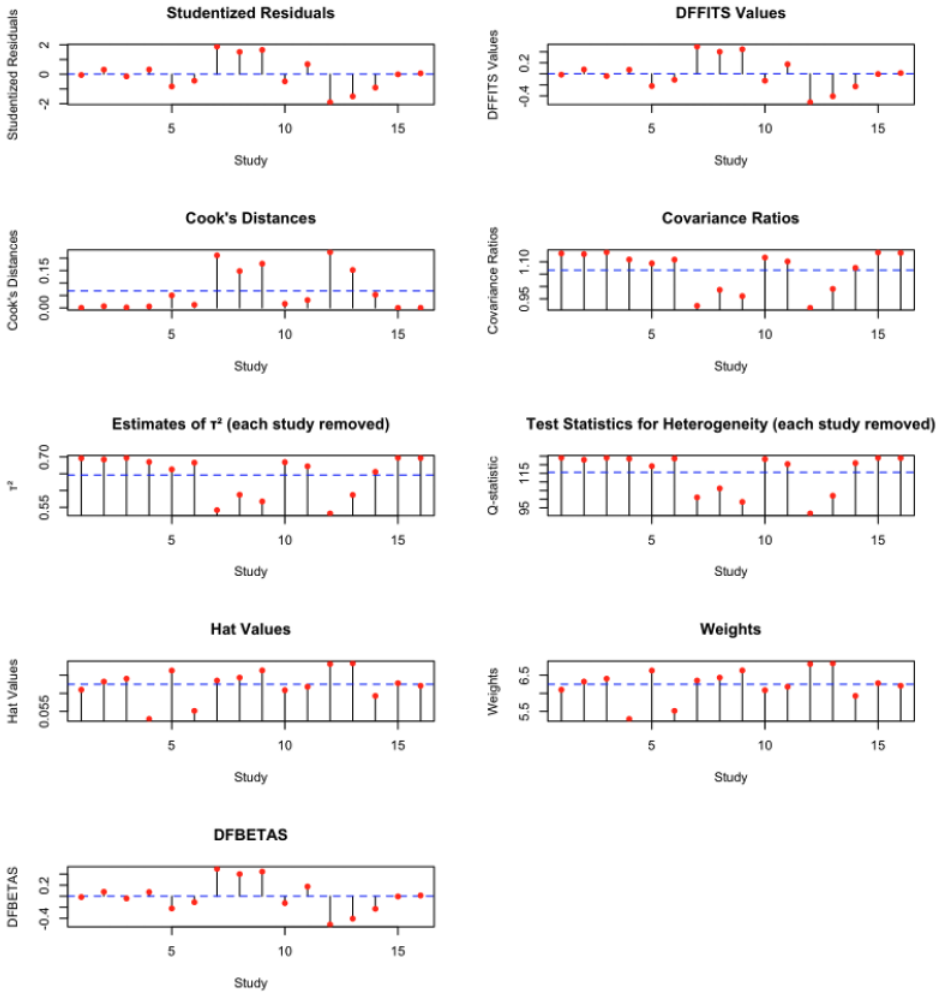
Supplementary Material 4 – Influence & Sensitivity Analyses

Sensitivity & Influence Analyses for Clinical Pain Studies

Influence analysis for CoV-Clinical Pain Studies

Fig. A: The figure presents an influence analysis for the meta-analytic model, illustrating various diagnostic measures to identify influential studies. The plots include externally studentized residuals, DFFITS values, Cook's distances, covariance ratios, estimates of heterogeneity (τ^2 & Q-statistic) when each study is removed, hat values, weights and DFBETAS. On the y-axis are the values of each measure, and on the x-axis are the study numbers, with the first author of each study listed in the adjacent table. The blue line in each plot represents the mean of each parameter across all studies. Studies that cause significant changes in these diagnostics when excluded are considered influential, indicating their substantial impact on the model's fit and the overall results. If there is an influential case, this is depicted with a red asterisk next to the author's name in the table.

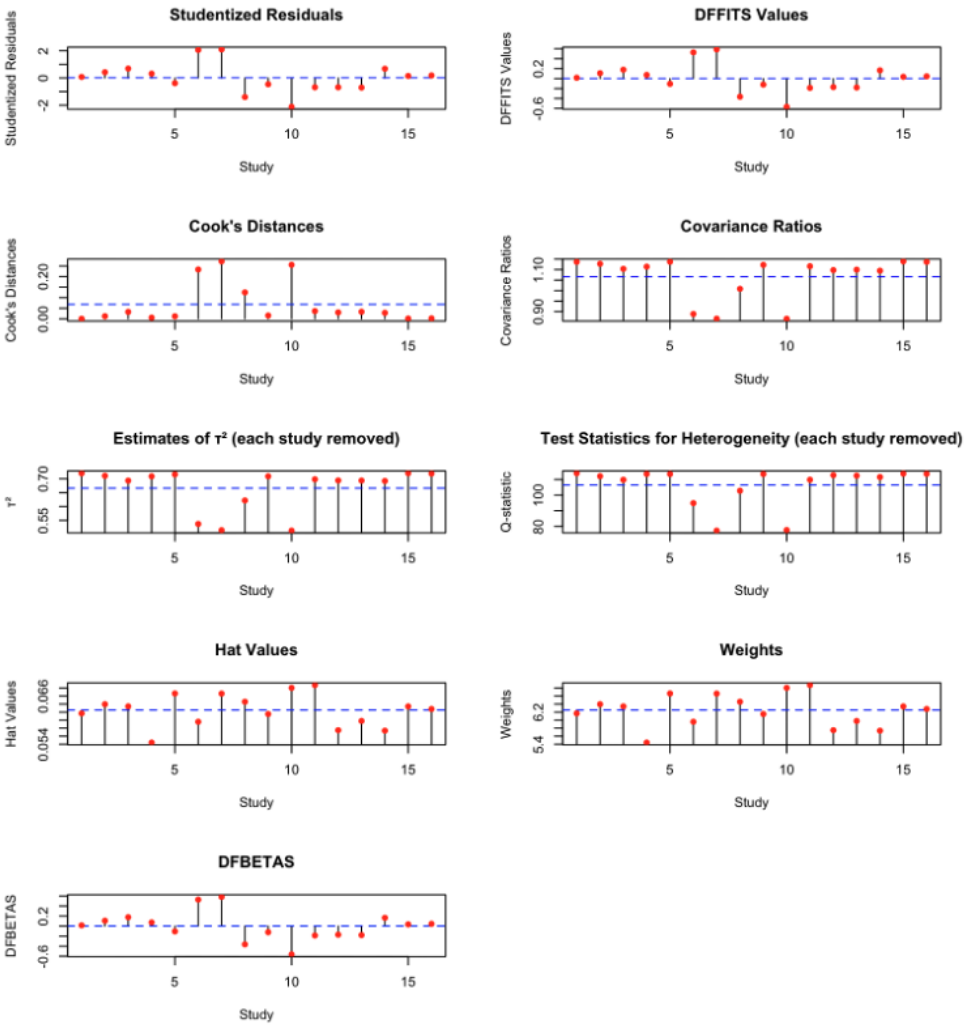
Study	First Author
1	Arvanitidis 2022
2	Arvanitidis 2024c
3	Arvanitidis 2024c
4	Bandholm 2006
5	Camargo 2009
6	Falla 2010
7	Ferreira 2021
8	Ferreira 2021
9	Magni 2021
10	Miura 2014
11	Muceli 2011
12	Overbeek 2020
13	Overbeek 2020
14	Testa 2017
15	Wang 2018
16	Wang 2020



Influence analysis for SD-Clinical Pain Studies

Fig. B: The figure presents an influence analysis for the meta-analytic model, illustrating various diagnostic measures to identify influential studies. The plots include externally studentized residuals, DFFITS values, Cook's distances, covariance ratios, estimates of heterogeneity (τ^2 & Q-statistic) when each study is removed, hat values, weights and DFBETAS. On the y-axis are the values of each measure, and on the x-axis are the study numbers, with the first author of each study listed in the adjacent table. The blue line in each plot represents the mean of each parameter across all studies. Studies that cause significant changes in these diagnostics when excluded are considered influential, indicating their substantial impact on the model's fit and the overall results. If there is an influential case, this is depicted with a red asterisk next to the author's name in the table.

Study	First Authors
1	Arvanitidis 2022
2	Arvanitidis 2024c
3	Arvanitidis 2024c
4	Bandholm 2006
5	Camargo 2009
6	Hortobagyi 2004
7	Magni 2021
8	Mista 2018
9	Miura 2014
10	Overbeek 2020
11	Overbeek 2020
12	Testa 2015
13	Testa 2017
14	Testa 2018
15	Wang 2018
16	Wang 2020



Sensitivity Analyses for CoV – Leaving One Study Out

Table A. The table presents the results of a sensitivity analysis conducted by leaving one study out at a time to evaluate the influence on the overall combined effect size for **Force/Torque CoV** on clinical pain studies. The analysis aims to determine how each individual study impacts the robustness and consistency of the overall findings.

Excluded study. Author, year	Combined effect size (95% CI)	p-value	I^2(%; 95% CI)	Q	Tau^2	df
Arvanitidis 2022	0.80 [0.28, 1.33]	***0.006***	89 [83, 92]	124.06	0.60	14
Arvanitidis 2024c (Trunk Ext & Flex)	0.79 [0.26, 1.33]	***0.007***	89 [84, 93]	122.86	0.61	13
Bandholm 2006	0.78 [0.26, 1.30]	***0.006***	89 [83, 92]	123.47	0.59	14
Camargo 2009	0.86 [0.35, 1.37]	***0.003***	88 [82, 92]	119.19	0.56	14
Falla 2010	0.83 [0.31, 1.35]	***0.004***	89 [83, 92]	123.61	0.59	14
Ferreira 2021 (Hip & Knee)	0.67 [0.21, 1.13]	***0.007***	84 [74, 90]	80.29	0.42	13
Magni, 2021	0.68 [0.22, 1.15]	***0.007***	86 [78, 91]	98.43	0.45	14
Miura, 2014	0.83 [0.31, 1.35]	***0.004***	89 [83, 92]	123.26	0.59	14
Muceli, 2011	0.75 [0.23, 1.27]	***0.008***	88 [83, 92]	120.38	0.58	14
Overbeek, 2020 (Abd & Add)	0.93 [0.48, 1.39]	***<0.001***	79 [65, 87]	61.84	0.41	13
Testa, 2017	0.86 [0.35, 1.37]	***0.003***	88 [83, 92]	120.94	0.55	14
Wang, 2018	0.80 [0.27, 1.33]	***0.006***	89 [83, 92]	124.01	0.61	14
Wang, 2020	0.79 [0.27, 1.32]	***0.006***	89 [83, 92]	123.90	0.60	14

**Significant results are highlighted by bolding the p-values.

Sensitivity Analyses for SD – Leaving One Study Out

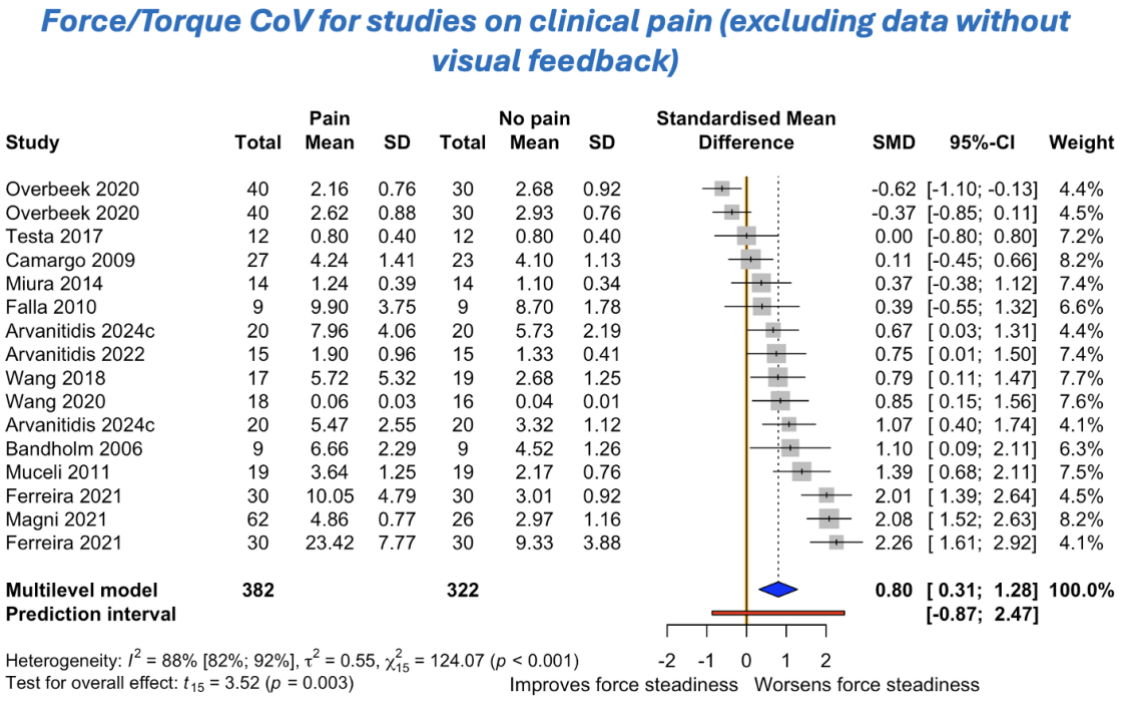
Table B. The table presents the results of a sensitivity analysis conducted by leaving one study out at a time to evaluate the influence on the overall combined effect size for **Force/Torque SD** on clinical pain studies. The analysis aims to determine how each individual study impacts the robustness and consistency of the overall findings.

Excluded study. Author, year	Combined effect size (95% CI)	p-value	I^2(%; 95% CI)	Q	Tau^2	df
Arvanitidis, 2022	0.61 [0.07, 1.15]	***0.030***	88 [81, 92]	113.97	0.72	14
Arvanitidis 2024c (Trunk Ext & Flex)	0.56 [0.01, 1.11]	***0.047***	88 [81, 92]	107.23	0.73	13
Bandholm, 2006	0.59 [0.06, 1.13]	***0.032***	88 [81, 92]	113.52	0.71	14
Camargo, 2009	0.64 [0.10, 1.18]	***0.023***	88 [81, 92]	113.46	0.71	14
Hortobagyi,2004	0.49 [0.02, 0.96]	***0.043***	85 [77, 90]	94.84	0.53	14
Magni, 2021	0.48 [0.02, 0.95]	***0.044***	82 [71, 89]	77.30	0.50	14
Mista, 2018	0.70 [0.20, 1.20]	***0.010***	86 [79, 91]	102.77	0.60	14
Miura, 2014	0.64 [0.11, 1.18]	***0.022***	88 [81, 92]	113.46	0.70	14
Overbeek, 2020 (Abd & Add)	0.72 [0.22, 1.22]	***0.008***	81 [70, 88]	69.23	0.56	13
Testa, 2015	0.66 [0.13, 1.18]	***0.019***	88 [81, 92]	112.74	0.69	14
Testa, 2017	0.66 [0.13, 1.19]	***0.018***	88 [81, 92]	112.40	0.69	14
Testa, 2018	0.57 [0.04, 1.10]	***0.037***	87 [81, 92]	111.50	0.69	14
Wang, 2018	0.60 [0.06, 1.14]	***0.031***	88 [81, 92]	113.69	0.72	14
Wang, 2020	0.60 [0.06, 1.14]	***0.032***	88 [81, 92]	113.58	0.72	14

**Significant results are highlighted by bolding the p-values.

Sensitivity Analyses for CoV – Forest Plot – (excluding studies that did not provide visual force feedback)

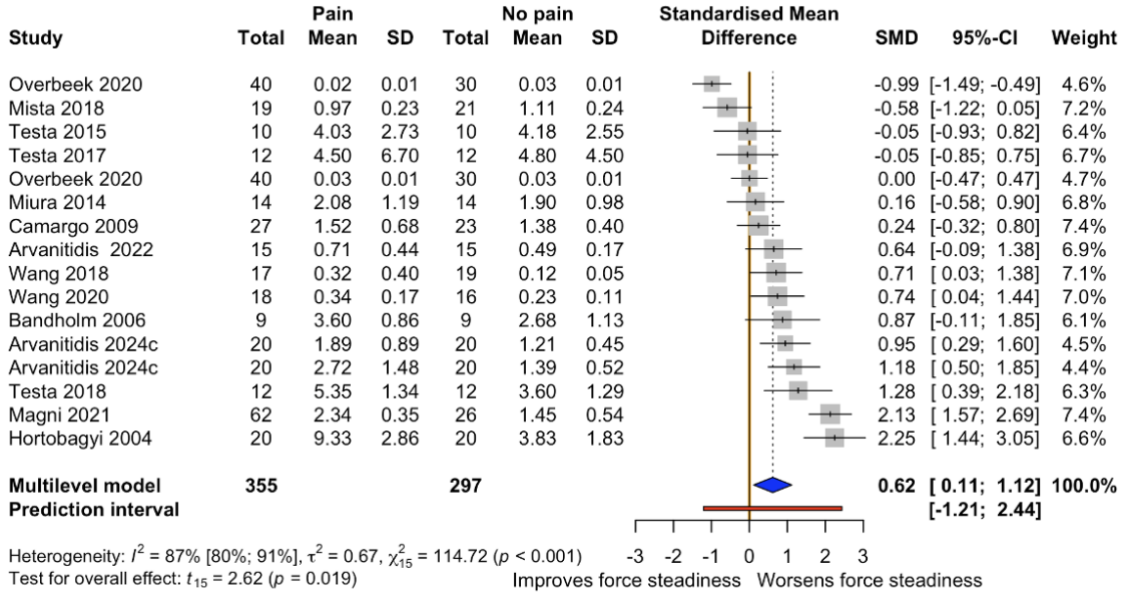
Fig. C. This figure presents a forest plot of the sensitivity analysis conducted after removing Torque CoV data from the study by Testa et al., (2017), during the condition without visual feedback. This step was taken to ensure that the confounding factor of visual feedback does not influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.



Sensitivity Analyses for SD – Forest Plot – (excluding studies that did not provide visual force feedback)

Fig. D. This figure presents a forest plot of the sensitivity analysis conducted after removing Torque SD data from the study by Testa et al., (2017) and (2018), during the condition without visual feedback. This step was taken to ensure that the confounding factor of visual feedback does not influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque SD for studies on clinical pain (excluding data without visual feedback)

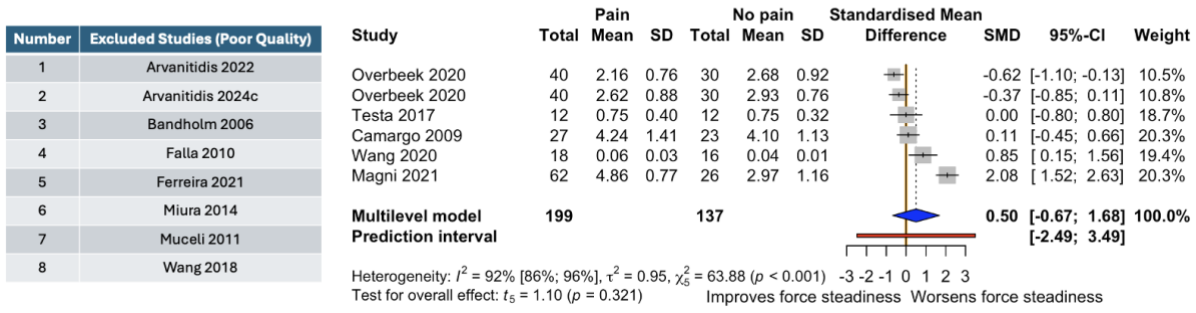


Sensitivity Analyses for CoV – Forest Plot – Removing Studies of Poor Quality

Fig. E. This figure presents a forest plot of the sensitivity analysis conducted after removing studies of poor quality (presented in the table next to the forest plot). This step was taken to explore how removing these studies of high risk of bias will influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque CoV for studies on clinical pain (excluding studies of poor quality)

Number	Excluded Studies (Poor Quality)
1	Arvanitidis 2022
2	Arvanitidis 2024c
3	Bandholm 2006
4	Falla 2010
5	Ferreira 2021
6	Miura 2014
7	Muceli 2011
8	Wang 2018

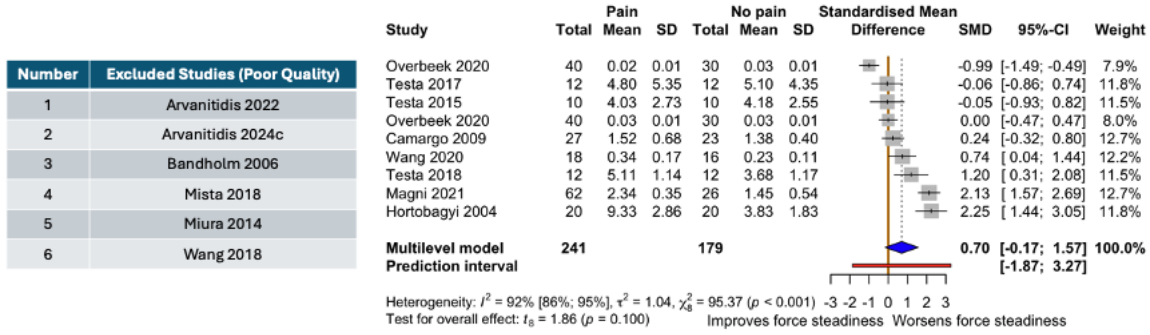


Sensitivity Analyses for SD – Forest Plot – Removing Studies of Poor Quality

Fig. F. This figure presents a forest plot of the sensitivity analysis conducted after removing studies of poor quality (presented in the table next to the forest plot). This step was taken to explore how removing these studies of high risk of bias will influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque SD for studies on clinical pain (excluding studies of poor quality)

Number	Excluded Studies (Poor Quality)
1	Arvanitidis 2022
2	Arvanitidis 2024c
3	Bandholm 2006
4	Mista 2018
5	Miura 2014
6	Wang 2018

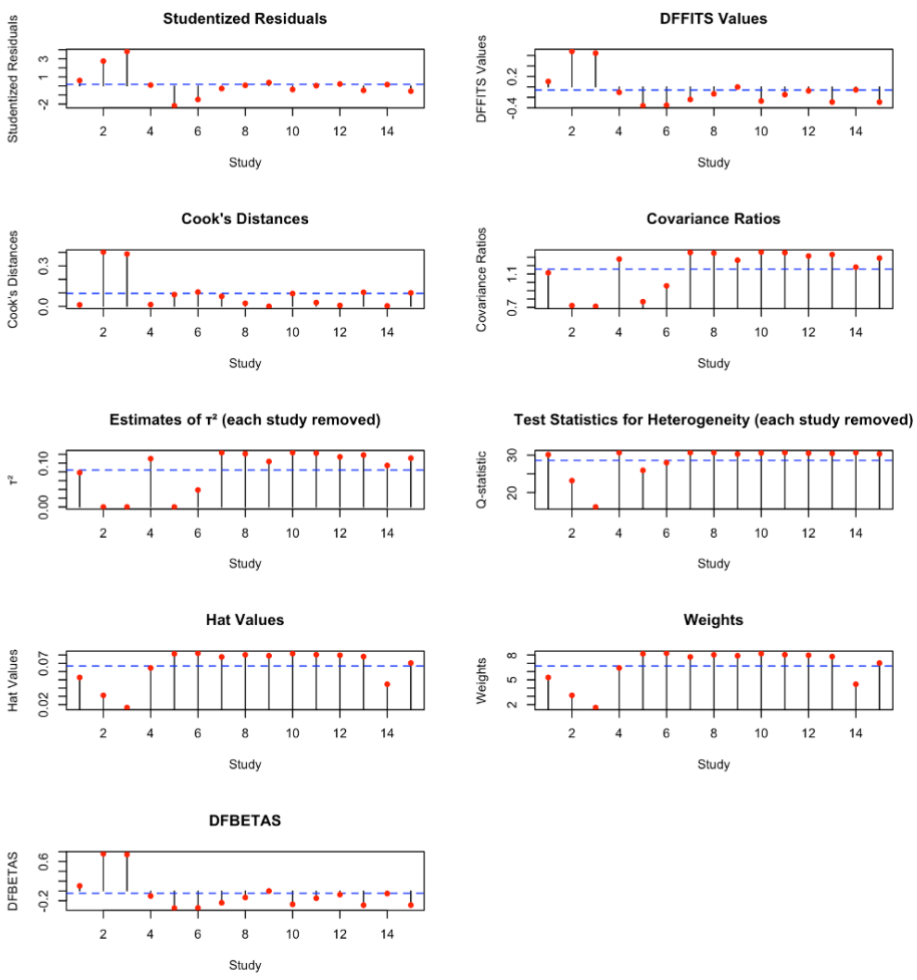


Sensitivity & Influence Analyses for Experimental Pain Studies

Influence analysis for CoV-Experimental Pain Studies

Fig. G: The figure presents an influence analysis for the meta-analytic model, illustrating various diagnostic measures to identify influential studies. The plots include externally studentized residuals, DFFITS values, Cook's distances, covariance ratios, estimates of heterogeneity (τ^2 & Q-statistic) when each study is removed, hat values, weights and DFBETAS. On the y-axis are the values of each measure, and on the x-axis are the study numbers, with the first author of each study listed in the adjacent table. The blue line in each plot represents the mean of each parameter across all studies. Studies that cause significant changes in these diagnostics when excluded are considered influential, indicating their substantial impact on the model's fit and the overall results. If there is an influential case, this is depicted with a red asterisk next to the author's name in the table.

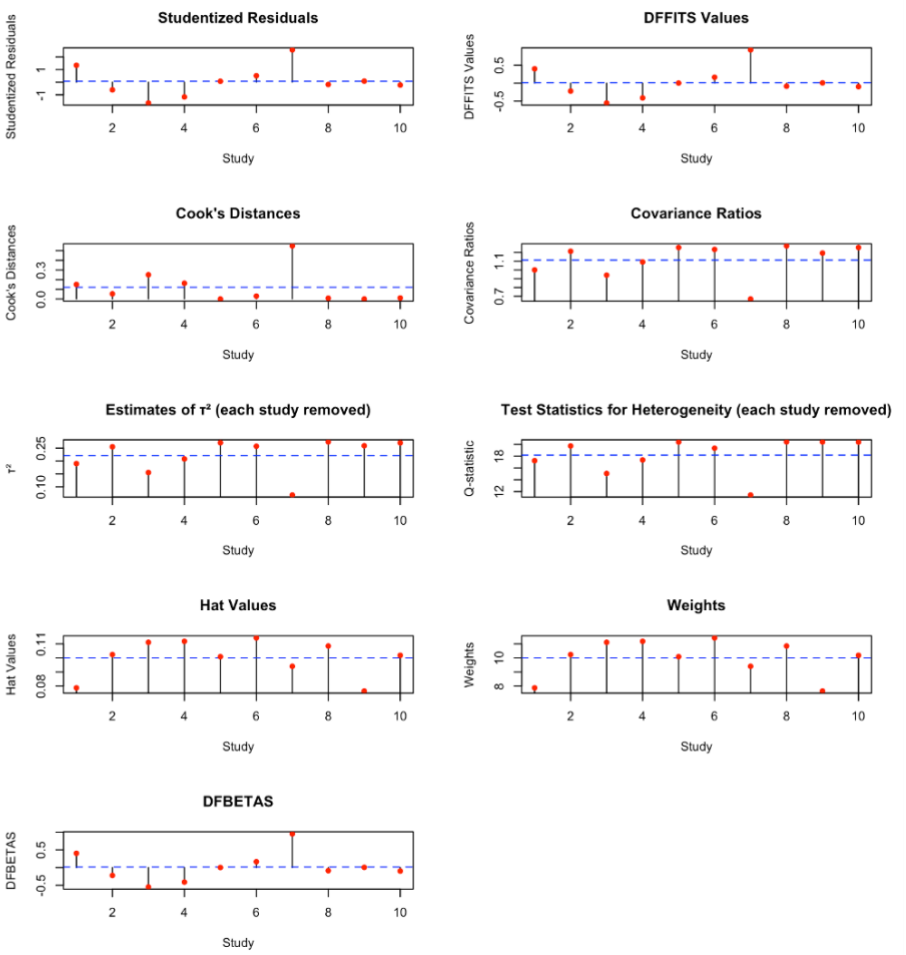
Study	First Author
1	Bandholm 2008
2	Del Santo 2007
3	Del Santo 2007
4	Farina 2012
5	Martinez-Valdes 2020
6	Martinez-Valdes 2021
7	Rice 2015
8	Salomoni 2012
9	Salomoni 2012
10	Salomoni 2012
11	Salomoni 2012
12	Salomoni 2013
13	Smith 2021
14	Yavuz 2015
15	Yavuz 2015



Influence analysis for SD-Experimental Pain Studies

Fig. H: The figure presents an influence analysis for the meta-analytic model, illustrating various diagnostic measures to identify influential studies. The plots include externally studentized residuals, DFFITS values, Cook's distances, covariance ratios, estimates of heterogeneity (τ^2 & Q-statistic) when each study is removed, hat values, weights and DFBETAS. On the y-axis are the values of each measure, and on the x-axis are the study numbers, with the first author of each study listed in the adjacent table. The blue line in each plot represents the mean of each parameter across all studies. Studies that cause significant changes in these diagnostics when excluded are considered influential, indicating their substantial impact on the model's fit and the overall results. If there is an influential case, this is depicted with a red asterisk next to the author's name in the table.

Study	First Author
1	Bandholm 2008
2	Hirata 2015
3	Martinez-Valdes 2020
4	Martinez-Valdes 2021
5	Mista 2015
6	Poortvliet 2019
7	Rice 2015 *
8	Smith 2021
9	Yavuz 2015
10	Yavuz 2015



Sensitivity Analyses for Experimental Pain Studies

Table C. The table presents the results of a sensitivity analysis conducted by leaving one study out at a time to evaluate the influence on the overall combined effect size for **Force/Torque CoV** on experimental pain studies. The analysis aims to determine how each individual study impacts the robustness and consistency of the overall findings.

Excluded study. Author, year	Combined effect size (95% CI)	p-value	I^2(%; 95% CI)	Q	Tau^2	df
Bandholm 2008	0.48 [-0.07, 1.03]	*0.082*	57 [22, 76]	30.12	0.44	13
Del Santo 2007 (Elbow Flex & Fifth finger Abd)	0.34 [0.07, 0.60]	***0.017***	0 [0, 58]	8.15	<0.01	13
Farina 2012	0.51 [-0.06, 1.07]	*0.074*	58 [23, 77]	30.66	0.47	13
Martinez-Valdes 2020	0.59 [0.09, 1.09]	***0.024***	50 [7, 73]	25.92	0.33	13
Martinez-Valdes 2021	0.58 [0.04, 1.11]	***0.036***	54 [15, 75]	28.00	0.40	13
Rice 2015	0.53 [-0.04, 1.10]	*0.066*	58 [23, 77]	30.66	0.47	13
Salomoni 2012 (All muscles)	0.51 [-0.09, 1.12]	*0.087*	67 [37, 82]	30.07	0.50	10
Salomoni 2013	0.50 [-0.07, 1.07]	*0.079*	57 [23, 77]	30.52	0.47	13
Smith 2021	0.54 [-0.03, 1.10]	*0.060*	57 [23, 76]	30.45	0.46	13

Yavuz 2015 (Ankle DF & Fifth Finger Abd)	0.58 [-0.09, 1.25]	*0.085*	63 [32, 80]	29.98	0.59	13

**Significant results are highlighted by bolding the p-values.

Table D. The table presents the results of a sensitivity analysis conducted by leaving one study out at a time to evaluate the influence on the overall combined effect size for **Force/Torque SD** on experimental pain studies. The analysis aims to determine how each individual study impacts the robustness and consistency of the overall findings.

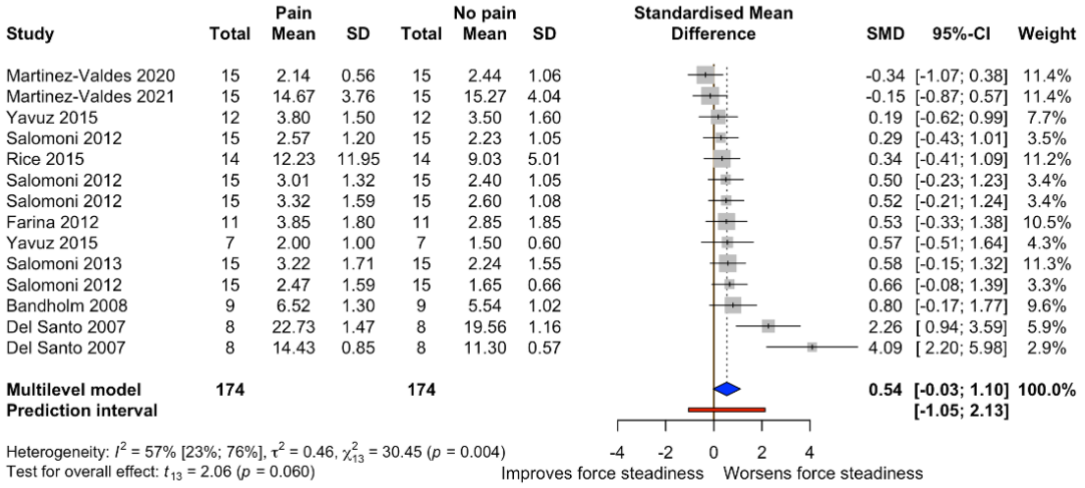
Excluded study. Author, year	Combined effect size (95% CI)	p-value	I^2(%; 95% CI)	Q	Tau^2	df
Bandholm 2008	0.36 [-0.13, 0.85]	*0.131*	54 [1, 78]	17.23	0.22	8
Hirata 2015	0.49 [-0.06, 1.04]	*0.072*	59 [15, 81]	19.73	0.29	8
Martinez-Valdes 2020	0.55 [0.07, 1.03]	***0.029***	47 [0, 75]	15.06	0.18	8
Martinez-Valdes 2021	0.53 [0.01, 1.05]	***0.027***	54 [2, 78]	17.36	0.24	8
Mista 2015	0.44 [-0.12, 1.00]	*0.105*	61 [19, 81]	20.38	0.31	8
Poortvliet 2019	0.41 [-0.15, 0.96]	*0.129*	59 [14, 80]	19.35	0.30	8
Rice 2015	0.29 [-0.10, 0.68]	*0.128*	30 [0, 68]	11.42	0.08	8
Smith 2021	0.46 [-0.10, 1.03]	*0.094*	61 [19, 81]	20.41	0.32	8
Yavuz 2015 (Ankle DF & Fifth Finger Abd)	0.46 [-0.13, 1.05]	*0.110*	66 [27, 84]	20.35	0.32	7

**Significant results are highlighted by bolding the p-values.

Sensitivity Analyses for CoV – Forest Plot – (excluding studies that did not provide visual force feedback)

Fig. I. This figure presents a forest plot of the sensitivity analysis conducted after removing Torque CoV data from the study by Smith et al., 2021, during the condition without visual feedback. This step was taken to ensure that the confounding factor of visual feedback does not influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque CoV for studies on experimental pain (excluding data without visual feedback)

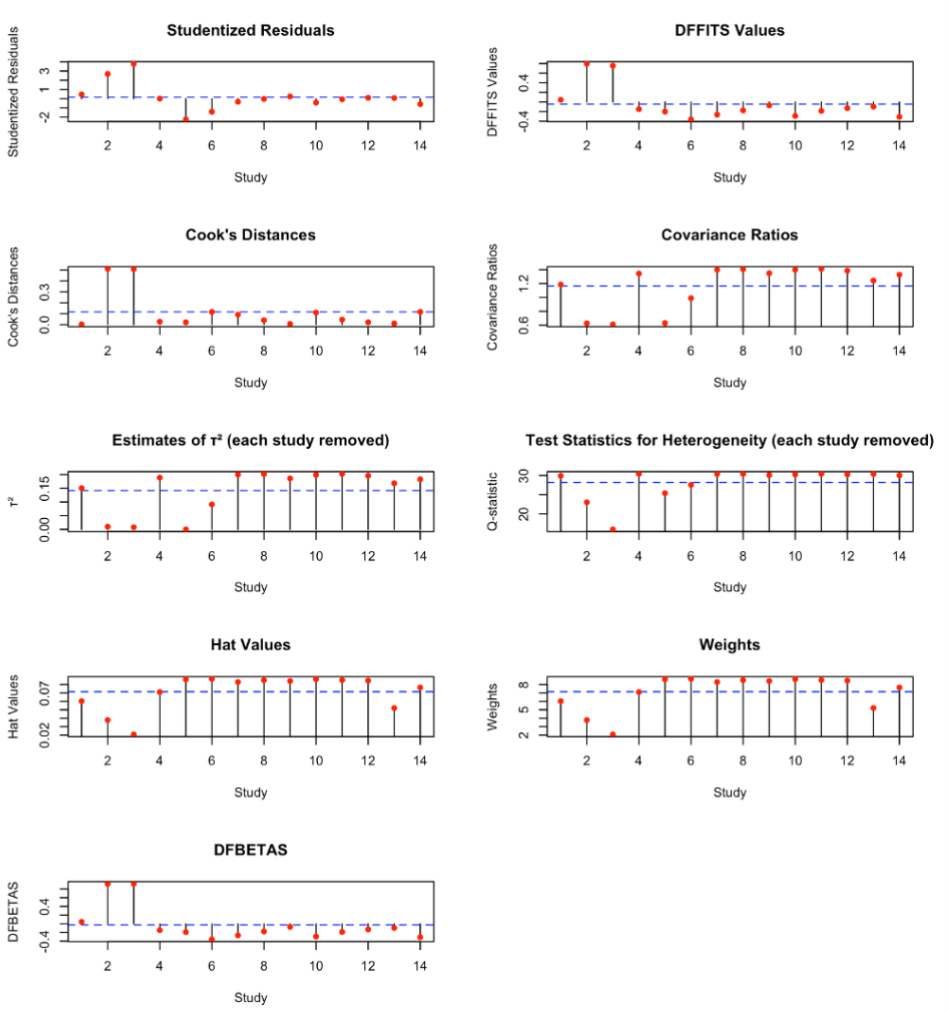


This analysis resulted in a change of the overall effect (i.e., there was no influence of experimental pain on force steadiness). However, this exclusion resulted in identifying a potential outlier in our analysis. Specifically, the data from Del Santo 2007 were identified as potential outliers after performing the influence analysis presented below:

Additional Influence analysis for CoV-Experimental Pain Studies (excluding studies that did not provide visual force feedback)

Fig. J: The figure presents an influence analysis for the meta-analytic model after the exclusion of the study by Smith et al., (2021), which did not use visual feedback, illustrating_various diagnostic measures to identify influential studies. The plots include externally studentised residuals, DFFITS values, Cook's distances, covariance ratios, estimates of heterogeneity (τ^2 & Q-statistic) when each study is removed, hat values, weights and DFBETAS. On the y-axis are the values of each measure, and on the x-axis are the study numbers, with the first author of each study listed in the adjacent table. The blue line in each plot represents the mean of each parameter across all studies. Studies that cause significant changes in these diagnostics when excluded are considered influential, indicating their substantial impact on the model's fit and the overall results. If there is an influential case, this is depicted with a red asterisk next to the author's name in the table.

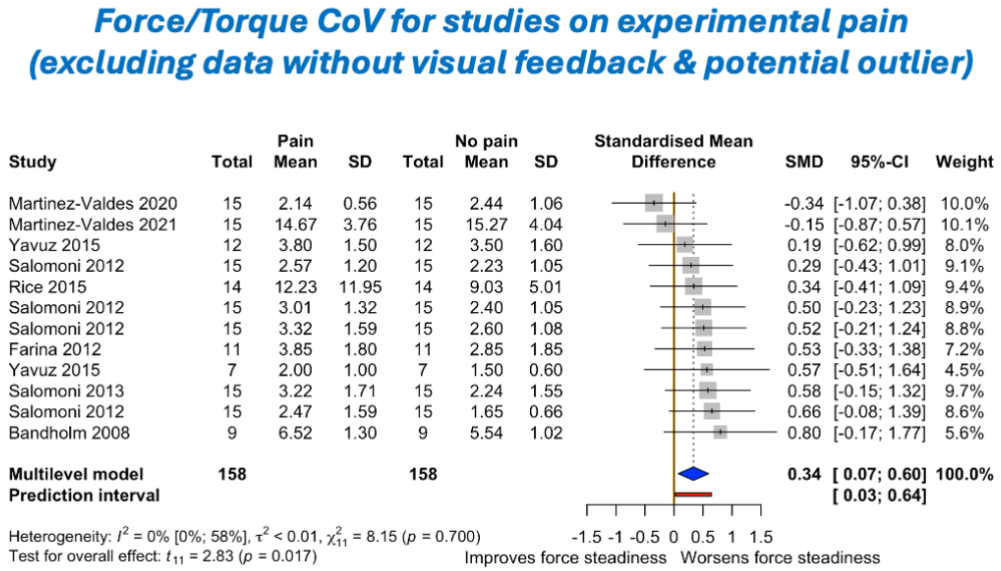
Study	First Author
1	Bandholm 2008
2	Del Santo 2007 *
3	Del Santo 2007 *
4	Farina 2012
5	Martinez-Valdes 2020
6	Martinez-Valdes 2021
7	Rice 2015
8	Salomoni 2012
9	Salomoni 2012
10	Salomoni 2012
11	Salomoni 2012
12	Salomoni 2013
13	Yavuz 2015
14	Yavuz 2015



This analysis showed that after removing the study by Smith et al., (2021), the study by Del Santo et al., (2007) was detected as a potential outlier. Therefore, we excluded this study to further explore how the overall effect of our meta-analysis would be affected. This is presented in the forest plot below:

Additional Sensitivity Analyses for CoV – Forest Plot – (excluding studies that did not provide visual force feedback)

Fig. K. This figure presents a forest plot of the sensitivity analysis conducted after removing Torque CoV data from the study by Smith et al., (2021), during the condition without visual feedback and a potential outlier study by Del Santo et al., (2007). This step was taken to ensure that the confounding factor of visual feedback and a potential outlier does not influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

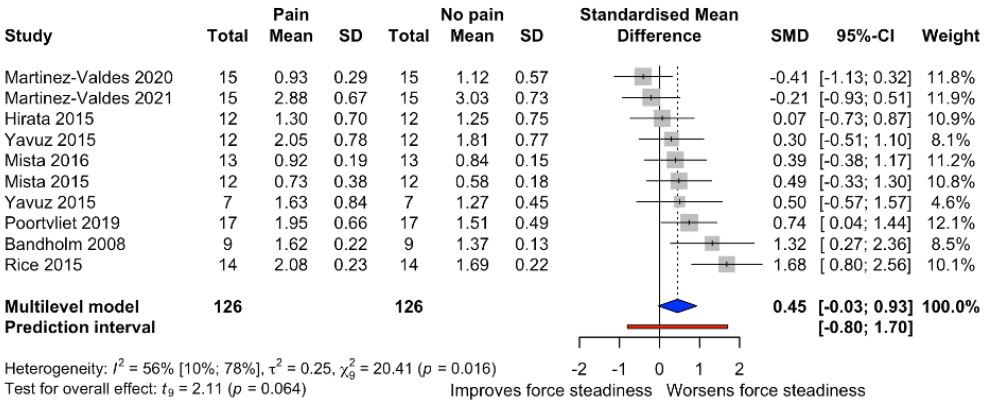


Removing the study that performed the tests without visual feedback and a potential outlier resulted in observing the same result of our main analysis (i.e., force steadiness being impaired in the presence of experimentally induced pain) and importantly led to a significant reduction in heterogeneity.

Sensitivity Analyses for SD – (excluding studies that did not provide visual force feedback)

Fig. L. This figure presents a forest plot of the sensitivity analysis conducted after removing Torque SD data from the study by Smith et al., (2021), during the condition without visual feedback. This step was taken to ensure that the confounding factor of visual feedback does not influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque SD for studies on experimental pain (excluding data without visual feedback)

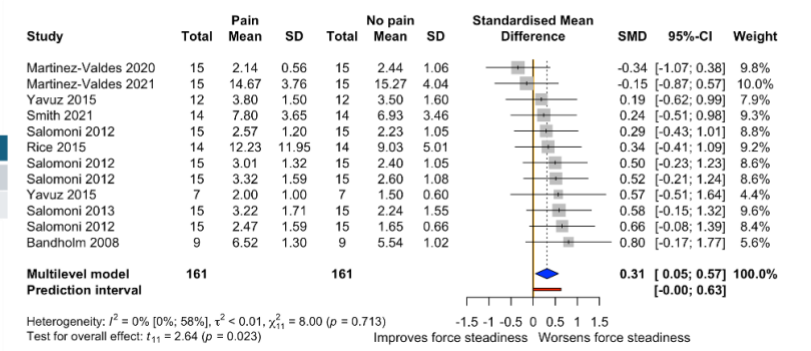


Sensitivity Analyses for CoV – Forest Plot – Removing Studies of Poor Quality

Fig. M. This figure presents a forest plot of the sensitivity analysis conducted after removing studies of poor quality (presented in the table next to the forest plot). This step was taken to explore how removing these studies of high risk of bias will influence the overall analysis. The meta-analysis examines the effect of clinical pain on force steadiness during different submaximal voluntary contractions. The mean ± SD of each outcome measure and sample size for each group are reported, alongside the SMD and 95% CI for each study. All heterogeneity measures and overall effect size tests are reported below the forest plot, with the prediction interval depicted as a red line within the graph. The forest plots are organised in ascending order of their effect sizes.

Force/Torque CoV for studies on experimental pain (excluding studies of poor quality)

Number	Excluded Studies (Poor Quality)
1	Del Santo 2007
2	Farina 2012



This analysis was not performed for the force/torque SD-based meta-analysis, as none of the studies were of poor quality.