Movement variability in people with neck pain disorders

By

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Abstract

Neck pain, a common source of morbidity and disability, not only affects people physically, but can have significant social and psychological impact. People with chronic neck pain (CNP) may present with number of symptoms and signs associated with their condition, including decreased range of motion (RoM), increased fatigue, neuromuscular dysfunction and altered joint position sense. An abundance of research has examined how the quantity of neck movement is modified when people have neck pain, however, the quality or variability of movement has received much less attention, even though it may be a better indicator of ongoing neuromuscular dysfunction in people with CNP. This thesis presents unique research to investigate whether the variability of movement is modified in people with neck pain disorders, and seeks to understand the mechanisms underlying these changes. Three experimental studies were undertaken to examine movement variability during active cervical movements and gait in people with neck pain. These studies revealed consistent findings of reduced movement variability and developed further insights regarding mechanisms underlying movement variability changes in people with neck pain disorders. Specifically, the first study aimed to investigate movement variability during active neck movements, and assessed correlations between movement variability parameters and clinical features. It found reduced movement variability in people with CNP compared to asymptomatic participants during flexion-extension and rotation movements, and also documented a negative correlation between fear of movement and movement variability for all neck rotation conditions. For the second study, the aim was to examine the variability of neck and trunk rotation during single- and dual-task gait in people with CNP relative to asymptomatic participants, and also to evaluate the correlation between the variability of neck and trunk rotation and clinical features. The results showed that people with CNP displayed reduced variability of trunk rotation during dual-task gait compared to asymptomatic

people. The third study aimed to investigate the effects of acute neck-muscle soreness, induced via eccentric exercise, in asymptomatic participants on neck movement variability during active neck movements. The findings demonstrated reduced neck movement variability immediately after, 24 hours after and 48 hours after eccentric exercise, consistent with the findings observed in people with CNP. The fourth study was a systematic review, which was subsequently conducted to explore the existing evidence regarding whether differences in the quality of movement, including movement variability, exist in people with CNP compared to asymptomatic people, based on the available literature. In addition, this review was used to determine the characteristics of the measurements used to investigate movement changes and quality. This review revealed that further investigation is required to evaluate movement variability, for example by examining variability during more challenging tasks such as walking with head rotation and in activities of daily living. Findings indicated that using the average of standard deviation as a parameter to measure movement variability has potential to detect changes in kinematics. Overall, examining movement variability and understanding the mechanisms underlying its changes in people with neck pain has shown potential to provide important insights into the impact of neck pain disorders on those affected.

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List of Papers and Conference Abstracts

During the candidate's PhD course in the School of Sport, Exercise and Rehabilitation Sciences, the following papers directly related to the thesis have either been published, presented at conferences, or were under review at the time of thesis submission. Therefore, sections of this thesis include verbatim text from published work. Sections of the thesis developed from published work will resemble this work in terms of structure and content, with additional changes as required to build the argument of the overall thesis. A summary of each paper and its use within this thesis is provided at the start of each relevant chapter.

Published Articles

Alsultan, F., Cescon, C., De Nunzio, A.M., Barbero, M., Heneghan, N.R., Rushton, A. & Falla, D. 2019. Variability of the helical axis during active cervical movements in people with chronic neck pain. *Clinical Biomechanics*, 62, 50-57. **(Appendix 1)**

Alsultan, F., De Nunzio, A.M., Rushton, A., Heneghan, N.R. and Falla, D. 2020. Variability of neck and trunk movement during single-and dual-task gait in people with chronic neck pain. *Clinical Biomechanics*, 72, pp. 31-36. **(Appendix 2)**

Alsultan, F., Cescon, C., Heneghan, N.R., Rushton, A., Barbero, M. and Falla, D. 2020. Eccentric exercise and delayed onset muscle soreness reduce the variability of active cervical movements. *Journal of Biomechanics*, 111, 109962. **(Appendix 3)**

Articles Under Review

Alsultan, F., Cescon, C., Alalawia, A., Heneghan, N.R., Rushton, A., and Falla, D. Is the quality of spinal movement altered in people with chronic neck pain?: A systematic review. (Under Review)

Conference Presentations

Platform Presentations

Alsultan, F., Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. People with chronic neck pain perform active neck movements in a less variable way. Presentation, Physiotherapy UK conference, Birmingham. November 2018.

Alsultan, F., Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. People with chronic neck pain perform active neck movements in a less variable way. Presentation, World Confederation of Physical Therapy conference, Geneva. May 2019.

Alsultan, F., De Nunzio, A.M., Rushton, A, Heneghan, N.R. & Falla, D. Investigating neck and trunk movement variability during single and dual-task gait in people with Chronic Neck Pain. Presentation, Physiotherapy UK conference, Birmingham. November 2019.

Poster Presentations

Alsultan, F., Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. Does neck pain change the way people move? Research Poster Conference 2018, University of Birmingham. June 2018.

Alsultan, F., Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. People with chronic neck pain perform active neck movements in a less variable way. Presentation, Physiotherapy UK conference, Birmingham. November 2018.

Alsultan, F., De Nunzio, A.M., Rushton, A, Heneghan, N.R., & Falla, D. Does neck pain change the way people move during a challenging walking task? Presentation, Research Poster Conference 2018, University of Birmingham. June 2019.

Alsultan, F., De Nunzio, A.M., Rushton, A, Heneghan, N.R. & Falla, D. Investigating neck and trunk movement variability during single and dual-task gait in people with Chronic Neck Pain. Presentation, Physiotherapy UK conference, Birmingham. November 2019.

Alsultan, F., De Nunzio, A.M., Rushton, A, Heneghan, N.R. & Falla, D. Investigating neck and trunk movement variability during single and dual-task gait in people with Chronic Neck Pain. Presentation, Pain Science in Motion Conference, Savona. May 2019.

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ABBREVIATIONS

2D	Two-dimensional
3D	Three-dimensional
AE	Absolute error
CINP	Chronic idiopathic neck pain
CNP	Chronic neck pain, including pain of idiopathic or traumatic origin
CE	Constant Error
C	Control (asymptomatic)
CON	Control Participant
DHI	Dizziness Handicap Inventory
EMG	Electromyography
ES	Erector Spinae
HA	Helical Axis
HRA	Head Repositioning Accuracy
IPAQ	International Physical Activity Questionnaire
JPE	Joint Position Error
MVC	Maximum voluntary contractions
MA	Mean Angle
MD	Mean Distance
NDI	Neck Disability Index
NA	Not applicable
PPT	Pressure pain threshold
RoM	Range of Motion
RMSE	Root Mean Square Error
Dizziness NRS	Self-reported dizziness NRS
SD	Standard Deviation
TSK	Tampa Scale for Kinesiophobia
VE	Variable Error
VAS	Visual analogue scale
ANOVA	Analysis of variance
WAD	Whiplash Associated Disorders
WAD ND	Whiplash Associated Disorders not complaining of dizziness
WAD D	Whiplash Associated Disorders with dizziness

CHAPTER 1

NECK PAIN DISORDERS AND MOVEMENT VARIABILITY

1.1. Overview and incidence of neck pain disorders

Neck pain disorders are a common source of morbidity and disability (McLean et al., 2010; Hurwitz et al., 2018). Neck pain was ranked as the fourth most frequently reported condition leading to disability worldwide in 2015, according to the Global Burden of Disease study (Hurwitz et al., 2018), with approximately four out of five individuals affected by neck pain at some point during their lives (De Pauw et al., 2018). Neck pain can affect patients not only physically, including causing activity limitation, but also can have social and psychological impacts (Hogg-Johnson et al., 2008).

Neck pain impacts economic health costs (Hoy et al., 2014) as it is a common reason to visit health practitioners, including physicians and physiotherapists (Bussieres et al., 2016). Approximately 25 % of 869 participants with neck pain in one study had visited health practitioners within the four weeks before the study commenced (Côté et al., 2001), and 31% of these participants had seen more than one of type of practitioner, including medical doctors, chiropractors and physiotherapists.

Based on data from the Labour Force Survey in 2016, neck pain was one of the top conditions reported by approximately 2.3 million working people in the United Kingdom (Work et al., 2016). Medical service costs, including hospital/clinic, doctor's office and emergency department fees (Rondoni et al., 2017; Kleinman et al., 2014), and costs related to prescription

drugs produce the greatest financial burdens associated with neck pain. According to Comer (2017), neck pain was one of the conditions that most frequently led to sickness absence in the United Kingdom, resulting in roughly 30 million lost workdays in 2016. High socioeconomic costs associated with neck pain have also been documented in the United States, totalling approximately $9 billion, and in Europe, with estimates for neck pain-related expenditures across the EU of around €10 billion per year (Hassan and Meguid, 2018; Tenenbaum et al., 2017). The overall cost of neck pain was reported to be nearly $686 million per year in the Netherlands alone (Krott et al., 2018).

The monthly prevalence of neck pain disorders is 213 per 1000 individuals (Al-Nimer, 2010; Gross et al., 2013). According to Pink et al. (2014), the incidence of neck pain is approximately 400,000 per year in the United Kingdom. In addition, the point prevalence of neck pain in any one month is around 14%, and is higher among women compared to men in the United Kingdom (Webb et al., 2003).

1.1.1 Classification of neck pain disorders

Neck pain disorders are typically classified according to the mechanism of onset (Jull et al., 2018). The most common classifications are insidious onset (i.e. mechanical, idiopathic or non-specific), traumatic onset (e.g. whiplash associated disorders [WAD]), and degenerative onset (e.g. radiculopathies) (Jull et al., 2018), These classifications reflect differences in the origin of these neck pain disorders, but also relate to the biopsychosocial model, which takes into account biological, psychological and social factors related to a patient's neck pain presentation. Although neck pain can be associated with degenerative disorders (e.g. cervical radiculopathy and myelopathy), most common neck pain presentations relate to disorders of the cervical musculoskeletal system (Jull et al., 2008).

In addition to classification of neck pain disorders by mechanism of onset and origin, neck pain is commonly described according to the duration of symptoms, as are other pain disorders, i.e. acute, subacute or chronic. Acute pain (present for less than three months) is described as pain resulting from a condition that is likely to recover automatically by natural healing, while chronic pain (present for more than three months) refers to a condition unlikely to recover automatically by natural healing (King, 2013). Subacute pain, a part of acute pain, describes continuing acute pain that presents for between six weeks and three months following onset. Neck pain becomes chronic in about one-third of cases (Nakamaru et al., 2019; Karakaş and Gök, 2020).

Specifically in relation to WAD, which is a result of a whiplash injury (defined as rapid acceleration and deceleration of the neck), a further classification system commonly utilised in research as well as in clinical settings is that of the Quebec Task Force (QTF)(Pastakia and Kumar, 2011; Teasell et al., 2010; Spitzer, 1995). First introduced in 1995, the QTF system is used extensively in recent studies (Björsenius et al., 2020; Spitzer, 1995; Lanhers et al., 2020). In the QTF classification, whiplash injury is classified as follows, based on the type of signs and symptoms and their severity (Spitzer, 1995):

- Grade 0: No complaint regarding neck pain and no physical signs
- Grade 1: No physical signs, but complaints of neck pain, stiffness or tenderness are reported
- Grade 3: Neck complaint, musculoskeletal and neurological signs
- Grade 4: Neck complaint and fracture or dislocation

Most WAD conditions are classified as grade 1 or 2 (Robinson et al., 2007). Only those with grades 2 and 3 WAD are likely to develop chronic symptoms (Agnew et al., 2015). In previous studies that examined cervical kinematics for both traumatic and mechanical neck pain, no

significant differences regarding cervical motion were observed between these groups (Woodhouse and Vasseljen, 2008; Sjolander et al., 2008a).

1.1.2 Manifestations of chronic neck pain

In addition to pain, people with chronic neck pain (CNP) may present with unpleasant, tiring, and potentially disabling symptoms and signs associated with the condition, including decreased range of motion (RoM), fatigue, dizziness, headaches, cognitive dysfunction, motor dysfunctions, joint position sense impairments, reduced postural stability, difficulties with head-eye movement control, reduced muscle strength and reduced endurance (Della Casa et al., 2014; Ischebeck et al., 2017; De Pauw et al., 2017; Ferrari and Russell, 2003; Saadat et al., 2018). In addition, CNP can be associated with psychological issues, including kinesiophobia, depression and anxiety, and other impairments that can intensify the experience of neck pain (Dimitriadis et al., 2015; Falla et al., 2006).

1.2 Movement behaviour and chronic neck pain

Movement behaviour is a visible movement or altered posture of the body as a result of musculoskeletal performance (Cratty, 1967; Kluka, 1999). Movement behaviour is a broad term and has several variants, including skilled performance, and reflex actions which are movements referring to a reaction to stimuli without consciousness (Cratty, 1967; Kluka, 1999). When examining movement behaviour, both the nature and the cause of movement are of interest, leading researchers to study movement in terms of physiological (motor control) and psychological (motor learning) factors, which can interact with each other (Ives, 2013). Examples of movement behaviour include moving the body through space (locomotion), posture and balance, and manipulative tasks (e.g. kicking a ball) (Ives, 2013).

According to Kluka (1999), movement behaviour is the visible result of motor control and motor learning, where motor control (or neuromuscular control) points to the study of internal processes that drive performances and postures. These processes are the mechanisms guiding muscles and joints. Motor control mainly reflects systems performing movements, especially neurophysiological and musculoskeletal systems (Ives, 2013).

Changes in movement behaviour are commonly observed in people with spinal pain (Key, 2010). These changes can be protective or maladaptive strategies triggered by pain, representing a patient's attempt to adapt to a new situation. In several studies, changes in motor performance have been observed in people with neck pain in terms of quality of movement as well as quantity of movement (Stenneberg et al., 2017; Sjolander et al., 2008b; de Vries et al., 2015; Stanton et al., 2016). For example, reduced active cervical RoM (Stenneberg et al., 2017) and increased jerk index (used to evaluate smoothness of the movement) (Sjolander et al., 2008b) and joint position sense error (used to assess proprioception) were documented in people with CNP compared to asymptomatic individuals (de Vries et al., 2015; Stanton et al., 2016).

1.2.1 Measurement of motor performance

Motor performance can be assessed via quantitative and/or qualitative assessments (Kluka, 1999; Kroes et al., 2002) A quantitative assessment can refer to measuring the speed or number of movements (e.g. measuring peak velocity during active neck rotations), while qualitative assessments examine the pattern or technique of movement performance (e.g. measuring smoothness of movement during active neck rotations) (see *Figure 1.1*). With regards to quantitative assessment, numerous studies have examined quantitative parameters, especially RoM, in people with CNP (Dvir et al., 2006; Woodhouse and Vasseljen, 2008; Cagnie et al., 2007). However, assessing the quality of movement may be a more sensitive method for identifying

kinematics disturbances in people with neck pain disorders, and could provide further insights regarding movement behaviour (Baydal-Bertomeu et al., 2011; Guo et al., 2019). In previous work, active neck movements were investigated in people with CNP compared to asymptomatic group (Sjolander et al., 2008b) using quantitative (RoM and peak velocity) and qualitative (RoM variability and jerk index) parameters. Assessing the quality of movement has the potential to capture information about a combination of aspects (van Dijk et al., 2017), including:

- Biomechanical data, which is associated with the way an individual links to space, and how this link impacts postural alignment and the path and form of movement, according to the anatomy of the body;
- Physiological data, which is associated with the way an individual links to time and how this link affects movement quality according to physiological processes;
- Psycho-socio-cultural data, which is associated with the way an individual links to internal mental processes and external socio-cultural elements, and how these elements affect human movements;
- Information about existential processes, which are associated with the way an individual links to the element of self-awareness, and how this element affects movement quality.

When the quality of movement is found to be disturbed in people with neck pain, it may indicate neuromuscular changes, which can result from disturbed patterns and control of movements (Jull et al., 2018). Thus, understanding changes in the quality of spinal movement is fundamental to better understand the functional changes accompanying neck pain (Guo et al., 2019; Jull et al., 2018).

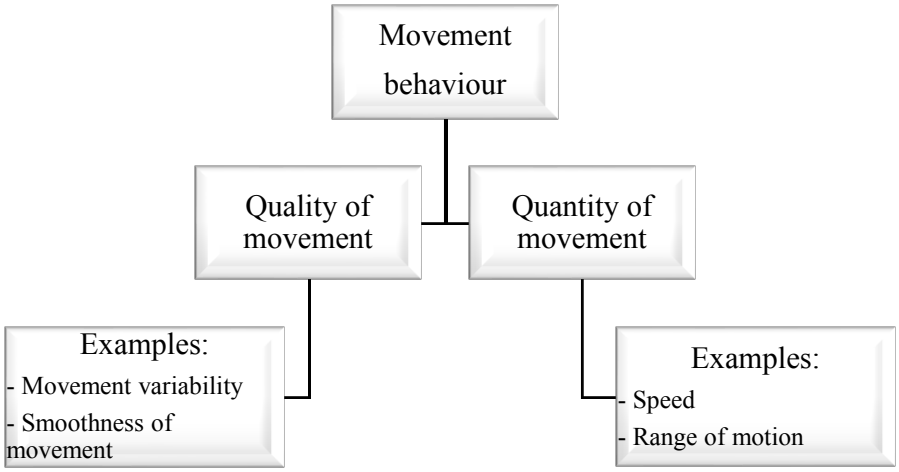


***Figure 1.1*: Representation of quantify versus quality of movement, and examples for each measurement type.**

1.2.2 Quality of movement

The quality of movement can be quantified using various outcome measures including movement acuity, smoothness of movement and movement variability, all of which can provide more knowledge regarding movement behaviour in people with CNP (Sjolander et al., 2008b; Alsultan et al., 2019; Dugailly et al., 2015).

In particular, movement variability is a topic of increased interest among researchers and clinicians (Srinivasan and Mathiassen, 2012; Heiderscheit, 2000). In addition to its role in motor control and learning, movement variability is considered to be a crucial area of attention when researching movement (Moseley and Hodges, 2006). It can be measured by collecting data regarding several parameters, including muscle activity and kinematics related to movement patterns (Srinivasan and Mathiassen, 2012). Specifically, kinematics can be investigated in connection with several movement features, including movement speed, which is rarely examined but plays a key role in pathological conditions (Bonnechere et al., 2014), and also continuous whole

movement cycles, which have been demonstrated to provide knowledge regarding movement changes and strategies in people with neck pain (Baydal-Bertomeu et al., 2011). Initial evidence suggests that movement variability can differentiate asymptomatic individuals from people with chronic musculoskeletal disorders, including CNP (Abboud et al., 2014; Lomond and Côté, 2010; Madeleine, 2010).

1.3 Movement variability

Movement variability can be described as the normal variations that occur in motor performance during a repeated task (Stergiou et al., 2006). For example, if someone tries to replicate a movement, some differences may be present between repetitions, regardless of familiarity with the movement (Preatoni et al., 2013; Stergiou and Decker, 2011). The meaning behind these physiological changes in kinematics is subject to debate. Some theories propose that movement variability could be largely random (error or noise) (Stergiou et al., 2006; Stergiou and Decker, 2011). However, others suggest that movement variability is often not random, and may therefore provide crucial information about the natural movement pattern or behaviour, as well as evidencing any changes in function caused by pain or impairment, with potentially important implications for clinicians.

1.3.1 Limitations of traditional perspectives on movement variability

Traditional perspectives do not adequately consider some behaviours that appear to be stable, but are nonetheless performed in variable ways (Stergiou et al., 2006). This can be seen in elite sports players or musicians when they perform complex activities, such as taking a jump shot in basketball or playing the cello. Professionals' movements are more consistent compared to those of people who are less skilled at performing movements (Stergiou et al., 2006). Professionals, who

typically show a very stable behavioural state—stable behavioural states indicate less movement variability—are able to respond to changing conditions without loss of movement stability, as underlined by their 'rich' behavioural performances. With regards to skill acquisition, movement variability typically reduces once a skill is obtained (Harbourne and Stergiou, 2009). Of course, where fundamental motor skills, including complex activities like gait and posture, are concerned, every individual could typically be considered as having developed skill equal to that of Michael Jordan in their ability to navigate diverse and challenging terrains while walking (Stergiou and Decker, 2011). As a motor skill becomes fully embedded, movement variability does not reduce, it increases as individuals further develop and refine their skill to achieve a stable behavioural state (Stergiou et al., 2006). The outcome of movement variability is explained based on how it is measured (Stergiou and Decker, 2011). Regarding skill acquisition, movement variability reduces with skill acquisition in term of the motor learning model, but the movement variability associated with the motor skill increases through the development of a broader behavioural repertoire or state that permits successful adaptation to new environments.

1.3.2 An alternative theoretical model of human movement variability

Recently, an alternative theoretical framework has been suggested that may better explain the relationship between movement variability, motor learning and health (Stergiou et al., 2006; Stergiou and Decker, 2011). This research posits that motor skills and healthy states are linked, with optimal movement variability indicating greater adaptability of the underlying control system (Stergiou and Decker, 2011). By contrast, reduced movement variability refers to more predictable, rigid motor behaviour, with greatly increased variability indicating unpredictable and unstable motor behaviour. Both markedly higher and lower levels of movement variability can result in

decreased adaptability to disturbances, and can indicate underlying health or physical function problems (Niederer et al., 2017; Stergiou and Decker, 2011).

To enhance the understanding of the human movement and evaluate movement variability, it is essential to perform quantitative movement analysis in three-dimensional (3D) space(Camomilla et al., 2018).

1.4 Movement Analysis

Analysing movement behaviour using a quantitative method can provide useful data about the functions of movement sub-systems, as well as permitting analysis of motor activity (Camomilla et al., 2018), Both forms of analysis can lead to improved understanding of significant factors that relate to movement, including alteration of movement in response to injury, motor control, and how movement can adapt and change due to muscle fatigue or injury. Subject-specific analysis via quantitative methods can be used to monitor and measure outcomes, contributing to several areas of research and practice, including prevention, early diagnosis and intervention (Camomilla et al., 2018).

Quantitative movement analysis is dependent on measurements. These can be derived using motion capture systems and computational modelling, to generate mathematical models related to the anatomy and physiology of movement and the physical structures that underpin it (Camomilla et al., 2018). Data is typically recorded using optoelectronic motion capture systems or magnetic and inertial measurement units (MIMU).

In recent years, optoelectronic motion capture systems based on stereophotogrammetry have become widely used (Duffy, 2016; Bolink et al., 2016). These are now seen as the ‘gold standard’ amongst methods to measure human body kinematics. Such systems require several cameras in

order to record the position of markers placed on the skin of the subject's body (Duffy, 2016; Bolink et al., 2016). The 3D marker positions are estimated after two-dimensional (2D) marker positions have been recorded at each frame, with the 3D positions based on stereophotogrammetric methods. Simply put, the function of this system is based on each camera using infrared light to identify reflective surfaces (markers) (Abdel-Malek and Arora, 2013) (see *Figure 1.2*).

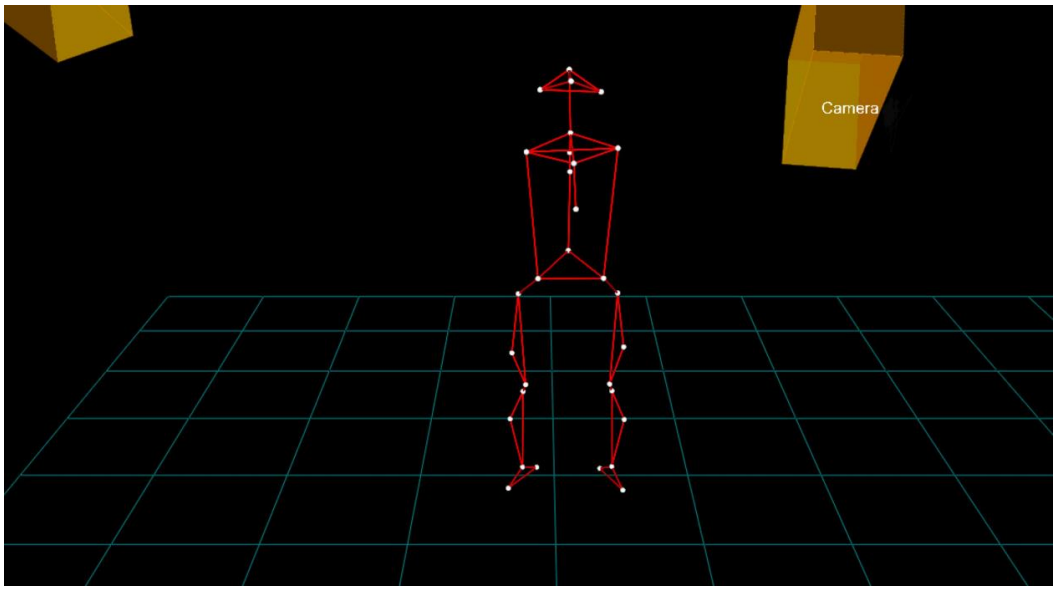


***Figure. 1.2*: Recording with a movement analysis laboratory equipped with an optoelectronic motion capture system: reflective markers were placed on subject's skin to record body kinematics.**

MIMU is commonly used as an alternative to optoelectronic motion capture systems (Camomilla et al., 2018). A MIMU system includes an accelerometer, sensors and a magnetometer; data acquired by sensors is quantified based on the axis of a unit-embedded technical frame (Camomilla et al., 2018), Algorithms are employed to screen out redundant information, and to modify data collection by taking sensor noise and drift into account.

1.4.1 Methods for measuring movement variability

There are two key aspects to movement variability: the amount of variability and the structure of variability. These can vary independently (Baida et al., 2018). The amount of movement variability can be assessed using linear statistical methods, while the structure of variability requires nonlinear methods. Linear methods can be described as one-dimensional measures of centrality, which allow researchers to calculate the amount or magnitude of variability in a time series (e.g. gait fluctuations) (Smith et al., 2014; Stergiou and Decker, 2011). There are several linear methods that can be used to measure variability, including standard deviation (SD), variance and range (Urdan, 2016).

SD is the most commonly used measure of variability. SD employs the average of the distribution as a reference, then quantifies variability via the distance between each score and the average (Gravetter, 2018). In other words, SD gives a measure of the mean distance (MD) from the average, as well as reflecting the degree of dispersion of scores around the average.

Nonlinear methods include sample entropy, approximate entropy and largest Lyapunov exponent, which quantifies the mean divergence or convergence of trajectories related to directions in state space, amongst others (Baida et al., 2018; Peixoto et al., 2018). These methods calculate the structure or organisation of variability in a time series (e.g. alteration observed in gait fluctuations) (Stergiou and Decker, 2011; Baida et al., 2018). With regards to the results of movement variability examination, linear and nonlinear methods provide different information (Smith et al., 2014). For example, Harbourne and Stergiou (2009) used the example of postural sway when standing to illustrate the outcomes of evaluating movement variability using linear and nonlinear methods. When an individual displays an increased range of sway while standing, a higher amount of variability will be seen when using a linear measure, while a nonlinear measure will reveal that the

sway becomes more regular with more repetition of movement patterns. This observation reveals that the individual is performing a particular strategy—swaying—to modify balance when the range of sway increases, otherwise they would fall (Harbourne and Stergiou, 2009).

Although nonlinear methods can be used to examine complexity of movement over a period of time, ranging from seconds to days, these techniques are challenging to use in a clinical environment. Concurrent utilisation of linear measures is also needed in order to understand the relationships between data and movement strategies, and to identify clinical meaning (Harbourne and Stergiou, 2009). In contrast, linear methods are easier to use in clinical settings, and are easier to interpret (Schumacher, 2004; Urdan, 2016). Furthermore, standard motor learning curves are composed by utilising linear statistics regarding variability measures of movement performance (Stergiou, Harbourne and Cavanaugh, 2006). Linear statistical methods measure the magnitude of variation in a set of values based on their order in the distribution (Stergiou, Harbourne and Cavanaugh, 2006). As motor learning happens, the magnitude of variation constantly reduces, and eventually plateaus.

The helical axis (HA) has been used to describe three-dimensional motion of rigid bodies (Spoor, 1984; Galbusera and Wilke, 2018). The HA can give a comprehensive description of movements; it describes the rotation and translation of a body along an axis (see *Figure. 1.3*) (Middleton et al., 1999; Spoor, 1984). HA has been used to investigate movement in several body regions, including the arm, ankle, knee and neck (Graf and Stefanyshyn, 2012; Grip and Hager, 2013; Venegas et al., 2020; Grip et al., 2008). According to Venegas et al. (2020), the HA is reliable for examining differences in coordination of intervertebral movement during cyclic neck movements in asymptomatic individuals. In addition, HA is sensitive to variability and able to identify specific patterns of movement (Venegas et al., 2020). Therefore, HA data could provide important information regarding functional changes in people with CNP since it can be affected by

motor control, and can identify movement changes in people with neck pain disorders (Barbero et al., 2017).

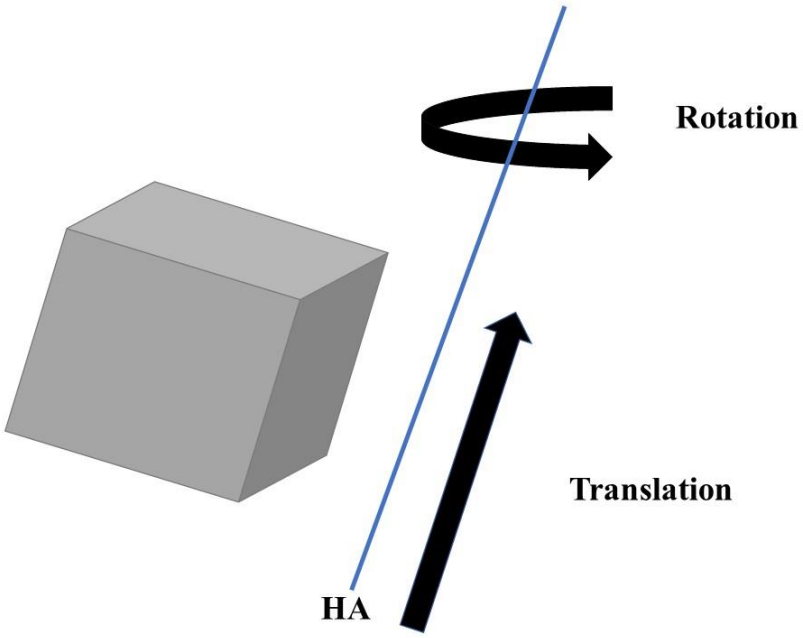


***Figure. 1.3*: Representation of the helical axis (HA) of an object with rotation and translation along the instantaneous axis.**

Recently, novel measurements were suggested to reflect the behaviour of the HA while performing active neck movements in asymptomatic individuals (Barbero et al., 2017). The mean angle (MA) and distribution in space of the HA parameters were used to examine movement variability in the neck area (Cescon et al., 2014; Barbero et al., 2017). The MD and MA of the HA were calculated as defined previously (Barbero et al., 2017). The MD represents the distance between all intersection points between the HA and a transversal plane from their barycenter, while the MA is defined by calculating the MA of each axis and the total average. Notably, the observed MA changes during the active neck movements clearly exceed the standard error of the measurement as well as the minimal detectable change reported in a recent study (Barbero et al., 2017). This indicates good response stability, a measure that reflects consistency of repeated responses over a period of time, which indicates that the changes could be related to the

participant's condition (Mohammad et al., 2011). Thus, HA parameters have the potential to describe movement behaviour in people with neck pain disorders (Barbero et al., 2017; Lomond and Côté, 2010).

1.5 Movement variability and chronic neck pain

Several studies of movement variability have found differences between people with painful conditions and asymptomatic individuals. For example, in a study investigating the variability of kinematics during repetitive arm movement (Madeleine et al., 2008), findings showed decreased variability of arm and trunk acceleration in participants with chronic neck-shoulder pain as compared to asymptomatic people. In addition, less variability of transverse thoracic movement, which is described as rotation of the trunk and pelvis and includes lumbar rotations, has been observed in people with low back pain as compared to asymptomatic controls during treadmill gait trials (Lamoth et al., 2006).

With regards to CNP, few studies investigated movement variability as an outcome measure. Vogt et al. (2007) used coefficients of variation to quantify movement variability at the maximum oscillation amplitude levels (the maximum displacement of an object from its mean position during an oscillation is defined as a repetitive variation in time) (Fitzpatrick, 2018; Sawhney, 2016). This research also found statistically significant differences in movement variability between people with CNP and asymptomatic subjects during active neck movements in all directions. An age-matched group of 18 healthy participants and 16 CNP participants were included in the study (at the time of the test, the CNP participants had an average level of pain of 3.7, measured via visual analogue scale) (Vogt et al., 2007). Furthermore, people with CNP displayed larger RoM variability compared to asymptomatic individuals during left and right neck rotation movements (Sjolander et

al., 2008b). However, changes in movement behaviour with regards to movement variability in people with CNP remains unclear, and therefore further investigation is required.

1.6 Thesis Aims and Objectives

The general aim of this thesis was to understand whether changes in movement variability exist in people with neck pain disorders and to better understand the mechanisms underlying these changes. To pursue the aim of this thesis, four studies were conducted. Specifically, a focus was on examining movement variability via novel approaches, in order to shed light on changes in movement variability during active cervical movements and during gait in people with CNP, and to understand the mechanisms underlying these changes.

1.6.1 Specific objectives of this thesis:

1. To examine movement variability using novel kinematics parameters of the HA during active cervical movements in people with CNP, and to assess correlations between these parameters and clinical features.

2. To examine movement variability of the spine, including both neck and trunk, during gait in people with CNP, and to evaluate the correlation between movement variability and reported clinical features.

3. Using a novel approach to induce acute neck pain in asymptomatic individuals, to examine the immediate effects of neck pain on movement variability during active cervical movements.

4. To synthesise the evidence investigating the quality of spinal movement, including movement variability, in people with CNP and to determine the characteristics of the measurements used.

For a visual representation of the objectives of the thesis, see *Figure 1.4*.

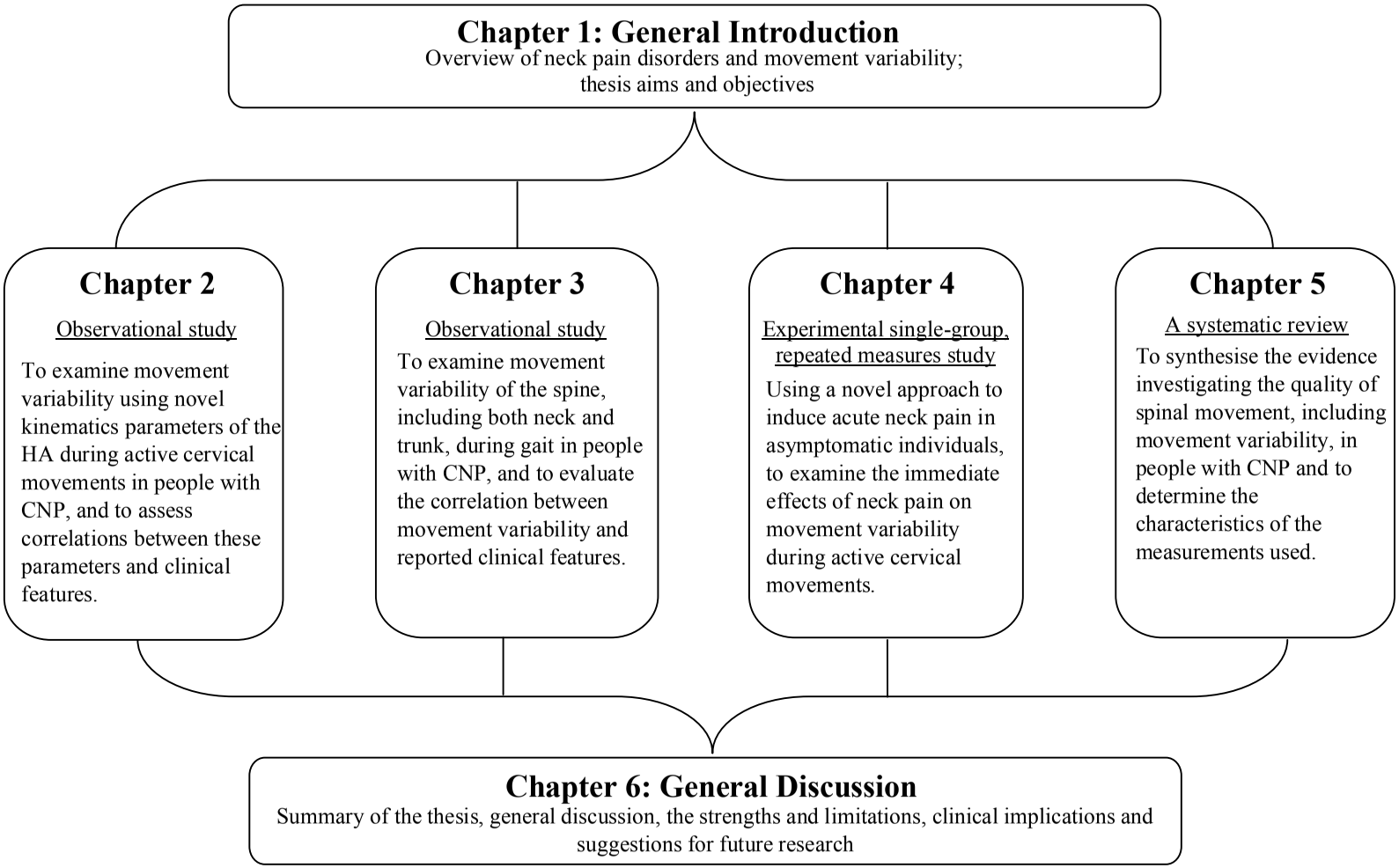


***Figure 1.4*: Visual representation of the thesis, including the objectives of each chapter.**

1.6.2 Thesis Chapter Overview

Chapter One has provided an overall summary of current research investigating movement in people with neck pain disorders and sets the scene for the following chapters. *Chapter Two* reports the results of an observational study focused on using novel parameters of the HA to investigate changes in movement variability in people with CNP compared to asymptomatic individuals, in order to provide further information regarding movement behaviour during active neck movements in people with neck pain. *Chapter Three* reports the results of an observational study, which focused on investigating changes in the variability of neck and trunk rotation during gait in people with CNP relative to asymptomatic individuals. *Chapters Two and Three* also explore correlations between kinematics parameters and clinical features in people with CNP.

Chapter Four reports results of an experimental single-group repeated measures study, which examines a novel approach using eccentric exercise to induce acute neck pain in order to determine whether pain can induce an immediate change in neck movement variability. *Chapter Five* reports a systematic review, which focuses on summarising-and critically appraising the literature investigating whether people with CNP differ from asymptomatic individuals in terms of the quality (including movement variability) of spinal movement. In addition, it emphasises the outcome measures and parameters used in current research to assess the quality of spinal movement. *Chapter Six* presents further discussion of the four studies documented in *Chapters Two, Three, Four and Five*. This final chapter summarises the main research outcomes of the thesis, and includes a general discussion of the research, reflections on the strengths and limitations of the work, a discussion of clinical implications, and suggestions for future research.

The results of the series of studies presented in this thesis are intended to assist researchers and healthcare practitioners to further understand movement behaviour in terms of movement

variability, therefore providing insights to support better examination and intervention for people with neck pain disorders.

CHAPTER 2

VARIABILITY OF THE HELICAL AXIS DURING ACTIVE CERVICAL MOVEMENTS IN PEOPLE WITH CHRONIC NECK PAIN: AN OBSERVATIONAL CASE-CONTROL STUDY

This chapter reports in full the contents of a published manuscript by the thesis author (Alsultan et al., 2019). It includes verbatim text from the published manuscript and some changes employed for the purpose of this thesis.

Publications and Presentations

1. **Alsultan, F.**, Cescon, C., De Nunzio, A.M., Barbero, M., Heneghan, N.R., Rushton, A. & Falla, D. 2019. Variability of the helical axis during active cervical movements in people with chronic neck pain. *Clinical Biomechanics*, 62, 50-57. **(Appendix 1)**

2. **Alsultan, F.**, Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. Does neck pain change the way people move? Research Poster Conference 2018, University of Birmingham. June 2018.

3. **Alsultan, F.**, Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. People with chronic neck pain perform active neck movements in a less variable way. Presentation, Physiotherapy UK conference, Birmingham. November 2018.

4. **Alsultan, F.**, Cescon, C., De Nunzio, A., Heneghan, N., Rushton, A., Barbero, M. & Falla, D. People with chronic neck pain perform active neck movements in a less variable way. Presentation, World Confederation of Physical Therapy conference, Geneva. May 2019.

2.1 Abstract

Recent work describes parameters of the HA in asymptomatic people as having potential for investigating kinematic changes in the cervical region. This approach could provide novel information on movement variability in people with neck pain, but this has not yet been investigated. This chapter aimed to investigate movement variability during active neck movements performed at different speeds in people with and without CNP.

This observational case-control study examined 18 participants with CNP of either idiopathic or traumatic origin and 18 gender-matched asymptomatic participants, aged between 18 and 70. The mean (SD) for age of participants was 32.2 (13.4) years for CNP group and 25.8 (7.3) years for asymptomatic group. For the CNP participants, the mean (SD) for level of pain was 4.08 (1.89), i.e. mild, while for the level of disability it was 12.94 (6.84), also mild. The mean (SD) of the Tampa Scale for Kinesiophobia (TSK) score was 36.53 (6.58).

Cervical kinematics were captured with 3D motion capture as people with and without CNP performed flexion-extension, bilateral lateral flexion and bilateral rotation at different speeds (natural, slow, and fast). The MD and MA parameters of the HA were extracted to describe 3D motion and quantify movement variability.

A smaller MD was observed in those with neck pain compared to the asymptomatic participants during flexion-extension ($p = 0.019$) and rotation movements ($p = 0.007$). The CNP group displayed smaller values for the MA during rotation movements with different speeds ($p = 0.01$). These findings indicate less variable movement for those with CNP relative to the asymptomatic participants. No difference in the MA was observed between groups for flexion-extension and lateral flexion. People with CNP displayed less movement variability during flexion-extension and rotation movements compared to healthy individuals, as shown by the MD and MA

measurements. For the CNP group, a negative correlation was observed between TSK and MA measured for all neck rotation conditions. The findings showed the importance of data derived from kinematic measures, and its potential for providing clinicians with further insight into the quality of active neck movements in people with CNP

2.2 Introduction

As discussed in the *Chapter One*, a number of studies have examined neck movement characteristics in people with CNP, with reduced active neck RoM a common observation, regardless of the aetiology of the neck pain disorder (Alricsson et al., 2001; Lee et al., 2005; Peolsson et al., 2007). However, most studies have focused on the quantity of movement, and typically on static variables of planar cervical motion. The quality or variability of movement may be a better indicator of ongoing neuromuscular dysfunction in people with CNP (Anderst et al., 2017; Baydal-Bertomeu et al., 2011; Edmondston et al., 2005; Preatoni et al., 2013). Furthermore, investigating kinematic variables across multiple axes can provide more precise information regarding changes during active movements (Ellingson et al., 2013).

Measures of the HA can be used to describe three-dimensional motion in the cervical region. Recently, novel parameters were proposed to describe the behaviour of the HA during active neck movements in healthy volunteers, and the reliability of these parameters were established: intra-session and inter-session reliability during rotation (ICC) ≥ 0.80), with a 95% confidence interval (CI) (0.55-0.91) (Barbero et al., 2017). The distribution in space of the HA and the MA of the HA measurements (Barbero et al., 2017; Cescon et al., 2014) demonstrated potential for investigating the variability of neck movement. HA parameters could therefore provide novel information regarding movement behaviour in people with CNP (Barbero et al., 2017; Lomond and Côté, 2010). It was hypothesized that movement variability would be reduced in people with CNP, based on previous studies that examined variability in people with pain (Lamoth et al., 2006; Madeleine et al., 2008).

This chapter addresses the aims of this thesis as follows: The primary objective was to investigate movement variability using novel parameters during active neck movements at different

speeds, in people with and without CNP, in order to understand whether changes in movement variability exist in people with CNP disorders. The secondary objective was to assess correlations between HA parameters and levels of pain, disability, fear of movement, physical activity and dizziness in the participants with neck pain in order to understand the mechanisms underlying movement variability changes.

2.3 Methods

2.3.1 Design

An observational case-control study was conducted between May and November 2017. Ethical approval for the study was granted by the Ethics Committee of the University of Birmingham, UK (CM06/03/171: see *Appendix 4*) and the study was conducted according to the Declaration of Helsinki. Convenience sampling was used to recruit participants from among students and staff of the University of Birmingham. The main purpose of the study and the methods that would be used were explained to participants before they were asked to give written informed consent. In designing and reporting the study, the researcher adhered to the guidelines of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement (von Elm et al., 2014) (see *Appendix 5*).

2.3.2 Participants

The sample size included 36 male and female gender-matched participants aged between 18 and 70, including 18 asymptomatic people and 18 people with CNP of either idiopathic or traumatic origin. Participants attended a single laboratory session. An a priori sample size could not be determined, since no previous study had evaluated parameters of the HA in people with CNP and therefore no data were available for sample size calculation. Thus, the sample size was estimated

based on a previous study evaluating other features of cervical kinematics in people with and without CNP (Vogt et al., 2007).

Inclusion criteria

Participants with neck pain were included in the study if they presented with painful symptoms for at least three months (King, 2013). In the case of those with WAD, only individuals with grades I, II, or III symptoms according to the Quebec Task Force Classification (Spitzer, 1995) were included. In addition, the participants had to report their neck pain intensity over the last four weeks as at least 4 (mild pain) out of 10 on a Numerical Rating Scale (NRS) with two anchor points: 0 = "no pain" and 10 = "worst pain imaginable" (Boonstra et al., 2016; Kamper et al., 2015). The NRS is a valid and reliable instrument for self-reported pain intensity (Williamson and Hoggart, 2005). Self-rating of pain intensity was found to be sensitive based on the method of pain measurement used and the length of recall time: for example, when participants are asked to rate pain over a period of four weeks, they will report a higher pain score than when asked to only rate immediate pain (Kamper et al., 2015).

Asymptomatic participants were recruited to act as a control group, which was matched for age and gender. To be included, they must have had no history of a neck injury or neck pain in the last two years that required treatment from a health care practitioner. Participant selection was in line with previous studies, which also included CNP and asymptomatic groups (Misailidou et al., 2010; Falla et al., 2017; Vogt et al., 2007).

Exclusion criteria

Participants were excluded from either group if they presented with any of the following: previous spinal surgery, rheumatic condition, current or chronic respiratory condition, having an ongoing compensation claim related to an injury. In line with (Spitzer, 1995), additional exclusion

criteria for the CNP group included currently receiving active management, and neck injury that resulted in a spinal fracture (Grade 4 of QTF). The exclusion criteria were selected based on previous studies that also included CNP and asymptomatic groups (Misailidou et al., 2010; Falla et al., 2017).

2.3.3 Questionnaires

All participants were required to complete the International Physical Activity Questionnaire (IPAQ), which was used to characterise the sample with respect to their physical activity levels (Craig et al., 2003). Additionally, for the participants with CNP, their average pain level over the last four weeks was recorded using the NRS (Kamper et al., 2015) and their perceived neck disability was assessed using the Neck Disability Index (NDI), with a possible score range of 0–50 (Vernon, 2008; Vernon and Mior, 1991). The test-retest reliability value was 0.89 ($P < 0.05$).The Dizziness Handicap Inventory (DHI) was used to determine self-reported levels of dizziness (Jaco and Graig, 1990). The test-retest reliability for the DHI total score was excellent ($r = .97$, $df= 12$, $p< 0.0001$). Additionally, self-reported dizziness intensity at rest and during activity was measured following testing, using an NRS from 0 to 10, where 0 was “no symptoms” and 10 was “worst symptoms” (Kammerlind et al., 2005; Kamper et al., 2015). Finally, the 17-item TSK questionnaire was employed to evaluate fear of movement and related behavioural problems, including avoidance and disability (Miller et al., 1991). TSK has previously been found to be a valid and reliable measure (Hudes, 2011).

2.3.4 Cervical Kinematics

An optoelectronic system (Milan, Italy: BTS Bioengineering) was used to record cervical kinematics following system calibration. The kinematic data was acquired at a standard frequency

of 250 fps. The system consists of eight infrared cameras with a resolution of 2,2 Mpixels (2048 × 1088 pxs) (Bioengineering, 2020). The cameras tracked the 3D motion of retroreflective markers attached to the subject's skin over the following body landmarks, with at least three placed on each body segment as recommended by Camomilla et al. (2018) (Drillis et al., 1964): two markers on the sternum, superior at the jugular notch and inferior at the xiphoid process, 7th cervical vertebra, 5th thoracic vertebrae, 9th thoracic vertebrae. In addition, a helmet was placed on the subject's head, with four reflective markers as follows: on the head apex, the front, and right and left sides of the helmet (see *Figure 2.1*) (Cescon et al., 2015). The helmet also contained a laser pointer, which has been used in previous studies to examine the quality of movement (Quartey et al., 2019; Sarig Bahat et al., 2020; Woodhouse et al., 2010b).

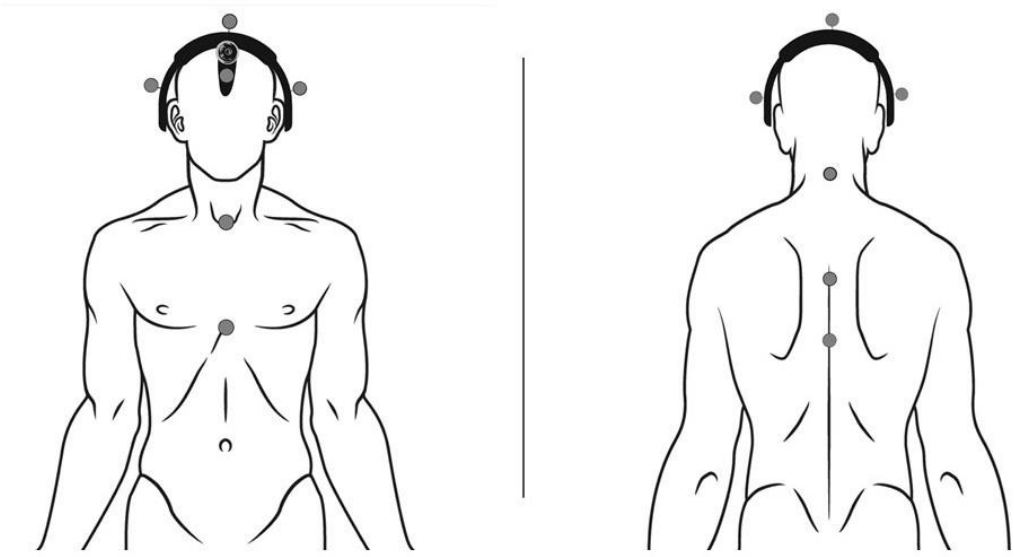


***Figure 2.1*: Illustration of the retroreflective markers attached to the front and back of the subject's body.**

2.3.5 Procedure

Following placement of the reflective markers, the participant was seated upright on a chair with their head in a neutral position, and they were instructed to avoid shoulder movements and to

relax their arms (Barbero et al., 2017; Grip et al., 2008). The participant was seated 220 cm in front of a wall and with the head in neutral, the point of the laser was marked on the wall to define the starting reference position (0°). Using a goniometer, the subjects head was then rotated 45° to the left and right and these positions were marked (see *Figure 2.2*).

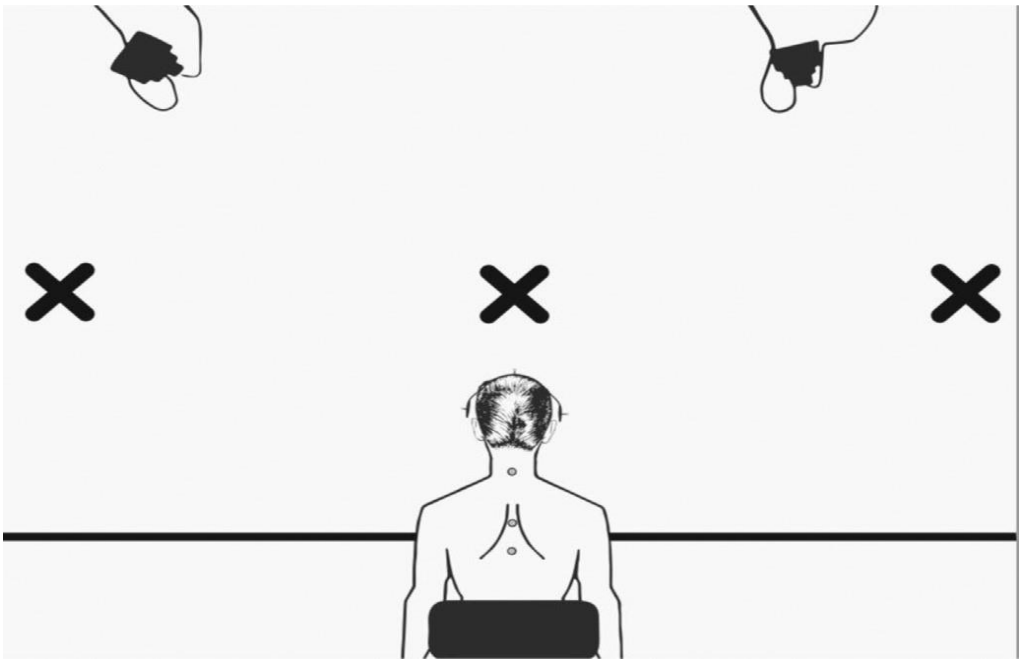


***Figure 2.2*: Illustration of the experimental setup. Marks were placed on the wall in front of the subject to identify the starting position and, as illustrated here, 45° of right and left rotation. Markers were placed on a helmet and on the subject to track head movement in three-dimensional (3D) space.**

Flexion and extension to 45° were also performed and these positions were marked on the ceiling and floor. The participants performed the following neck movements: flexion-extension, bilateral lateral flexion, and bilateral rotation. Each movement was performed in three conditions: at a natural self-selected speed, slow speed (30 beats per second [bps]) and fast speed (60 bps) (see *Table 2.1*). The movement speed was controlled using a metronome beats mobile application, and conditions were randomised in order to minimise the risk of order as a confounding variable (Castelein et al., 2016).

***Table 2.1*: Overview of the movements and conditions measured.**

Movements	Conditions
Flexion-extension	1. Natural speed 2. Slow speed 3. Fast speed
Bilateral lateral flexion	4. Natural speed 5. Slow speed 6. Fast speed
Bilateral rotation	7. Natural speed 8. Slow speed 9. Fast speed

Participants were instructed to start every movement from the reference point at 0° and then perform continuous neck movements without stopping in the midline (Baydal-Bertomeu et al., 2011). The subjects were instructed to maintain the laser at 0° while performing lateral flexion, move between the 45° reference points while performing rotation, and move up and down between the 45° reference points while performing flexion-extension. The RoM was limited, since performing functional tasks and activities of daily living does not usually require the full active RoM (Bennett et al., 2002; Bible et al., 2010), Therefore, reference points were set at 45 °, a range expected to be appropriate for most everyday activities. In addition, the position and orientation of the HA depend on the RoM (Barbero et al., 2017).

Kinematic data were acquired for 10 repetitions of each condition following the protocol described by Barbero et al. (2017). Ten was selected as the number of cycles to be performed for two reasons. First, obtaining a representative sample of natural head movements required a reasonably large number of repetitions. Second, it was also important to avoid requiring a number of cycles that would lead to muscle fatigue or dizziness in the patient. After completing a pilot study, an acceptable number of cycles was found to be 10 movements, meeting both of these criteria.

Familiarisation with each test condition preceded data acquisition. A rest period of 30 seconds was given between each condition to prevent fatigue and ensure that the participant returned to the neutral position between conditions (Miura and Sakuraba, 2014).

2.3.6 Data analysis

To investigate variability during active neck movements, the MD and MA of the HA were calculated as defined previously (Barbero et al., 2017) (see *Figure 2.3*).

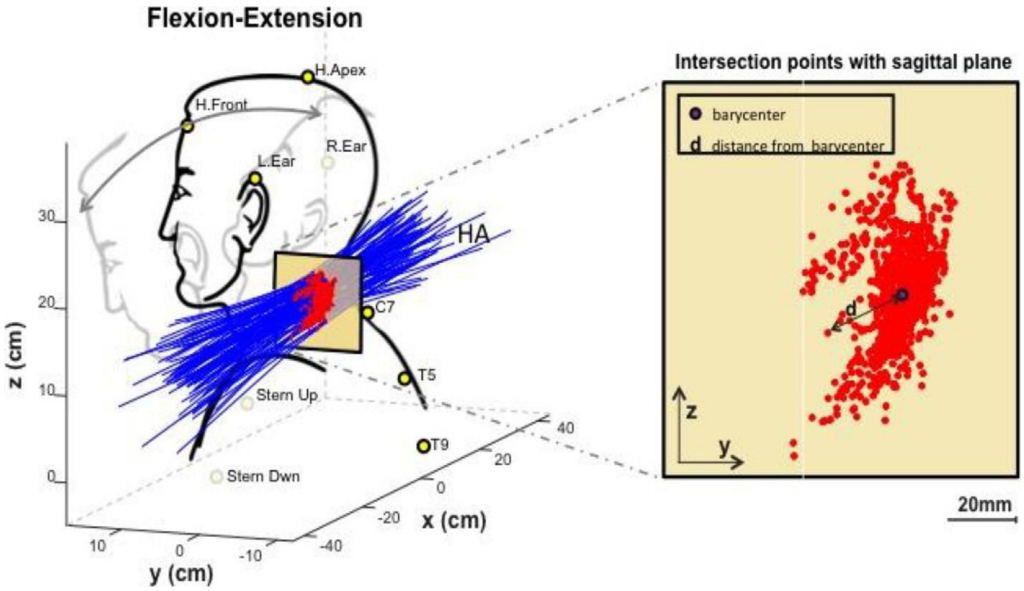


***Figure 2.3*: Demonstration of the Helical Axis (HA) parameters used in the experimental protocol. Mean Distance (MD) intersection points are represented in red, while Mean Angle (MA) angles of axis lines are represented in blue.**

Lower values of the MD and MA imply that the movement is less variable. The RoM was quantified by calculating the mean difference between the maximal flexion and extension movements, while the mean difference of neck rotation and lateral flexion were computed between the left and right movements (Barbero et al., 2017).

Data from eight repetition movement cycles were analysed following exclusion of the first and last cycle in order to avoid artefacts or alterations in angular velocity (Cescon et al., 2014). After completing the pilot study, it was observed that patients often performed the first and the last movements differently from the others, reflecting adaptation of the subject to the task. Removing the first and last movement of the 10 cyclic movements allowed researchers to reduce the impact of these transitional phases of movement initiation and termination. In gait analysis research, analysis is also sometimes performed on a sub-portion of gait cycles, usually excluding the first and last, for the same reason (Temporiti et al., 2020). The degree of variability of neck movements across the whole movement cycle was measured by calculating the SD of the mean.

2.3.7 Statistical analysis

Mean and SD were calculated to describe MD and MA parameters. In addition, mean and SD were used to demonstrate the range and distribution of participant demographics and questionnaire responses. Two-way analysis of variance (ANOVA) was applied to evaluate the MD, MA and RoM during the flexion-extension movements, lateral flexion movements and rotation movements, with group (control, CNP) and condition (slow, natural and fast speed) as factors (Field, 2013). Significant differences revealed by ANOVA were followed up by post-hoc Student Newman-Keuls (SNK) pair-wise comparisons.

The parametric test assumptions, including testing data for normality, have not been met. However, the sample sizes used in the research reported in this *Chapter* were above 30, a size that is considered large enough to avoid serious problems (Pallant and Manual, 2007; Ghasemi and Zahediasl, 2012). As these authors suggest, when a sample size is large enough, it should tolerate violations of assumptions. Thus, parametric procedures can be used even when the data are not normally distributed (Ghasemi and Zahediasl, 2012). Outliers were kept since they were considered

as different, not “wrong” (Kozak and Piepho, 2018). Also, analysis of variance can stand up to violations of the assumption of homogeneity of variance in a robust fashion, as long as the groups compared as relatively similar (Pallant and Manual, 2007).

To assess the correlation between movement variability and reported clinical features in people with CNP, Pearson or Spearman correlations (depending on the distribution of each form of questionnaire data) were performed to assess the relationship between MA and MD of the neck movements and the following six variables (Field, 2013): NDI, DHI and self-reported dizziness intensity (NRS), level of average pain intensity (NRS), TSK, and IPAQ. The strength of the correlation was interpreted as: small correlation < 0.3, moderate correlation between 0.3 and 0.5, and strong correlation > 0.5 (Cohen, 1988a). Results are reported as mean and SD in the text and figures. Statistical analyses were performed with SPSS Version 22.0 (Armonk, NY: IBM Corp.). Statistical significance was set at $p < 0.05$.

2.3.8 Missing data

Before the study began, an effort has been made to prevent missing data from occurring through the design of the data collection procedure. Where missing data are present in the study, precise examination of missing data was performed in order to determine mechanism, rate, and pattern related to missing data and the data distribution, before selecting an appropriate method to deal with the missing data (Dong and Peng, 2013).

2.4 Results

A total of 36 participants completed the study, with 8 men and 10 women in each group. Those with CNP had a mean (SD) age of 32.2 (13.4) years, while the mean (SD) age of the control

group was 25.8 (7.3) years, which was not significantly different (U = 109.500, z = −1.664, p = 0.097).

There were six CNP participants who had experienced a whiplash injury: two with grade I, three with grade II, and one with grade III. Participant demographics for both groups are presented in *Table 2.2*. One participant in the CNP group did not complete the TSK questionnaire. There were 7 missing values across all kinematic variables: two values of RoM for flexion-extension at fast speed and lateral flexion at slow speed in the control group, and 5 values of MD for two conditions for lateral flexion at slow and fast speed, one condition for rotation slow speed in the control group, and two conditions for flexion-extension slow and lateral flexion natural speed in the CNP group. These occurred due to artefacts in data acquisition. Statistical analysis was considered to be biased if more than 10% of data was missing (Dong and Peng, 2013). Therefore, the procedures of statistical analysis tests were performed.

***Table 2.2*: Participant demographics and self-report questionnaires.**

		Control group	CNP group
Age	Mean (SD)	25.89 (7.34)	32.22 (13.41)
Height (cm)	Mean (SD)	168.80 (7.71)	170.77 (10.34)
Weight (kg)	Mean (SD)	64.67 (14.41)	68.39 (14.69)
Total IPAQ score	Mean (SD)	3940.97 (3163.72)	5175.61 (4569.36)
NDI	Mean (SD)	NA	12.94 (6.84)
Average pain intensity	Mean (SD)	NA	4.08 (1.89)
TSK	Mean (SD)	NA	36.53 (6.58)
DHI	Mean (SD)	NA	20.78 (17.32)
Dizziness NRS	Mean (SD)	NA	1.65 (2.12)

Figure 2.4 presents representative data from a control subject and person with CNP acquired during rotation at a natural speed. The observations from this representative example were confirmed at the group level, as presented in *Figure 2.5* and detailed below.

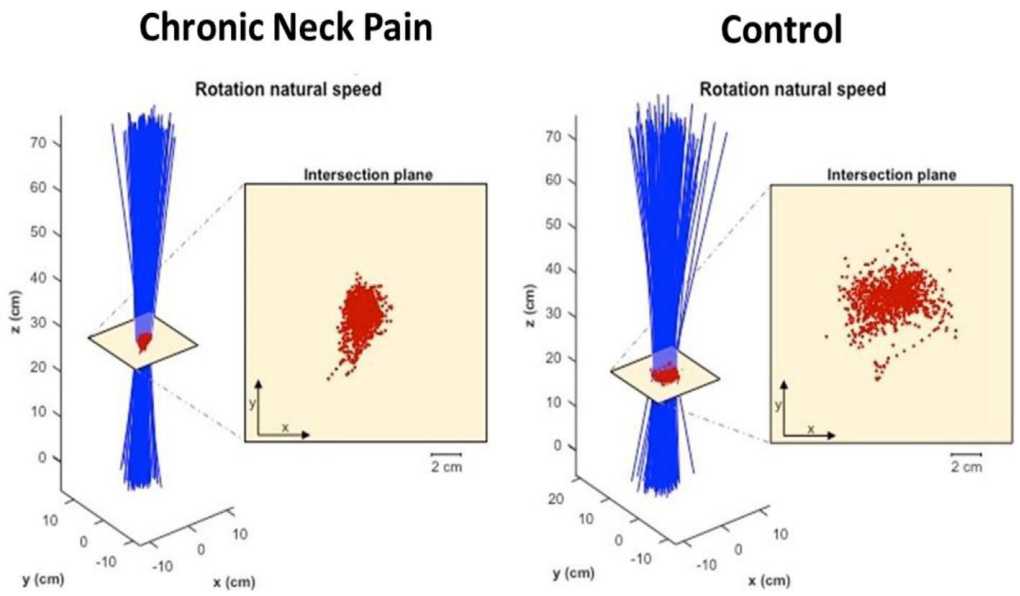


***Figure 2.4*: Representative data acquired from a patient and control subject during head rotation performed at a natural speed. Note the smaller mean distance (MD) and mean angle (MA) for the participant with chronic neck pain (CNP) compared to the control subject.**

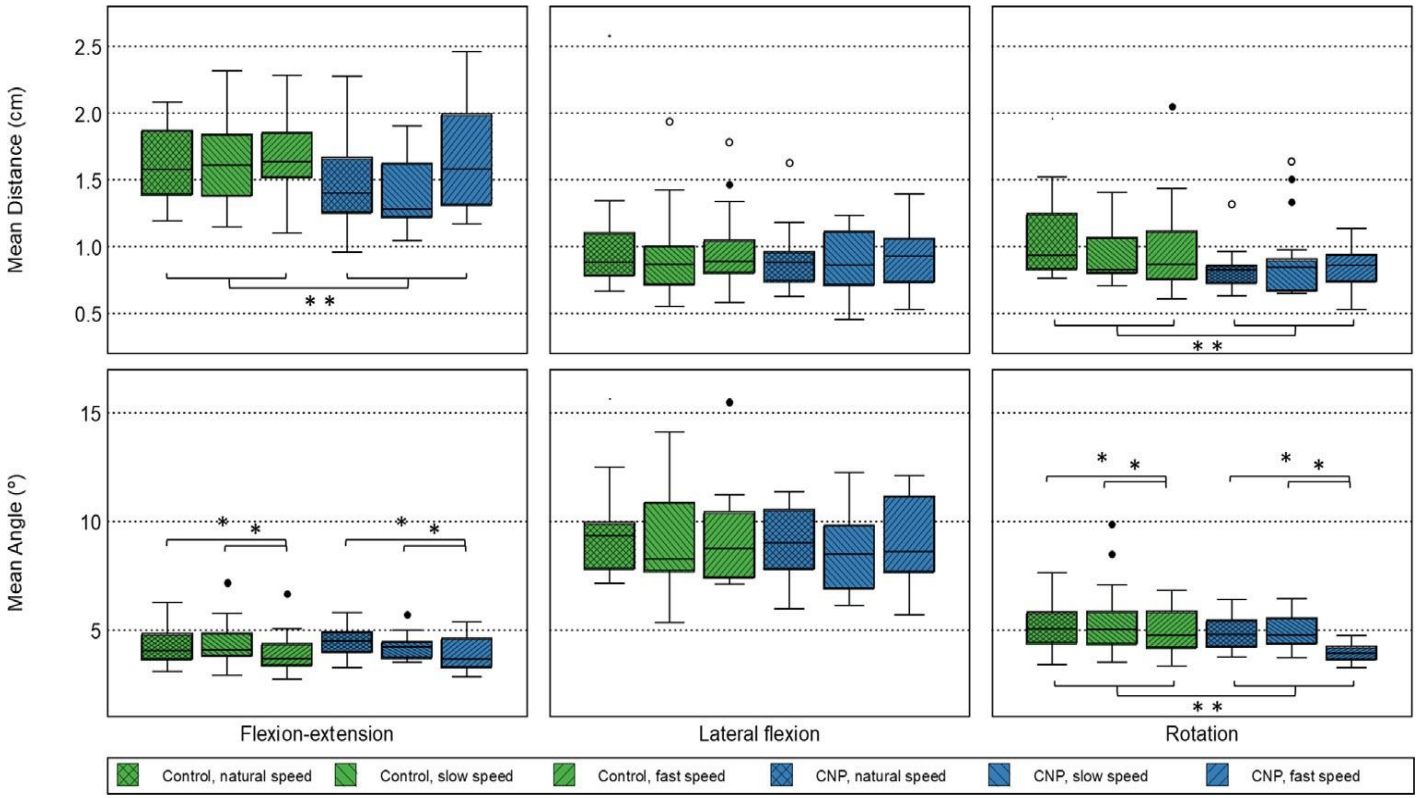


***Figure 2.5*: Boxplots representing the descriptive results, mean and standard division of the mean distance (MD), and mean angle (MA) for all the neck movement conditions investigated.**

* Statistically significant difference between conditions < 0.05

** Statistically significant difference between groups < 0.05

2.4.1 Mean distance (MD)

Flexion-extension

The CNP group displayed a smaller MD for the flexion-extension movements regardless of the condition (main effect for group: $F = 5.7$, $p = 0.019$). Despite a trend, the MD did not vary across flexion-extension movement conditions ($F = 3.0$, $p = 0.051$) and was not dependent on the interaction between group and condition ($F = 0.7$, $p = 0.47$). The MD decreased in the CNP group as compared to control group for the flexion-extension movements. The mean (SD) of CNP group were as follows; natural speed condition 1.46 cm (0.33 cm), slow condition 1.39 cm (0.25 cm), fast condition 1.65 cm (0.39 cm); whereas in the control group the values for the natural speed condition were 1.61 cm (0.28 cm), slow condition 1.63 cm (0.31 cm), and fast condition 1.71 cm (0.31 cm).

Lateral flexion

The MD did not vary across groups ($F = 1.1$, $p = 0.28$) or condition ($F = 0.2$, $p = 0.82$) for the lateral flexion movements, and was not dependent on the interaction between group and condition ($F = 0.2$, $p = 0.83$). The mean (SD) of the CNP group were: natural speed condition 0.91 cm (0.23 cm), slow condition 0.90 cm (0.23 cm), and fast condition 0.91 cm (0.25 cm); while for the control group, natural speed condition values were 1.02 cm (0.44 cm), slow condition 0.93 cm (0.34 cm), and fast condition 0.97 cm (0.31 cm).

Rotation

Consistent with the results for flexion-extension, the CNP group displayed smaller MD values for the rotation movements regardless of condition (main effect for group: $F = 7.48$, $p = 0.007$). The MD did not vary across rotation movement conditions ($F = 0.19$, $p = 0.82$) and was not dependent on the interaction between group and condition ($F = 1.53$, $p = 0.22$).

The MD for the rotation movements decreased in the CNP group as compared to the control group. The mean (SD) of the CNP group were as follows: natural speed condition 0.83 cm (0.15 cm), slow condition 0.90 cm (0.29 cm), and fast condition 0.84 cm (0.15 cm). The control group mean (SD) were: 1.07 cm (0.33 cm) in the natural speed condition, slow condition 0.93 cm (0.22 cm), and fast condition 0.99 cm (0.35 cm).

2.4.2 Mean angle (MA)

Flexion-extension

No difference was observed between groups for the MA during the flexion-extension movements ($F = 0.1$, $p = 0.92$), and no interaction between group and condition was observed ($F = 5.2$, $p = 0.59$). However, the MA did vary across conditions ($F = 4.0$, $p = 0.02$), with smaller MA observed during the fast speed condition compared to the slow and natural speed conditions (both SNK: $p < 0.05$).

The MA for the flexion-extension movements was reduced in the fast speed condition as compared to other conditions. The mean (SD) values during the fast speed condition were as follows: CNP group 3.88° (0.75°) and control group 3.89° (0.92°); whereas for the CNP group the values were 4.51° (0.73°) for natural speed condition and 4.22° (0.57°) for slow condition; and for the control group, 4.29° (0.91°) for natural speed condition and 4.39° (0.99°) for slow condition.

Lateral flexion

The MA did not vary across groups ($F = 1.5$, $p = 0.21$) or condition ($F = 0.3$, $p = 0.68$) for the lateral flexion movements, and was not dependent on the interaction between group and condition ($F = 0.2$, $p = 0.82$). The mean (SD) of the CNP group were as follows: natural speed condition 8.96° (1.62°), slow condition 8.61° (1.92°), and fast condition 9.04° (2.07°); while for the

control group, the values were natural speed condition 9.70° (2.16°), slow condition 9.21° (2.42°), and fast condition 9.20° (2.11°).

Rotation

The MA during the rotation movements was dependent on group ($F = 9.30$, $p = 0.003$) and condition ($F = 4.82$, $p = 0.010$), but not the interaction between group and condition ($F = 1.34$, $p = 0.26$). The post-hoc analysis revealed that the CNP group displayed smaller values for the MA during rotation movements with different speeds (SNK: $p < 0.01$) (see *Table 2.3*).

***Table 2.3*: Results of the ANOVA to evaluate differences in the mean distance (MD) and mean angle (MA) for each movement direction.**

Parameters	Conditions	Group * conditions (Sig.)	Group (Sig.)	Conditions (Sig.)
MD (cm)	Rotation	0.22	0.007*	0.82
	Flexion-extension	0.47	0.019*	0.051
MA (°)	Lateral flexion	0.83	0.28	0.82
	Rotation	0.26	0.003*	0.010*
	Flexion-extension	0.59	0.92	0.02*
	Lateral flexion	0.82	0.21	0.68

* Statistically significant difference: $p < 0.05$.

The MA for the rotation movements decreased in the CNP group as compared to the control group. The mean (SD) for the CNP group were as follows: natural speed condition 4.98° (0.85°), slow condition 4.89° (0.71°), and fast condition 3.98° (0.42°). The control group values were: natural speed condition 5.21° (1.04°), slow condition 5.44° (1.64°), and fast condition 4.99° (1.02°) (see *Table 2.4*).

***Table 2.4*: Mean and standard deviation of the Mean Distance (MD) and Mean Angle (MA) recorded during each movement direction and each condition, for both the control and Chronic Neck Pain (CNP) groups.**

Parameter	MD (cm)		MA (°)	
Group	Control	CNP	Control	CNP
Movement	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Flexion-extension natural	1.61 (0.28) [1.47, 1.75]	1.46 (0.33) [1.31, 1.62]	4.29 (0.91) [3.85, 4.74]	4.51 (0.73) [4.19, 4.84]
Flexion-extension slow	1.63 (0.31) [1.49, 1.77]	1.39 (0.25) [1.23, 1.55]	4.39 (0.99) [3.95, 4.83]	4.22 (0.57) [3.89, 4.54]
Flexion-extension fast	1.71 (0.31) [1.57, 1.85]	1.65 (0.39) [1.50, 1.81]	3.89 (0.92) [3.44, 4.33]	3.88 (0.75) [3.56, 4.21]
Lateral flexion natural	1.02 (0.44) [0.84, 1.19]	0.91 (0.23) [0.79, 1.02]	9.70 (2.16) [8.65, 10.76]	8.96 (1.62) [8.07, 9.85]
Lateral flexion slow	0.93 (0.34) [0.75, 1.11]	0.90 (0.23) [0.79, 1.02]	9.21 (2.42) [8.16, 10.27]	8.61 (1.92) [7.72, 9.50]
Lateral flexion fast	0.97 (0.31) [0.79, 1.15]	0.91 (0.25) [0.80, 1.02]	9.20 (2.11) [8.14, 10.25]	9.04 (2.07) [8.15, 9.93]
Rotation natural	1.07 (0.33) [0.93, 1.22]	0.83 (0.15) [0.74, 0.92]	5.21 (1.04) [4.60, 5.83]	4.98 (0.85) [4.56, 5.41]
Rotation slow	0.93 (0.22) [0.78, 1.08]	0.90 (0.29) [0.81, 0.99]	5.44 (1.64) [4.83, 6.05]	4.89 (0.71) [4.47, 5.32]
Rotation fast	0.99 (0.35) [0.84, 1.14]	0.84 (0.15) [0.76, 0.93]	4.99 (1.02) [4.38, 5.61]	3.98 (0.42) [3.56, 4.41]

2.4.3 RoM

The RoM for flexion-extension movements was consistent across conditions ($F = 0.4$, $p = 0.62$) and groups ($F = 1.9$, $p = 0.16$), with no interactions present ($F = 0.4$, $p = 0.66$). The same was true for lateral flexion, with no differences between conditions ($F = 2.4$, $p = 0.09$) and groups ($F = 2.0$, $p = 0.15$) and no interactions present ($F = 0.0$, $p = 0.98$). For rotation, there were no effect of conditions ($F = 2.60$, $p = 0.07$), no effect of group ($F = 0.74$, $p = 0.39$), and no interaction present ($F = 1.07$, $p = 0.34$). The results of the RoM confirmed that all neck movement conditions were performed within the range of movement required by the experimental protocol.

2.4.4 Correlations between kinematic variables and subjective descriptors

To understand the mechanisms underlying changes in movement variability, the correlation between the questionnaires scores and MA and MD variables are shown in *Table 2.5*. Significant correlations were found between MA and MD with the following variables: NDI, level of average pain intensity (NRS), TSK, and IPAQ.

***Table 2.5*: Correlations between questionnaire responses and helical axis (HA) parameters.**

Questionnaires	Parameters	Neck movements	Correlation coefficient	Sig. (2 tailed)
NDI	MD (cm)	Flexion-extension with fast speed	0.490*	0.039
Pain (average)	MD (cm)	Flexion-extension with fast speed	0.514*	0.029
TSK	MA (°)	Rotation natural	−0.563*	0.015
		Rotation slow	−0.561*	0.015
		Rotation fast	−0.805**	0.000
	MD (cm)	Lateral flexion fast	−0.481*	0.044
IPAQ	MA (°)	Lateral flexion natural	−0.346*	0.039
	MD (cm)	Lateral flexion fast	−0.346*	0.042

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Mean distance (MD)

There was a moderate positive correlation between NDI and the MD measured during flexion-extension neck movements at the fast speed ($r = 0.490$, $p = 0.039$). A strong positive correlation was found between the average pain intensity (NRS) and the MD measured during flexion-extension neck movement at the fast speed ($r = 0.514$, $p = 0.029$). Furthermore, a moderate negative correlation was documented between the TSK score and MD during lateral flexion performed and at the fast speed ($r = −0.481$, $p = 0.044$). A moderate negative correlation was found between the IPAQ score and the MD during lateral flexion performed at the fast speed ($r = −0.346$, $p = 0.042$).

Mean angle (MA)

There was a moderate negative correlation between the IPAQ score and the MA during lateral flexion performed at the natural speed ($r = -0.346$, $p = 0.039$). In addition, there was a strong negative correlation between the TSK score and the MA during neck rotation and at a natural speed ($r = -0.563$, $p = 0.015$), slow speed ($r = -0.561$, $p = 0.015$), and fast speed ($r = -0.805$, $p = 0.000$).

2.5 Discussion

This study is the first to evaluate the variability of active neck movement in people with CNP by utilising parameters of the HA. The findings revealed less variability of movement in people with CNP during flexion-extension and rotation movement compared to healthy controls as shown by the MD measurements. The results also showed reduced variability of movement during rotation in people with CNP as compared to asymptomatic people as seen in the MA measurements.

2.5.1 Movement variability

The results of the present study are congruent with previous research findings that people with pain may move with less variability (Lamoth et al., 2006; Madeleine et al., 2008). Madeleine et al. (2008) reported reduced variability of arm and trunk acceleration in people with chronic neck-shoulder pain as compared to asymptomatic people during a repetitive arm movement task. Reduced variability of transverse thoracic and lumbar rotations has also been observed in people with low back pain as compared to asymptomatic controls while participants were walking (Lamoth et al., 2006). However, some other studies suggest the opposite. For example, Vogt et al. (2007) found that movement variability was significantly higher in people with CNP when compared to an asymptomatic group. However, they examined movement variability only in the maximum oscillation amplitudes (Vogt et al., 2007), whereas the present study investigated a larger cycle of

neck movement. Continuous cyclical movement trials are more likely to able to provide information regarding movement behaviour associated with CNP. For example, (Baydal-Bertomeu et al., 2011) observed reductions in RoM, velocity and acceleration during active neck movements in people with CNP compared to asymptomatic individuals.

One previous study that investigated full active range of neck movements found that motion patterns were characterised by less flexibility and slower movement in people with neck pain as compared to healthy controls. Reduced flexibility, indicated by decreased cervical RoM and conjunct motion, was quantified with regards to the primary plane and the two associated movement planes at the maximum of the RoM (Meisingset et al., 2015b). The findings of the present study concur with these results even though different procedures were used in both studies. In Meisingset et al. (2015b), participants were asked to move as far as possible while performing neck movements at a self-determined speed, while the participants in this study were requested to move between fixed points at both a natural speed as well as fixed speed. The findings from the present study, as in those of Meisingset et al. (2015b), could be interpreted as evidence of a more cautious movement strategy by people with neck pain, presumably employed as a protective strategy to decrease or potentially avoid neck pain.

Even though the level of pain reported in this study was low (mild) in the CNP group, differences in movement behaviour and movement variability were nevertheless observed between the groups. This is consistent with other research, and with current theories about the impact of pain on movement and motor control (Moseley and Hodges, 2006), Indeed, some people may continue to display less variability in movements even when they are free from pain. This association could be controlled by evaluative processes that play a role in motor variability: when a movement is associated with pain, the patient performs that movement differently, and over a period of time this change in movement becomes ingrained (Moseley and Hodges, 2006). Furthermore, motor

adaptations to pain could lead to protection from vulnerability to pain or injury, and contribute to changes in mechanical behaviour (Hodges and Tucker, 2011). For example, a protective movement strategy was employed by healthy people when they anticipated that a movement could cause harm to their back (Moseley and Hodges, 2006). Thus, the lower movement variability identified in the CNP group in the current study could reflect an adapted movement behaviour due to pain.

2.5.2 The influence of movement speed

In the current study, reduced movement variability was observed in the CNP group as compared to the control group for flexion-extension as revealed by differences in the MD. Furthermore, decreased movement variability during flexion-extension was seen via the MA when performed at the faster speed than when performed at the slower and self-selected speeds, and this was the case for both groups. Vikne et al. (2013) also observed a significant reduction in movement speed and displacement during flexion-extension movements when performed at a faster speed compared to the preferred or slower speed. In addition to the observed reduction of movement variability during flexion-extension at the faster speed, positive correlations were also found between the MD during flexion-extension performed at the faster speed, and the level of disability (NDI), and the level of average pain intensity (NRS). Based on the current and on previous observations, faster movements could be emphasised during the clinical examination of people with CNP especially since people with neck pain often complain of difficulty performing rapid movement of their head (Sarig Bahat et al., 2010).

2.5.3 Correlation between movement parameters and clinical features

A negative correlation was found for the CNP group between TSK and MA measured for all neck rotation conditions. Thus, movement variability decreased with higher levels of fear of

movement. The fear avoidance model of pain indicates that when pain is present and leads to fear that movement could cause harm, this fear leads to avoidance of physical activities (Bahat et al., 2014), These findings confirm the effect of avoidance behaviour on physical functioning.

2.5.4 Clinical implications

Examining the variability of neck movement as done in this study is not trivial to perform in a clinical setting (Lamoth et al., 2006). However, our findings show that such data derived from kinematic measures have the potential to provide clinicians with important insights into active neck movement behaviour in people with CNP. Further research should evaluate whether simplified measures of movement e.g. with inertial sensors, which can be more easily implemented in a clinical setting, are capable of detecting such changes in movement quality in people with CNP.

2.5.5 Methodological considerations

Our current sample of CNP participants presented with relatively low levels of pain and disability compared to the typical CNP population (average pain intensity ~4/10 and NDI score ~13/50) (Goode et al., 2010), and the study sample size was not calculated a priori, thus the generalisability of study findings is likely reduced. The sample size also prevented comparisons between those with idiopathic neck pain versus trauma-induced neck pain or a comparison between genders. This could be explored in future studies. Nevertheless, the kinematic variables in this study were able to detect differences in the quality of cervical motion between groups and provided information about the nature of these differences. This is one of very few studies examining whole-cycle movement at different speeds in people with CNP.

2.6 Conclusion

In this chapter, the use of parameters of the HA to observe differences in movement variability during neck flexion-extension and rotation movements in people with CNP is described and discussed. Findings indicate that these measurements may be useful in future studies to evaluate the effects of interventions, including exercise, to enhance movement control in people with CNP. Based on the findings presented in this chapter, the third chapter explores the variability of spinal movement in people with neck pain disorders but now during the task of gait.

CHAPTER 3

VARIABILITY OF NECK AND TRUNK MOVEMENT DURING SINGLE- AND DUAL-TASK GAIT IN PEOPLE WITH CHRONIC NECK PAIN: AN OBSERVATIONAL CASE-CONTROL STUDY

This chapter reports in full the contents of a published manuscript (Alsultan et al., 2020a), including verbatim text of the published manuscript and changes for the purpose of this thesis.

Publications and Presentations

1. **Alsultan, F.**, De Nunzio, A.M., Rushton, A., Heneghan, N.R. and Falla, D. 2020. Variability of neck and trunk movement during single-and dual-task gait in people with chronic neck pain. *Clinical Biomechanics*, 72, pp. 31-36. **(Appendix 2)**

2. **Alsultan, F.**, De Nunzio, A.M., Rushton, A, Heneghan, N.R., & Falla, D. Does neck pain change the way people move during a challenging walking task? Presentation, Research Poster Conference 2018, University of Birmingham. June 2019.

3. **Alsultan, F.**, De Nunzio, A.M., Rushton, A, Heneghan, N.R. & Falla, D. Investigating neck and trunk movement variability during single and dual-task gait in people with Chronic Neck Pain. Presentation, Physiotherapy UK conference, Birmingham. November 2019.

4. **Alsultan, F.**, De Nunzio, A.M., Rushton, A, Heneghan, N.R. & Falla, D. Investigating neck and trunk movement variability during single and dual-task gait in people with Chronic Neck Pain. Presentation, Pain Science in Motion Conference, Savona. May 2019.

3.1 Abstract

Previous findings have reported that people with CNP walk with a reduced range of trunk rotation, especially when walking in more challenging conditions, including walking with head rotation. Quantification of the quality of neck and trunk movement during gait could provide further insight into biomechanical changes that occur in people with neck pain. This chapter presents a unique comparison of the variability of trunk and neck rotation during single-task and dual-task gait in people with CNP and asymptomatic individuals.

An observational case-control study was conducted on 20 asymptomatic individuals and 24 people with CNP of idiopathic or traumatic origin, aged between 18 and 70. The mean (SD) of age was 31.50 (12.50) years for CNP group and 28.65 (11.03) years for asymptomatic group. The mean (SD) of the level of pain reported by people with CNP was 3.96 (1.91) (mild), and the mean (SD) of the level of disability was 11.92 (6.70) (mild), with mean (SD) of TSK scores 35.43 (8.26).

Participants performed rectilinear (straight line) walking whilst keeping the head in a neutral position (single-task) and whilst rotating the head at a natural speed (dual-task). Trunk and head rotation angles were averaged across gait cycles for the task trials. The data were normalised in time, and the average variability of angular distribution along the normalised cycle was extracted.

During single-task gait, there were no group differences for the variability of trunk ($p = 0.862$) or neck ($p = 0.427$) rotation. For dual-task gait, there was no difference between groups for the variability of neck rotation ($p = 0.636$), however, the participants with neck pain displayed reduced variability of trunk rotation ($p = 0.021$). The neck pain group also walked at a significantly slower speed during dual-task gait ($p = 0.043$) compared to asymptomatic individuals and the speed of their gait was associated with the extent of fear of movement. The strategy observed in participants with CNP likely reflects adaptive behaviour when faced with more challenging conditions for postural control.

3.2 Introduction

The results presented in *Chapter Two* confirmed significant differences in movement variability between people with CNP and asymptomatic individuals during active neck movements. Surprisingly, few studies have examined whether gait is modified in people with CNP even though walking is one of the most common activities of daily living, and is closely related to health status and physical function (Sitthipornvorakul et al., 2015; Uthaikhup et al., 2014). Those that have been conducted, have revealed that some people with CNP walk with a narrower step width, a shorter step length and a slower gait speed (Poole et al., 2008; Sjostrom et al., 2003; Uthaikhup et al., 2014). Moreover, a recent study documented reduced trunk rotation during walking in people with CNP compared to asymptomatic individuals, especially when walking was accompanied by a task of maintaining the neck in 30º of rotation (Falla et al., 2017).

Dual tasks, in which two tasks are performed at the same time, are commonly used when investigating gait, since such tasks more appropriately reflect typical activities of daily living and therefore stand to reveal more relevant differences in gait biomechanics (Freire Junior et al., 2017; Liu et al., 2018). For instance, a previous study observed a significant difference in gait speed, stride and step time, and single-support time between fallers and non-fallers when dual-task gait was performed, whereas no changes were observed during the single-task condition (Toulotte et al., 2006). In addition, Sjostrom et al. (2003) recorded reduced head and trunk rotation in people with chronic WAD when performing head rotation during walking.

Although the evaluation of RoM is a typical component of the clinical examination of people with neck pain, quantifying the quality and variability of movement is also essential to understand the day-to-day impact of a patient's condition (Edmondston et al., 2005). Based on the research results presented in *Chapter Two* and other studies that examined variability in people with

pain (Lamoth et al., 2006; Madeleine et al., 2008; Alsultan et al., 2019), it was hypothesized that movement variability of the spine would be reduced in people with CNP during gait.

This chapter addresses the objectives of the thesis via research focused on two aims. The first aim was to investigate the variability of neck and trunk rotation during gait in people with CNP relative to asymptomatic participants. Participants were evaluated during both single- and dual-task gait, with the expectation that if differences were to exist between groups, this would be more evident during dual-task gait. The dual-task condition consisted of walking whilst rotating the head, a common daily activity. The second aim was to evaluate the correlation between the variability of neck and trunk rotation during gait and the extent of neck pain intensity, level of neck pain-related disability and fear of movement.

3.3 Methods

3.3.1 Design

An observational case-control study congruent with the Declaration of Helsinki principles was conducted from May to November 2017. Ethical approval was obtained from the Ethics Committee of the University of Birmingham, UK (CM06/03/17-1: see *Appendix 4*). Participants were recruited from the staff and student population of the University of Birmingham using a convenience sampling method. Written informed consent was obtained from all participants after the purpose and methods of the study were explained. The guidelines of the STROBE Statement (von Elm et al., 2014) were employed to design and report this study (see *Appendix 6*).

3.3.2 Participants

A sample of 44 participants aged between 18 and 70, including 20 healthy individuals and 24 people with CNP of either idiopathic or traumatic origin, attended a single laboratory session.

Sample size was estimated based on previous studies that examined parameters during gait in people with CNP (Falla et al., 2017; Poole et al., 2008). Following data collection, a post-hoc effect size (Cohen's d) was calculated for the primary variable outcome using the program G*Power 3.1 for Windows. The one-way ANOVA F-test was used, with an α error level probability of 0.05. The effect size was calculated for the variability of trunk rotation during the dual gait task of the CNP group (mean 1.46°[1.13°]). The effect size was 0.43, which indicates a large effect (Cohen, 1988b).

Inclusion and Exclusion criteria

Recruitment, inclusion and exclusion criteria were identical to those described in *Chapter Two* (Alsultan et al., 2019).

3.3.3 Anthropometric measurements

Anthropometric measurements were recorded for all subjects according to Davis's guidelines (Davis III et al., 1991). The measurements include height, weight, leg length, the distance between the two anterior superior iliac spines (ASIS), pelvis depth bilaterally, knee diameter bilaterally, malleolus width bilaterally.

3.3.4 Questionnaires

The participants with CNP were required to complete three questionnaires, the NRS, NDI and TSK, which were also used in the study described in *Chapter Two* (Alsultan et al., 2020a).

3.3.5 Cervical and trunk kinematics

An optoelectronic system (Milan, Italy: BTS Bioengineering) identical to the system used in the study described in *Chapter Two* was employed to record cervical and trunk kinematics (Alsultan et al., 2019). The cameras tracked the 3D motion of retroreflective markers attached to the subject's

skin over body landmarks, similar to the biomechanical model described in (Davis et al., 1991). At least three were placed on each body segment, as recommended by Camomilla et al. (2018). Two markers were placed on the sternum (superior at the jugular notch and inferior at the xiphoid process), and additional markers were placed bilaterally on the anterior superior iliac spine (ASIS), great trochanters, lateral femoral condyles, lateral bars (located on centre between great trochanter and lateral femoral condyles markers), the head of the fibula, lateral bars (centred between the head of the fibula and lateral malleolus markers), lateral malleolus, the fifth metatarsal head and heels. Posteriorly, markers were placed bilaterally on the acromion process, seventh cervical vertebra, fifth thoracic vertebrae, ninth thoracic vertebrae and second sacral vertebra (S2). Furthermore, to track head motion, the participants wore a helmet which included four reflective markers (head apex, front, and right and left of the helmet) (see *Figure 3.1*) (Cescon et al., 2015).

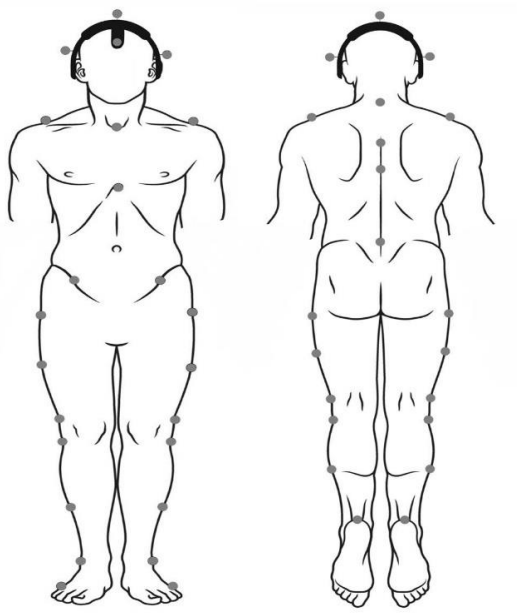


***Figure 3.1*: Illustration of the retroreflective markers attached to body landmarks on the subject's skin, front and back.**

3.3.6 Procedure

Once the reflective markers were positioned, the participants completed single- and dual-task gait trials, which each consisted of six repetitions of walking along a rectilinear path for approximately five steps (three meters) (Davis III et al., 1991; Poole et al., 2008; Sjostrom et al., 2003; Uthaikhup et al., 2014), during single-task gait, the participants were asked to walk while keeping their head in a natural position (three repetitions executed), whereas the dual-task waking trial consisted of walking whilst rotating the head continuously at a natural speed (three repetitions executed). In this trial, participants were asked to rotate their neck as far as they comfortably could without causing pain, but the RoM was not imposed (Sjostrom et al., 2003). The trials were randomised to minimise the risk of order as a confounding variable and a rest period of 30 seconds was provided between each trial (Uthaikhup et al., 2014). Familiarisation with each gait task was performed before data acquisition. These procedures are similar to those used in previous studies investigating movement in people with neck pain (Davis III et al., 1991; Poole et al., 2008; Sjostrom et al., 2003; Uthaikhup et al., 2014).

3.3.7 Data analysis

To investigate the variability of neck and trunk rotation during gait, trunk and head rotation angles (degrees) were averaged across gait cycles for the single-task gait trials. Data were normalised in time (% gait cycle), and the average variability of the angular distribution along the normalised cycle was extracted. The same analysis was conducted for the dual-task gait trials, using the head rotation angular peaks as events to define the cycles during gait.

Gait speed was averaged across gait cycles for both the single- and dual-task trials. Gait speed data were then normalised to the participants' height. The average variability of trunk and neck rotation across the gait cycles was measured by calculating the SD (SD) of the mean.

3.3.8 Statistical analysis

Mean and SD of trunk and neck rotation were extracted to describe the average and variability of their motion in the horizontal plane, as well as mean speed. The Shapiro-Wilk test was applied to evaluate the data distribution for all extracted variables (Field, 2013). One-way ANOVA or Kruskal-Wallis H tests, for normally and non-normally distributed data respectively, were performed to analyse differences between the asymptomatic participants and the CNP group, for the variability of trunk and neck rotation, RoM, and mean gait speed during single- and dual-task gait. As in *Chapter Two*, outliers have been retained: these were considered as different, but not "wrong" (Kozak and Piepho, 2018). The Kruskal-Wallis H test was used instead of ANOVA when the data are not normally distributed, as recommended by MacFarland and Yates (2016).

A cross-correlation test was performed between trunk and neck movements to examine movements of these two body segments during single-task and dual-task gait, with results from the CNP group then compared to those of the healthy group. Independent-samples t-test for normally distributed data or Kruskal-Wallis H tests for non-normally distributed data analysed differences between the groups (Field, 2013). To evaluate the correlation between movement variability and reported clinical features in people with CNP, Pearson or Spearman correlations for normally and non-normally distributed data, respectively, were performed to assess the relationship between the variability of trunk and neck rotation, mean gait speed, and: i. perceived disability (NDI), ii. average neck pain intensity (NRS) and iii. fear of movement (TSK). Mean and SD findings are reported in the text and figures. Statistical analyses were completed using SPSS Version 25.0 (Armonk, NY: IBM Corp.). Statistical significance was set at $p<0.05$.

3.3.9 Missing data

The procedure for dealing with missing data was planned as described in *Chapter Two* (Alsultan et al., 2019).

3.4 Results

Participant demographics for CNP and healthy groups are presented in *Table 3.1*. The groups did not differ in age ($t(42)=0.135$, $p=0.893$) or gender ($U = 288.000$, $z = 1.133$, $p = 0.257$). Eight of the 24 participants with CNP had experienced a whiplash injury: four with grade I, three with grade II, and one with grade III. Kinematic data were missing for 28 out of 440 measures due to artefacts. Statistical analysis was completed since less than 10% of data were missing.

Table 3.1: **Participant demographics and results of self-report questionnaires—range of Standard Deviation (SD) scores is reported in parentheses. Higher scores indicate high level of disability according to Neck Disability Index (NDI), pain in average pain intensity, or greater fear of movement.**

		Control Group	CNP Group
Gender	Women	10	14
	Men	10	10
Age	Mean (SD)	28.65 (11.03)	31.50 (12.50)
Height (cm)	Mean (SD)	169 (7.34)	169.88 (9.72)
Weight (kg)	Mean (SD)	65.66 (14.09)	66.87 (13.28)
NDI (0-50)	Mean (SD)	NA	11.92 (6.70), mild
Average pain intensity (0-10)	Mean (SD)	NA	3.96 (1.91), mild
TSK (17 – 68)	Mean (SD)	NA	35.43 (8.26)

3.4.1 Single-task gait

Variability of trunk and neck rotation

The mean variability (SD) of trunk rotation for the CNP group was 0.62° (0.43°) versus 0.60° (0.48°) for the asymptomatic group; whereas the variability of neck rotation was 0.48° (0.34°)

for the CNP group versus 0.46° (0.52°) for the asymptomatic group. No significant differences was observed between groups for the variability of trunk rotation (F [1, 42] = 0.031, p=0.862) or neck rotation χ^2 (1)= 0.631, p=0.427) during single-task gait.

Range of motion (RoM) for trunk and head rotation

The mean (SD) RoM of trunk rotation for the CNP group was 9.19° (3.56°) versus 8.82° (2.87°) for the asymptomatic group. The mean RoM of head rotation was 4.95° (2.49°) for the CNP group versus 4.56° (1.24°) for the asymptomatic group. There were no significant differences between groups for the mean RoM of trunk rotation (F [1, 42] = 0.141, p=0.710) or neck rotation (χ^2 (1)= 0.142, p=0.706) during single-task gait.

Gait speed

Gait speed during single-task gait trials was not significantly different between groups (F [1, 42] =0.702, p=0.407). The mean (SD) gait speed for the CNP group was 0.68 (0.10 ht/s), while for the control group, the mean (SD) was 0.71 (0.12).

3.4.2 Dual-task gait

Variability of trunk and neck rotation

The CNP group (mean 1.46° [1.13°]) displayed significantly reduced variability of trunk rotation (F [1, 42] =5.773, p=0.021) during the dual gait task compared to the asymptomatic group (2.43° [1.54°]). However, no difference was observed between groups for the variability of neck rotation (F [1, 42] =0.227, p=0.636; CNP group: 29.55° [6.23°]; asymptomatic group: 28.39° [9.66°]).

Range of motion (RoM) for trunk and head rotation

The mean RoM of the trunk rotation for the CNP group was 12.16° (4.53°) versus 11.81° (3.14°) for the asymptomatic group (χ^2 (1)= 0.101, p=0.750). The mean RoM of head rotation for the CNP group was 91.59° (18.44°) versus 99.17° (17.15°) for the asymptomatic group (F [1, 42] = 1.963, p=0.169).

Gait speed

The CNP group walked at a significantly slower speed during dual-task gait trials (F [1, 42] =4.337, p=0.043) (see *Table 3.2*) with a mean (SD) 0.57 (0.10) for the CNP group and 0.64 (0.11) for the control group (see *Table 3.3*).

***Table 3.2*: Results of the ANOVA or Kruskal-Wallis H to evaluate differences in variability of trunk and neck rotation, range of motion (RoM) for trunk and head rotation, as well as gait speed for each task.**

	Task	Group (Sig.)
Variability of trunk rotation	Single [a]	0.862
	Dual[a]	0.021*
Variability of neck rotation	Single [b]	0.427
	Dual[a]	0.636
Gait speed	Single [a]	0.407
	Dual[a]	0.043*
RoM for trunk rotation	Single [a]	0.710
	Dual [b]	0.750
RoM for head rotation	Single [b]	0.706
	Dual[a]	0.169

Statistically significant difference; * $p < 0.051$.
[a] One-way ANOVA performed.
[b] Kruskal-Wallis H is performed.

***Table 3.3*: Mean and Standard Deviation (SD) of the variability of trunk and neck rotation, Range of Motion (RoM) for trunk and head rotation, and gait speed for each task, for both the control group and Chronic Neck Pain (CNP) group.**

	Variability of trunk rotation		Variability of neck rotation		RoM of trunk rotation		RoM of head rotation		Gait speed	
Group	Control	CNP	Control	CNP	Control	CNP	Control	CNP	Control	CNP
Task	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Simple	0.60° (0.48°) [0.37, 0.82]	0.62° (0.43°) [0.44, 0.80]	0.46° (0.52°) [0.22, 0.70]	0.48° (0.34°) [0.33, 0.62]	8.82° (2.87°) [7.48, 10.17]	9.19° (3.56°) [7.69, 10.70]	4.56° (1.24°) [3.98, 5.14]	4.95° (2.49°) [3.90, 6.00]	0.71 (0.12) [0.65, 0.77]	0.68 (0.10) [0.64, 0.72]
Dual	2.43° (1.54°) [1.71, 3.15]	1.46° (1.13°) [0.99, 1.94]	28.39° (9.66°) [23.73, 33.04]	29.55° (6.23°) [26.92, 32.18]	11.81° (3.14°) [10.34, 13.28]	12.16° (4.53°) [10.25, 14.07]	99.17° (17.15°) [91.14, 107.19]	91.59° (18.44°) [83.80, 99.37]	0.64 (0.11) [0.59, 0.69]	0.57 (0.10) [0.53, 0.61]

3.4.3 Correlation between the variability of trunk or neck rotation and gait speed

No statistically significant correlation was observed between gait speed and the variability of trunk rotation for either group: healthy group during single-task gait (r =-0.359, p=0.120) and dual-task gait (r =-0.130, p=0.585); CNP group during single-task gait (r =0.148, p=0.533) and dual-task gait (r =-0.125, p=0.599). Likewise, no correlation was observed between gait speed and the variability of neck rotation for either group: healthy group during single-task gait (r =-0.394, p=0.085) and dual-task gait (r =-0.034, p=0.891); for the CNP group, variability of trunk rotation during single-task gait (r =0.120, p=0.614) and during dual-task gait (r =-0.105, p=0.659).

3.4.4 Correlations between kinematic variables and patient reported outcome measures

Variability of trunk rotation

No significant correlation was found between the variability of trunk rotation during single-task gait and scores on the NDI (r= -0.208, p=0.329), NRS pain intensity (r = -0.232, p=0.274), or TSK (r =0.039, p=0.867). Similarly, no significant correlation was found between the variability of

trunk rotation during dual-task gait and scores on the NDI (r = -0.096, *p*=0.655), NRS pain intensity (r = -0.141, *p*=0.510), and TSK (r =-0.022, *p*=0.925).

Variability of neck rotation

No correlation was observed between the variability of neck rotation during single-task gait and scores on the NDI (r = -0.400, *p*=0.053), NRS pain intensity (r = -0.341, *p*=0.103), and TSK (r =-0.076, *p*=0.742). Likewise, no correlation was observed between the variability of neck rotation during dual-task gait and the NDI score (r = -0.123, *p*=0.567), NRS pain intensity scores (r = -0.122, *p*=0.569), or TSK scores (r =-0.209, *p*=0.364) (see *Table 3.4*).

***Table 3.4*: Correlations between questionnaire responses and variability of trunk and neck rotation parameters**

	Questionnaires	Task	Correlation Coefficient	Sig. (2-tailed)
Variability of trunk rotation	NDI	Single	-0.208	0.329
		Dual	-0.096	0.655
	NRS pain	Single	-0.232	0.274
		Dual	-0.141	0.510
	TSK	Single	0.039	0.867
		Dual	-0.022	0.925
Variability of neck rotation	NDI	Single	-0.400	0.053
		Dual	-0.123	0.567
	NRS pain	Single	-0.341	0.103
		Dual	-0.122	0.569
	TSK	Single	-0.076	0.742
		Dual	0.209	0.364

* Correlation is significant at the 0.05 level (2-tailed)

Gait speed

No significant correlations were found between gait speed during single-task gait and the NDI scores (r = -0.206, *p*=0.335), NRS pain intensity scores (r = 0.020, *p*=0.926), or TSK scores (r =-0.376, *p*=0.093). For dual-task gait, no significant correlations were found between gait speed and the NDI scores (r = -0.035, *p*=0.870) or NRS pain intensity scores (r = 0.019, *p*=0.931). However,

there was a significant but moderate negative correlation between gait speed during dual-task gait and TSK scores for the CNP group (r =-0.48, p=0.026) indicating slower movement in those with higher fear of movement.

3.5 Discussion

This study is the first to evaluate the variability of trunk and neck rotation in people with and without CNP when performing single-task versus dual-task gait. These findings uniquely demonstrate less variability of trunk rotation and slower gait speed in people with CNP as compared to asymptomatic individuals when performing a dual gait task. Interestingly, walking at a slower speed during the more challenging dual-task gait condition was associated with higher levels of fear of movement.

3.5.1 Single-task gait

The current study observed no differences in the variability of trunk and neck rotation between those with and without CNP during single-task gait trials. These findings are in line with previous research (Falla et al. (2017) that compared variability of trunk and neck rotation between asymptomatic individuals and people with CNP during a simple walking task, albeit performed on a treadmill. In contrast, Van Den Hoorn et al. (2012) reported reduced variability of trunk rotation in people with low back pain as compared to healthy individuals during normal walking on a treadmill. Our results show similar gait speed between groups during single-task gait, which is consistent with previous research investigating gait speed during simple walking tasks between asymptomatic individuals and people with CNP (Falla et al., 2017; Poole et al., 2008; Uthaikhup et al., 2014).

3.5.2 Dual-task gait

A significant reduction in the variability of trunk rotation during dual-task gait was observed between asymptomatic individuals and people with CNP. Reduced variability of movement has been observed in other chronic musculoskeletal pain disorders and during different tasks. For example, Lamoth et al. (2006) found reduced variability of transverse thoracic and lumbar rotations between healthy participants and people with low back pain during walking. Another study observed reduced variability of arm and trunk acceleration during a repetitive arm task in people with chronic neck/shoulder pain as compared to asymptomatic individuals (Madeleine et al., 2008). Furthermore, reduced variability of active flexion-extension and rotation has been reported in people with CNP as compared to healthy individuals (Alsultan et al., 2019).

The findings of the current study contrast to those of an earlier study that reported no difference in the variability of trunk rotation between people with and without CNP (Falla et al., 2017). Nevertheless, the tasks examined are not entirely comparable, since in the current study the participants walked on a floor whilst performing continuous cyclic head rotation, whereas in the study by Falla et al. (2017), the participants walked on a treadmill while keeping their heads fixed in 30º rotation. Both the current study and Falla et al. (2017) showed no difference in the variability of neck rotation movement between asymptomatic individuals and people with CNP. These findings suggest that people with CNP tend to reduce the variability of their trunk rotation during more challenging conditions, such as dual-task gait. These observations give credence to the importance of examining movement behaviour during functional tasks that include walking, as simulated by dual-gait tasks used in this and similar studies, in people with CNP in order to detect changes in movement variability.

The participants with CNP also walked at a slower speed during dual-task gait as compared to asymptomatic individuals. Both Uthaikhup et al. (2014) and Poole et al. (Poole et al., 2008) also found that people with CNP reduced their walking speed when gait was performed while rotating the head. In addition, we observed a negative correlation between gait speed during the dual-task and the extent of fear of movement, suggesting that gait modifications in people with CNP may at least partially reflect adaptive behaviour, particularly when faced with conditions that are more challenging for postural control.

3.5.3 Methodological considerations

The participants with CNP presented with low levels of neck pain intensity (average pain intensity =3.96 /10) and mild (5 - 14 points) neck disability (average NDI score =11.92 /50) (Vernon and Mior, 1991). Although this is relevant as it highlights that individuals with CNP can display biomechanical disturbances even with relatively mild pain and disability, further work is warranted to examine movement variability in people with moderate to severe disability. Furthermore, participants with CNP presented with low levels of fear of movement (Vlaeyen et al., 1995). Despite the relatively low levels of fear of movement, a negative correlation was still identified between fear of movement and gait speed during the dual-task gait for individuals with CNP.

3.6 Conclusion

This study demonstrates less variability of trunk rotation and slower gait speed in people with CNP as compared to asymptomatic individuals when performing a dual gait task. Current findings suggest that walking at a slower speed during the more challenging dual-task gait condition was associated with higher levels of fear of movement. These novel findings provide evidence of

subtle changes in the control of spinal movement in people with CNP and highlight the importance of a comprehensive examination of functional movement involving single and dual tasks to reflect activities of daily living.

CHAPTER 4

ECCENTRIC EXERCISE AND DELAYED-ONSET MUSCLE SORENESS REDUCE THE VARIABILITY OF ACTIVE CERVICAL MOVEMENTS: AN EXPERIMENTAL, SINGLE-ARM REPEATED MEASURES STUDY

This chapter reports in full the contents of a published manuscript (Alsultan et al., 2020b). It includes verbatim text from the published manuscript and changes made for the purpose of this thesis.

4.1 Abstract

Chapter Two revealed that people with CNP move their neck in a much less variable way as compared to asymptomatic people. It remains unknown whether neck movement variability is immediately altered when people have acute neck pain. This chapter examines the effects of acute neck muscle soreness induced via eccentric exercise in healthy volunteers on the variability of neck movement, by examining changes in parameters of the HA during active neck movements.

An experimental, single-arm repeated measures study recruited 32 healthy participants, male and female, aged between 18 to 55. Repetitive active neck movements (flexion-extension, bilateral lateral flexion and bilateral rotation) were performed at different speeds, either at full RoM or restricted to 45° RoM at baseline pre-exercise (T0), immediately following eccentric neck exercise (T1), 24 hours (T2) and 48 hours post exercise (T3). The MD and MA parameters of the HA were extracted to quantify movement variability.

MD, measured during movements performed at full RoM, reduced significantly at T2 compared to T0 ($p = 0.001$) regardless of direction or speed of movement. MA was significantly lower at T2 and T3 compared to T1 ($p = 0.029$ and $p = 0.033$, respectively). When RoM was restricted to 45°, significantly lower MD values were observed at T3 compared to T1 ($p = 0.034$), and significantly lower MA values were measured at T3 compared to T0, T1 and T2 (all $p<0.0001$).

This study uniquely demonstrates that neck movement variability is reduced immediately after, 24 hours after and 48 hours after eccentric exercise, indicating that acute neck muscle soreness affects the quality of neck movement.

4.2 Introduction

Active cervical movements are commonly measured by clinicians to evaluate function of the cervical spine (Stenneberg et al., 2017). It is common for people with CNP to move with less RoM during active neck movements compared to asymptomatic individuals (Sarig-Bahat et al., 2010; Vogt et al., 2007; Woodhouse and Vasseljen, 2008; Puglisi et al., 2004). In addition, the study reported in *Chapter Two* showed that, compared to asymptomatic individuals, people with CNP move in a less variable way during repeated active neck movements (Alsultan et al., 2019). Specifically, the MD and MA of the HA were used to quantify the variability of active neck movements, and people with CNP displayed lower values of the MD and MA; indicating less movement variability (Alsultan et al., 2019).

Few studies have investigated changes in neck movement in people experiencing acute pain. The research that does exist, has typically focused on the quantity of movement i.e., RoM, confirming reduced neck RoM soon after the onset of symptoms (Fernandez-Perez et al., 2012; Sterling et al., 2003; Kasch et al., 2001; Pedler and Sterling, 2011). It was hypothesised that changes in the *quality* of active neck movements also develop rapidly following the onset of symptoms, as per restricted RoM.

There could be multiple mechanisms underlying changes in the quality of movement in people with acute neck pain or different aetiology, including pain/soreness, articular dysfunction, and psychological factors, such as fear of movement (Zabihhosseinian et al., 2017; Bahat et al., 2014). One approach to understanding the mechanisms underlying neuromuscular and biomechanical adaptations to pain is the use of human experimental pain models, including injection of noxious substances into the neck muscles (most commonly hypertonic saline) (Mista et al., 2019; Qu et al., 2019; Christensen et al., 2019). However, hypertonic saline produces pain that

typically only lasts 5-10 minutes with a peak intensity of less than a few minutes (Falla et al., 2007).

Another potential experimental approach for inducing acute pain which has not yet been applied to the neck region, is delayed-onset muscle soreness (DOMS) which occurs following unaccustomed eccentric exercise (Hedayatpour et al., 2018; Hedayatpour and Falla, 2015; Mista et al., 2019; Qu et al., 2019). DOMS typically commences within 24 hours and lasts 48-72 hours following exercise (Tsatalas et al., 2013; Martin et al., 2004) and is experienced during movement rather than being constant (Hedayatpour and Falla, 2015; Lau et al., 2013). Eccentric exercise induces muscle fibre damage and as a subsequence, pain or DOMS, most likely due to the pathophysiological changes within the exercised muscle (Hedayatpour and Falla, 2014). Muscles soreness typically appears one or two days following exercise and mechanical hyperalgesia is commonly observed for the exercised muscle/s. The maximal force of the exercised muscle usually decreases immediately after the exercise and can remain 48 hours after exercise due to soreness (Doyle-Baker et al., 2018; Mense and Gerwin, 2010; Mista et al., 2019; Iguchi et al., 2008). Therefore, the soreness induced from eccentric exercise may more likely reflect clinical neck pain and would allow the effects of acute neck muscle soreness on the quality of neck movement to be evaluated over several days.

This chapter addresses the objectives of this thesis via testing a novel approach for inducing DOMS within the neck extensor muscles in healthy volunteers, and examining the immediate influence of DOMS on the quantity (RoM) and quality (movement variability measured via the MD and MA of the HA) of active neck movements. These results indicate whether pain can induce an immediate change in neck movement variability in healthy volunteers.

4.3 Methods

4.3.1 Design

An experimental single-group and repeated measures designed study was conducted at the Centre of Precision Rehabilitation for Spinal Pain (CPR Spine) between April and July 2019. Ethical approval was granted by the Ethics Committee of the University of Birmingham, UK (ERN_18-1273A: see *Appendix 7*), and the study was conducted according to the Declaration of Helsinki. Participants were recruited from students and staff at the University of Birmingham using a convenience sampling method. Recruitment methods included contacting participants on the CPR Spine patient register, printed advertisements, and an identical digital advertisement disseminated using the University's intranet. The main aim of the study and the methods were explained to participants in person, and were presented in a participant information sheet. Any questions or concerns regarding the study were addressed before participants signed an informed consent form. The guidelines of the STROBE Statement (von Elm et al., 2014) were used to report this study, as no specific guideline was recommended for this type of study design and it was the most appropriate available guideline (see *Appendix 8*).

4.3.2 Participants

Thirty-two healthy participants were recruited, including 18 men and 14 women. The sample size required was estimated using the program G*Power 3.1 for MacOS. Deriving four measurements from one group for neck rotation movements, with normal speed and the MA as a primary outcome, was found sufficient to achieve 80% statistical power (1-β error probability), with an α error level probability of 0.05 using ANOVA of repeated measures, within-factors, and a medium effect size of 0.24. The effect size was based on previous data describing the difference

between the means (0.23°) of two groups—people with CNP and healthy individuals—divided by their SD (0.94) (Alsultan et al., 2019). The non-sphericity correction ε was 0.5 (Bartlett, 2019). This calculation generated a required sample size of 32 participants.

Inclusion and exclusion criteria

Healthy participants (men and women aged between 18 and 55 years old) were included in the study if they did not have a history of neck injury or neck pain in the last five years that required treatment from a healthcare practitioner. Participants were excluded if they presented with previous spinal surgery, pregnancy, rheumatic conditions, current or chronic respiratory conditions, or an ongoing compensation claim related to any injury. Similar inclusion and exclusion criteria for healthy participants have been used in previous studies, as well as in the research presented in *Chapter Two* and *Chapter Three* (Misailidou et al., 2010; Falla et al., 2017; Vogt et al., 2007; Alsultan et al., 2020a; Alsultan et al., 2019).

4.3.3 Questionnaires

The following questionnaires have been used in this chapter to record clinical features of the participants. Participants completed the IPAQ to describe their physical activity levels (Craig et al., 2003). This questionnaire was used to compare IPAQ scores in asymptomatic individuals who experienced neck pain via eccentric exercise in the study described in this chapter and IPAQ scores in people with CNP in the study described in *Chapter Two* (Alsultan et al., 2019).

Furthermore, a visual analogue scale (VAS) was used to evaluate the degree of perceived muscle soreness experienced during neck movements, before (T0), immediately after (T1), 24 hours after (T2) and 48 hours after (T3) the eccentric exercise protocol with the endpoints ‘‘no soreness’’ to ‘‘extreme soreness.’’ Using a VAS has been found to be valid and reliable for assessing DOMS in other studies (Misailidou et al., 2010; Lau et al., 2013).

4.3.4 Cervical kinematics

A 3D motion capture system (Milan: BTS Bioengineering) was used to record cervical kinematics. It recorded the 3D motion of retroreflective markers attached to the participants' skin, based on the protocol described in *Chapter Two* (Alsultan et al., 2019).

Raw marker data were filtered with a Butterworth low-pass filter (cut-off 4Hz).

Clusters on trunk and head were defined as rigid bodies using the Single Value Decomposition (SVD) technique and their relative movement was calculated according to the HA model (Cappozzo et al., 1995; Söderkvist and Wedin, 1993). In particular, the movement of the head was computed with respect to the trunk at each timeframe as a composition of a rotation and translation around a fixed axis (HA) (Söderkvist and Wedin, 1993; Woltring et al., 1985; Grip et al., 2008). In accordance with previous studies, the HA was computed every 10 degrees of head motion along the plane (sagittal plane for flexion, and transversal plane for rotation) (Barbero et al., 2017; Cescon et al., 2014). The HA dispersion and orientation were described using the MD and the MA (Temporiti et al., 2019; Alsultan et al., 2019). MD represents the minimum mean distance between helical axes intersections with the plane (sagittal or transversal) and their barycenter, whereas MA is the mean value of the angles between each HA and Mean Axis (Temporiti et al., 2019) (see *Figure 4.1*). Data analysis was also performed on eight repetition movement cycles, as described in *Chapter Two* (Alsultan et al., 2019).

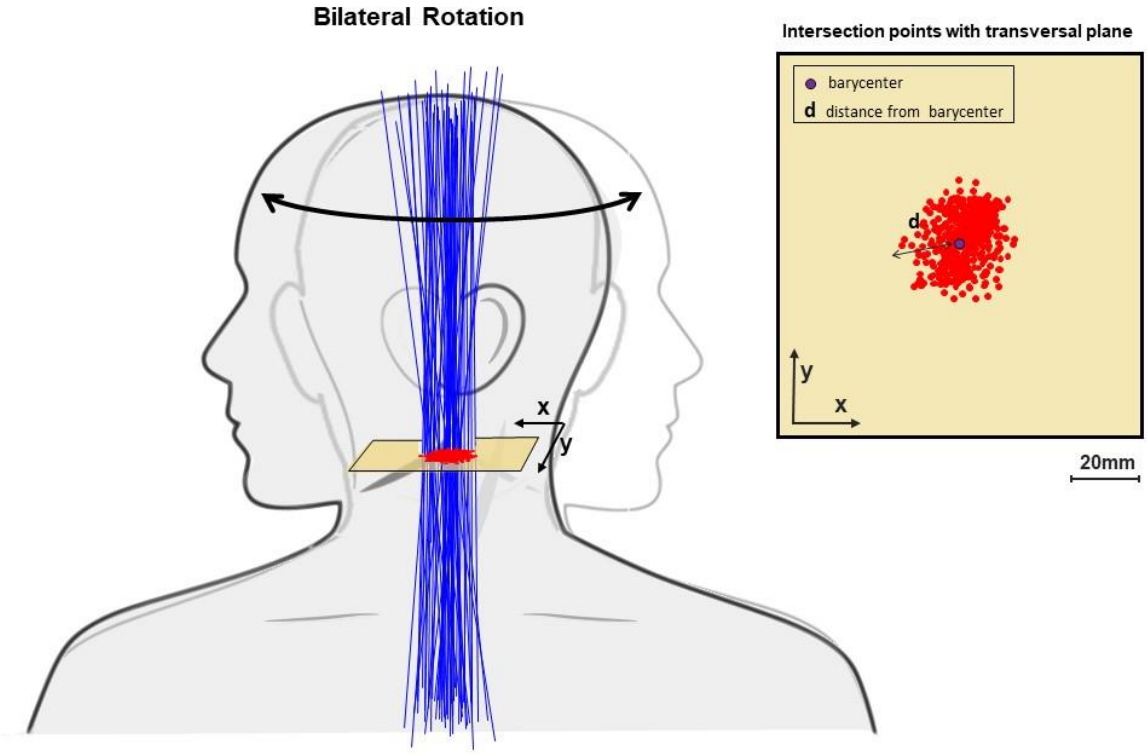


***Figure 4.1*: Quantifying the mean distance (MD) and mean angle (MA) of the Helical Axis (HA) parameters. MD is the intersection points shown in red, whereas MA is the angles of axis lines shown in blue.**

5.3.5 Procedure

Pressure pain threshold (PPT), active neck movement tasks, and maximum voluntary contractions (MVC) were performed in each of the three sessions. The eccentric exercise protocol (ref), detailed below, was only performed in session one.

Pressure pain threshold (PPT)

PPT was assessed using a pressure algometer (Sollentuna, Sweden: Somedic Algometer) with a $1cm^2$ rubber tip plunger, at an application rate of 40 kPa/s at predetermined locations over the following sites: bilaterally in the suboccipital muscle region, 2cm lateral to the spinous process

of the axis (prone); bilaterally over the neck extensors at the level of C5, 1cm lateral to the spinous process (prone); and bilaterally on the upper border of the trapezius muscle region, halfway between the midline and lateral border of the acromion (sitting). These muscle sites are known to be sensitive in people with neck pain while performing active cervical movements (Tsang et al., 2018; Ylinen et al., 2007). Each site was tested twice in a random order. The average of the two repetitions was considered for analysis (Lau et al., 2013). PPT was used to confirm the presence of eccentric exercise-induced DOMS.

Maximum voluntary contractions

The Multi-Cervical Unit (MCU; Hanover, MD: BTE Technologies) was used to measure the MVC of the neck extensors. The MCU is a reliable and validated device; ICCs for maximal isometric extension strength ranges from 0.95-0.99 for asymptomatic individuals (Chiu and Sing, 2002). Participants were briefed on the procedure, seated in the MCU, and a belt was applied over their waist and shoulders (see *Figure 4.2*). Participants performed three MVCs with standardised verbal encouragement provided to push as hard as they could. For each participant, MVC was determined as the highest force produced during three isometric contractions with the neck in a neutral position, each lasting five seconds (Lindstrom et al., 2011). The MVCs were used as a measure before and after the eccentric exercise to confirm the effectiveness of the eccentric exercise (Sewright et al., 2008).

Active neck movement tasks

Whilst seated on a chair in an upright posture, the participant performed repeated flexion-extension, bilateral lateral flexion and bilateral rotation at three different speeds whilst keeping their eyes open as described in *Chapter Two* (Alsultan et al., 2019). In addition to the protocol in

Chapter Two of performing each movement at 45° RoM, each movement was also repeated at full RoM to quantify RoM at T0, T1, T2, and T3 (Alsultan et al., 2019).

Eccentric exercise (Session 1 only)

Following familiarisation, the participants performed eccentric contractions of their neck extensors between 45° of extension and 0° (neutral), consisting of three sets of 15 repetitions against an average load of 20% MVC. Neck extension was performed passively to a limit of 45°, and then participants were asked to push their head against the head brace to control the load back to a neutral position (0°) (see *Figure 4.2*). There was no time restriction for completing the contractions, and a rest time of 60 seconds was given after every set.

A pilot was established, since no previous study had used eccentric exercise to induce DOMS in the neck area. Pilot testing results determined the appropriate load to induce DOMS. To determine the appropriate eccentric exercise protocol to induce DOMS whilst avoiding unnecessary levels of soreness, 45 repetitions at 20% was selected as appropriate for study purposes, as it was sufficient to induce soreness in healthy individuals. Note that the amount of soreness produced was comparable to other studies using eccentric exercise of the lower limbs to induce DOMS: for example, (Vila-Chã et al., 2012) found that 4/10 participants reported soreness 24 hours post-exercise.

With regards to eccentric exercise of neck extensors, neck pain was associated with holding the neck in flexion posture for a prolonged time and making repetitive movements (Nilsson and Söderlund, 2005), Patients with neck pain held significantly more neck flexion postures than healthy individuals, and the mean neck flexion posture in this group was found to be around 45 degrees. This neck flexion posture leads to an increase in gravitational load and altered neck

extensor muscle activity. Also, neck flexion at 45 degrees places stress on suboccipital muscles, the neck extensors region, and the upper border of the trapezius region (Russell, 2006).

Figure 4.2: **Illustration of the Multi-Cervical Unit (MCU) used to perform MVC and eccentric exercise (BTE Technologies, 2020).**

4.3.6 Statistical analysis

Mean and SD were used to describe participant demographics and MD and MA measurements, MVC measures, PPT and questionnaire responses.

Three-way repeated measures ANOVA were applied to evaluate the MD, MA and RoM for movements performed at full and 45º of motion, with time (T0, T1, T2, T3), direction of neck movement (flexion-extension, bilateral lateral flexion and bilateral rotation), and movement speed (slow, natural and fast) as factors.

Two-way repeated measures ANOVA was performed to examine PPT with time (T0, T2, T3), and location (suboccipital muscles, neck extensors, and trapezius) as factors. In addition, one-way repeated measures ANOVA were performed to test MVC and VAS, with time as the factor (T0, T1, T2, T3). The ANOVA tests were conducted, even though the assumptions were not met as in *Chapter Two*. The ANOVA tests can tolerate violations of assumptions when the sample size is above 30 (Pallant and Manual, 2007; Ghasemi and Zahediasl, 2012).

In all cases, significant differences revealed by ANOVAs were followed by Bonferroni post-hoc analyses (Field, 2013). Outcomes are reported as mean and SD in the tables. SPSS Version 26.0 (Armonk, NY: IBM Corp.) was used for statistical analyses. Statistical significance was set at $P < 0.05$.

4.3.7 Missing data

The procedure for dealing with missing data was planned as described in *Chapter Two* (Alsultan et al., 2019).

4.4 Results

All 32 participants completed the study. Participant demographics and descriptive data are presented in *Table 4.1*. Kinematic data were missing for 15 out of 8433 measures due to artefacts. Statistical analysis was performed since less than 10% of data were missing.

Table 4.1: **Participant demographics and descriptive data.**

Characteristic	Mean (SD) [95% CI]
Age (years)	25.53 (6.33)
Height (cm)	166.60 (29.04)
Weight (Kg)	71.22 (14.41)
IPAQ	6317.95 (6272.15)
MVC (lb) T1	33.03 (12.35)
MVC T2	28.20 (10.26)
MVC T3	28.24 (10.53)
MVC T4	30.89 (12.12)
PPT Suboccipital (kPa) T0	249.55 (64.23) [226.39, 272.70]
PPT Suboccipital T2	211.47 (71.11) [185.83, 237.10]
PPT Suboccipital T3	216.38 (63.81) [193.39, 239.40]
PPT Erector spinae T0	262.47 (71.08) [236.86, 288.12]
PPT Erector spinae T2	219.33 (72.37) [193.25, 245.44]
PPT Erector spinae T3	234.27 (70.94) [208.72, 259.88]
PPT Trapezius T0	375.82 (103.32) [338.60, 413.10]
PPT Trapezius T2	354.63 (92.95) [321.14, 388.16]
PPT Trapezius T3	324.77 (84.72) [294.25, 355.34]
VAS (0-10) T0	0.00
VAS T1	4.32 (2.67)
VAS T2	2.25 (2.34)
VAS T3	1.54 (1.72)

Standard deviations (SD) are reported in parentheses. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after the eccentric exercise, (T2) 24 hours after and (T3) 48 hours after eccentric exercise.

The participants reported mean (SD) VAS scores of 4.32 (2.67), 2.25 (2.34), and 1.54 (1.72) at T1, T2 and T3, respectively, which were all significantly ($p < 0.001$) higher compared to VAS at T0 that was 0. The VAS score at T2 and T3 were both significantly ($p < 0.005$ and $p<0.001$) lower compared to the VAS score at T1.

The PPTs decreased significantly with time confirming the presence of eccentric exercise-induced DOMS ($F = 20.442$, $p<0.0001$) with significantly lower values for all locations at T2 ($p < 0.0001$) and T3 ($p < 0.001$) compared to T0. The MVC also depended on time ($F = 4.616$, $p<0.01$) with a significant reduction found at T2 compared to T0 ($p < 0.01$) (see *Table 4.2*), although MVC had returned to baseline at T3.

Table 4.2: **Results of the ANOVA to evaluate differences.**

Parameters	Significance	Baseline -T0	Immediate Post - T1	24 h - T2	48 h – T3	Post hoc
PPT (kPa)	0	295.96 (98.65)	261.82 (102.68)	258.5(87.11)	NA	T0 > T1, T0 > T2
MVC (lb)	0.005	33.03 (12.35)	28.2 (10.26)	28.24 (10.53)	30.89 (12.12)	T0 > T2
VAS (0-10)	0	0	4.32 (2.67)	2.25 (2.34)	1.54 (1.72)	T1 >T0, T2 >T0, T3 >T0, T1 > T2, T1 >T3

Pressure pain threshold (PPT), maximum voluntary contractions (MVC), and visual analogue scale (VAS) across time. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after the eccentric exercise, (T2) 24 hours after and (T3) 48 hours after eccentric exercise.

4.4.1 Movements performed to full RoM

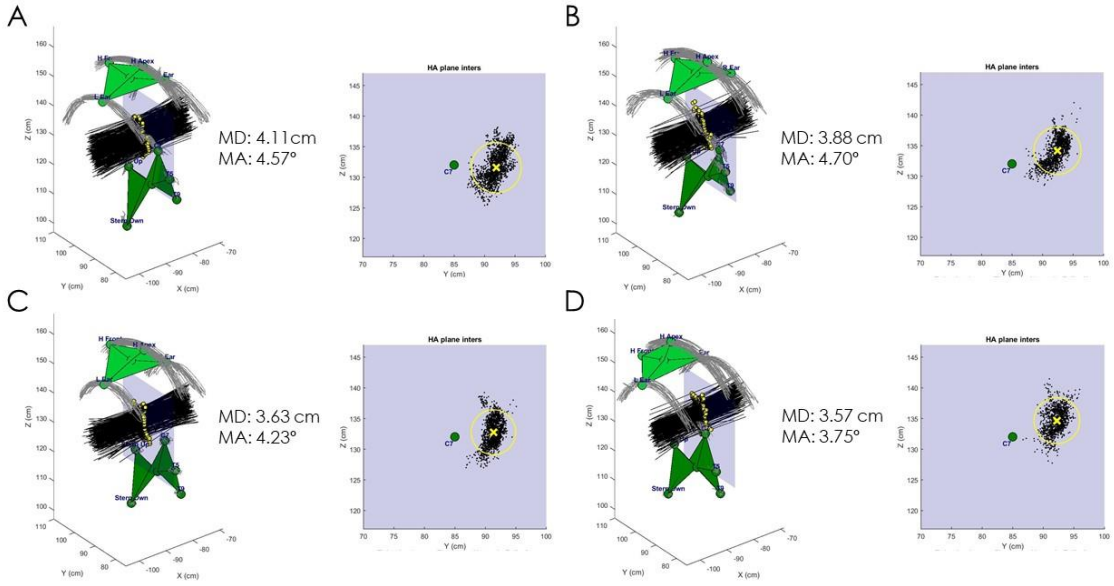
The mean and SD for all measures in each movement direction and at all time points are presented in *Table 4.3,* and significant differences are highlighted in *Table 4.4*. A representative example illustrating the MA and MD measured at each time point for the task of rotation is presented in *Figure 4.3*.

Table 4.3: **Mean and standard deviation (SD) of the mean distance (MD) and mean angle (MA) at full range of motion, recorded for all active neck movement tasks. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after eccentric exercise, (T2) 24 hours after and (T3) 48 hours after eccentric exercise.**

Parameter			MD (cm)			MA (°)		
Time	T0	T1	T2	T3	T0	T1	T2	T3
Movement	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Flexion-extension natural	4.05 (0.76) [3.78, 4.38]	3.81 (0.8) [3.56, 4.18]	3.66 (0.8) [3.41, 4.02]	3.90 (0.76) [3.62, 4.21]	4.34 (0.78) [4.01, 4.53]	4.7 (0.69) [4.42, 4.95]	4.4 (0.57) [4.24, 4.66]	4.59 (0.71) [4.32, 4.85]
Flexion-extension slow	3.72 (0.97) [3.35, 4.13]	3.80 (0.84) [3.56, 4.19]	3.62 (0.95) [3.28, 4.03]	3.67 (0.73) [3.43, 3.98]	4.26 (0.67) [3.98, 4.46]	4.74 (0.75) [4.43, 4.98]	4.45 (0.53) [4.28, 4.68]	4.62 (0.85) [4.31, 4.95]
Flexion-extension fast	3.86 (0.9) [3.50, 4.20]	3.63 (0.78) [3.34, 3.93]	3.63 (0.97) [3.25, 4.01]	3.81 (0.96) [3.42, 4.16]	3.88 (0.65) [3.61, 4.08]	4.3 (0.7) [4.02, 4.56]	4.24 (0.69) [3.95, 4.45]	4.13 (0.71) [3.87, 4.38]
Lateral flexion natural	2.6 (0.45) [2.43, 2.77]	2.74 (0.76) [2.44, 3.04]	2.67 (0.73) [2.37, 2.94]	2.58 (0.72) [2.30, 2.86]	10.27 (2.87) [9.19, 11.42]	9.95 (3.54) [8.49, 11.27]	9.88 (4.32) [8.13, 11.43]	9.06 (2.01) [8.27, 9.85]
Lateral flexion slow	2.78 (0.72) [2.48, 3.04]	2.77 (0.85) [2.47, 3.12]	2.63 (0.65) [2.39, 2.89]	2.81 (0.9) [2.51, 3.20]	10.39 (4.55) [8.54, 12.11]	10.19 (3.66) [8.60, 11.42]	9.51 (2.19) [8.61, 10.32]	10.05 (2.77) [9.04, 11.16]
Lateral flexion fast	2.76 (0.8) [2.41, 3.03]	2.72 (0.92) [2.39, 3.11]	2.52 (0.64) [2.26, 2.77]	2.65 (0.96) [2.29, 3.04]	9.64 (3.55) [8.14, 10.85]	9.52 (3.73) [8.17, 11.12]	9.14 (2.5) [8.18, 9.90]	8.83 (2.3) [8.01, 9.78]
Rotation natural	3.06 (0.72) [2.84, 3.40]	2.93 (0.63) [2.71, 3.18]	2.94 (0.72) [2.72, 3.26]	3.02 (0.68) [2.79, 3.31]	4.78 (0.75) [4.47, 5.07]	4.99 (0.94) [4.66, 5.39]	4.71 (0.65) [4.45, 4.96]	4.82 (0.76) [4.51, 5.11]
Rotation slow	2.96 (0.78) [2.70, 3.30]	2.95 (0.67) [2.70, 3.21]	3.07 (0.82) [2.79, 3.42]	3.07 (0.74) [2.80, 3.37]	4.71 (0.75) [4.40, 5.00]	5.23 (0.91) [4.90, 5.62]	5.07 (0.84) [4.76, 5.42]	4.89 (0.88) [4.49, 5.17]
Rotation fast	3.05 (0.76) [2.80, 3.38]	2.81 (0.61) [2.61, 3.07]	2.95 (0.73) [2.70, 3.24]	2.98 (0.76) [2.72, 3.30]	4.72 (1.07) [4.33, 5.14]	4.87 (1.11) [4.47, 5.34]	4.7 (0.75) [4.46, 5.03]	4.63 (0.72) [4.33, 4.89]

Table 4.4: **Mean and standard deviation of the mean distance (MD) and mean angle (MA), and range of motion (RoM) at full and 45° RoM recorded, for all active neck movement tasks. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after eccentric exercise, (T2) 24 hours after and (T3) 48 hours after eccentric exercise.**

Parameters	RoM	T0	T1	T2	T3	Post hoc
MD (cm)	Full	3.21 (0.91)	3.13 (0.88)	3.08 (0.89)	3.17 (0.93)	T0 > T2, T2 < T3
MA (°)	Full	6.31 (3.47)	6.48 (3.25)	6.22 (2.98)	6.16 (2.69)	T1 > T2, T1 > T3
RoM (°)	Full	115.09 (28.13)	111.37 (27.04)	111.21 (27.17)	113.43 (28.4)	T0 > T1, T0 > T2, T0 > T3 , T1 < T3 , T2 < T3
MD (cm)	45°	2.40 (0.68)	2.48 (0.70)	2.42 (0.69)	2.41 (0.61)	T0 < T1, T1 > T3
MA (°)	45°	5.76 (2.71)	5.78 (2.53)	5.69 (2.37)	5.43 (2.23)	T0 > T3, T1 > T3, T2 > T3
RoM (°)	45°	81.54 (15.04)	82.55 (14.10)	81.60 (15.03)	82.01 (14.94)	T1 > T2



***F*igure 4.3. Representative data obtained from a participant during flexion-extension movements performed at natural speed and full range of motion at baseline (T0) (A), immediately after eccentric exercise (T1) (B), 24 hours after (T2) (C) and 48 hours after eccentric exercise (T3) (D). Note the smaller mean distance (MD) for the participant particularly at T2 as compared to T0 and T3. Similarly, the mean angle (MA) is lower when measured at T2 and T3.**

A significant difference of the MD was observed over time regardless of the movement direction or speed ($F = 4.662$, $p<0.01$). Pairwise comparisons showed significantly reduced MD (i.e. reduced movement variability) when measured at T2 compared to T0 ($p < 0.001$) and T3 ($p < 0.05$). A significant difference of the MA was also observed over time regardless of the movement direction or speed ($F = 3.573$, $p<0.05$). The MA was significantly lower at T2 and T3 compared to the MA recorded at T1 (both $p<0.05$). A significant difference in RoM was also identified over time ($F = 23.197$, $p<0.0001$); pairwise comparisons showed that the RoM was significantly reduced for all movement directions at T1, T2 and T3 compared to T0 (all $p<0.01$). Additionally, RoM was significantly lower at T1 ($p < 0.01$), T2 ($p < 0.0001$), compared to RoM measured at T3, indicating some recovery of RoM by 48 hours.

4.4.2 Movements performed to 45° RoM

The mean and SD for all measures in each movement direction and at all points are presented in *Table 4.5* and the significant differences are highlighted in *Table 4.4*. A significant difference ($F = 3.606$, $p<0.05$) was observed over time for MD with pairwise comparisons demonstrating lower values of MD at T3 compared to T1 ($p < 0.05$). A significant difference ($F = 10.829$, $p<0.0001$) was also observed over time for MA with the pairwise comparisons revealing significantly lower values of MA at T3 compared to T0, T1 and T2 (all $p<0.0001$). Finally, RoM also differed over time ($F = 2.734$, $p<0.05$) regardless of the speed or direction of movement with the pairwise comparisons, revealing significantly less RoM at T2 compared to T1 ($p < 0.05$).

Table 4.5: **Mean and standard deviation (SD) of the mean distance (MD) and mean angle (MA) at 45° range of motion, recorded for all active neck movement tasks. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after eccentric exercise, (T2) 24 hours after and (T3) 48 hours after eccentric exercise.**

Parameter	MD (cm)				MA (°)			
Time	T0	T1	T2	T3	T0	T1	T2	T3
Movement	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Flexion-extension natural	2.99 (0.67) [2.72, 3.19]	2.85 (0.63) [2.60, 3.06]	2.85 (0.72) [2.56, 2.98]	2.75 (0.47) [2.55, 2.88]	4.38 (0.91) [4.11, 4.78]	4.53 (0.83) [4.26, 4.89]	4.24 (0.68) [3.99, 4.52]	4.21 (0.70) [3.99, 4.52]
Flexion-extension slow	2.8 (0.61) [2.56, 2.97]	2.92 (0.65) [2.64, 3.13]	2.85 (0.68) [2.57, 3.01]	2.73 (0.48) [2.54, 2.90]	4.28 (0.95) [3.96, 4.68]	4.55 (0.95) [4.27, 4.97]	4.45 (0.64) [4.23, 4.72]	4.32 (0.72) [4.10, 4.64]
Flexion-extension fast	3.18 (0.74) [2.88, 3.39]	3.05 (0.72) [2.75, 3.21]	3.01 (0.91) [2.67, 3.06]	3.06 (0.6) [2.82, 3.23]	3.93 (0.69) [3.69, 4.22]	4.04 (0.72) [3.80, 4.35]	4.1 (0.7) [3.86, 4.39]	3.89 (0.64) [3.65, 4.15]
Lateral flexion natural	2.25 (0.43) [2.09, 2.42]	2.46 (0.59) [2.23, 2.66]	2.27 (0.54) [2.07, 2.48]	2.22 (0.54) [2.01, 2.40]	9.25 (2.63) [8.21, 9.42]	9.11 (1.56) [8.49, 9.68]	8.59 (1.93) [7.80, 9.28]	8.07 (1.76) [7.30, 8.43]
Lateral flexion slow	2.19 (0.55) [2.05, 2.42]	2.38 (0.65) [2.17, 2.64]	2.28 (0.64) [2.06, 2.54]	2.28 (0.53) [2.12, 2.50]	8.68 (1.7) [8.07, 9.35]	8.68 (1.72) [8.16, 9.40]	8.55 (1.41) [8.02, 9.08]	8.23 (1.31) [7.75, 8.74]
Lateral flexion fast	2.2 (0.47) [2.02, 2.38]	2.4 (0.75) [2.13, 2.50]	2.3 (0.5) [2.12, 2.50]	2.28 (0.63) [2.03, 2.44]	9.15 (2.08) [8.20, 9.52]	8.72 (2.21) [7.72, 9.22]	8.66 (1.83) [7.85, 9.19]	8.03 (1.92) [7.24, 8.38]
Rotation natural	1.97 (0.41) [1.81, 2.12]	2.09 (0.46) [1.91, 2.26]	2.03 (0.43) [1.87, 2.20]	2.07 (0.42) [1.91, 2.23]	4.06 (0.83) [3.78, 4.40]	4.25 (1.02) [3.87, 4.64]	4.15 (0.98) [3.80, 4.54]	4.00 (0.95) [3.66, 4.38]
Rotation slow	1.96 (0.39) [1.81, 2.11]	2.06 (0.49) [1.86, 2.24]	2.08 (0.37) [1.93, 2.21]	2.14 (0.47) [1.96, 2.32]	4.02 (0.81) [3.75, 4.36]	4.19 (0.96) [3.87, 4.60]	4.35 (0.87) [4.08, 4.73]	4.28 (0.98) [3.96, 4.70]
Rotation fast	2.02 (0.4) [1.85, 2.15]	2.1 (0.48) [1.90, 2.27]	2.11 (0.46) [1.92, 2.27]	2.11 (0.51) [1.89, 2.27]	4.09 (0.79) [3.83, 4.42]	3.99 (1.17) [3.60, 4.48]	4.18 (0.85) [3.85, 4.51]	3.91 (0.85) [3.60, 4.25]

4.5 Discussion

This study is the first to investigate the effect of acute pain on the variability of active cervical movements, based on an experimental protocol involving eccentric exercise. The MVC of the neck extensors decreased 24 hours post exercise and PPT decreased at 24 and 48 hours after exercise confirming the effectiveness of the eccentric exercise protocol for inducing DOMS. The key finding of this study was that eccentric exercise of the neck extensor muscles and the resultant DOMS, caused reduced neck movement variability, which was observed across all neck movement tasks, regardless of the movement direction or speed. In addition to the influence on the quality of active neck movements, the neck RoM was also affected by DOMS of the neck extensors.

4.5.1 Eccentric exercise as a means to induce DOMS of the neck extensors

This is the first study to use an eccentric exercise protocol of the neck muscles with the aim of inducing DOMS as an experimental neck pain model. Participants reported soreness of their neck extensor muscles both 24 and 48 hours post exercise, likely due to the damage of the contractile elements and connective tissue (Hedayatpour and Falla, 2014). Following the injury of muscle fibres, phagocyte cell infiltration results in progressive necrosis of the contractile elements and inflammation, which will sensitise the intramyofibril group IV afferents (Smith, 1991; Hedayatpour and Falla, 2014). The PPTs measured over the neck region were lower both 24 and 48 hours post exercise confirming local sensitisation. Additionally, the maximal force of the neck extensors decreased 24 hours post exercise, likely reflecting reduced neural drive to the muscle because of an inhibitory effect mediated by nociception ref. These findings are consistent with the effects of eccentric exercise of different muscle groups including the elbow flexors (Lau et al., 2013) and knee extensors (Hedayatpour et al., 2008; Hedayatpour and Falla, 2014), confirming the appropriateness of our model to induce DOMS.

4.5.2 Variability of active neck movements

Earlier work observed reduced movement variability in people with CNP as compared to healthy individuals (Alsultan et al., 2019). Additionally, reduced RoM of the neck is a common finding in people with chronic or acute neck pain (Woodhouse and Vasseljen, 2008; Puglisi et al., 2004; Fernandez-Perez et al., 2012; Sterling et al., 2003). Our findings uniquely demonstrate that both the quality and quantity of neck movement can change rapidly in the presence of neck muscle soreness. Specifically, we observed reduced movement variability 24 hours and 48 hours post-eccentric exercise revealed through measures of the MD and MA, regardless of the movement direction or speed. Likewise, RoM was significantly reduced post-eccentric exercise when neck pain was present. Even though there may be multiple mechanisms contributing to impaired movement control in people with acute neck pain, the current findings suggest soreness can induce rapid changes in both the quality and quantity of neck movement.

Importantly, the MD and MA values recorded in this study had approximately similar means, regardless of the movement direction or speed, as compared to those found in a previous study (see *Chapter Two*) examining active neck movements in people with and without CNP (Alsultan et al., 2019). The mean difference of the MD varied up to 0.24 cm between the healthy participants and those with CNP in a previous study (see *Chapter 2*; Alsultan et al., 2019). In the current study, the mean difference of the MD between baseline and immediately after eccentric exercise ranged between 0.08 and 0.21 cm and when measured at 24 hours and 48 hours post exercise when soreness was present, the mean of difference of MD values relative to baseline ranged between 0.02 and 0.24 cm. Similarly, in the study examining active neck movements in people with and without CNP (Alsultan et al., 2019), the mean difference of the MA varied up to 1.01º between the healthy participants and those with CNP (see *Chapter 2*; Alsultan et al., 2019). In the current study, the mean difference of the MA between baseline and immediately after eccentric

exercise was up to 0.43º and when measured at 24 hours and 48 hours post exercise when soreness was present, the mean of difference of MA values relative to baseline was up to 1.18º. A similar reduction of the HA parameters in people with CNP and following eccentric exercise-induced neck muscle soreness is relevant when attempting to understand factors underlying impaired movement quality in people with pain. Although speculative, the reduced variability of neck movement may reflect a strategy to reduce or avoid pain during repeated neck movement (Arendt-Nielsen and Falla, 2009). Future studies should investigate neck muscle activation concurrently with measures of neck movement quality over a period of time.

4.5.3 Methodological considerations

The participant sample in this study was a convenience sample, and may not be representative of the general population. Therefore careful consideration is required regarding generalisation of the results (SMITH, 1998). In addition, a 3D motion capture system was used to collect data on the quality and quantity of movement, which might not be accessible for use in clinics. Nevertheless, both the quality and quantity of movement could be assessed using portable virtual reality-based devices and 3D motion–tracking systems, which have been validated to detect neck movements for people with chronic neck pain and asymptomatic individuals (Kiper et al., 2020).

4.6 Conclusion

Using a novel approach to induce acute neck pain, changes in neck movement variability were observed immediately after, 24 hours after and 48 hours after eccentric exercise, indicating that the presence of acute neck pain affects the quality of neck movement. These findings indicate the importance of examining the quality of neck movement in addition to the quantity of movement

in order to better characterise movement dysfunction in people with painful neck disorders, including during the acute stage. Furthermore, the neck pain model induced by eccentric exercise revealed an immediate change in neck movement variability in healthy volunteers. Further research is needed to validate this protocol for inducing acute neck pain.

CHAPTER 5

IS THE QUALITY OF SPINAL MOVEMENT ALTERED IN PEOPLE WITH CHRONIC NECK PAIN?: A SYSTEMATIC REVIEW

This chapter reports in full the contents of a manuscript that has been submitted for publication. It combines verbatim text from the original manuscript with changes employed for the purpose of this thesis.

5.1 Abstract

This is the first systematic review that aims to investigate how the quality of spinal motion differs between people with CNP and healthy individuals.

This systematic review followed a published and PROSPERO-registered protocol (CRD42019137411), and is reported in line with the PRISMA statement. Seven databases and reference lists of relevant articles were searched on 26 June 2020 to identify studies that met the eligibility criteria. Two reviewers independently assessed relevant articles and extracted data. Risk of bias for each study included was assessed independently by the two reviewers using the Newcastle-Ottawa Scale (NOS) and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to assess the overall quality of evidence across studies

Seventeen studies were identified that met the eligibility criteria: 14 case-control studies and three cross-sectional studies, providing information about 826 people with CNP and 586 asymptomatic individuals. Quality of motion outcome measures, including proprioception, smoothness of movement and movement variability, were identified. All studies that evaluated proprioception and smoothness of movement outcome measures and in which neck movements were performed separately found statistically significant differences between people with CNP and asymptomatic people. The results of studies that examined movement variability outcome measures were not consistent. For risk of bias, fourteen studies were at low risk, two at medium risk, and one at high risk of bias. Although the overall quality of evidence was very low for outcomes of interest across the included studies based on GRADE criteria, the quality of spinal movement did differ between people with CNP and healthy individuals. Nevertheless, further, high-quality research is still required to corroborate this finding.

5.2 Introduction

As emphasised in *Chapter One*, most research that has investigated neck movements in people with CNP has focused on quantifying changes in RoM. Nevertheless, changes in the pattern of movement may exist, even when RoM is normal (Waeyaert et al., 2016; Guo et al., 2019). These more subtle variations can be detected by examining quality of movement, a feature that appears to be sensitive to changes in movement due to neck pain disorders, as was found in previous studies, including those reported in *Chapter Two* and *Chapter Three* (Guo et al., 2019; Alsultan et al., 2020a; Alsultan et al., 2019).

A variety of outcome measures have been used to examine the quality of movement in people with CNP (Vogt et al., 2007; Dugailly et al., 2015; Waeyaert et al., 2016) and studies have examined the quality of movement in different spinal regions (Descarreaux et al., 2010; Alsultan et al., 2020a; Portelli and Reid, 2018). For example, Sjolander and colleagues showed that people with CNP display a significantly larger jerk index and RoM variability during active cervical movement compared to asymptomatic individuals (Sjolander et al., 2008b).

In *Chapter Two* and *Chapter Three*, we examined the quality of movement in terms of movement variability in people with CNP compared to asymptomatic individuals. Reduced movement variability was observed during active neck movements and also gait tasks (Alsultan et al., 2020a; Alsultan et al., 2019). However, other studies have shown contrasting results, with Waeyaert et al. (2016) observing no significant differences between groups when examining the jerk index during active neck movements.

To date, no previous research has systematically summarised and critically appraised the studies investigating whether people with CNP differ from asymptomatic individuals in terms of quality of spinal movement. In addition, the reasons for conflicting findings between studies

examining the quality of spinal movement between CNP and asymptomatic individuals remain unclear. Therefore, this chapter presents a systematic review with two objectives that address the aim of the thesis. The primary objective was to identify, based on current literature (including published articles that form part of this thesis), whether the quality of spinal movement differs between people with CNP and asymptomatic individuals, especially as regards movement variability. The secondary objective was to determine the characteristics of the quality of movement measurements used in the literature.

5.3 Methods

5.3.1 Protocol and registration

This systematic review was registered on PROSPERO (International Prospective Register of Systematic Reviews) with registration number CRD42019137411 and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2015).

5.3.2 Eligibility criteria

Eligibility criteria were defined according to the participants, interventions, comparisons, outcomes and study design (PICOS) framework (Smith et al., 2011; Shamseer et al., 2015), which was also used to structure the systematic review objectives.

Participants

Studies that included participants with CNP of either idiopathic or traumatic origin and pain symptoms of at least three months were included (Misailidou et al., 2010). Studies in which CNP was attributed to a specific disease, or in which participants presented with widespread pain, were

excluded. Asymptomatic people were required to be pain-free at the time of the test and have no history of neck pain or injury, and to be included in the context of a comparative control. Only studies involving participants aged 18 years or above were included, since this age was selected by most studies, according to the review by Misailidou et al. (2010).

Interventions

Studies were included if they examined the quality of movement involving any region of the spine, including the cranio-cervical, cervical, thoracic and lumbar regions. Studies investigating movement of the mandible, eye, tongue, or the upper and lower extremities were excluded.

Comparisons

Studies were included if they involved a comparison between people with CNP and an asymptomatic group.

Outcomes

Studies were included if they investigated outcome measures describing the quality of spinal movement, such as variability of trunk and neck rotation, and smoothness of neck movement that could be quantified by jerk index. Studies investigating quantitative outcome measures only, such as speed or number (countable units) of movements, including RoM, were not included (Kroes et al., 2002).

Study design

All forms of observational studies (cohort, case control, single case study) were included. Studies were excluded if their main aim was to assess reliability or diagnostic accuracy of tests or techniques to measure the quality of spinal movement.

5.3.3 Information sources

A specific search strategy was adopted based on each database format. The search process was limited to articles in English, based on a human sample, and for which full text was available. A systematic search was conducted on each of the following databases: PubMed, PEDro (Physiotherapy Evidence Database), MEDLINE, Cochrane Library, Embase, AMED (Allied and Complementary Medicine Database) and CINAHL (Index to Nursing and Allied Health). In addition, reference lists of the studies included were checked for additional sources. The search process and collation of search results was completed on 26 June 2020.

5.3.4 Data management

Citation results were uploaded, and duplicates were removed by using Covidence (Innovation, 2017). Eligibility screening processes for titles and abstracts were completed by two reviewers (FA, AA) using Covidence. Full texts of relevant studies were uploaded into EndNote X8 (Philadelphia, PA: Clarivate), and assessed independently for inclusion criteria by both reviewers. Studies were included if both reviewers agreed (Analytics, 2016) and in case of disagreement, a third reviewer (DF) mediated.

5.3.5 Search strategy

The search strategy included terms related to the outcomes; targeted population was not specified in the search to ensure all relevant research was captured. This database search was completed by FA, and the design was informed by the PICOS framework. Terms and keywords used were as follows: ‘neck pain’ or ‘whiplash’ or ‘whiplash associated disorders’ or ‘whiplash-associated disorder’ or ‘WAD’ or ‘neck disorders’ or ‘whiplash injury’ AND ‘movement’ or

'motion' or 'motor' or 'motor control.' For an example of the search strategy used with the MEDLINE database, see *Table 5.1*.

***Table 5.1*: Terms and keywords used in the search strategy for the MEDLINE database.**

1. neck pain.mp.
2. whiplash.mp.
3. whiplash associated disorders.mp.
4. whiplash-associated disorder.mp.
5. WAD.mp.
6. neck disorders.mp.
7. whiplash injur*.mp.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. movement.mp.
10. movement*.mp.
11. motion.mp.
12. motion*.mp.
13. motor.mp.
14. motor control.mp.
15. 9 or 10 or 11 or 12 or 13 or 14
16. 8 and 15

5.3.6 Study selection

After removing duplicate studies, FA and AA independently screened titles and abstracts for eligibility, and excluded studies that were irrelevant to the objectives of this systematic review. If eligibility criteria were met or eligibility was not clear from the title or abstract, FA and AA read the full text of the study to further assess eligibility. If there was no consensus between the two reviewers, the third reviewer (DF) mediated.

5.3.7 Data collection process

Two reviewers (FA and AA) independently extracted data using a data extraction form. This form was based on the objectives of this systematic review and eligible studies found during the process of data extraction, and was checked by both reviewers for accuracy. A third reviewer (DF)

mediated any disagreement at this stage. If clarification was needed or missing data might affect the eligibility of a study, the corresponding author of the original study was contacted. Also, a reminder was sent when no response was received after two weeks. If no response was received after a month, the study was excluded.

5.3.8 Data items

Data regarding the authors and year of publication, study design, sample size, participant characteristics, spinal region, task performed, outcomes of interest, and parameters were extracted by FA and then reviewed by AA.

5.3.9 Risk of bias

Risk of bias for each study included was assessed independently by the two reviewers (FA and AA) utilising the NOS (Wells et al., 2018). Although it has not been determined a universally preferable tool to assess risk of bias, NOS was considered to be the best tool for this study since it is easy to use, has item clarity, and has the potential to be an excellent instrument for rating observational studies (Sanderson et al., 2007; Hootman et al., 2011). There is no gold standard to test the validity of NOS tool against, but the its developers have stated that the validity and reliability have been established, with no further data published (Hartling et al., 2013; Losilla et al., 2018). Regarding the reliability of NOS, previous studies found that NOS demonstrated low reliability (k 5 0.29, 95% CI 5 0.10, 0.47) but also moderate to good reliability between reviewers (ICC = 0.52; 95% CI = 0.14–0.76) (Hartling et al., 2013; Hootman et al., 2011). Thus, areas of uncertainty regarding potential bias were resolved by discussion between the reviewers (FA and AA), and a third reviewer (DF) mediated if the two reviewers disagreed.

The NOS form includes eight items with three subscales, where the maximum score is 9, and was adopted for case-control and cross-sectional studies. Some questions in the NOS form were modified to suit this review, and justification of these adaptations was stated (see *Table 5.2)*. The quality of a study was categorised based on its scores as follows: High quality ≥6, medium quality 3-5 and low quality ≤2 (Sookoian and Pirola, 2018).

Table 5.2: **Assessment of risk of bias represents the original Newcastle-Ottawa Scale (NOS) form and adapted form.**

	Original NOS for case control and cross-sectional studies	Revised item	Type of change	Justification
Selection	1) Is the case definition adequate? a) yes, with independent validation * b) yes, e.g. record linkage or based on self-report c) no description	1) Is CNP definition adequate? a) yes (defining neck pain by time CNP), with clinical assessment *	Reworded	The item was revised to be more suitable for the targeted population of people with CNP and therefore to avoid bias. Also, the first option was modified to 'clinical assessment,' since CNP is typically diagnosed using clinical assessment.
	2) Representativeness of the cases a) consecutive or obviously representative series of cases * b) potential for selection biases or not stated	None	None	None
	3) Selection of Controls a) community controls * b) hospital controls c) no description	None	None	None
	4) Definition of Controls a) no history of disease (endpoint) *	None	None	None

	b) no description of source			
Comparability	1) Comparability of cases and controls on the basis of the design or analysis a) study controls for _____ (Select the most important factor.) * b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)	Gender and age	Added	The item was revised to be more suitable for the target population with CNP and therefore to avoid bias. Gender and age factors typically matched to avoid bias in several research studies for CNP.
Exposure	1) Ascertainment of exposure a) secure record (e.g. surgical records) * b) structured interview where blind to case/control status * c) interview not blinded to case/control status d) written self-report or medical record only e) no description	a) objective outcomes that are valid and reliable (e.g. 3D motion) * b) data collected by blinded assessors * c) assessors not blinded to case/control status	Reworded and added	Items revised to be more suitable for this systematic review. The main variable (quality of movement) is usually measured using objective outcomes. In order to avoid bias, studies obtain a score for objective outcomes that are valid and reliable. Also, data for these measures are typically collected by researchers or assessors.
	2) Same method of ascertainment for cases and controls a) yes * b) no	None	None	None

	3) Non-Response rate a) same rate for both groups * b) non-respondents described c) rate different and no designation	None	None	This question is used to assess trials and tasks, since case-control and cross-sectional studies included in this systematic review do not have follow-up.

5.3.10 Data synthesis and analysis

A quantitative synthesis combining study results that shared the same outcome measures was planned in order to perform a meta-analysis. This could not be carried out due to dissimilar kinematic variables, methods of measurement, and tasks performed across studies. Subgroup analysis could not be performed for the same reasons. For example, neck movements in various studies were investigated as one continuous movement or two separate movements (bilateral rotation vs rotation right and left) (Alsultan et al., 2019; Baydal-Bertomeu et al., 2011; Vogt et al., 2007), with participants in different positions (sitting vs standing), and at different speeds (natural or preferred vs fast speed) (Sjolander et al., 2008b; Woodhouse and Vasseljen, 2008). Furthermore, some studies reported overall group findings for all conditions instead of reporting each condition (Woodhouse and Vasseljen, 2008; Roren et al., 2009). Regarding groups, some studies grouped idiopathic CNP and chronic WAD participants into one group, while others categorised them into two separate groups (Kristjansson et al., 2003; Alsultan et al., 2020a). Thus, a qualitative synthesis of studies included was performed to analyse the data and achieve the objective of this review: to identify whether the quality of spinal movement differs between people with CNP and asymptomatic individuals.

In addition, the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to grading evidence in systematic reviews and guidelines was used to assess the overall quality of evidence for each outcome across studies (Schünemann, 2013; Guyatt et al., 2011a). According to the GRADE guidelines, observational studies are rated low for the quality of evidence (Balshem et al., 2011). The quality of evidence for individual outcomes of interest can be rated up or down, but it is common to rate observational studies down according to factors that

include risk of bias, inconsistency, indirectness, imprecision and publication bias (Guyat t G and Alk, 2011; Goldet and Howick, 2013).

The overall score of the NOS form was incorporated under the "risk of bias" factor (Schünemann et al., 2019). Risk of bias was downgraded to Very Serious limitations (−2) if an outcome measure scored as low quality in most studies, and to Serious (−1) limitations if an outcome measure scored as medium quality in most studies (Guyatt et al., 2011d; Stevens et al., 2014). Risk of bias was not upgraded or downgraded (No serious limitations) if an outcome measure scored as high quality in most studies (Balshem et al., 2011).

Inconsistency was downgraded to Very Serious (−2) or Serious inconsistency (−1) if variability, which was represented by p-values, existed per outcome measure across studies (Guyatt et al., 2011e). Regarding indirectness, this factor was downgraded to Serious (−1) indirectness if differences in patient groups (CNP or chronic WAD) were present per outcome measure across studies (Guyatt et al., 2011b). Imprecision was downgraded to Serious (−1) imprecision if sample size and CI were not calculated or reported per outcome measure across studies (Guyatt et al., 2011c). Publication bias was downgraded to Undetected (−1), as suggested by Guyatt et al. (2011f), since it is difficult to be confident that publication bias is not present where there are a number of potential reasons for bias, including the possibility that authors would not submit work involving uninteresting results to well-known journals.

5.4 Results

5.4.1 Study selection

A total of 17 studies (number of all participants = 1412), including 14 case-control and three cross-sectional studies, met the eligibility criteria (Alsultan et al., 2019; Portelli and Reid, 2018;

Williams et al., 2017; Falla et al., 2017; Alahmari et al., 2017; Waeyaert et al., 2016; Dugailly et al., 2015; Vikne et al., 2013; Tsang et al., 2013; Baydal-Bertomeu et al., 2011; Hill et al., 2009; Sjolander et al., 2008b; Woodhouse and Vasseljen, 2008; Vogt et al., 2007; Grip et al., 2007; Kristjansson et al., 2003; Alsultan et al., 2020a). The process of study selection is shown in *Figure 5.2*, and the list of excluded studies, as well as reasons for exclusion, is provided in *Table 5.3*.

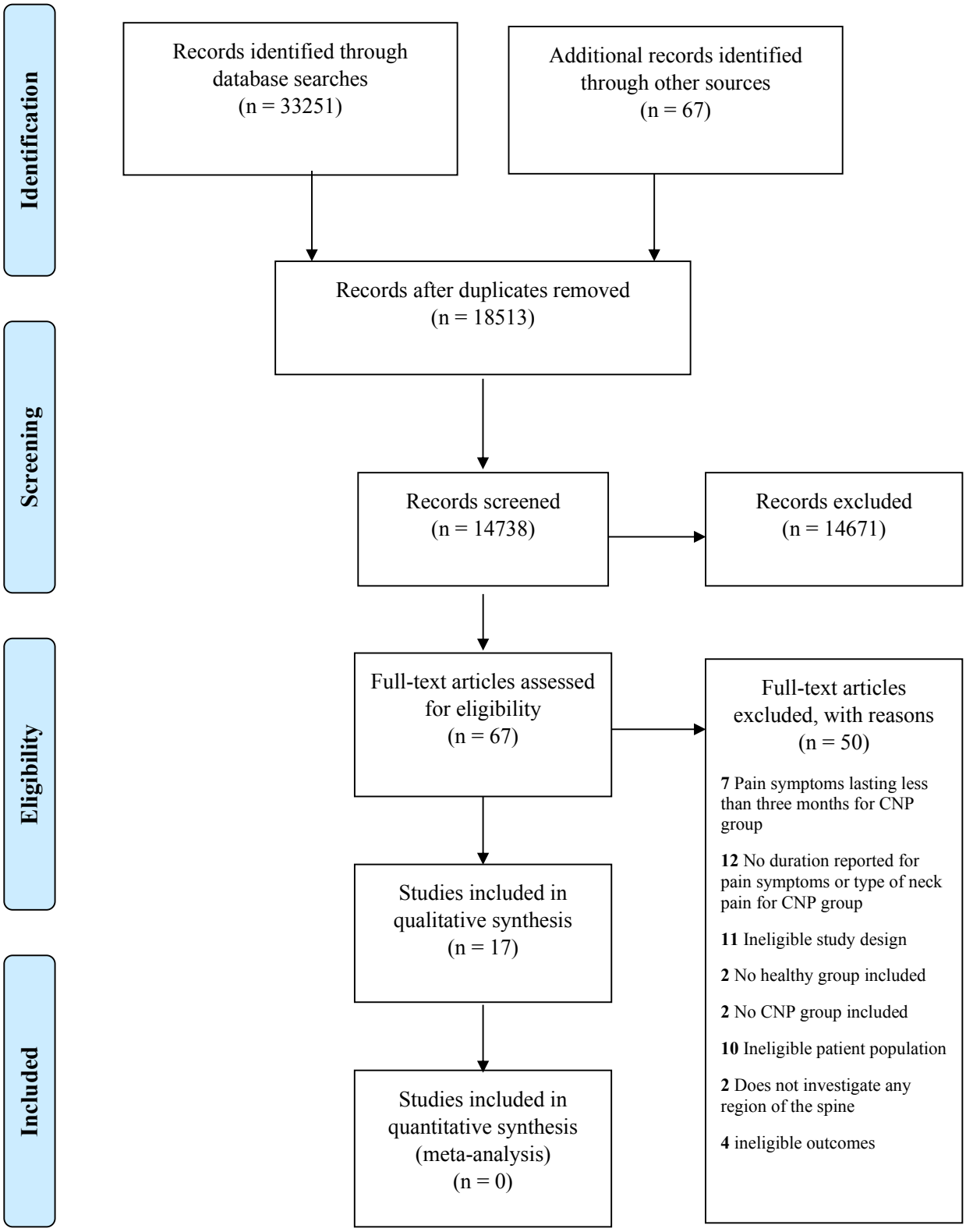


***Figure 5.2*: Flow diagram of systematic review process.**

***T*able 5.3: Excluded studies and reasons for exclusion.**

Number of studies	Excluded studies	Reasons
7	(De Loose et al., 2009; Stensdotter et al., 2019; Sarig Bahat et al., 2010; Rix and Bagust, 2001; Guo et al., 2012; Feipel et al., 2006; Meisingset et al., 2015a)	Pain symptoms lasting less than three months for CNP group
12	(Constand and MacDermid, 2013; Yang et al., 2012; Yang et al., 2014; Teng et al., 2007; Rutledge et al., 2013; Rudolfsson et al., 2017; Revel et al., 1991; Loudon et al., 1997; Lemmers et al., 2018; Heikkila and Wenngren, 1998; Harvie et al., 2016; Descarreaux et al., 2010)	No duration reported for pain symptoms or type of neck pain for CNP group
11	(Armstrong et al., 2005; Woodhouse et al., 2010a; Niederer et al., 2015; Kristjansson et al., 2004; Ellingson et al., 2013; Cheng et al., 2010; Roren et al., 2009; De Pauw et al., 2020; Lin et al., 2020; Gonçalves and Silva, 2019; Sarig Bahat et al., 2020)	Ineligible study design
2	(Kristjansson et al., 2016; Madeleine et al., 2004)	No healthy group included
2	(Sirikantharajah et al., 2015; Vibert et al., 2006)	No CNP group included
10	(Amevo et al., 1992; Woltring et al., 1994; Uthaikhup et al., 2012; Sjostrom et al., 2003; Sarig Bahat et al., 2015; Roijezon et al., 2010; Quartey et al., 2019; Prushansky et al., 2006; Elsig et al., 2014; De Pauw et al., 2018)	Ineligible patient population (CNP associated with other disease, in addition to pain in other areas of the body, or acute neck pain)
2	(Baarbe et al., 2016; Treleaven and Takasaki, 2015)	Does not investigate any region of the spine
4	(Grip et al., 2008; Woodhouse et al., 2010b; Treleaven et al., 2019; Ohberg et al., 2003)	ineligible outcomes

5.4.2 Study characteristics

Characteristics of the included studies are reported in *Table 5.4*. A number of quality of spinal movement outcome measures, including movement variability, proprioception (including joint position and movement sense (kinesthesia) and smoothness of movement were identified (see *Table 5.5*) (Röijezon et al., 2015).

Table 5.4: **Characteristics of studies included**

Authors and year of publication	Sample size	Study design	Age mean (SD)/ range years	Gender (women) %	Type of chronic neck pain (Grade of WAD)
Alsultan et al. (2019)	Total = 36 CNP = 18 C = 18	Case-control	• CNP 32.2 (13.4) • C 25.8 (7.3)	• CNP 55.56 • C 55.56 **	Idiopathic and WAD only (Grades I, II or III)
Vogt et al. (2007)	Total = 34 CINP = 16 C = 18	Case-control	• CINP 55.8 (2.8) • C 56.6 (3.5) *	• CINP 62.50 • C 55.56**	Idiopathic neck pain
Baydal-Bertomeu et al. (2011)	Total = 59 WAD = 30 C = 29	Case-control	• WAD 20–50 • C 20–50 *	• WAD 50 • C 50 **	WAD grades II and III
Alsultan et al. (2020a)	Total = 44 CNP = 24 C = 20	Case-control	• CNP 31.50 (12.50) • C 28.65 (11.03) *	• CNP 58.33 • C 50 **	Idiopathic and WAD only (Grades I, II or III)
Grip et al. (2007)	Total = 67 CINP = 21 WAD = 22 C = 24	Case-control	• CINP 49 (16) • WAD 49 (15) • C 50 (18)	• CINP 66.67 • WAD 77.27 • C 66.67	Non-specific neck pain group and WAD group grade 1–2
Falla et al. (2017)	Total = 28 CNP = 14 C = 14	Case-control	• CNP 28.0 (6.9) • C 24.0 (4.3) *	• CNP 78 • C 78 **	Chronic non-specific neck pain

Woodhouse and Vasseljen (2008)	Total = 173 CINP = 57 WAD = 56 C = 57	Case-control	• CINP 43.7(12.6) • WAD 38.19(10.8) • C 38.2(10.9)	• CINP 66.67 • WAD 60.71 • C 49.12 **	WAD grades I-II and chronic non-traumatic neck pain
Sjolander et al. (2008b)	Total = 32 CINP = 9 WAD = 7 C = 16	Case-control	• CINP 40 (9) • WAD 45 (11) • C 41 (9) *	• CINP 100 • WAD 71.43 • C 81.25**	Patients with insidious neck pain and patients with WAD graded as II or III
Dugailly et al. (2015)	Total = 71 CNP = 35 C = 36	Case-control	• CNP 42 (5) • C 42 (8)	• CNP 68.57 • C 61.11	Not stated
Portelli and Reid (2018)	Total = 44 CNP = 22 C = 22	Case-control	• CNP 21.0 (3.5) • C 20.1 (1.2) *	• CNP 59.09 • C 68.18**	Not stated
Hill et al. (2009)	Total = 150 WAD (dizziness) = 50 WAD (Not dizziness) = 50 C = 50	Case-control	• WAD D 35.5 (8.1) • WAD ND 35.0 (9.5) • C 29.5 (8.3)	• WAD 76 • WAD ND 76 • C 46	Whiplash complaining of dizziness (WAD D) and whiplash not complaining of dizziness (WAD ND); WAD classifiable as WAD 11
Kristjansson et al. (2003)	Total = 63 CINP = 20 WAD = 22 C = 21	Case-control	• CNP 30.0 (9.1) • WAD 33.4 (10.6) • C 26.9 (6.4) *	• CNP 22 • WAD 140.91 • C 52.38**	Insidious onset neck pain and neck pain following a whiplash injury Grade not stated.

Alahmari et al. (2017)	Total = 84 CNP = 42 C = 42	Cross-sectional	• CNP 47.4 (15.8) • C 47.8 (15.2) *	• Not stated	Not stated
Williams et al. (2017)	Total = 40 CNP = 20 C = 20	Pilot cross sectional	• CNP 48.3 (13.6) • C 45 (12.8) *	• CNP 55 • C 50 **	Not stated
Waeyaert et al. (2016)	Total = 187 CNP (Asymmetric a (16) and Symmetrical (21) = 37 C = 150	Cross-sectional	• Asymmetrical CNP 49.40 (12.20) • Symmetrical CNP 43.10 (13.53) • C 40.85 (13.19) *	• Asymmetrical CNP 68.75 • Symmetrical CNP 80.95 • C 39.33	Non-specific neck pain Subgroups based on pain location (Asymmetrical and Symmetrical)
Tsang et al. (2013)	Total = 68 CNP = 34 C = 34	Case-control	• CNP 38.44 (10.87) C 34.35 (9.08)	• CNP 73.52 • C 73.52	Not stated
Vikne et al. (2013)	Total = 30 WAD = 15 C = 15	Case-control	• WAD 40.1 (8.7) • C 38.7 (8.8) *	• WAD 60 • C 60 **	Chronic WAD classified as grade 2

Abbreviation: CNP: Chronic neck pain, including pain of idiopathic or traumatic origin; C: Control (asymptomatic); WAD: chronic Whiplash Associated Disorders; CINP: Chronic idiopathic neck pain.

* Age: Matched or no significant difference

** Gender: Matched or no significant difference

Table 5.5: **Characteristics of outcomes, parameters, tasks performed, and spinal region used in studies included.**

Outcome measure	Authors and year of publication	Spinal region	Task performed	Measurement variables
Movement Variability	Alsultan et al. (2019)	Neck	Flexion-extension, bilateral lateral flexion, and bilateral rotation	Movement variability was measured by calculating the SD of the mean distance and mean angle parameters of the helical axis.
	Vogt et al. (2007)	Neck	Flexion, extension, rotation left and right, and lateral flexion left and right	Movement variability was quantified by Coefficients of Variation to assess intra-subject variability maximum oscillation amplitudes.
	Baydal-Bertomeu et al. (2011)	Neck	Flexion–extension	Movement variability was calculated by Phase Area Ratio, which calculates intra-subject variability across cycles.
	Alsultan et al. (2020a)	Neck and Trunk	Walking on floor with head in neutral position (single-task) and whilst rotating head at natural speed (dual-task).	Movement variability of trunk and neck rotation across the gait cycles was quantified by calculating the SD of the mean.
	Falla et al. (2017)	Neck and Trunk	Walked on a treadmill with head in a neutral position or rotated	Variability of trunk and neck rotations was measured by median as a measure of variability.
	Woodhouse and Vasseljen (2008)	Neck	Axial rotation, side-bending and flexion/extension	The variability of maximal RoM was calculated via SD for each primary neck movement plane.
	Sjolander et al. (2008b)	Neck	Rotation left and right	RoM variability was measured by the average SD of the movements.
	Dugailly et al. (2015)	Neck	Flexion, extension and rotation left and right	Head repositioning accuracy was measured by the following parameters: • CE as the mean of raw repositioning errors • RMSE accuracy, estimated by computing RMSE considering horizontal, vertical and x–y components.
	Portelli and Reid (2018)	Neck	Flexion, extension and rotation left and right	HRA was quantified by mean and SD of the HRA as a measure of cervical spine proprioception.
	Hill et al. (2009)	Neck	Left and right rotations and extension	Cervical joint position error or head repositioning accuracy was calculated by the following parameters:

Proprioception				• AE describes the average AE • CE represents the average magnitude and direction of the errors • VE measures the variability • RMSE represents a measure the way of achieving the target.
	Kristjansson et al. (2003)	Neck	Cervicocephalic relocation tests, including relocation to the natural head posture (NHP), relocation to the 30° rotation position, preset trunk rotation, figure-of-eight relocation, and figure-of-eight movement	Relocation accuracy was measured via Absolute Value of the error calculated for angular motion.
	Sjolander et al. (2008b)	Neck	Left and right rotations	Repositioning acuity was measured by CE and VE. CE is the mean value of the algebraic errors, and VE is the SD of the algebraic errors.
	Alahmari et al. (2017)	Neck	Flexion, extension, and left and right rotation	JPE represents cervical joint position sense, and is a measure of proprioception.
	Woodhouse and Vasseljen (2008)	Neck	Axial rotation, side-bending and flexion/extension	JPE is a measure of proprioception.
	Williams et al. (2017)	Neck	Flexion/extension and rotation	Accuracy of head motion was calculated by Accuracy Error: the accumulated error between head motion and target motion in the accuracy module.
	Grip et al. (2007)	Neck	Flexion, extension, and rotation left and right	Proprioceptive ability was quantified via AE, VE, CE, and variation in axis position and direction. SD of the angles xi was calculated to estimate variance in direction. Total length of the trajectory was calculated to estimate variance in position.
Smoothness of movement	Sjolander et al. (2008b)	Neck	Rotation left (Out-Left and In-Left) and right (Out-Right and In-Right)	Jerk index was calculated by normalizing the jerk cost with respect to angular excursion and movement time.
	Waeyaert et al. (2016)	Neck	Axial rotation, lateral bending, flexion-extension	Smoothness of movement parameters: standard error of measurement on the deviation of the original data and a sixth polynomial function and the jerk index

	Vikne et al. (2013)	Neck	Forward flexion from Natural Position (NP), extension back to NP, extension from NP and flexion back to NP	Normalised Jerk Cost (NJC) is calculated to evaluate the smoothness of the movement
	Williams et al. (2017)	Neck	Flexion/extension and rotation	The number of velocity peaks is the number of times that the acceleration curve changed from acceleration to deceleration, and vice versa.
Spontaneity of movement	Baydal-Bertomeu et al. (2011)	Neck	Flexion–extension	Harmonicity, defined as the absolute value of the correlation coefficient between $\ddot{\theta}$ and θ.
Time to peak velocity percentage	Williams et al. (2017)	Neck	Flexion/extension and rotation	Percentage of time from motion start to peak velocity.
Movement coordination	Tsang et al. (2013)	Neck and Thoracic	Flexion and extension, left and right side bending, and neck rotation	Coefficient of cross-correlation analysis calculates correlation between the two regions during dynamic neck movements.

Abbreviation: Standard Deviation (SD), Range of Motion (RoM), Head Repositioning Accuracy (HRA), Absolute error (AE), Constant Error (CE), Variable Error (VE), Root Mean Square Error (RMSE), Joint Position Error (JPE)

5.4.3 Risk of bias

A modified NOS form for both case-control and cross-sectional studies was used to assess the risk of bias for all studies included. Most studies scored 6 and higher (low risk of bias) (Alsultan et al., 2019; Portelli and Reid, 2018; Williams et al., 2017; Falla et al., 2017; Alahmari et al., 2017; Vikne et al., 2013; Tsang et al., 2013; Baydal-Bertomeu et al., 2011; Woodhouse and Vasseljen, 2008; Sjolander et al., 2008b; Vogt et al., 2007; Grip et al., 2007; Kristjansson et al., 2003; Alsultan et al., 2020a), whereas two studies scored between 3 and 5 (medium risk of bias) (Waeyaert et al., 2016; Hill et al., 2009), and one study scored 2 or less (high risk of bias) (Dugailly et al., 2015). The results of study risk of bias assessment are shown in *Table 5.6*.

Table 5.6: **Results of the Newcastle Ottawa Scale (NOS) for case-control and cross-sectional studies.**
Total Score: Maximum = 9: Low risk of bias ≥6; Medium risk of bias 3-5; High risk of bias ≤2.

Authors and Year of publication	Quality indicators from Newcastle-Ottawa Scale								
	Selection of study groups'				Comparability of groups	Ascertain of exposure (outcome)			Score total
Alahmari et al. (2017)	0	1	1	1	1	1	1	1	7
Alsultan et al. (2019)	0	1	1	1	2	1	1	1	8
Alsultan et al. (2020a)	0	1	1	1	2	1	1	1	8
Baydal-Bertomeu et al. (2011)	1	1	0	1	2	1	1	1	8
Dugailly et al. (2015)	0	0	0	1	1	0	0	0	2
Falla et al. (2017)	1	1	0	1	2	1	1	1	8
Grip et al. (2007)	1	1	1	1	1	1	1	0	7
Hill et al. (2009)	0	0	1	1	0	1	1	0	4
Kristjansson et al. (2003)	0	1	1	1	2	1	1	0	7
Portelli and Reid (2018)	0	1	1	1	2	0	1	1	7
Sjolander et al. (2008b)	1	1	1	1	2	1	1	1	9
Tsang et al. (2013)	0	1	1	1	2	1	1	1	8
Vikne et al. (2013)	1	1	0	0	2	1	1	1	7
Vogt et al. (2007)	1	1	1	1	1	1	1	1	8
Waeyaert et al. (2016)	0	0	0	0	1	1	1	0	3
Williams et al. (2017)	0	1	1	1	2	1	0	1	7
Woodhouse and Vasseljen (2008)	1	1	1	1	1	1	1	0	7

5.4.4 Synthesis of results

The findings from cross-sectional and case-control studies across are detailed in *Table 5.7*. The quality of movement variables extracted for this review were used to identify whether the quality of spinal movement differs between people with CNP and asymptomatic individuals for each study included. The overall body of evidence based on GRADE criteria was very low for outcomes of interest (movement variability, proprioception, smoothness of movement, spontaneity of movement, time to peak velocity percentage and movement coordination) across the studies included (see *Table 5.8*). Studies were grouped based on outcome measures, including movement variability, proprioception and smoothness of movement. Studies were marked as "uncategorised" when no similar outcome measures were found in other studies included.

Table 5.7: **Summary of findings.**

Outcome measure	Authors and year of publication	Spinal region	Comparing of chronic neck pain group to asymptomatic group
Movement Variability	Alsultan et al. (2019)	Neck	CNP group displayed less movement variability compared to C group for flexion-extension (MD) and rotation (MD and MA)($p < 0.05$)
	Vogt et al. (2007)	Neck	CNP group showed higher movement variability compared to C group in all neck directions ($p < 0.01$).
	Baydal-Bertomeu et al. (2011)	Neck	No significant difference was found between groups for variability of movement ($p > 0.05$).
	Alsultan et al. (2020a)	Neck and Trunk	During single-task gait, no group differences found for variability of trunk ($p > 0.05$) or neck ($p > 0.05$) rotation. For dual-task gait, no difference observed between groups for variability of neck rotation ($p > 0.05$). However, CNP group displayed reduced variability of trunk rotation compared to C group ($p < 0.05$).
	Falla et al. (2017)	Neck and Trunk	No significant differences were observed between groups for neck and trunk rotation variability ($p > 0.05$)
	Woodhouse and Vasseljen (2008)	Neck	No significant differences were observed between groups for maximal RoM variability ($p > 0.05$).
	Sjolander et al. (2008b)	Neck	CNP group showed larger RoM variability ($p <0.01$) for right and left rotation to C group.
	Dugailly et al. (2015)	Neck	CNP group showed higher mean of head repositioning accuracy measured by CE and RMSE compared to C group for all neck directions ($p < 0.05$).
	Portelli and Reid (2018)	Neck	CNP group showed higher mean of repositioning errors compared to C group for flexion movement ($p < 0.005$). For other cervical movements, there was no difference between groups ($p > 0.05$).

Proprioception	Hill et al. (2009)	Neck	CNP (WAD D and WAD ND) group showed greater means of CE compared to C group for left rotation and extension movements ($p < 0.05$). CNP (WAD ND) group showed lower means of CE compared to C group for right rotation ($p < 0.05$). CNP (WAD D) group showed greater means of AE and RMSE compared to C group for right and left rotation movement ($p < 0.05$). No differences were seen with VE between groups for all movements or AE and RMSE for extension movements ($p > 0.05$).
	Kristjansson et al. (2003)	Neck	CNP group showed higher mean of repositioning errors compared to C group for rotation movement ($p < 0.005$).
	Sjolander et al. (2008b)	Neck	CNP group showed larger VE ($p <0.01$) for right and left rotation to C group. No significant differences were observed between groups for CE ($p > 0.05$).
	Alahmari et al. (2017)	Neck	CNP group showed larger JPE compared to C group for flexion, extension, and left and right rotation ($p < 0.001$).
	Woodhouse and Vasseljen (2008)	Neck	No significant differences were observed between groups regarding joint position error for axial rotation, side-bending and flexion/extension ($p > 0.05$).
	Williams et al. (2017)	Neck	No significant differences were seen between groups for accuracy of head motion for flexion/extension and rotation ($p > 0.05$).
	Grip et al. (2007)	Neck	WAD group showed larger constant repositioning error compared to C group during flexion ($p < 0.05$), but no significant difference was observed between the groups for other movements ($p > 0.05$). CNP and WAD groups showed more variation in axis direction compared to C group during axial rotation to the left ($p < 0.05$), but no significant difference was observed between groups for other movements ($p > 0.05$). No significant difference was found between groups for variation in axis position, Absolute Error and Variable Errors ($p > 0.05$).
Smoothness of movement	Sjolander et al. (2008b)	Neck	CNP group showed larger jerk index ($p < 0.05$) for right and left rotation (Out-Left ($p <0.01$) and In-Left ($p < 0.05$) to C group.
	Waeyaert et al. (2016)	Neck	CNP (symmetrical) group showed less harmonic motion patterns for the conjunct lateral bending than C group, expressed by the deviation from the polynomial fit for axial rotation ($p < 0.005$). No significant differences were observed between groups for jerk index for all directions ($p > 0.05$).

	Vikne et al. (2013)	Neck	CNP group showed higher mean of normalized jerk cost during flexion back to natural position and maximum speed ($p < 0.01$).
	Williams et al. (2017)	Neck	No significant differences were seen between groups for number of velocity peaks for flexion/extension and rotation ($p > 0.05$).
Spontaneity of movement	Baydal-Bertomeu et al. (2011)	Neck	No significant difference was found between groups for spontaneity of movement ($p > 0.05$)
Time to peak velocity percentage	Williams et al. (2017)	Neck	CNP group showed lower time to peak velocity percentage compared to C group ($p < 0.05$).
Movement coordination	Tsang et al. (2013)	Neck and Thoracic	CNP group showed lower cross-correlation analysis values compared to C group in all movement directions for the time history of velocity and acceleration of the cervical and upper thoracic spines, except the left and right rotation angular displacements with $p < 0.005$.

Table 5.8: **Quality of evidence assessment based on Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria (Balshem et al., 2011)**

Outcome measure	No of studies (No of patients with chronic neck pain)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of a body of evidence
Movement Variability	7 studies (n = 197) (Vogt et al., 2007; Baydal-Bertomeu et al., 2011; Alsultan et al., 2019; Falla et al., 2017; Woodhouse and Vasseljen, 2008; Sjolander et al., 2008b; Alsultan et al., 2020a)	✓	×	×	×	×	Very low
Proprioception	9 studies (n = 433) (Dugailly et al., 2015; Grip et al., 2007; Hill et al., 2009; Portelli and Reid, 2018; Kristjansson et al., 2003; Sjolander et al., 2008b; Alahmari et al., 2017; Woodhouse and Vasseljen, 2008; Williams et al., 2017)	✓	✓	×	×	×	Very low
Smoothness of movement	4 study (n = 88) (Sjolander et al., 2008b; Waeyaert et al., 2016; Vikne et al., 2013; Williams et al., 2017)	✓	✓	×	×	×	Very low
Time to peak velocity percentage	1 study (n = 20) Williams et al. (2017)	✓	✓	✓	×	×	Very low

Spontaneity of movement	1 study (n = 30) Baydal-Bertomeu et al. (2011)	✓	✓	✓	×	×	Very low
Movement coordination	1 study (n = 34) Tsang et al. (2013)	✓	✓	✓	×	×	Very low

- No serious (✓) means not rated down or up for the factor of quality of evidence
- Serious or undetected (×) means rated down one for the factor of quality of evidence

Movement Variability

Seven studies compared variability of spinal movement in groups of people with CNP and asymptomatic people (Alsultan et al., 2019; Vogt et al., 2007; Baydal-Bertomeu et al., 2011; Falla et al., 2017; Woodhouse and Vasseljen, 2008; Sjolander et al., 2008b; Alsultan et al., 2020a). There were inconsistencies regarding differences between groups across studies. Four studies (all at low risk of bias) found significant differences: less movement variability in the neck region in CNP group compared to asymptomatic group for flexion-extension and rotation (Alsultan et al. (2019), $p < 0.05$), less movement variability of trunk rotation in CNP group compared to asymptomatic group during dual-task gait (Alsultan et al. (2020a), $p < 0.05$), higher movement variability in the neck region in CNP group compared to asymptomatic group for all neck directions (Vogt et al. (2007), $p < 0.01$), and higher movement variability for left and right rotation movements (Sjolander et al. (2008b), $p < 0.01$).

Three studies (all at low risk of bias) reported no difference between groups for flexion/extension in the neck region (Baydal-Bertomeu et al. (2011), $p > 0.05$); for rotation, side-bending and flexion/extension (Woodhouse and Vasseljen (2008), $p < 0.05$); and for neck and trunk rotation variability during gait (Falla et al. (2017), $p < 0.05$). Inconsistent results among studies are present, as four studies found differences between groups, but three other studies reported no differences. There was very low quality of evidence for movement variability, and its inconsistency factors were rated “Serious.”

Proprioception

Nine studies assessed proprioception in the neck area (Dugailly et al., 2015; Hill et al., 2009; Portelli and Reid, 2018; Kristjansson et al., 2003; Sjolander et al., 2008b; Alahmari et al., 2017; Woodhouse and Vasseljen, 2008; Williams et al., 2017; Grip et al., 2007). Four studies (one high

risk of bias and three at low risk of bias) reported reduced proprioception in people with CNP compared to asymptomatic controls, for flexion, extension and rotation left and right (Dugailly et al. (2015), $p < 0.05$); for flexion movement (Portelli and Reid (2018), $p < 0.05$); for rotation movement (Kristjansson et al. (2003); and for flexion, extension, and left and right rotation (Alahmari et al. (2017), $p < 0.001$). However, two studies (both at low risk of bias) found no significant differences in proprioception between the groups: for axial rotation, side-bending and flexion/extension (Woodhouse and Vasseljen (2008), $p > 0.05$); and for flexion/extension and rotation (Williams et al. (2017), $p > 0.05$).

Three studies (2 low risk of bias, 1 medium risk of bias) used several parameters to calculate proprioception, and delivered conflicting findings. The CNP group were seen to exhibit reduced proprioception compared to asymptomatic group for flexion movements (Grip et al. (2007), $p < 0.05$); for right and left rotation and extension movements (Hill et al. (2009), $p < 0.05$); and for right and left rotation (Sjolander et al. (2008b), $p < 0.05$). At the same time, no significant differences were seen between groups in some studies ($p > 0.05$) (Grip et al., 2007; Sjolander et al., 2008b; Hill et al., 2009), and increased proprioception was observed in those with CNP during right rotation movements ($p < 0.05$) (Hill et al., 2009). Eight out of the nine studies looking at proprioception reported significant differences between groups. For proprioception, the overall quality of evidence was very low. This outcome of interest was rated "No Serious" in terms of inconsistency factors across the studies.

Smoothness of movement

Four studies investigated smoothness of movement (Sjolander et al., 2008b; Waeyaert et al., 2016; Vikne et al., 2013; Williams et al., 2017). Two studies (both at low risk of bias) observed reduced smoothness of movement in people with CNP compared to an asymptomatic group for

right and left rotation (Sjolander et al. (2008b), $p < 0.05$), and for flexion back to natural position and maximum speed (Vikne et al. (2013), $p < 0.001$). However, no significant differences between groups were found for flexion/extension and rotation in one study with a low risk of bias (Williams et al. (2017), $p > 0.05$).

Waeyaert et al. (2016) (medium risk of bias) used two parameters to measure smoothness of movement and reported different results. They found lower smoothness of movement in the CNP group compared to the asymptomatic group regarding one parameter ($p < 0.005$), while no difference was observed between groups regarding another parameter ($p > 0.05$) (Waeyaert et al., 2016). Three out of the four studies found significant differences between groups. For smoothness of movement, the overall quality of evidence was very low, and this outcome measure was rated "No Serious" in terms of inconsistency factors across the studies.

Uncategorised

Three studies (all low risk of bias) (Williams et al., 2017; Baydal-Bertomeu et al., 2011; Tsang et al., 2013) examined unique outcome measures, and are therefore placed in the "uncategorised" outcomes category. People with CNP displayed a lower quality of neck movement regarding velocity for flexion/extension and rotation compared to asymptomatic group ($p < 0.005$) (Williams et al., 2017), while no group difference was found when examining spontaneity of movement during flexion-extension (Baydal-Bertomeu et al., 2011).

Tsang et al. (2013) used several parameters to assess movement coordination between the cervical and thoracic regions. They observed lower movement coordination for all movement directions regarding three parameters, except for the left and right of one parameter ($p < 0.005$) (Tsang et al., 2013). The overall quality of evidence for measures of spontaneity of movement, time to peak velocity percentage, and movement coordination was very low for all three parameters.

5.5 Discussion

The main objective of this study was to synthesis the evidence base for differentiating between people with CNP compared to asymptomatic individuals regarding quality of spinal movement. Through a comprehensive search, 17 studies were located that fulfilled the criteria for inclusion in this review. Most of these found significant differences in the quality of spinal movement between people with CNP and asymptomatic individuals, regardless of the outcome measures and parameters. Most studies were at low risk of bias on the NOS scale, although the overall quality of evidence for proprioception, smoothness of movement and movement variability outcome measures was very low.

Movement Variability

Seven studies examined variability outcomes (Alsultan et al., 2019; Vogt et al., 2007; Baydal-Bertomeu et al., 2011; Falla et al., 2017; Woodhouse and Vasseljen, 2008; Sjolander et al., 2008b; Alsultan et al., 2020a). The results of these studies were not in agreement. The inconsistent findings might be due to the use of different types of measurements, parameters and protocols used to investigate movement variability across these studies (see *Table 3*).

With regards to measurements and parameters, movement variability was measured differently in the included studies, using the standard deviation (SD) of the mean of helical axis parameters for whole neck movement cycles (Alsultan et al., 2019), coefficients of variation for assessing variability of neck maximum oscillation amplitudes (Vogt et al., 2007), phase area ratio parameter for measuring the variability across neck movement cycles (Baydal-Bertomeu et al., 2011), SD to measure maximal neck RoM (Woodhouse and Vasseljen, 2008), SD to measure the average of neck RoM (Sjolander et al., 2008b), median across all gait cycles to measure variability

of trunk and neck rotations (Falla et al., 2017), and SD of the mean to measure variability of trunk and neck rotation across gait cycles (Alsultan et al., 2020a).

Regarding protocols used in the included studies, in three studies movement variability was investigated where different RoM of neck movements, including full or limited RoM, were performed (Alsultan et al., 2019; Baydal-Bertomeu et al., 2011; Vogt et al., 2007). In addition, two studies examined neck movement variability as a continuous movement (e.g. full flexion to full extension as one movement) (Alsultan et al., 2019; Baydal-Bertomeu et al., 2011), while Vogt et al. (2007) investigated neck movement variability regarding separate neck movements (e.g. flexion and extension movements separately).

Although Woodhouse and Vasseljen (2008) and Sjolander et al. (2008b) both examined neck RoM variability, and both separated CNP participants into idiopathic and traumatic groups, they used different positions (sitting versus standing), speeds (natural versus fast), and eye conditions (open versus closed) while neck movements were performed. Also, Woodhouse and Vasseljen (2008) measured the variability of maximal neck RoM, whereas Sjolander et al. (2008) calculated the average of movements.

In variability of trunk and neck rotation was investigated as participants walked on a treadmill, with head in a neutral position or rotated at 30° (Falla et al., 2017). No differences were found between CNP and asymptomatic groups. However, Alsultan et al. (2020a) observed that participants with CNP displayed reduced variability of trunk rotation when walking on a level surface and performing continuous head rotations. The different way tasks and parameters were used in these two studies might explain the conflicting findings.

Although findings are not in agreement across all studies included and the quality of evidence was low for movement variability, in all cases examining variability using the average of

SD was able to differentiate the CNP group from the asymptomatic group, regardless of the method of measurement and the region of the spine (Sjolander et al., 2008b; Alsultan et al., 2019; Alsultan et al., 2020a). Further research is needed to investigate movement variability in people with CNP, particularly using SD as a parameter.

Proprioception

Seven studies examined proprioception outcomes and measured each neck movement separately (Dugailly et al., 2015; Grip et al., 2007; Hill et al., 2009; Portelli and Reid, 2018; Kristjansson et al., 2003; Sjolander et al., 2008b; Alahmari et al., 2017). In these studies, significant differences between the CNP group and asymptomatic group were found, regardless of how CNP groups were categorised, parameters, or method of measurement. In contrast, other studies assessed proprioception outcomes and calculated neck movements as one movement (Woodhouse and Vasseljen, 2008; Williams et al., 2017). These studies reported no significant differences between the groups.

With regards to the studies that used several parameters to calculate proprioception, these parameters could be utilised to obtain different aspects of proprioception (Hill et al., 2009; Sjolander et al., 2008b). For example, Variable Errors (VE) calculates variability within the findings, while Root Mean Square Error (RMSE) measures the overall results. These differences might explain the conflicting findings when different parameters are used to examine proprioception in the CNP group compared to an asymptomatic group.

Based on the findings of the studies included in this review, most studies that examined proprioception could identify significant differences between the CNP group and asymptomatic group, regardless of parameters, although the overall quality of evidence across studies was very low for proprioception. Examining proprioception outcome measure by calculating each neck

movements (e.g. flexion, extension and rotation) separately was more likely to distinguish between the CNP group and asymptomatic group.

Smoothness of movement

Two studies used jerk index to calculate smoothness of movement, and found a significant difference in the CNP group compared to asymptomatic group (Sjolander et al., 2008b; Vikne et al., 2013). However, Waeyaert et al. (2016) used the same parameter as these two studies, and found no significant differences between groups. The different findings of these studies might be due to the different neck movements that were examined and the way neck movements were calculated. Two studies measured each neck movement separately (Sjolander et al., 2008b; Vikne et al., 2013), whereas the neck movements were calculated as one movement in Waeyaert et al. (2016). In addition, no significant difference was found between the groups when the number of velocity peaks was used to measure smoothness of movement as one movement (Williams et al., 2017). Based on these findings, even though the overall quality of evidence across studies was very low for smoothness of movement, smoothness of movement outcomes could differentiate between the CNP group and asymptomatic group when neck movements were performed separately.

Uncategorised

Three studies examined spinal movement quality measures that were not investigated in other included studies. Baydal-Bertomeu et al. (2011) examined spontaneity of movement in neck region by calculating the harmonicity variable. The quality of neck movement regarding velocity was measured by time to peak velocity percentage (Williams et al., 2017). Movement coordination between the cervical and thoracic regions was investigated by coefficient of cross-correlation analysis for the time history of velocity, acceleration, and angular displacements (Tsang et al.,

2013). Further investigation is needed to determine whether these spinal movement quality measures differentiate between CNP group compared to asymptomatic group.

5.5.1 Strengths and limitations

The strengths of this review include utilising an *a priori* protocol registered on PROSPERO, as well as adherence to the PRISMA guideline (see *Appendix 9*). In addition, the modified NOS for evaluating the risk of bias in each study, and the GRADE criteria to assess the overall quality of the evidence, were both used in this review. Likewise, this review has limitations: randomised controlled trial study designs that might examine the quality of spinal movement at baseline were not considered during the search strategy. Thus, studies that potentially met the inclusion criteria may have been omitted. Furthermore, some studies did not report data regarding mean and SD, or reported an overall mean and SD for all neck movement conditions. Meta-analysis and sub-group analysis were not carried out, since the studies included were heterogeneous in terms of kinematic variables, methods of measurement and tasks performed.

Although the evidence presented by the studies included was found to be very low quality based on GRADE criteria, the results nevertheless offer preliminary evidence that the quality of spinal movement could differentiate CNP participants from asymptomatic individuals, regardless of outcome measures. This was the case in most studies in this review, regardless of quality outcomes. In addition, most studies included in this review had a low risk of bias based on the NOS form. Although few studies have investigated quality of movement outcomes in people with CNP, and especially movement variability, by measuring the average of SD, the findings of this review indicate that this method has potential to differentiate between people with CNP and asymptomatic individuals. Thus, a gap seems to exist in the literature, which should be filled by developing reliable, high-quality evidence.

5.6 Conclusion

Most studies examining quality of spinal movement carried a low risk of bias, and most showed significant differences between people with CNP and asymptomatic individuals, regardless of outcome measures employed even though the quality of the body of evidence for all outcomes of interest across the included studies is very low based on GRADE criteria. With regards to movement variability outcome measures, further investigation is required due to inconsistent findings in the included studies. Regarding proprioception and smoothness of movement outcome measures, the included studies observed differences between the CNP group and asymptomatic group when neck movements were performed separately.

CHAPTER 6

GENERAL DISCUSSION

6.1 Summary of Findings

The main goal of this thesis was to understand whether changes in movement variability exist in people with neck pain disorders, and to gain knowledge about the mechanisms underlying these changes. *Chapter One* covered the background regarding neck pain disorders, as well as movement behaviours that are typically altered in people with CNP. In addition, the importance of investigating quality of movement, including movement variability and understanding changes in movement variability in people with neck pain disorders, were highlighted (Guo et al., 2019; Jull et al., 2018). Areas of research that have not been fully documented in the literature were therefore determined to be objectives for this thesis.

Chapter Two presents an observational case-control study, focused on examining movement variability during active cervical movements (flexion-extension, lateral flexion and rotation) (Alsultan et al., 2019). These were performed as continuous movements at different speeds (natural, slow, and fast) by people with CNP and asymptomatic individuals (Alsultan et al., 2019). MD and MA measures of the HA were used to calculate movement variability.

Regarding movement variability, a smaller MD was found in people with CNP compared to asymptomatic individuals during flexion-extension and rotation movements (Alsultan et al., 2019), Also, people with CNP demonstrated smaller MA during rotation movements. These results reflect reduced movement variability in people with CNP relative to asymptomatic individuals.

In *Chapter Three*, an observational case-control study is presented that investigated the variability of neck and trunk rotation during gait in a CNP group as compared to an asymptomatic group (Alsultan et al., 2020a). Both groups were evaluated during both single-task (walking with head in a natural position) and dual-task (walking whilst rotating the head) gait. For single-task gait, no group differences were observed for the variability of trunk or neck rotation (Alsultan et al., 2020a), For dual-task gait, no difference between groups was found for the variability of neck rotation, but the CNP group showed reduced variability of trunk rotation compared to the asymptomatic group.

In *Chapter Four*, an experimental single-group and repeated measures study examined neck movement variability in asymptomatic individuals before and after eccentric exercise (Alsultan et al., 2020b). This is the first work that has been done to induce acute pain via eccentric exercise and examine the immediate influence of neck pain on the quantity and quality of active neck movements, and especially on movement variability. This experiment addressed the thesis aim of determining whether pain mechanisms contribute to modification of movement variability during active cervical movements. Movements including flexion-extension, lateral bending and rotation performed at different speeds, either at full RoM or restricted to 45° RoM at baseline pre-exercise, immediately following eccentric neck exercise, and 24 hours and 48 hours post exercise. Similar to the measures used in *Chapter Two*, the MD and MA measures of the HA were used to calculate movement variability (Alsultan et al., 2019).

Performing cervical movements at full RoM, MD reduced significantly at 24 hours post exercise relative to baseline pre-exercise, regardless of direction or speed of movement. In addition, MA was significantly decreased at 24 hours and 48 hours post exercise relative to MA immediately following eccentric neck exercise. Performing cervical movements at 45° RoM, MD was significantly reduced at 48 hours post exercise relative to immediately following eccentric neck

exercise, and MA was significantly decreased at 48 hours post exercise relative to baseline pre-exercise, immediately following eccentric neck exercise, and 24 hours post exercise.

The findings presented in *Chapter Four* showed that movement variability was reduced 24 hours after and 48 hours after eccentric exercise, providing evidence that acute neck pain does modify the quality of neck movement in terms of movement variability (Alsultan et al., 2020b).

Chapter Five presented a systematic review that examined whether the quality of spinal motion differs between people with CNP and healthy individuals, and identified the outcome measures for quality of movement currently used in research literature. In this systematic review, it was determined that six different outcome measures were used to examine the quality of spinal motion. Compared to other outcome measures, inconsistent findings were only found for the movement variability outcome measure. Overall, a very low quality of evidence was found in studies using movement variability outcome measures. However, the two studies included in this thesis (see *Chapter Two* and *Chapter Three*), which are also included in the systematic review, revealed an important feature of examining movement variability, which demonstrates potential for detecting differences between groups (Alsultan et al., 2020a; Alsultan et al., 2019).

With regards to the correlation between movement variability parameters and clinical features, a negative correlation was found between TSK and MA measured for all neck rotation conditions in people with CNP in *Chapter Two* (Alsultan et al., 2019). This finding confirms that movement variability is reduced when fear of movement is high. For *Chapter Three*, no significant correlations were found between movement variability parameters and clinical features in people with CNP (Alsultan et al., 2020a).

Regarding descriptive results, people with CNP presented with similar mean (SD) TSK scores: 36.53 (6.58) in *Chapter Two* and 35.43 (8.26) in *Chapter Three* (Alsultan et al., 2020a;

Alsultan et al., 2019). In addition, people with CNP reported their exact level of pain using NRS in *Chapter Two* as mild, with an average SD of 4.08 (1.89), and also in *Chapter Three* as mild, with an average SD of 3.96 (1.91). With regards to NDI, the level of disability was reported as mild (5-14 scores) in *Chapter Two*—12.94 (6.84)—and also as mild in *Chapter Three*: 11.92 (6.70) (Vernon and Mior, 1991; Alsultan et al., 2020a; Alsultan et al., 2019). Level of physical activity, scored via IPAQ, was high in people with CNP—5175.61 (4569.36)—in *Chapter Two,* as well as in asymptomatic individuals who experienced acute neck pain induced by eccentric exercise: 6317.95 (6272.15) in *Chapter Four* (Alsultan et al., 2019; Alsultan et al., 2020b).

In this concluding chapter (*Chapter Six*), the goal is to summarise the key findings of this thesis, draw conclusions, document the strengths and limitations of the research presented, and discuss clinical implications and suggestions for future research.

6.2 Movement variability and Neck Pain Disorders

In order to answer the thesis question regarding whether changes in movement variability exist in people with neck pain, three empirical studies were conducted. The study reported in *Chapter Two* found significant differences in movement variability, as shown by the MD and MA measurements, between people with CNP compared to asymptomatic individuals during active cervical movements (Alsultan et al., 2019). Findings reflected in *Chapter Three* also documented significant differences in the variability of trunk rotation between people with CNP compared to asymptomatic individuals during dual-task gait (Alsultan et al., 2020a). In *Chapter Four*, asymptomatic individuals performed movements with eccentric exercise-induced acute pain, which mimicked characteristics of clinical neck pain (Alsultan et al., 2020b). Here, the findings showed significant differences in neck movement variability before and after eccentric exercise-induced neck pain. Taking the results of the research reported in *Chapter Two, Chapter Three* and *Chapter*

Four, significant changes in movement variability were documented in people with neck pain during active neck movements, as well as while walking (Alsultan et al., 2019; Alsultan et al., 2020a; Alsultan et al., 2020b). Furthermore, in the systematic review presented in *Chapter Five,* four out of seven studies that examined movement variability found significant differences in people with CNP, regardless of the measurements and parameters used.

6.3 Mechanisms underlying movement variability changes

As discussed in *Chapter One*, movement variability is typically described as a normal variation that happens during movement performance (Niederer et al., 2017). However, movement variability can also provide knowledge regarding movement behaviour and underlying health or functional impairments, and therefore can contribute to clinical insights (Stergiou et al., 2006; Stergiou and Decker, 2011). A relatively new theoretical model proposes that a relationship between movement variability, motor learning, and health may exist (Harbourne and Stergiou, 2009; Stergiou et al., 2006). The researchers who developed this model have suggested mechanisms of change regarding movement variability, suggesting that motor skills and healthy states are associated, and that optimal movement variability points to greater adaptability of the underlying control system (Stergiou and Decker, 2011). Reduced movement variability refers to more predictable behaviour, while increased variability refers to unpredictable behaviour (Niederer et al., 2017; Stergiou and Decker, 2011). Both reduced and increased variability can lead to or reflect decreased adaptability due to disturbances.

The results reported in *Chapter Two* and *Chapter Three* showed consistent findings of reduced movement variability in people with CNP during active cervical movements, as well as when walking whilst rotating the head (Alsultan et al., 2020a; Alsultan et al., 2019). In order to

know whether pain itself contributes to changed movement variability, the research reported in *Chapter Four* was conducted (Alsultan et al., 2020b).

In *Chapter Four*, the effects of acute neck muscle soreness induced via eccentric exercise on the variability of neck movement were examined (Alsultan et al., 2020b). Findings indicated that asymptomatic individuals moved differently during active cervical movements after eccentric exercise. Similar to the observations of people with CNP in *Chapter Two* and *Chapter Three*, reduced movement variability was also displayed by healthy individuals when they experienced acute, experimentally induced neck pain (Alsultan et al., 2020a; Alsultan et al., 2019; Alsultan et al., 2020b). As well as reduced movement variability, the level of neck pain reported by participants with neck pain in the three studies was approximately similar: 4 out of 10. Furthermore, similar level of physical activity, which were high, were for people with CNP in *Chapter Two* and also for asymptomatic individuals who experienced acute neck pain induced by eccentric exercise during active neck movement in *Chapter Four* (Alsultan et al., 2019; Alsultan et al., 2020b). Thus, these results mirrored observations in the previous chapters, suggesting that decreased movement variability indicates an adaptive strategy employed by people with neck pain. This strategy is most likely adopted in order to avoid or decrease pain, suggesting an impact of avoidance behaviour on physical functioning (Bahat et al., 2014).

According to Moseley and Hodges (2006), asymptomatic individuals display movement strategies when anticipating harm due to movement. This association may lead to persistent changes in movement variability, which could become embedded over a period of time in people with CNP, (Moseley and Hodges, 2006), even when their pain has decreased, as observed in *Chapter Two* and *Chapter Three* (Alsultan et al., 2020a; Alsultan et al., 2019). In addition to a mild level of pain, people with CNP presented with similar mean TSK scores and a mild level of disability in the research reflected in *Chapter Two* and *Chapter Three* (Alsultan et al., 2020a; Alsultan et al., 2019).

Furthermore, a negative correlation was observed in people with CNP when movement variability reduced and fear of movement increased during cervical movements (Alsultan et al., 2019), This strategy could be considered as a predictable behaviour reflecting decreased adaptability of motor control in people with neck pain disorders. Thus, this thesis provides further insights into the potential mechanisms underlying changes in movement variability in people with neck pain disorders, which could drive further research in the future and therefore contribute to more appropriate clinical examination in turn, leading to provision of more effective interventions.

6.4 Measuring movement variability

As discussed in *Chapter One*, examining movement behaviour could provide further knowledge with regards to the functions of movement sub-systems and motor activity systems (Camomilla et al., 2018), This information could lead towards better understanding of significant factors associated with movement, and could be used in prevention, early diagnosis and intervention. Furthermore, *Chapter One* addressed the importance of examining the quality of movement, including movement variability. It focused on investigating the amount of variability, since it is easy to interpret and simple to implement in a clinical setting (Schumacher, 2004; Urdan, 2016).

Several previous studies used the average of SD to measure movement variability. According to Madeleine et al. (2008), significant differences in movement variability exist between people with chronic neck-shoulder pain and asymptomatic individuals. Also, Lamoth et al. (2006) observed differences in movement variability in people with lower back pain compared to asymptomatic individuals. Both of these studies used the average of SD to measure movement variability across a whole cycle of movement. Furthermore, movement variability was found to be reduced in a CNP group compared asymptomatic individuals during rotation neck movements

(Sjolander et al., 2008b), and this was also quantified by measuring the average of SD for neck movement.

Chapter Two reported research results that investigated movement variability by utilising novel parameters of the HA and quantifying movement variability by the average of SD across whole neck movement cycles (Alsultan et al., 2019). The findings showed differences between people with CNP and asymptomatic individuals for neck flexion-extension and rotation movements. Furthermore, *Chapter Three* documented observations of significant differences between people with CNP and asymptomatic individuals during a dual-gait task (Alsultan et al., 2020a) and used the average of SD to measure movement variability.

Research reported in *Chapter Four* used the same measurement and movement variability parameters as the research documented in *Chapter Two*, and again significant differences were found in asymptomatic individuals during active neck movements before and after eccentric exercise-induced acute pain (Alsultan et al., 2019; Alsultan et al., 2020b). The systematic review presented in *Chapter Five* confirmed that the type of parameters used to quantify movement variability might play a key role in the detection differences between symptomatic and asymptomatic individuals. Unlike other parameters, when the average of SD was used to quantify movement variability, the results consistently showed differences between the CNP group and asymptomatic group in all included studies.

Based on the findings of the studies presented in *Chapter Two, Chapter Three* and *Chapter Four*, as well as previous studies, the ability of average of SD to detect differences between and within subjects has been demonstrated, and the difference was obvious in people with pain (Alsultan et al., 2020a; Alsultan et al., 2019; Alsultan et al., 2020b). Using the average of SD as a

parameter revealed consistent findings of reduced movement variability in people with neck pain in all our experimental studies.

6.5 Quality of evidence for the conclusions of this thesis

Assessment of the quality of the evidence in this thesis has been applied to support drawing meaningful conclusions. All of the studies reported in *Chapter Two*, *Chapter Three* and *Chapter Four* of this thesis (Alsultan et al., 2020a; Alsultan et al., 2019; Alsultan et al., 2020b) were conducted according to the Declaration of Helsinki, which is not only concerned with ethics, but also with ensuring high quality research (Riis, 2003). Also, the studies reflected in *Chapter Two* and *Chapter Three* (Alsultan et al., 2020a; Alsultan et al., 2019) followed the guidelines of the STROBE statement regarding study design and reporting of results (von Elm et al., 2014). In addition, the modified NOS was used to assess two observational studies (*Chapter Two* and *Chapter Three*) in the systematic review (*Chapter Five)* (Alsultan et al., 2020a; Alsultan et al., 2019).

In *Chapter Five*, the systematic review was assessed using a critical appraisal tool, A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) (Shea et al., 2017). Most AMSTAR-2 checklist items were reported, while two items, including a comprehensive literature search strategy and a list of excluded studies and justification for exclusions, were partially reported.

Moreover, the systematic review was registered on PROSPERO and conducted according to PRISMA guidelines (Moher et al., 2015). The PICOS framework was used to define the eligibility criteria and to structure the systematic review questions. A comprehensive search strategy was adopted and completed using several databases, with two independent reviewers, alongside completing the study selection and data extraction processes. Furthermore, the reasons for

excluding studies and the number of full-text studies assessed were reported. The modified NOS was used to evaluate the risk of bias in each study, and the GRADE criteria were utilised to assess the overall quality of the evidence for outcome measures across studies (Schünemann, 2013; Guyatt et al., 2011a; Wells et al., 2018).

With regards to the quality of evidence for outcome measures, the included studies were found to be very low quality based on GRADE criteria. In addition, the systematic review included only observational studies, which are rated as low-quality evidence although they are the most appropriate study form for exploring differences without intervention (Guyatt et al., 2011a; Gilmartin-Thomas et al., 2018). However, most studies included in this review were found to be at low risk of bias according to the modified NOS. In this thesis, effort has been made to ensure that bias is limited, and that results are presented clearly.

6.6 Overall strengths, limitations and implications for clinical and future research

This thesis highlighted the importance of examining the quality of movement, and especially movement variability, in people with neck pain disorders. Based on the findings of *Chapter Two* and *Chapter Four*, the MA and MD parameters used to evaluate movement variability were found capable of detecting changes in people with neck pain, a method that had not been explored before (Alsultan et al., 2019; Alsultan et al., 2020b). A 3D motion-capture system was used in this thesis to collect kinematic data, including the quality and quantity of movement. This might not be available in clinical settings, reducing direct applicability of the methodology to clinical practice. Thus, further studies should examine measurement approaches available for use in clinical practice that are capable of identifying changes in movement quality and quantity in people with CNP. In

addition, the MD and MA measurements might be used in future research to examine the effects of interventions for improving movement control in people with CNP.

It was confirmed that the methodology used in *Chapter Two* and *Chapter Four* (Alsultan et al., 2019; Alsultan et al., 2020b), including examining active neck movements via continuous cycling movements and different speeds, could play an important role in identifying differences in people with neck pain disorders (Bonnechere et al., 2014; Baydal-Bertomeu et al., 2011).

In *Chapter Three*, examining simple and challenging gait tasks in people with CNP highlighted the importance of examining challenging and functional tasks in the spinal region (Alsultan et al., 2020a).

Establishing a neck pain model via eccentric exercise in *Chapter Four* was found to be an effective way to induce acute pain, which allows researchers to examine and understand changes in people with neck pain symptoms across a few days (Alsultan et al., 2020b).

However, limitations do exist. In this thesis, a first attempt has been made to use the parameters of HA to examine active neck movement behaviour in people with CNP, and therefore the measurement properties (including the reliability) of these parameters in people with CNP have not been investigated. However, these parameters of HA have shown the potential to identify changes in people with cervical spine disorders (Barbero et al., 2017). In addition, movement variability was examined mainly in people with CNP (including CNP of insidious and traumatic onset) in this thesis, and the findings might be different in people with other neck pain disorders, such as neck pain of degenerative onset or cervical radiculopathy.

The sample used in this thesis was a convenience sample, which likely decreases the generalisability of findings (Alsultan et al., 2020a; Alsultan et al., 2019). In addition, the sample size in *Chapter Two* and *Chapter Three* was not estimated *a priori* in these studies (Alsultan et al.,

2020a; Alsultan et al., 2019). However, the sample size was confirmed to be sufficient to proceed with statistical tests, since it was considered large enough to avoid serious problems and should tolerate violations of ANOVA assumptions (Pallant and Manual, 2007; Ghasemi and Zahediasl, 2012). Furthermore, a post-hoc effect size (Cohen's d) for the primary variable outcome was performed after the data collection, as noted in *Chapter Three* (Alsultan et al., 2020a), and showed that the effect size was 0.43, which indicates a large effect (Cohen, 1988b).

With regards to the sample of people with CNP in the observational studies presented in *Chapter Two* and *Chapter Three* (Alsultan et al., 2020a; Alsultan et al., 2019), the means for age (32.22 and 31.50), pain (4.08 and 3.96), and levels of disability (12.94 and 11.92) were low compared to an average CNP population (mean age 48.9 years, NRS 6.2 out of 10, and NDI 31 out 50) (Goode et al., 2010). Therefore, future research is needed to corroborate these findings in people with higher pain and disability and older age.

Finally, as observed in *Chapter Five*, few studies have examined movement variability in people with CNP, and inconsistent findings are also found in the literature. That has to date limited understanding regarding whether changes in movement variability exist in people with neck pain disorders. However, the findings reported in *Chapter Five* reveal that the average of SD as a parameter of movement variability is more likely to detect changes in people with neck pain disorders. Therefore, further investigations are suggested to explore movement variability using this parameter in people with neck pain disorders.

6.7 Conclusion

This thesis has provided evidence of changes in movement variability in people with neck pain disorders, and contributed to knowledge regarding the underlying mechanisms contributing to changes in movement variability. The results emphasise the importance of investigating movement

behaviour, and in particular movement variability, in people with CNP. Novel parameters of HA were used to quantify movement variability in two of the studies within this thesis. These were able to provide further insight regarding movement behaviour when people have neck pain. Furthermore, it was found that examining dual-gait tasks, could identify movement differences in people with CNP. Examining movement variability, and understanding the mechanisms underlying the changes observed, have provided insights that can inform improved clinical practice in people with neck pain.

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APPENDICES

Appendix 1 – Alsultan et al. (2019)

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Appendix 1 – Alsultan et al. (2019)

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Variability of the helical axis during active cervical movements in people with chronic neck pain

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ABSTRACT

Background: Recent work described parameters of the helical axis in asymptomatic people with potential for investigating kinematic changes in the cervical region. This approach could provide novel information on movement variability in people with neck pain, however this has never been investigated. This study aimed to investigate movement variability during active neck movements performed at different speeds in people with and without chronic neck pain.

Methods: This observational case-control study examined 18 participants with chronic neck pain of either idiopathic or traumatic origin and 18 gender-matched asymptomatic participants. Cervical kinematics were captured with 3D motion capture as people with and without chronic neck pain performed flexion-extension, bilateral lateral flexion and bilateral rotation at different speeds (natural, slow, and fast). The mean distance and mean angle parameters of the helical axis were extracted to describe 3D motion and quantify movement variability.

Findings: A smaller mean distance was observed in those with neck pain compared to the asymptomatic participants during flexion-extension ($P = 0.019$) and rotation movements ($P = 0.007$). The neck pain group displayed smaller values for the mean angle during rotation movements with different speeds ($P = 0.01$). These findings indicate less variable movement for those with neck pain relative to the asymptomatic participants. No difference in the mean angle was observed between groups for flexion-extension and lateral flexion.

Interpretation: The findings reiterate the importance of data derived from kinematic measures, and its potential for providing clinicians with further insight into the quality of active neck movements in people with chronic neck pain.

1. Introduction

Chronic neck pain (CNP) is one of the most common musculoskeletal disorders affecting adults, with reported prevalence ranging between 16.7% and 75.1% each year (Genebra et al., 2017). In addition to the individual physical, social, and psychological impact, CNP contributes greatly to health service costs (Coppieters et al., 2017; Genebra et al., 2017).

Besides pain, individuals with CNP may present with a number of disturbances in physical function including reduced proprioception, neuromuscular impairments, and difficulties with head-eye movement control (De Pauw et al., 2017; Della Casa et al., 2014; Ischebeck et al., 2017). Furthermore, people with CNP may experience fear of movement, symptoms of dizziness, a decrease of physical activity, and usually complain of disability during performance of daily activities (Cheng et al., 2015; Soderlund et al., 2018; Sremakaew et al., 2018; Yalcinkaya et al., 2017). A number of studies have examined neck movement characteristics in people with CNP with reduced active neck range of motion (RoM) a common observation regardless of the etiology of the neck pain disorder (Alricsson et al., 2001; Lee et al., 2005; Peolsson et al., 2007). Yet, most studies have focused on the quantity of movement and typically static variables of planar cervical motion. The quality or variability of movement may be a better indicator of ongoing neuromuscular dysfunction in people with CNP (Anderst et al., 2017;

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Baydal-Bertomeu et al., 2011; Edmondston et al., 2005; Preatoni et al., 2013). Furthermore, investigating kinematic variables across multiple axes can provide more precise information regarding changes during active movements (Ellingson et al., 2013).

Measures of the helical axis (HA) can be used to describe three-dimensional motion in the cervical region. Recently, novel parameters were proposed to describe the behaviour of the helical axis during active neck movements in healthy volunteers and the reliability of these parameters was established (intra and inter-session reliability (ICC) ≥ 0.80) (Barbero et al., 2017). The distribution in space of the HA and the mean angle of the HA measurements (Barbero et al., 2017; Cescon et al., 2014) demonstrated potential for investigating the variability of neck movement. HA parameters could therefore provide novel information regarding movement behaviour in people with CNP (Barbero et al., 2017; Lomond and Cote, 2010).

The objective of this study was to investigate movement variability during active neck movements inclusive of flexion-extension, lateral flexion and rotation performed at different speeds in people with and without neck pain. People with CNP of either idiopathic or traumatic origin were included. The secondary objective was to assess correlations between HA parameters and levels of pain, disability, fear of movement, physical activity and dizziness in the participants with neck pain.

2. Methods

2.1. Design

An observational case-control study was conducted from May to November 2017. Ethical approval for the study was granted by the Ethics Committee of the University of Birmingham, UK (CM06/03/17-1) and the study was conducted according to the Declaration of Helsinki. Convenience sampling was used to recruit participants from among students and staff of the University of Birmingham. The main purpose of the study and the methods that would be used were explained to participants before they were asked to give written informed consent. The guidelines of the STROBE statement (Strengthening the Reporting of Observational Studies in Epidemiology) were adhered to (Von Elm et al., 2014).

2.2. Participants

The sample size included 36 male and female gender-matched participants, including 18 asymptomatic people and 18 people with CNP of either idiopathic or traumatic origin. Participants attended a single laboratory session. An a priori sample size could not be determined, since no previous study had evaluated parameters of the HA in people with CNP and therefore no data were available for sample size calculation. Thus, sample size was estimated based on a previous study evaluating cervical kinematics in people with and without CNP (Vogt et al., 2007).

2.3. Inclusion criteria

Participants with neck pain were included in the study if they presented with painful symptoms for at least three months. In the case of those with whiplash-associated disorder (WAD), only grades I, II, or III according to the Quebec Task Force Classification (Spitzer, 1995) were included. In addition, the participants had to report their neck pain intensity over the last four weeks as at least 4 (mild pain) out of 10 on a Numerical Rating Scale (NRS) with two anchor points: 0 = “no pain” and 10 = “worst pain imaginable” (Boonstra et al., 2016; Kamper et al., 2015). The NRS is a valid and reliable instrument for self-reported pain intensity (Williamson and Hoggart, 2005). Asymptomatic participants were recruited to act as a control group. To be included they must have had no history of a neck injury or neck pain in the last two years that required treatment from a health care practitioner.

2.4. Exclusion criteria

Participants were excluded from either group if they presented with any of the following: previous spinal surgery, rheumatic condition, current or chronic respiratory condition, having an ongoing compensation claim related to an injury. Additional exclusion criteria for the CNP group included currently receiving active management, and neck injury that resulted in a spinal fracture.

2.5. Questionnaires

All participants were required to complete the International Physical Activity Questionnaire (IPAQ), which was used to characterise the sample with respect to their physical activity levels (Craig et al., 2003). Additionally, for the participants with CNP, their average pain level over the last four weeks was recorded using the NRS (Kamper et al., 2015) and their perceived neck disability was assessed using the Neck Disability Index (NDI), with a possible score range of 0–50 (Vernon, 2008; Vernon and Mior, 1991). The Dizziness Handicap Inventory (DHI) was used to determine self-reported levels of dizziness (Jaco and Graig, 1990). Additionally, self-reported dizziness intensity at rest and during activity was measured following testing, using an NRS from 0 to 10, where 0 was “no symptoms” and 10 was “worst symptoms” (Kammerlind et al., 2005; Kamper et al., 2015). Finally, the Tampa Scale for Kinesiophobia (TSK), a 17-item questionnaire, was employed to evaluate fear of movement and related behavioural problems, including avoidance and disability (Miller et al., 1991).

2.6. Cervical Kinematics

An optoelectronic system (BTS Bioengineering, Milan, Italy) was used to record cervical kinematics following system calibration. The kinematic data was acquired at a standard frequency of 250 fps. The system consists of eight infrared cameras with a resolution of 2,2 Mpixels (2048 × 1088 pxs). The cameras tracked the 3D motion of retroreflective markers attached to the subject's skin over the following body landmarks: two markers on the sternum, superior at the jugular notch and inferior at the xiphoid process, 7th cervical vertebra, 5th thoracic vertebrae, 9th thoracic vertebrae. In addition, a helmet was placed on the subject's head, with four reflective markers as follows: on the head apex, the front, and right and left sides of the helmet (Cescon et al., 2015). The helmet also contained a laser pointer.

2.7. Procedure

Following placement of the reflective markers, the participant was seated upright on a chair with their head in a neutral position and they were instructed to avoid shoulder movements and to relax their arms. The participant was seated 220 cm in front of a wall and with the head in neutral, the point of the laser was marked on the wall to define the starting reference position (0°). Using a goniometer, the subjects head was then rotated 45° to the left and right and these positions were marked (Fig. 1). Flexion and extension to 45° was also performed and these positions were marked on the ceiling and floor. The participants performed the following neck movements: flexion-extension, bilateral lateral flexion, and bilateral rotation. Each movement was performed in three conditions: at a natural self-selected speed, slow speed (30 beats per second (bps)) and fast speed (60 bps) (Table 1). The movement speed was controlled using a metronome beats mobile application and the conditions were randomized in order to minimize the risk of order as a confounding variable.

Participants were instructed to start every movement from the reference point at 0° and then perform continuous neck movements without stopping in the midline. The subjects were instructed to

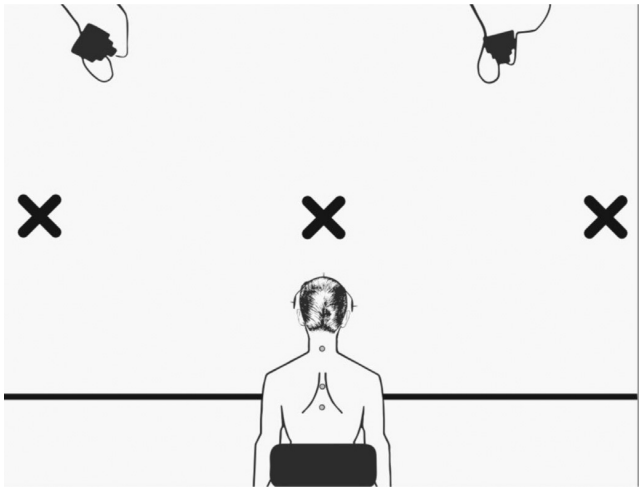

Fig. 1. Illustration of the experimental setup. Marks were placed on the wall in front of the subject to identify the starting position and, as illustrated here, 45° of right and left rotation. Markers were placed on a helmet and on the subject to track the movement of their head in 3D space.

Table 1
Overview of the movements and conditions measured.

Movements	Conditions
Flexion-extension	1. Natural speed
	2. Slow speed
	3. Fast speed
Bilateral lateral flexion	4. Natural speed
	5. Slow speed
	6. Fast speed
Bilateral rotation	7. Natural speed
	8. Slow speed
	9. Fast speed

maintain the laser at 0° while performing lateral flexion, move between the 45° reference points while performing rotation, and move up and down between the 45° reference points while performing flexion-extension. The range of motion was limited since performing functional tasks and activities of daily living does not usually require the full active range of motion (Bennett et al., 2002; Bible et al., 2010). In addition, the position and the orientation of the HA depends on the range of motion (Barbero et al., 2017).

Kinematic data were acquired for 10 repetitions of each condition following the protocol described by Barbero et al. (2017). Familiarisation with each test condition preceded data acquisition. A rest period of 30 s was given between each condition to prevent fatigue and ensure that the participant returned to the neutral position between conditions (Miura and Sakuraba, 2014).

2.8. Data analysis

The mean distance (MD) of the HA and mean angle (MA) of the HA were calculated as defined previously (Barbero et al., 2017). The MD represents the distance between all intersection points between the HA and a transversal plane from their barycenter, while the MA is defined by calculating the MA of each axis and the total average (Fig. 2). Lower values of the MD and MA imply that the movement is less variable. The RoM was quantified by calculating the mean difference between the maximal flexion and extension movements, while the mean difference of neck rotation and lateral flexion were computed between the left and right movements (Barbero et al., 2017).

Data from eight repetition movement cycles were analysed following exclusion of the first and last cycle in order to avoid artefacts or alterations in angular velocity (Cescon et al., 2014). The degree of variability of neck movements across the whole movement cycle was measured by calculating the standard deviation (SD) of the mean.

2.9. Statistical analysis

Mean and SD were calculated to describe MD and MA parameters. In addition, mean and SD were used to demonstrate the range and distribution of participant demographics and questionnaire responses. Two-way analysis of variance (ANOVA) was applied to evaluate the MD, MA and RoM during the flexion-extension movements, lateral flexion movements and rotation movements, with group (control, CNP) and condition (slow, natural and fast speed) as factors. Significant differences revealed by ANOVA were followed up by post-hoc Student-Newman-Keuls (SNK) pair-wise comparisons.

Pearson or Spearman correlations (depending on the distribution of each questionnaire data) were performed to assess the relationship between MA and MD of the neck movements and the following six variables: NDI, DHI and self-reported dizziness intensity (NRS), level of average pain intensity (NRS), TSK, and IPAQ. The strength of the correlation was interpreted as: small correlation < 0.3, moderate correlation between 0.3 and 0.5, and strong correlation > 0.5 (Cohen, 1988).

Results are reported as mean and SD in the text and figures. Statistical analyses were performed with SPSS Version 22.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

3. Results

A total of 36 participants completed the study with 8 men and 10 women in each group. Those with CNP had a mean (SD) age of 32.2 (13.4) years, while the mean (SD) age of the control group was 25.8 (7.3) years which was not significantly different ($U = 109.500$, $z = -1.664$, $P = 0.097$.).

There were 6 CNP participants who had experienced a whiplash injury: two with grade I, three with grade II, and one with grade III. Participant demographics for both groups are presented in Table 2. One participant in the CNP group did not complete the TSK questionnaire. There were 7 missing values across all kinematic variables: 2 values of RoM for flexion- extension at fast speed and lateral flexion at slow speed in the control group, and 5 values of MD for two conditions for lateral flexion at slow and fast speed, one condition for rotation slow speed in the control group, and two conditions for flexion-extension slow and lateral flexion natural speed in the CNP group. These occurred due to artefacts in data acquisition.

Fig. 3 presents representative data from a control subject and person with CNP acquired during rotation at a natural speed. The observations from this representative example were confirmed at the group level as presented in Fig. 4 and detailed below.

3.1. Mean distance (MD)

3.1.1. Flexion-extension

The CNP group displayed a smaller MD for the flexion-extension movements regardless of the condition (main effect for group: $F = 5.7$, $P = 0.019$). Despite a trend, the MD did not vary across flexion-extension movement conditions ($F = 3.0$, $P = 0.051$) and was not dependent on the interaction between group and condition ($F = 0.7$, $P = 0.47$). The MD decreased in the CNP group as compared to control group for the flexion-extension movements. The mean (SD) of CNP group were as follows; natural speed condition 1.46 cm (0.33 cm), slow condition 1.39 cm (0.25 cm), fast condition 1.65 cm (0.39 cm); whereas in the control group the values for the natural speed condition were 1.61 cm (0.28 cm), slow condition 1.63 cm (0.31 cm), and fast condition 1.71 cm (0.31 cm).

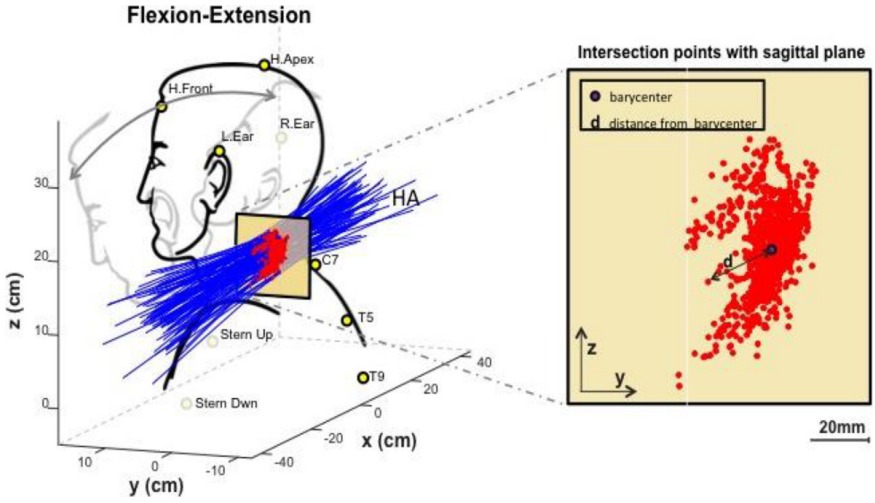

Fig. 2. Demonstration of the HA parameters that were used in the experimental protocol. Mean distance (MD) intersection points are represented in red, while mean angle (MA) angles of axis lines are represented in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Participant demographics and self-report questionnaires. Standard deviations (SD) are reported in parentheses.

		Control group	CNP group
Age	Mean (SD)	25.89 (7.34)	32.22 (13.41)
Height (cm)	Mean (SD)	168.80 cm (7.71 cm)	170.77 cm (10.34 cm)
Weight (kg)	Mean (SD)	64.67 kg (14.41 kg)	68.39 kg (14.69 kg)
Total IPAQ score	Mean (SD)	3940.97 (3163.72)	5175.61 (4569.36)
NDI	Mean (SD)	Not applicable	12.94 (6.84)
Average pain intensity	Mean (SD)	Not applicable	4.08 (1.89)
TSK	Mean (SD)	Not applicable	36.53 (6.58)
DHI	Mean (SD)	Not applicable	20.78 (17.32)
Dizziness NRS	Mean (SD)	Not applicable	1.65 (2.12)

Abbreviations: International Physical Activity Questionnaire (IPAQ), Neck Disability Index (NDI), Average pain level over the last four weeks was recorded using NRS (average pain), Tampa Scale for Kinesiophobia (TSK), Dizziness Handicap Inventory (DHI), self-reported dizziness NRS (dizziness NRS), Not applicable (NA).

3.1.2. Lateral flexion

The MD did not vary across groups (F = 1.1, $P = 0.28$) or condition (F = 0.2, $P = 0.82$) for the lateral flexion movements, and was not dependent on the interaction between group and condition (F = 0.2, $P = 0.83$). The mean (SD) of the CNP group were: natural speed condition 0.91 cm (0.23 cm), slow condition 0.90 cm (0.23 cm), and fast condition 0.91 cm (0.25 cm); while for the control group, natural speed condition values were 1.02 cm (0.44 cm), slow condition 0.93 cm (0.34 cm), and fast condition 0.97 cm (0.31 cm).

3.1.3. Rotation

Consistent with the results for flexion-extension, the CNP group displayed smaller MD values for the rotation movements regardless of condition (main effect for group: F = 7.48, $P = 0.007$). The MD did not vary across rotation movement conditions (F = 0.19, $P = 0.82$) and was not dependent on the interaction between group and condition (F = 1.53, $P = 0.22$).

The MD for the rotation movements decreased in the CNP group as compared to the control group. The mean (SD) of the CNP group were as follows: natural speed condition 0.83 cm (0.15 cm), slow condition 0.90 cm (0.29 cm), and fast condition 0.84 cm (0.15 cm). The control group mean (SD) were: 1.07 cm (0.33 cm) in the natural speed condition, slow condition 0.93 cm (0.22 cm), and fast condition 0.99 cm (0.35 cm).

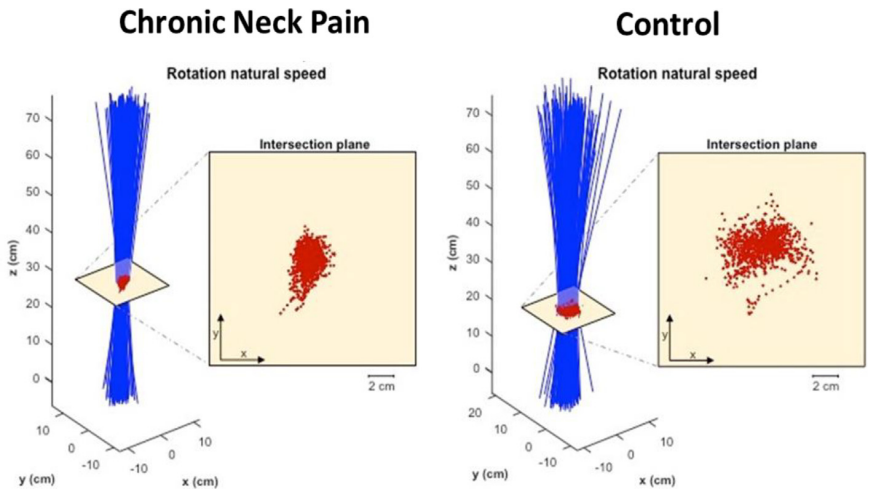

Fig. 3. Representative data acquired from a patient and control subject during head rotation performed at a natural speed. Note the smaller mean distance (MD) and mean angle (MA) for the participant with chronic neck pain compared to the control subject.

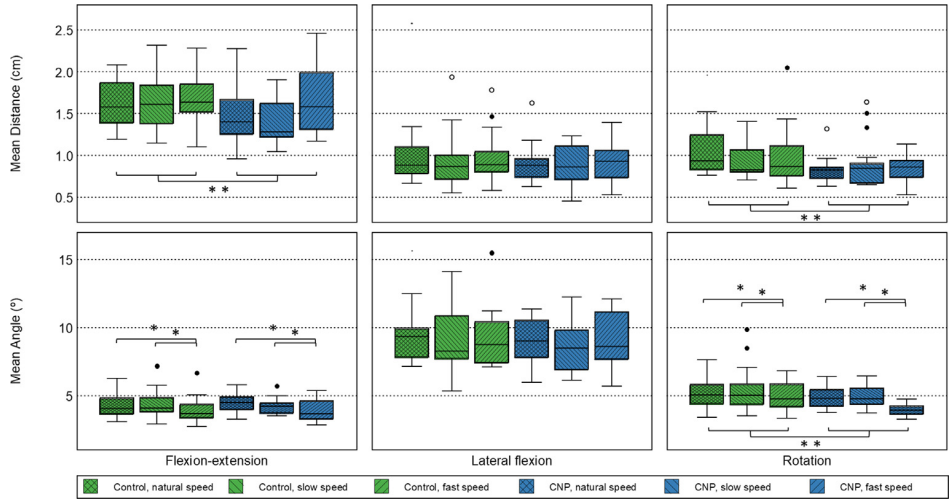

Fig. 4. Boxplots representing the descriptive results, mean and standard division of the mean distance (MD), and mean angle (MA) for all the neck movement conditions investigated. Statistically significant difference between groups; $^{**}P < 0.05$. Statistically significant difference between conditions; $^{*}P < 0.05$.

3.2. Mean angle (MA)

3.2.1. Flexion-extension

No difference was observed between groups for the MA during the flexion-extension movements ($F = 0.1$, $P = 0.92$), and no interaction between group and condition was observed ($F = 5.2$, $P = 0.59$). However, the MA did vary across conditions ($F = 4.0$, $P = 0.02$), with smaller MA observed during the fast speed condition compared to the slow and natural speed conditions (both SNK: $P < 0.05$).

The MA for the flexion-extension movements was reduced in the fast speed condition as compared to other conditions. The mean (SD) values during the fast speed condition were as follows: CNP group 3.88° (0.75°) and control group 3.89° (0.92°); whereas for the CNP group the values were 4.51° (0.73°) for natural speed condition and 4.22° (0.57°) for slow condition; and for the control group, 4.29° (0.91°) for natural speed condition and 4.39° (0.99°) for slow condition.

3.2.2. Lateral flexion

The MA did not vary across groups ($F = 1.5$, $P = 0.21$) or condition ($F = 0.3$, $P = 0.68$) for the lateral flexion movements, and was not dependent on the interaction between group and condition ($F = 0.2$, $P = 0.82$). The mean (SD) of the CNP group were as follows: natural speed condition 8.96° (1.62°), slow condition 8.61° (1.92°), and fast condition 9.04° (2.07°); while for the control group, the values were natural speed condition 9.70° (2.16°), slow condition 9.21° (2.42°), and fast condition 9.20° (2.11°).

3.2.3. Rotation

The MA during the rotation movements was dependent on group ($F = 9.30$, $P = 0.003$) and condition ($F = 4.82$, $P = 0.010$), but not the interaction between group and condition ($F = 1.34$, $P = 0.26$). The post-hoc analysis revealed that the CNP group displayed smaller values for the MA during rotation movements with different speeds (SNK: $P < 0.01$) (Table 3).

The MA or the rotation movements decreased in the CNP group as compared to the control group. The mean (SD) for the CNP group were as follows: natural speed condition 4.98° (0.85°), slow condition 4.89° (0.71°), and fast condition 3.98° (0.42°). The control group values were: natural speed condition 5.21° (1.04°), slow condition 5.44° (1.64°), and fast condition 4.99° (1.02°) (Table 4).

3.3. RoM

The RoM for flexion-extension movements was consistent across conditions ($F = 0.4$, $P = 0.62$) and groups ($F = 1.9$, $P = 0.16$), with no interactions present ($F = 0.4$, $P = 0.66$). The same was true for lateral flexion, with no differences between conditions ($F = 2.4$, $P = 0.09$) and groups ($F = 2.0$, $P = 0.15$) and no interactions present ($F = 0.0$, $P = 0.98$). For rotation, there were no effect of conditions ($F = 2.60$, $P = 0.07$), no effect of group ($F = 0.74$, $P = 0.39$), and no interaction present ($F = 1.07$, $P = 0.34$). The results of the RoM confirmed that all neck movement conditions were performed within the range of movement required by the experimental protocol.

3.4. Correlations between kinematic variables and subjective descriptors

The correlation between the questionnaires scores and MA and MD variables are shown in Table 5. Significant correlations were found between MA and MD with the following variables: NDI, level of average pain intensity (NRS), TSK, and IPAQ.

3.5. Mean distance (MD)

There was a moderate positive correlation between NDI and the MD measured during flexion-extension neck movements at the fast speed ($r = 0.490$, $P = 0.039$). A strong positive correlation was found between the average pain intensity (NRS) and the MD measured during flexion-extension neck movement at the fast speed ($r = 0.514$, $P = 0.029$). Furthermore, a moderate negative correlation was documented between the TSK score and MD during lateral flexion performed and at the fast speed ($r = -0.481$, $P = 0.044$). A moderate negative correlation was found between the IPAQ score and the MD during lateral flexion performed at the fast speed ($r = -0.346$, $P = 0.042$).

3.6. Mean angle (MA)

There was a moderate negative correlation between the IPAQ score and the MA during lateral flexion performed at the natural speed ($r = -0.346$, $P = 0.039$). In addition, there was a strong negative correlation between the TSK score and the MA during neck rotation and at a natural speed ($r = -0.563$, $P = 0.015$), slow speed ($r = -0.561$, $P = 0.015$), and fast speed ($r = -0.805$, $P = 0.000$).

Table 3
Results of the ANOVA to evaluate differences in the mean distance (MD) and mean angle (MA) for each movement direction.

Parameters	Conditions	Group * conditions (Sig.)	Group (Sig.)	Conditions (Sig.)
MD (cm)	Rotation	0.22	0.007*	0.82
	Flexion-extension	0.47	0.019*	0.051
	Lateral flexion	0.83	0.28	0.82
MA (°)	Rotation	0.26	0.003*	0.010*
	Flexion-extension	0.59	0.92	0.02*
	Lateral flexion	0.82	0.21	0.68

Statistically significant difference.
* $P < 0.05$.

4. Discussion

This study is the first to evaluate the variability of active neck movement in people with CNP by utilising parameters of the HA. The findings revealed less variability of movement in people with CNP during flexion-extension and rotation movement compared to healthy controls as shown by the MD measurements. The results also showed reduced variability of movement during rotation in people with CNP as compared to asymptomatic people as seen in the MA measurements.

4.1. Movement variability

The results of the present study are congruent with previous research findings that people with pain may move with less variability. Madeleine et al. (2008) reported reduced variability of arm and trunk acceleration in people with chronic neck-shoulder pain as compared to asymptomatic people during a repetitive arm movement task. Reduced variability of transverse thoracic and lumbar rotations has also been observed in people with low back pain as compared to asymptomatic controls while participants were walking (Lamoth et al., 2006). However, some other studies suggest the opposite. For example, Vogt et al. (2007) found that movement variability was significantly higher in people with CNP when compared to an asymptomatic group. However, they examined movement variability only in the maximum oscillation amplitudes (Vogt et al., 2007), whereas the present study investigated a larger cycle of neck movement. Continuous cyclical movement trials are more likely to able to provide information regarding movement behaviour associated with CNP (Baydal-Bertomeu et al., 2011).

One previous study which investigated full active neck movements, found that motion patterns were characterised by less flexibility and slower movement in people with neck pain as compared to healthy controls. Reduced range of neck movement was observed for motion in the primary plane and the two correlated movement planes at the maximum of the RoM (conjunct motion) (Meisingset et al., 2015). The findings of the present study concur with these results even though different procedures were used in both studies. In Meisingset et al. (2015), participants were asked to move as far as possible while performing neck movements at a self-determined speed, while the participants in this study were requested to move between fixed points at both a natural speed as well as fixed speed. The findings from the present study, as in those of Meisingset et al. (2015), could be interpreted as evidence of a more cautious movement strategy by people with neck pain, presumably employed as a protective strategy to decrease or potentially avoid neck pain.

Even though the level of pain reported in this study was low in the CNP group, differences in movement behaviour and movement variability were observed between groups. This is congruent with other research and with current theories about the impact of pain on movement and motor control. Some people may continue to display less variability in movements even when they are free from pain (Moseley and Hodges, 2006). Moreover, an association may exist between motor variability and learning in pain disorders (Moseley and Hodges, 2006). This association could be controlled by evaluative processes that play a role in motor variability: when a movement is associated with pain, the patient performs that movement differently, and over a period of time this change in movement becomes ingrained (Moseley and Hodges, 2006). Furthermore, motor adaptations to pain could lead to protection from vulnerability to pain or injury, and contribute to changes in mechanical behaviour (Hodges and Tucker, 2011). For example, a protective movement strategy was employed by healthy people when they anticipated that a movement could cause harm to their back (Moseley and Hodges, 2006). Thus, the lower movement variability identified in the CNP group in the current study could reflect an adapted behaviour due to pain.

4.2. The influence of movement speed

In the current study, reduced movement variability was observed in the CNP group as compared to the control group for flexion-extension as revealed by differences in the MD. Furthermore, decreased

Table 4
Mean and standard deviation of the mean distance (MD) and mean angle (MA) recorded during each movement direction and each condition for both the control and chronic neck pain (CNP) groups.

Parameter	MD (cm)		MA (°)	
Group	Control	CNP	Control	CNP
Movement	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Flex/Ext natural	1.61 cm (0.28 cm)	1.46 cm (0.33 cm)	4.29° (0.91°)	4.51° (0.73°)
Flex/Ext slow	1.63 cm (0.31 cm)	1.39 cm (0.25 cm)	4.39° (0.99°)	4.22° (0.57°)
Flex/Ext fast	1.71 cm (0.31 cm)	1.65 cm (0.39 cm)	3.89° (0.92°)	3.88° (0.75°)
LatFlex natural	1.02 cm (0.44 cm)	0.91 cm (0.23 cm)	9.70° (2.16°)	8.96° (1.62°)
LatFlex slow	0.93 cm (0.34 cm)	0.90 cm (0.23 cm)	9.21° (2.42°)	8.61° (1.92°)
LatFlex fast	0.97 cm (0.31 cm)	0.91 cm (0.25 cm)	9.20° (2.11°)	9.04° (2.07°)
Rotation natural	1.07 cm (0.33 cm)	0.83 cm (0.15 cm)	5.21° (1.04°)	4.98° (0.85°)
Rotation slow	0.93 cm (0.22 cm)	0.90 cm (0.29 cm)	5.44° (1.64°)	4.89° (0.71°)
Rotation fast	0.99 cm (0.35 cm)	0.84 cm (0.15 cm)	4.99° (1.02°)	3.98° (0.42°)

Abbreviations: mean distance (MD), mean angle (MA), standard deviation (SD).

Table 5
Correlations between questionnaire responses and helical axis parameters.

Questionnaires	Parameters	Neck movements	Correlation coefficient	Sig. (2-tailed)
NDI	MD (cm)	Flexion-extension with fast speed	0.490*	0.039
Pain (average)	MD (cm)	Flexion-extension with fast speed	0.514*	0.029
TSK	MA (°)	Rotation natural	−0.563*	0.015
		Rotation slow	−0.561*	0.015
		Rotation fast	−0.805**	0.000
	MD (cm)	Lateral flexion fast	−0.481*	0.044
IPAQ	MA (°)	Lateral flexion natural	−0.346*	0.039
	MD (cm)	Lateral flexion fast	−0.346*	0.042

Abbreviations; mean distance (MD), mean angle (MA), Neck Disability Index (NDI), average pain level over the last four weeks was recorded using NRS (average pain), Tampa Scale for Kinesiophobia (TSK), International Physical Activity Questionnaire (IPAQ).

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

movement variability during flexion-extension was seen via the MA when performed at the faster speed than when performed at the slower and self-selected speeds, and this was the case for both groups. Vikne et al. (2013) also observed a significant reduction in movement speed and displacement during flexion-extension movements when performed at a faster speed compared to the preferred or slower speed. In addition to the observed reduction of movement variability during flexion-extension at the faster speed, positive correlations were also found between the MD during flexion-extension performed at the faster speed, and the level of disability (NDI), and the level of average pain intensity (NRS). Based on the current and on previous observations, faster movements could be emphasised during the clinical examination of people with CNP especially since people with neck pain often complain of difficulty performing rapid movement of their head (Bahat et al., 2010).

4.3. Correlation between movement parameters and clinical features

A negative correlation was found for the CNP group between TSK and MA measured for all neck rotation conditions. Thus, movement variability decreased with higher levels of fear of movement. These findings confirm the effect of avoidance behaviour on physical functioning (Bahat et al., 2014).

4.4. Clinical implications

Examining the variability of neck movement as done in this study is not trivial to perform in a clinical setting (Lamoth et al., 2006). However, our findings show that such data derived from kinematic measures has the potential to provide clinicians with important insights into active neck movement behaviour in people with CNP. Further research should evaluate whether simplified measures of movement e.g. with inertial sensors, which can be more easily implemented in a clinical setting, are capable of detecting such changes in movement quality in people with CNP.

4.5. Methodological considerations

Our current sample of CNP participants presented with relatively low levels of pain and disability (average pain intensity ~4/10 and NDI score ~13/50) and the study sample size was not calculated a priori thus the generalisability of study findings is likely reduced. The sample size also prevented comparisons between those with idiopathic neck pain versus trauma induced neck pain or a comparison between genders. This could be explored in future studies. Nevertheless, the kinematic variables in this study were able to detect differences in the quality of cervical motion between groups and provided information about the nature of these differences. This is one of very few studies examining whole-cycle movement at different speeds in people with CNP.

5. Conclusion

Through parameters of the HA we observed differences in movement variability during neck flexion-extension and rotation movements in people with CNP. These measurements may be useful in future studies to evaluate the effects of interventions, including exercise, to enhance movement control in people with CNP.

Declarations of interest

None.

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Appendix 2 – Alsultan et al. (2020a)

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Variability of neck and trunk movement during single- and dual-task gait in people with chronic neck pain

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ABSTRACT

Background: Previous findings reported that people with chronic neck pain walk with reduced range trunk rotation, especially when walking in more challenging conditions. Quantification of the quality of neck and trunk movement during gait could provide further insight into biomechanical changes that occur in people with neck pain. This study uniquely compared the variability of trunk and neck rotation during single-task and dual-task gait in people with chronic neck pain and asymptomatic individuals.

Methods: An observational case-control study was conducted on 20 asymptomatic individuals and 24 people with chronic neck pain of idiopathic or traumatic origin. Participants performed rectilinear walking whilst keeping the head in a neutral position (single-task) and whilst rotating the head at a natural speed (dual-task). Trunk and head rotation angles were averaged across gait cycles for the task trials. The data were normalised in time, and the average variability of angular distribution along the normalised cycle was extracted. The Tampa Scale for Kinesiophobia was used to assess fear of movement.

Findings: During single-task gait, there were no group differences for the variability of trunk ($p = 0.862$) or neck ($p = 0.427$) rotation. For dual-task gait, there was no difference between groups for the variability of neck rotation ($p = 0.636$), however, the participants with neck pain displayed reduced variability of trunk rotation ($p = 0.021$). The neck pain group also walked at a significantly slower speed during dual-task gait ($p = 0.043$) compared to asymptomatic individuals and the speed of their gait was associated with the extent of fear of movement.

Interpretation: The strategy observed in participants with chronic neck pain likely reflects adaptive behaviour when faced with more challenging conditions for postural control.

1. Introduction

Neck pain is a common musculoskeletal disorder that four out of five individuals will experience at some point during their lives (De Pauw et al., 2018; Nam et al., 2016; Sremakaew et al., 2018). Besides pain and disability, people with chronic neck pain (CNP) may display fear of movement in addition to a number of neuromuscular and biomechanical disturbances (Cheng et al., 2015; De Pauw et al., 2018; Falla et al., 2017; Uthaikhup et al., 2014).

Surprisingly, few studies have examined whether gait is modified in people with CNP even though walking is one of the most common activities of daily living, which is closely related to health status and physical function (Sitthipornvorakul et al., 2015; Uthaikhup et al., 2014). Those that have been conducted, have revealed that some people with CNP walk with a narrower step width, a shorter step length and a slower gait speed (Poole et al., 2008; Sjostrom et al., 2003). Moreover, a recent study documented reduced trunk rotation during walking in people with CNP compared to asymptomatic individuals, especially when walking was accompanied by a task of maintaining the neck in 30° of rotation (Falla et al., 2017).

Dual tasks, in which two tasks are performed at the same time, are commonly used when investigating gait, since such tasks more appropriately reflect typical activities of daily living and therefore stand to reveal more relevant differences in gait biomechanics (Freire Junior et al., 2017; Liu et al., 2018). For instance, a previous study observed a significant difference in gait speed, stride and step time, and single-

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support time between fallers and non-fallers when dual-task gait was performed, whereas no changes were observed during the single-task condition (Toulotte et al., 2006). In addition, Sjostrom et al. (2003) recorded reduced head and trunk rotation in people with chronic whiplash associated disorders when performing head rotation during walking.

Although the evaluation of range of motion is a typical component of the examination of people with neck pain, quantifying the quality and variability of movement is also essential to understand the day-to-day impact of a patient's condition (Edmondston et al., 2005). Yet, very few studies have attempted to quantify the quality of movement in people with CNP, including the quantification of movement variability that may be a better marker of ongoing neuromuscular dysfunction (Lomond and Cote, 2010).

In this study, we investigate the variability of neck and trunk rotation in people with CNP during gait relative to pain-free participants. Participants were evaluated during both single and dual-task gait with the expectation that if differences were to exist between groups, this would be more evident during dual-task gait. The dual-task condition consisted of walking whilst rotating the head; a common daily activity. We also evaluate the correlation between the variability of neck and trunk rotation during gait and the extent of neck pain intensity, level of neck pain related disability and fear of movement.

2. Methods

2.1. Design

An observational case-control study congruent with the Declaration of Helsinki principles was conducted from May to November 2017. Ethical approval was obtained from the Ethics Committee of the University of Birmingham, UK . Participants were recruited from the staff and student population of the University of Birmingham using a convenience sampling method. Written informed consent was obtained from all participants after the purpose and methods of the study were explained. The guidelines of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement were employed to design and report this study (Von Elm et al., 2014).

2.2. Participants

A sample of 44 participants, including 20 healthy individuals and 24 people with CNP of either idiopathic or traumatic origin, attended a single laboratory session. Sample size was estimated based on previous studies that examined parameters during gait in people with CNP (Falla et al., 2017; Poole et al., 2008).

2.2.1. Inclusion criteria

Participants with CNP were eligible if they: (1) reported their average neck pain intensity over the last four weeks as at least 4 out of 10 on a Numerical Rating Scale (NRS) with two anchor points: 0 = “no pain” and 10 = “worst pain imaginable” (Boonstra et al., 2016; Kamper et al., 2015), and (2) had experienced neck pain for at least three months. For individuals with a history of a whiplash trauma, only persons with grades I, II, or III according to the Quebec Task Force Classification (Spitzer, 1995; Williamson and Hoggart, 2005) were eligible. Healthy participants were eligible if they had no history of a neck injury or neck pain in the last two years that required treatment from a health care practitioner.

2.2.2. Exclusion criteria

Participants were excluded from either group if they had any of the following: previous spinal surgery, rheumatologic condition, current or chronic respiratory condition, or an ongoing compensation claim related to an injury. Additionally, participants were excluded from the CNP group if they were currently receiving active management, or had experienced a neck injury that resulted in a spinal fracture.

2.3. Anthropometric measurements

Anthropometric measurements were recorded for all subjects according to Davis's guidelines (Davis III et al., 1991). The measurements include height, weight, leg length, the distance between the two anterior superior iliac spines (ASIS), pelvis depth bilaterally, knee diameter bilaterally, malleolus width bilaterally.

2.4. Questionnaires

The participants with CNP were required to complete three questionnaires. The average pain level over the last four weeks was recorded using a NRS (Kamper et al., 2015). In addition, their perceived neck disability was evaluated using the Neck Disability Index (NDI) questionnaire, which has a score range of 0–50 (Vernon, 2008; Vernon and Mior, 1991). The Tampa Scale for Kinesiophobia (TSK), a 17-item questionnaire, was used to assess fear of movement as well as problems related to movement behaviours, such as avoidance and disability (Hudes, 2011; Miller et al., 1991).

2.5. Cervical and trunk kinematics

An optoelectronic system (BTS Bioengineering, Milan, Italy) was used to record cervical and trunk kinematics. The kinematic data were acquired at a sampling frequency of 250fps. The system consisted of eight infrared cameras with a resolution of 2,2 Mpixels (2048 × 1088pxs). The cameras tracked the 3D motion of retro-reflective markers attached to the subject's skin over body landmarks according with the biomechanical model described in (Davis et al., 1991). Two markers were placed on the sternum (superior at the jugular notch and inferior at the xiphoid process), and additional markers were placed bilaterally on the anterior superior iliac spine (ASIS), great trochanters, lateral femoral condyles, lateral bars (located on centre between great trochanter and lateral femoral condyles markers), the head of the fibula, lateral bars (centred between the head of the fibula and lateral malleolus markers), lateral malleolus, the fifth metatarsal head and heels. Posteriorly, markers were placed bilaterally on the acromion process, seventh cervical vertebra, fifth thoracic vertebrae, ninth thoracic vertebrae and second sacral vertebra (S2). Furthermore, to track head motion, the participants wore a helmet which included four reflective markers (head apex, front, and right and left of the helmet) (Cescon et al., 2015).

2.6. Procedure

Once the reflective markers were positioned, the participants completed single- and dual-task gait trials, which each consisted of six repetitions of walking along a rectilinear path for approximately five steps (three meters). During single-task gait, the participants were asked to walk whilst keeping their head in a natural position (three repetitions executed), whereas the dual-task walking consisted of walking whilst rotating their head right and left continuously at a natural speed (three repetitions executed). The participants were asked to rotate their neck as far as they comfortably could but without causing pain, but the range of motion was not imposed. The trials were randomised to minimise the risk of order as a confounding variable and a rest period of 30 s was provided between each trial. Familiarisation with each gait task was performed before data acquisition.

2.7. Data analysis

Trunk and head rotation angles (degrees) were averaged across gait cycles for the single-task gait trials. Data were normalised in time (% gait cycle), and the average variability of the angular distribution along

the normalised cycle was extracted. The same analysis was conducted for the dual-task gait trials, using the head rotation angular peaks as events to define the cycles during gait.

Gait speed was averaged across gait cycles for both the single- and dual-task trials. Gait speed data were then normalised to the participants' height. The average variability of trunk and neck rotation across the gait cycles was measured by calculating the standard deviation (SD) of the mean.

2.8. Statistical analysis

Mean and SD of trunk and neck rotation were extracted to describe the average and variability of their motion in the horizontal plane, as well as mean speed. The Shapiro-Wilk's test was applied to evaluate the data distribution for all the extracted variables. One-way analysis of variance (ANOVA) or Kruskal-Wallis H tests, for normally and non-normally distributed data respectively, were performed to analyse differences between the asymptomatic participants and the CNP group, for the variability of trunk and neck rotation, range of motion (ROM), and mean gait speed during single- and dual-task gait.

A cross-correlation test was performed between trunk and neck movements to examine movements of these two body segments during single-task and dual-task gait, with results from the CNP group then compared to those of the healthy group. Independent-samples *t*-test for normally distributed data or Kruskal-Wallis H tests for non-normally distributed data analysed differences between the groups. For the CNP group, Pearson or Spearman correlations for normally and non-normally distributed data respectively, were performed to assess the relationship between the variability of trunk and neck rotation, mean gait speed, and: i. perceived disability (NDI), ii. average neck pain intensity (NRS) and iii. fear of movement (TSK). Mean and SD findings are reported in the text and figures. Statistical analyses were completed using SPSS Version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$.

3. Results

Participant demographics for CNP and healthy groups are presented in Table 1. The groups did not differ in age ($t(42) = 0.135$, $p = 0.893$) or gender ($U = 288.000$, $z = 1.133$, $p = 0.257$). Eight of the 24 participants with CNP had experienced a whiplash injury: four with grade I, three with grade II, and one with grade III.

Table 1
Participant demographics and results of self-report questionnaires—standard deviations (SD) are reported in parentheses.

		Control group	CNP group
Gender	Women	10	14
	Men	10	10
Age	Mean (SD)	28.65 (11.03)	31.50 (12.50)
Height (cm)	Mean (SD)	169 cm (7.34 cm)	169.88 cm (9.72 cm)
Weight (kg)	Mean (SD)	65.66 kg (14.09 kg)	66.87 kg (13.28 kg)
NDI (0–50)	Mean (SD)	NA	11.92 (6.70) (low)
Average pain intensity (0 – 10)	Mean (SD)	NA	3.96 (1.91) (mild)
TSK (17–68)	Mean (SD)	NA	35.43 (8.26)

Abbreviations: Neck disability index (NDI), Average pain level over the last four weeks was recorded using NRS (average pain), Tampa Scale for Kinesiophobia (TSK), not applicable (NA). The range of scores for the questionnaires is in parentheses. Higher scores indicate high disability in NDI, pain in average pain intensity, or fear of movement.

3.1. Single-task gait

3.1.1. Variability of trunk and neck rotation

The mean variability (SD) of trunk rotation for the CNP group was 0.62° (0.43°) versus 0.60° (0.48°) for the asymptomatic group; whereas the variability of neck rotation was 0.48° (0.34°) for the CNP group versus 0.46° (0.52°) for the asymptomatic group. No significant differences was observed between groups for the variability of trunk rotation ($F(1, 42) = 0.031$, $p = 0.862$) or neck rotation ($\chi^2(1) = 0.631$, $p = 0.427$) during single-task gait.

3.1.2. Range of motion for trunk and head rotation

The mean ROM of trunk rotation for the CNP group was 9.19° (3.56°) versus 8.82° (2.87°) for the asymptomatic group. The mean ROM of head rotation was 4.95° (2.49°) for the CNP group versus 4.56° (1.24°) for the asymptomatic group. There were no significant differences between groups for the mean ROM of trunk rotation ($F(1, 42) = 0.141$, $p = 0.710$) or neck rotation ($\chi^2(1) = 0.142$, $p = 0.706$) during single-task gait.

3.1.3. Gait speed

Gait speed during single-task gait trials was not significantly different between groups ($F(1, 42) = 0.702$, $p = 0.407$). The mean (SD) gait speed for the CNP group was 0.68 ht./s (0.10 ht./s), whilst for the control group, the mean (SD) was 0.71 ht./s (0.12 ht./s).

3.2. Dual-task gait

3.2.1. Variability of trunk and neck rotation

The CNP group (mean 1.46° (1.13°)) displayed significantly reduced variability of trunk rotation ($F(1, 42) = 5.773$, $p = 0.021$) during the dual gait task compared to the asymptomatic group (2.43° (1.54°)) (*see* Fig. 1). However, no difference was observed between groups for the variability of neck rotation ($F(1, 42) = 0.227$, $p = 0.636$; CNP group: 29.55° (6.23°), asymptomatic group: 28.39° (9.66°)).

3.2.2. Range of motion (ROM) for trunk and head rotation

The mean ROM of the trunk rotation for the CNP group was 12.16° (4.53°) versus 11.81° (3.14°) for the asymptomatic group (χ^2

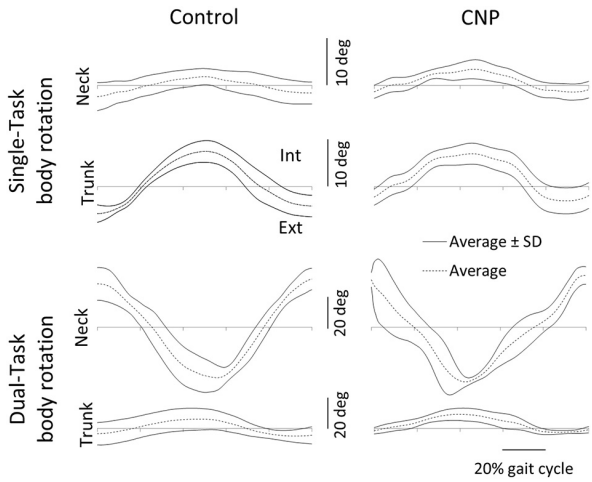

Fig. 1. Neck and trunk body segments' rotation (deg) of a representative asymptomatic (Control, left) and chronic neck pain (CNP, right) participant, during single-task (upper half) and dual-task (lower half) gait. Internal and external rotation ("Int" and "Ext") are reported as positive and negative values respectively. The average segments' rotation (dashed black line) is displayed, across the gait cycle (%), with its variability (solid black line) as ± one standard deviation (SD). A consistently smaller variability can be noted for trunk rotation during dual-task gait for the CNP participant (lower right graph).

Table 2
Results of the ANOVA or Kruskal-Wallis H to evaluate differences in variability of trunk and neck rotation, range of motion (ROM) for trunk and head rotation, as well as gait speed for each task.

	Task	Group (sig.)
Variability of trunk rotation	Single[a]	0.862
	Dual[a]	0.021*
Variability of neck rotation	Single[b]	0.427
	Dual[a]	0.636
Gait speed	Single[a]	0.407
	Dual[a]	0.043*
ROM for trunk rotation	Single[a]	0.710
	Dual[b]	0.750
ROM for head rotation	Single[b]	0.706
	Dual[a]	0.169

Statistically significant difference; *$p < 0.05$.
[a] One-way analysis of variance (ANOVA) is performed,
[b] Kruskal-Wallis H is performed.

(1) = 0.101, $p = 0.750$). The mean ROM of head rotation for the CNP group was 91.59° (18.44°) versus 99.17° (17.15°) for the asymptomatic group (F (1, 42) = 1.963, $p = 0.169$).

3.2.3. Gait speed

The CNP group walked at a significantly slower speed during dual-task gait trials (F (1, 42) =4.337, $p = 0.043$) (see Table 2) with a mean (SD) 0.57 ht./s (0.10 ht./s) for the CNP group and 0.64 ht./s (0.11 ht./s) for the control group (see Table 3).

3.3. Correlation between the variability of trunk or neck rotation and gait speed

No significant correlation was observed between gait speed and the variability of trunk rotation for either group: healthy group during single-task gait ($r = -0.359$, $p = 0.120$) and dual-task gait ($r = -0.130$, $p = 0.585$); CNP group during single-task gait ($r = 0.148$, $p = 0.533$) and dual-task gait ($r = -0.125$, $p = 0.599$). Likewise, no significant correlation was observed between gait speed and the variability of neck rotation for either group: healthy group during single-task gait ($r = -0.394$, $p = 0.085$) and dual-task gait ($r = -0.034$, $p = 0.891$); for the CNP group, variability of trunk rotation during single-task gait ($r = 0.120$, $p = 0.614$) and during dual-task gait ($r = -0.105$, $p = 0.659$).

3.4. Correlations between kinematic variables and patient reported outcome measures

3.4.1. Variability of trunk rotation

No significant correlation was found between the variability of trunk rotation during single-task gait and scores on the NDI ($r = -0.208$, $p = 0.329$), NRS pain intensity ($r = -0.232$, $p = 0.274$), or TSK ($r = 0.039$, $p = 0.867$). Similarly, no significant correlation was found between the variability of trunk rotation during dual-task gait and scores on the NDI ($r = -0.096$, $p = 0.655$), NRS pain intensity ($r = -0.141$, $p = 0.510$), and TSK ($r = -0.022$, $p = 0.925$).

Table 4
Correlations between questionnaire responses and variability of trunk and neck rotation parameters.

	Questionnaires	Task	Correlation coefficient	Sig. (2-tailed)
Variability of trunk rotation	NDI	Single	−0.208	0.329
		Dual	−0.096	0.655
	NRS pain	Single	−0.232	0.274
		Dual	−0.141	0.510
	TSK	Single	0.039	0.867
		Dual	−0.022	0.925
Variability of neck rotation	NDI	Single	−0.400	0.053
		Dual	−0.123	0.567
	NRS pain	Single	−0.341	0.103
		Dual	−0.122	0.569
	TSK	Single	−0.076	0.742
		Dual	0.209	0.364

*Correlation is significant at the 0.05 level (2-tailed).
Abbreviations: Neck disability index (NDI), Average pain level over the last four weeks was recorded using NRS (average pain), Tampa Scale for Kinesiophobia (TSK).

3.4.2. Variability of neck rotation

No significant correlation was observed between the variability of neck rotation during single-task gait and scores on the NDI ($r = -0.400$, $p = 0.053$), NRS pain intensity ($r = -0.341$, $p = 0.103$), and TSK ($r = -0.076$, $p = 0.742$). Likewise, no significant correlation was observed between the variability of neck rotation during dual-task gait and the NDI score ($r = -0.123$, $p = 0.567$), NRS pain intensity scores ($r = -0.122$, $p = 0.569$), or TSK scores ($r = -0.209$, $p = 0.364$) (Table 4).

3.4.3. Gait speed

No significant correlations were found between gait speed during single-task gait and the NDI scores ($r = -0.206$, $p = 0.335$), NRS pain intensity scores ($r = 0.020$, $p = 0.926$), or TSK scores ($r = -0.376$, $p = 0.093$). For dual-task gait, no significant correlations were found between gait speed and the NDI scores ($r = -0.035$, $p = 0.870$) or NRS pain intensity scores ($r = 0.019$, $p = 0.931$). However, there was a significant medium negative correlation between gait speed during dual-task gait and TSK scores for the CNP group ($r = -0.48$, $p = 0.026$) indicating slower movement in those with higher fear of movement (see Table 5).

3.4.4. Sample size confirmation

Following data collection, a post-hoc effect size (Cohen's d) was calculated for the primary variable outcome using the program G*Power 3.1 for Windows. The one-way analysis of variance (ANOVA)

Table 3
Mean and standard deviation (SD) of the variability of trunk and neck rotation and Range of Motion (ROM) for trunk and head rotation, as well as gait speed, for each task for both the control group and chronic neck pain (CNP) group.

	Variability of trunk rotation		Variability of neck rotation		RoM of trunk rotation		RoM of head rotation		Gait speed	
Group	Control	CNP	Control	CNP	Control	CNP	Control	CNP	Control	CNP
Task	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Simple	0.60° (0.48°)	0.62° (0.43°)	0.46° (0.52°)	0.48° (0.34°)	8.82° (2.87°)	9.19° (3.56°)	4.56° (1.24°)	4.95° (2.49°)	0.71 ht./s (0.12 ht./s)	0.68 ht./s (0.10 ht./s)
Dual	2.43° (1.54°)	1.46° (1.13°)	28.39° (9.66°)	29.55° (6.23°)	11.81° (3.14°)	12.16° (4.53°)	99.17° (17.15°)	91.59° (18.44°)	0.64 ht./s (0.11 ht./s)	0.57 ht./s (0.10 ht./s)

Abbreviations: standard deviation (SD), range of motion (ROM).

Table 5
Correlations between questionnaire responses and gait speed parameters.

	Questionnaires	Task	Correlation coefficient	Sig. (2-tailed)
Gait speed	NDI	Single	−0.206	0.335
		Dual	−0.035	0.870
	NRS pain	Single	0.020	0.926
		Dual	0.019	0.931
	TSK	Single	−0.376	0.093
		Dual	−0.48*	0.026

Abbreviations: Neck disability index (NDI), Average pain level over the last four weeks was recorded using NRS (average pain), Tampa Scale for Kinesiophobia (TSK).

* Correlation is significant at the 0.05 level (2-tailed).

F-test was used, with an α error level probability of 0.05. The effect size was calculated for the variability of trunk rotation during the dual gait task of the CNP group (mean 1.46°(1.13°)). The effect size was 0.43, which indicates a large effect (Cohn 1988).

4. Discussion

This study is the first to evaluate the variability of trunk and neck rotation in people with and without CNP when performing single-task versus dual-task gait. These findings uniquely demonstrate less variability of trunk rotation and slower gait speed in people with CNP as compared to asymptomatic individuals when performing a dual gait task. Interestingly, walking at a slower speed during the more challenging dual-task gait condition was associated with higher levels of fear of movement.

4.1. Single-task gait

The current study observed no differences in the variability of trunk and neck rotation between those with and without CNP during single-task gait trials. These findings are in line with previous research (Falla et al., 2017) that compared variability of trunk and neck rotation between asymptomatic individuals and people with CNP during a simple walking task, albeit performed on a treadmill. In contrast, (Van Den Hoorn et al., 2012) reported reduced variability of trunk rotation in people with low back pain as compared to healthy individuals during normal walking on a treadmill. Our results show similar gait speed between groups during single-task gait, which is consistent with previous research investigating gait speed during simple walking tasks between asymptomatic individuals and people with CNP (Falla et al., 2017; Poole et al., 2008; Uthaikhup et al., 2014).

4.2. Dual-task gait

A significant reduction in the variability of trunk rotation during dual-task gait was observed between asymptomatic individuals and people with CNP. Reduced variability of movement has been observed in other chronic musculoskeletal pain disorders and during different tasks. For example, Lamoth et al. (2006) found reduced variability of transverse thoracic and lumbar rotations between healthy participants and people with low back pain during walking. Another study observed reduced variability of arm and trunk acceleration during a repetitive arm task in people with chronic neck/shoulder pain as compared to asymptomatic individuals (Madeleine et al., 2008). Furthermore, reduced variability of active flexion-extension and rotation has been reported in people with CNP as compared to healthy individuals (Alsultan et al., 2019).

The findings of the current study contrast to those of an earlier study that reported no difference in the variability of trunk rotation between people with and without CNP (Falla et al., 2017). Nevertheless, the tasks examined are not entirely comparable, since in the current study the participants walked on a floor whilst performing continuous cyclic head rotation, whereas in the study by Falla et al. (2017), the participants walked on a treadmill whilst keeping their heads fixed in 30° rotation. Both the current study and Falla et al. (2017) showed no difference in the variability of neck rotation movement between asymptomatic individuals and people with CNP. These findings showed that people with CNP tend to reduce the variability of their trunk rotation during more challenging conditions, such as dual-task gait. These observations give credence to the importance of examining movement behaviour during functional tasks that include walking, as simulated by dual-gait tasks used in this and similar studies, in people with CNP in order to detect changes in movement variability.

The participants with CNP also walked at a slower speed during dual-task gait as compared to asymptomatic individuals. Both Uthaikhup et al. (2014) and Poole et al. (Poole et al., 2008) also found that people with CNP reduced their walking speed when gait was performed whilst rotating the head. In addition, we observed a negative correlation between gait speed during the dual task and the extent of fear of movement, indicating that gait modifications in people with CNP may at least partially reflect adaptive behaviour, particularly when faced with conditions that are more challenging for postural control.

4.2.1. Methodological considerations

The participants with CNP presented with relatively low levels of neck pain intensity (average pain intensity = 3.96/10) and mild to moderate neck disability (average NDI score = 11.92/50). Although this is relevant as it highlights that individuals with CNP can display biomechanical disturbances even with relatively mild pain and disability, further work is warranted to examine movement variability in people with moderate to severe disability. Furthermore, participants with CNP presented with low levels of fear of movement (Vlaeyen et al. 1995). Despite the relatively low level of fear of movement, a negative correlation was still identified between fear of movement and gait speed during the dual-task gait for individuals with CNP. Additionally, the length of the path used during the tests (3 m) likely implies that there was some effect of acceleration and deceleration. Nevertheless, we don't believe that this would impair the general validity of the results.

The difference in the mean ROM of head rotation was large between the asymptomatic group and the CNP group during the dual gait task, although the difference was not statistically significant. Furthermore, although several correlations were observed, most were non-significant. It should be considered that the use of a larger sample size might have captured a significant difference.

5. Conclusion

This study demonstrates less variability of trunk rotation and slower gait speed in people with CNP as compared to asymptomatic individuals when performing a dual gait task. Interestingly, walking at a slower speed during the more challenging dual-task gait condition was associated with higher levels of fear of movement. These novel findings provide evidence of subtle changes in the control of spinal movement in people with chronic neck pain and highlight the importance of a comprehensive examination of functional movement involving single and dual tasks to reflect activities of daily living.

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Declaration of competing interest

None.

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Eccentric exercise and delayed onset muscle soreness reduce the variability of active cervical movements

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ABSTRACT

People with acute neck pain commonly present with restricted neck movement. However, it is unknown whether the presence of acute pain affects the quality of neck movement, specifically neck movement variability. We examined the effects of acute neck muscle soreness induced via eccentric exercise in healthy volunteers, on the variability of neck movement by examining changes in parameters of the helical axis during active neck movements.

An experimental, single-arm repeated measures study recruited 32 healthy participants, male and female, aged between 18 and 55 years. Repetitive active neck movements (flexion–extension, bilateral lateral flexion and bilateral rotation) were performed at different speeds, either at full range of motion (RoM) or restricted to 45° RoM at baseline, pre-exercise (T0), immediately following eccentric neck exercise (T1), 24 h (T2) and 48 h post-exercise (T3). The mean distance (MD) and mean angle (MA) parameters of the helical axis were extracted to quantify movement variability.

MD, measured during movements performed at full RoM, reduced significantly at T2 compared to T0 ($P = 0.001$) regardless of direction or speed of movement. MA was significantly lower at T2 and T3 compared to T1 ($P = 0.029$ and $P = 0.033$, respectively). When RoM was restricted to 45°, significantly lower MD values were observed at T3 compared to T1 ($P = 0.034$), and significantly lower MA values were measured at T3 compared to T0, T1 and T2 (all $P < 0.0001$).

This study uniquely demonstrates that neck movement variability is reduced immediately after, 24 h and 48 h after eccentric exercise, indicating that acute neck muscle soreness modifies the quality of neck movement.

1. Introduction

Active cervical movements are commonly measured by clinicians to evaluate function of the cervical spine (Stenneberg et al., 2017). It is common for people with chronic neck pain to move with less range of motion (RoM) during active neck movements compared to asymptomatic individuals (Sarig-Bahat et al., 2010; Vogt et al., 2007; Woodhouse and Vasseljen, 2008; Puglisi et al., 2004). In addition, recent work showed that, compared to asymptomatic individuals, people with chronic neck pain move in a less variable way during repeated active neck movements (Alsultan et al., 2019). Specifically, the mean distance (MD) and mean angle (MA) of the helical axis were used to quantify the variability of active neck movements and people with chronic neck pain displayed lower values of MD and MA; indicating less movement variability (Alsultan et al., 2019).

Few studies have investigated changes in neck movement in people experiencing acute pain. The research that does exist, has typically focused on the quantity of movement i.e., RoM, confirming reduced neck RoM soon after the onset of symptoms (Fernández-Pérez et al., 2012; Sterling et al., 2003, Kasch et al., 2001; Pedler and Sterling, 2011). We hypothesised that changes in the *quality* of active neck movements also develops rapidly following the onset of symptoms as per restricted RoM.

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There could be multiple mechanisms underlying changes in the quality of movement in people with acute neck pain, including pain/soreness, articular dysfunction, and psychological factors, such as fear of movement (Zabihhosseinian et al., 2017; Bahat et al., 2014). One approach to understanding the mechanisms underlying neuromuscular and biomechanical adaptations to pain is the use of human experimental pain models, including injection of noxious substances into the neck muscles (most commonly hypertonic saline) (Mista et al., 2019; Qu et al., 2019; Christensen et al., 2019). However, hypertonic saline produces pain that typically only lasts 5–10 min with a peak intensity of less than a few minutes (Falla et al., 2007). Another potential experimental approach for inducing acute pain which has not yet been applied to the neck region, is delayed-onset muscle soreness (DOMS) which occurs following un-accustomed eccentric exercise (Hedayatpour et al., 2018; Hedayatpour and Falla, 2015; Mista et al., 2019; Qu et al., 2019). DOMS typically commences within 24 h, lasts 48–72 h post exercise (Tsatalas et al., 2013; Martin et al., 2004) and is experienced during movement rather than being constant (Hedayatpour and Falla, 2015; Lau et al., 2013). Therefore, the soreness induced from eccentric exercise may more likely reflect clinical neck pain and would allow the effects of acute neck muscle soreness on the quality of neck movement to be evaluated over multiple days.

In this study, we test a novel approach for inducing DOMS within the neck extensor muscles in healthy volunteers and examine the influence of DOMS on the quantity (RoM) and quality (MD and MA of the helical axis) of active neck movements. Movements included flexion–extension, lateral bending and rotation movements which were examined at full and 45° RoM at different speeds.

2. Methods

2.1. Design

An experimental single-group and repeated measures designed study was conducted at the Centre of Precision Rehabilitation for Spinal Pain (CPR Spine) between April and July 2019. Ethical approval was granted by the Ethics Committee of the University of Birmingham, UK (ERN_18-1273A), and the study was conducted according to the Declaration of Helsinki. The main aim of the study and the methods were explained to participants in person, and were presented in a participant information sheet. Any questions or concerns regarding the study were addressed before participants signed an informed consent form.

2.2. Participants

Participants were recruited from students and staff at the University of Birmingham using a convenience sampling method. Recruitment methods included contacting participants on the CPR Spine patient register, printed advertisements, and an identical digital advertisement disseminated using the University's intranet.

Thirty-two healthy participants were recruited, including 18 men and 14 women. The sample size required was estimated using the program G*Power 3.1 for MacOS. Deriving four measurements from one group for neck rotation movements, with normal speed and the mean angle as a primary outcome, was found sufficient to achieve 80% statistical power (1-β error probability), with an α error level probability of 0.05 using analysis of variance (ANOVA) of repeated measures, within-factors, and a medium effect size of 0.24. The effect size was based on our previous data describing the difference between the means (0.23) of two groups—people with chronic neck pain and healthy individuals, divided by their standard deviation (0.94) (Alsultan et al., 2019). The non-sphericity correction ε was 0.5. This calculation generated a sample size of 32 participants.

2.3. Inclusion and exclusion criteria

Healthy participants (men and women aged between 18 and 55 years old) were included in the study if they did not have a history of neck injury or neck pain in the last five years that required treatment from a healthcare practitioner. Participants were excluded if they presented with previous spinal surgery, pregnancy, rheumatic conditions, current or chronic respiratory conditions, or an ongoing compensation claim related to any injury.

2.4. Questionnaires

Participants completed the International Physical Activity Questionnaire (IPAQ), to describe participants with respect to their physical activity levels (Craig et al., 2003). Participants were also required to rate their perceived fatigue after the eccentric exercise protocol using Borg's CR-10 scale (Äng, 2008, Thuresson et al., 2005). This scale ranges from 0 to 10, where 0 equals no fatigue and 10 is maximal perceived fatigue (Borg, 1982).

A visual analogue scale (VAS) was used to evaluate the degree of perceived muscle soreness experienced during neck movements, before (T0), immediately after (T1), 24 h after (T2) and 48 h after (T3) the eccentric exercise protocol with the endpoints "no soreness" to "extreme soreness." The McGill Pain Questionnaire, which assesses pain quality and includes 15 elements, was completed 24 h (T2) and 48 h after (T3) the eccentric exercise protocol (Nie et al., 2005, Melzack, 1987).

2.5. Cervical kinematics

A 3D motion capture system (BTS Bioengineering, Milan, Italy) was used to record cervical kinematics at a standard frequency of 250fps. This system included eight infrared cameras with a full resolution of 2,2 Mpixels (2048x1088pxs), which recorded the 3D motion of retroreflective markers attached to the participants' skin, based on the protocol described in Alsultan et al. (2019). A total of nine retroreflective markers were used: two over the sternum, one over the 7th cervical vertebra, one over the 5th thoracic vertebrae and one over the 9th thoracic vertebrae. In addition, four markers were placed on a helmet that incorporated a laser pointer.

Raw marker data were filtered with a Butterworth low-pass filter (cut-off 4 Hz). Clusters on trunk and head were defined as rigid bodies using the Single Value Decomposition (SVD) technique and their relative movement was calculated according to the helical axis model (Cappozzo et al., 1995; Söderkvist and Wedin, 1993). In particular, the movement of the head was computed with respect to the trunk at each timeframe as a composition of a rotation and translation around a fixed axis (helical axis) (Söderkvist and Wedin, 1993; Woltring et al.,1985; Grip et al., 2008). In accordance with previous studies, the helical axis was computed every 10 degrees of head motion along the plane (sagittal plane for flexion, and transversal plane for rotation) (Cescon et al., 2014; Barbero et al., 2017). The helical axis dispersion and orientation were described using the MD and the MA (Temporiti et al., 2019; Alsultan et al., 2019). MD represents the minimum mean distance between helical axes intersections with the plane (sagittal or transversal) and their barycenter, whereas MA is the mean value of the angles between each helical axis and Mean Axis (Temporiti et al., 2019) (see Fig. 1). Data analysis was performed on eight repetition movement cycles after excluding the first and last movement to avoid changes in the angular velocity cycle (Cescon

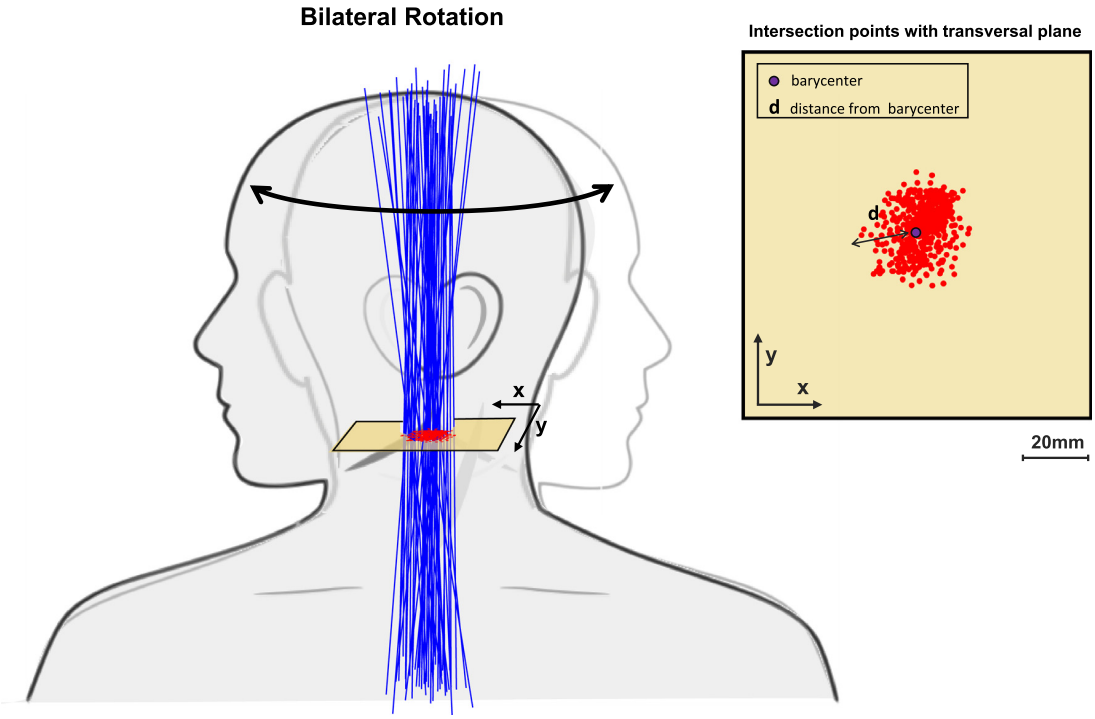

Fig. 1. Quantifying the mean distance (MD) and mean angle (MA) of the helical axis parameters. MD is the intersection points shown in red, whereas MA is the angles of axis lines shown in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

et al., 2014). The standard deviation (SD) of the mean was calculated to measure the degree of variability of neck movements across the whole movement cycle.

2.6. Procedure

Pressure pain threshold (PPT), active neck movement tasks, and maximum voluntary contractions (MVC) were performed in each of the three sessions. The eccentric exercise protocol was only performed in session one.

2.7. Pressure pain threshold (PPT)

PPT was assessed using a pressure algometer (Somedic Algometer, Sollentuna, Sweden) with a 1 cm^2 rubber tip plunger, at an application rate of 40 kPa/s at predetermined locations over the following sites: bilaterally in the suboccipital muscle region, 2 cm lateral to the spinous process of the axis (prone); bilaterally over the neck extensors at the level of C5, 1 cm lateral to the spinous process (prone); and bilaterally on the upper border of the trapezius muscle region, halfway between the midline and lateral border of the acromion (sitting). Each site was tested twice in a random order. The average of the two repetitions was considered for analysis.

2.8. Maximum voluntary contractions

The Multi-Cervical Unit (MCU; BTE Technologies, USA) was used to measure the MVC of the neck extensors. The MCU is a reliable and validated device (ICCs for maximal isometric extension strength ranges from 0.95 to 0.99 (Chiu and Lo, 2002). Participants were briefed on the procedure, seated in the MCU, and a belt was applied over their waist and shoulders. Participants performed three MVCs with standardised verbal encouragement provided. For each participant, MVC was determined as the highest force produced during three isometric contractions, each lasting five seconds (Lindstrøm et al., 2011).

2.9. Active neck movement tasks

Whilst seated on a chair in an upright posture, the participant performed repeated flexion-extension, bilateral lateral flexion and bilateral rotation at three different speeds—a natural self-selected speed, slow speed (30 beats per second [bps]) and fast speed (60 bps)—whilst keeping their eyes open. The speed of neck movement was controlled via a metronome beats mobile application. Each movement was repeated continuously 10 times at full RoM and with movement limited to 45°. To limit the movement to 45°, the participant was asked to move their head until the laser pointer attached to the helmet reached reference marks on the wall (Alsultan et al., 2019). We also examined movement variability during movements where the RoM was limited to 45°, since performing functional tasks and activities does not usually require full RoM (Bennett et al., 2002; Bible et al., 2010). Familiarisation with each neck movement task was completed a few times prior to data acquisition, after which the movements were completed in a random order.

2.10. Eccentric exercise (Session 1 only)

Following familiarisation, the participants performed eccentric contractions of their neck extensors between 45° of extension and 0° (neutral) consisting of three sets of 15 repetitions against an average load of 20% MVC. Neck extension was performed passively to a limit of 45° and then they were asked to push their head against the head brace to control the load back to a neutral position (0°). There was no time restriction for completing the contractions, and a rest time of 60 s was given after every set. Pilot testing confirmed that this protocol was sufficient to induce soreness in healthy individuals.

2.11. Statistical analysis

Mean and SD were used to describe participant demographics and MD and MA measurements, MVC measures, PPT and questionnaire responses.

Three-way repeated measures analysis of variance (ANOVA) were applied to evaluate the MD, MA and RoM for movements performed at full and 45° of motion, with time (T0, T1, T2, T3), direction of neck movement (flexion–extension, bilateral lateral flexion and bilateral rotation), and movement speed (slow, natural and fast) as factors.

Two-way repeated measures ANOVA was performed to examine PPT with time (T0, T2, T3), and location (suboccipital muscles, neck extensors, and trapezius) as factors. In addition, one-way repeated measures ANOVA were performed to test MVC and VAS, with time as the factor (T0, T1, T2, T3).

In all cases, significant differences revealed by ANOVAs were followed by Bonferroni post-hoc analyses. Outcomes are reported as mean and SD in the tables. SPSS Version 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Statistical significance was set at $P < 0.05$.

3. Results

All 32 participants completed the study. Participant demographics and descriptive data are presented in Table 1. Kinematic data were missing for 15 out of 8433 measures due to artefacts.

The participants reported mean (SD) VAS scores of 4.32 (2.67), 2.25 (2.34), and 1.54 (1.72) at T1, T2 and T3, respectively, which were all significantly ($P < 0.001$) higher compared to VAS at T0 that was 0. The VAS score at T2 and T3 were both significantly ($P < 0.005$ and $P < 0.001$) lower compared to the VAS score at T1. The mean (SD) Borg's score was 4.70 (2.56) at T1.

According to the McGill Pain Questionnaire, the most frequently selected word was "aching," chosen by 53% of participants when assessed both at T2 and at T3. The descriptions of "heavy," "tender" and "tiring-exhausting" were selected by 34%, 38% and 38% of participants at T2 and 28%, 31% and 25% at T3, respectively. The words "throbbing," "sharp," "cramping" and "grawing" were chosen by 13%, 16%, 25% and 13% of participants, respectively at T2 and 9%, 9%, 19% and 9% at T3.

The PPTs decreased significantly with time confirming the presence of eccentric exercise induced DOMS ($F = 20.442$, $P < 0.0001$) with significantly lower values for all locations at T2 ($P < 0.0001$) and T3 ($P < 0.001$) compared to T0. The MVC also depended on time ($F = 4.616$, $P < 0.01$) with a significant reduction found at T2 compared to T0 ($P < 0.01$) (see Table 2), although MVC had returned to baseline at T3.

Table 1
Participant demographics and descriptive data. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after the eccentric exercise, (T2) 24 h after and (T3) 48 h after eccentric exercise.

Characteristic	Mean (SD) [95% CI]
Age (years)	25.53 (6.33)
Height (cm)	166.60 (29.04)
Weight (Kg)	71.22 (14.41)
IPAQ	6317.95 (6272.15)
MVC (lb) T1	33.03 (12.35)
MVC T2	28.20 (10.26)
MVC T3	28.24 (10.53)
MVC T4	30.89 (12.12)
Borg T1	4.70 (2.56)
PPT Suboccipital (kPa) T0	249.55 (64.23) [226.39, 272.70]
PPT Suboccipital T2	211.47 (71.11) [185.83, 237.10]
PPT Suboccipital T3	216.38 (63.81) [193.39, 239.40]
PPT Erector spinae T0	262.47 (71.08) [236.86, 288.12]
PPT Erector spinae T2	219.33 (72.37) [193.25, 245.44]
PPT Erector spinaet T3	234.27 (70.94) [208.72, 259.88]
PPT Trapezius T0	375.82 (103.32) [338.60, 413.10]
PPT Trapezius T2	354.63 (92.95) [321.14, 388.16]
PPT Trapezius T3	324.77 (84.72) [294.25, 355.34]
VAS (0–10) T0	0.00
VAS T1	4.32 (2.67)
VAS T2	2.25 (2.34)
VAS T3	1.54 (1.72)

Abbreviations: International Physical Activity Questionnaire (IPAQ), maximum voluntary contractions (MVC), pressure pain threshold (PPT), a visual analogue scale (VAS).

3.1. Movements performed to full RoM

The mean and SD for all measures in each movement direction and at all time points are presented in Table 3 and the significant differences are highlighted in Table 4. A representative example illustrating the MA and MD measured at each time point for the task of rotation is presented in Fig. 2. A significant difference of the MD was observed over time regardless of the movement direction or speed ($F = 4.662$, $P < 0.01$). Pairwise comparisons showed significantly reduced MD (i.e. reduced movement variability) when measured at T2 compared to T0 ($P < 0.001$) and T3 ($P < 0.05$). A significant difference of the MA was also observed over time regardless of the movement direction or speed ($F = 3.573$, $P < 0.05$). The MA was significantly lower at T2 and T3 compared to the MA recorded at T1 (both $P < 0.05$). A significant difference in RoM was also identified over time ($F = 23.197$, $P < 0.0001$); pairwise comparisons showed that the RoM was significantly reduced for all movement directions at T1, T2 and T3 compared to T0 (all $P < 0.01$). Additionally, RoM was significantly lower at T1 ($P < 0.01$), T2 ($P < 0.0001$), compared to RoM measured at T3, indicating some recovery of RoM by 48 h.

3.2. Movements performed to 45° RoM

The mean and SD for all measures in each movement direction and at all points are presented in Table 5 and the significant differences are highlighted in Table 4. A significant difference ($F = 3.606$, $P < 0.05$) was observed over time for MD with pairwise comparisons demonstrating lower values of MD at T3 compared to T1 ($P < 0.05$). A significant difference ($F = 10.829$, $P < 0.0001$) was also observed over time for MA with the pairwise comparisons revealing significantly lower values of MA at T3 compared to T0, T1 and T2 (all $P < 0.0001$). Finally, RoM also differed over time ($F = 2.734$, $P < 0.05$) regardless of the speed or direction of movement with the pairwise comparisons revealing a significantly less RoM at T2 compared to T1 ($P < 0.05$).

4. Discussion

This study is the first to investigate the effect of eccentric exercise and DOMS on the variability of active cervical movements. The MVC of the neck extensors decreased 24 h post-exercise and PPT decreased at 24 and 48 h after exercise confirming the effectiveness of the eccentric exercise protocol for inducing DOMS. The key finding of this study was that eccentric exercise of the neck extensor muscles and the resultant DOMS, caused reduced neck movement variability, which was observed across all neck movement tasks, regardless of the movement direction or speed. In addition to the influence on the quality of active neck movements, the neck RoM was also affected by DOMS of the neck extensors.

Table 2
Results of the ANOVA to evaluate differences: pressure pain threshold (PPT), maximum voluntary contractions (MVC), and visual analogue scale (VAS) across time. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after the eccentric exercise, (T2) 24 h after and (T3) 48 h after eccentric exercise.

Parameters	Significance	Baseline - T0	Immediate Post - T1	24 h - T2	48 h – T3	Post hoc
PPT (kPa)	0.000	295.96 (98.65)	NA	261.82 (102.68)	258.5 (87.11)	T0 > T1, T0 > T2
MVC (lb)	0.005	33.03 (12.35)	28.2 (10.26)	28.24 (10.53)	30.89 (12.12)	T0 > T2
VAS (0–10)	0.000	0	4.32 (2.67)	2.25 (2.34)	1.54 (1.72)	T1 > T0, T2 > T0, T3 > T0, T1 > T2, T1 > T3

Table 3
Mean, standard deviation (SD) and 95% confidence interval (95% CI) of the mean distance (MD) and mean angle (MA) at full range of motion, recorded for all active neck movement tasks. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after eccentric exercise, (T2) 24 h after and (T3) 48 h after eccentric exercise.

Parameter	MD (cm)				MA (°)			
Time	T0	T1	T2	T3	T0	T1	T2	T3
Movement	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Flex/Ext natural	4.05 (0.76) [3.78, 4.38]	3.81 (0.8) [3.56, 4.18]	3.66 (0.8) [3.41, 4.02]	3.90 (0.76) [3.62, 4.21]	4.34 (0.78) [4.01, 4.53]	4.7 (0.69) [4.42, 4.95]	4.4 (0.57) [4.24, 4.66]	4.59 (0.71) [4.32, 4.85]
Flex/Ext slow	3.72 (0.97) [3.35, 4.13]	3.80 (0.84) [3.56, 4.19]	3.62 (0.95) [3.28, 4.03]	3.67 (0.73) [3.43, 3.98]	4.26 (0.67) [3.98, 4.46]	4.74 (0.75) [4.43, 4.98]	4.45 (0.53) [4.28, 4.68]	4.62 (0.85) [4.31, 4.95]
Flex/Ext fast	3.86 (0.9) [3.50, 4.20]	3.63 (0.78) [3.34, 3.93]	3.63 (0.97) [3.25, 4.01]	3.81 (0.96) [3.42, 4.16]	3.88 (0.65) [3.61, 4.08]	4.3 (0.7) [4.02, 4.56]	4.24 (0.69) [3.95, 4.45]	4.13 (0.71) [3.87, 4.38]
LatFlex natural	2.6 (0.45) [2.43, 2.77]	2.74 (0.76) [2.44, 3.04]	2.67 (0.73) [2.37, 2.94]	2.58 (0.72) [2.30, 2.86]	10.27 (2.87) [9.19, 11.42]	9.95 (3.54) [8.49, 11.27]	9.88 (4.32) [8.13, 11.43]	9.06 (2.01) [8.27, 9.85]
LatFlex slow	2.78 (0.72) [2.48, 3.04]	2.77 (0.85) [2.47, 3.12]	2.63 (0.65) [2.39, 2.89]	2.81 (0.9) [2.51, 3.20]	10.39 (4.55) [8.54, 12.11]	10.19 (3.66) [8.60, 11.42]	9.51 (2.19) [8.61, 10.32]	10.05 (2.77) [9.04, 11.16]
LatFlex fast	2.76 (0.8) [2.41, 3.03]	2.72 (0.92) [2.39, 3.11]	2.52 (0.64) [2.26, 2.77]	2.65 (0.96) [2.29, 3.04]	9.64 (3.55) [8.14, 10.85]	9.52 (3.73) [8.17, 11.12]	9.14 (2.5) [8.18, 9.90]	8.83 (2.3) [8.01, 9.78]
Rotation natural	3.06 (0.72) [2.84, 3.40]	2.93 (0.63) [2.71, 3.18]	2.94 (0.72) [2.72, 3.26]	3.02 (0.68) [2.79, 3.31]	4.78 (0.75) [4.47, 5.07]	4.99 (0.94) [4.66, 5.39]	4.71 (0.65) [4.45, 4.96]	4.82 (0.76) [4.51, 5.11]
Rotation slow	2.96 (0.78) [2.70, 3.30]	2.95 (0.67) [2.70, 3.21]	3.07 (0.82) [2.79, 3.42]	3.07 (0.74) [2.80, 3.37]	4.71 (0.75) [4.40, 5.00]	5.23 (0.91) [4.90, 5.62]	5.07 (0.84) [4.76, 5.42]	4.89 (0.88) [4.49, 5.17]
Rotation fast	3.05 (0.76) [2.80, 3.38]	2.81 (0.61) [2.61, 3.07]	2.95 (0.73) [2.70, 3.24]	2.98 (0.76) [2.72, 3.30]	4.72 (1.07) [4.33, 5.14]	4.87 (1.11) [4.47, 5.34]	4.7 (0.75) [4.46, 5.03]	4.63 (0.72) [4.33, 4.89]

Table 4
Mean and standard deviation of the mean distance (MD) and mean angle (MA), and range of motion (RoM) at full and 45° range of motion recorded, for all active neck movement tasks. The four repeated measures across time are defined as (T0) at baseline or before eccentric exercise, (T1) immediately after eccentric exercise, (T2) 24 h after and (T3) 48 h after eccentric exercise.

Parameters	RoM	T0	T1	T2	T3	Post hoc
MD (cm)	Full	3.21 (0.91)	3.13 (0.88)	3.08 (0.89)	3.17 (0.93)	T0 > T2, T2 < T3
MA (°)	Full	6.31 (3.47)	6.48 (3.25)	6.22 (2.98)	6.16 (2.69)	T1 > T2, T1 > T3
RoM (°)	Full	115.09 (28.13)	111.37 (27.04)	111.21 (27.17)	113.43 (28.4)	T0 > T1, T0 > T2, T0 > T3 , T1 < T3 , T2 < T3
MD (cm)	45°	2.40 (0.68)	2.48 (0.70)	2.42 (0.69)	2.41 (0.61)	T0 < T1, T1 > T3
MA (°)	45°	5.76 (2.71)	5.78 (2.53)	5.69 (2.37)	5.43 (2.23)	T0 > T3, T1 > T3, T2 > T3
RoM (°)	45°	81.54 (15.04)	82.55 (14.10)	81.60 (15.03)	82.01 (14.94)	T1 > T2

4.1. Eccentric exercise as a means to induce DOMS of the neck extensors

Eccentric exercise induces muscle fibre damage and as a subsequence, pain or DOMS, most likely due to the pathophysiological changes within the exercised muscle. Muscles soreness typically appears one or two days following exercise and mechanical hyperalgesia is commonly observed for the exercised muscle/s. The maximal force of the exercised muscle usually decreases immediately after the exercise and can remain 48 h after exercise due to soreness and fatigue (Doyle-Baker et al., 2018; Mense and Gerwin, 2010; Mista et al., 2019; Iguchi et al., 2008). This is the first study to use an eccentric exercise protocol of the neck muscles with the aim of inducing DOMS as an experimental neck pain model. Participants reported soreness of their neck extensor muscles both 24 and 48 h post exercise, likely due to the damage of the contractile elements and connective tissue. Following the injury of muscle fibres, phagocyte cell infiltration results in progressive necrosis of the contractile elements and inflammation, which will sensitise the intramyofibril group IV afferents (Smith, 1991; Hedayatpour and Falla, 2014). The PPTs measured over the neck region were lower both 24 and 48 h post exercise confirming local sensitisation. Additionally, the maximal force of the neck extensors decreased 24 h post exercise, likely reflecting reduced neural drive to the muscle because of an inhibitory effect mediated by nociception. These findings are consistent with the effects of eccentric exercise

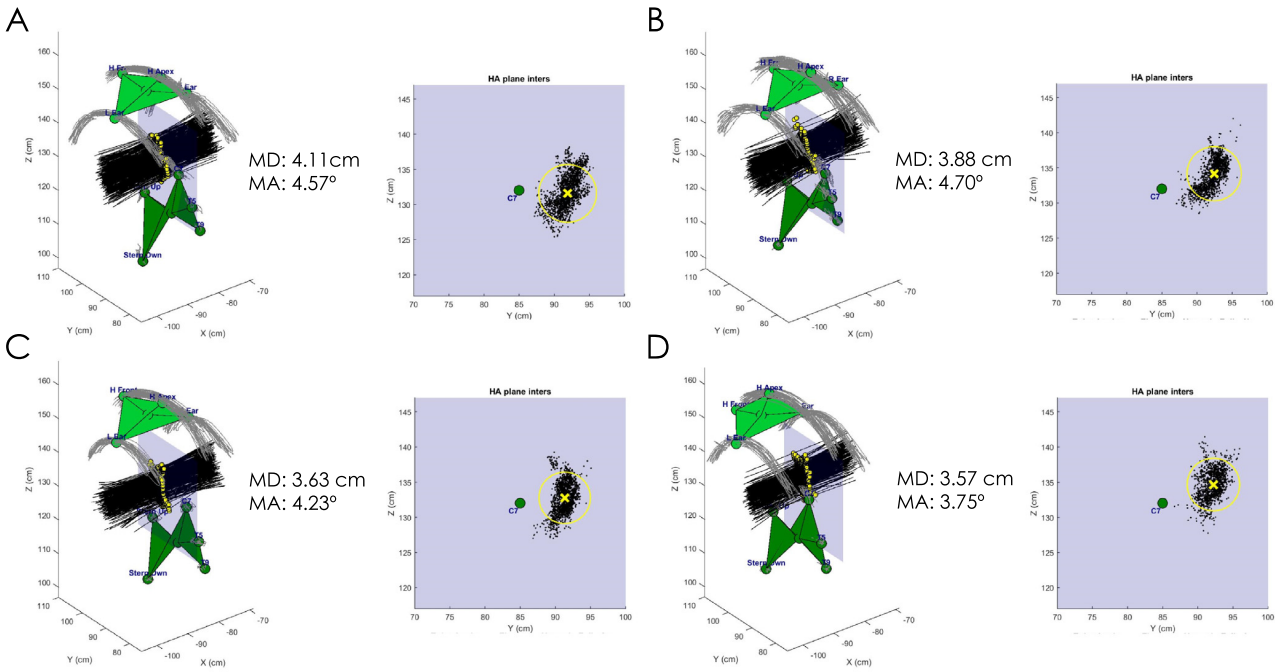

Fig. 2. Representative data obtained from a participant during flexion–extension movements performed at natural speed and full range of motion at baseline (T0) (A), immediately after eccentric exercise (T1) (B), 24 h after (T2) (C) and 48 h after eccentric exercise (T3) (D). Note the smaller mean distance (MD) for the participant particularly at T2 as compared to T0 and T3. Similarly, the mean angle (MA) is lower when measured at T2 and T3.

Table 5
Mean, standard deviation (SD) and 95% confidence interval (95% CI) of the mean distance (MD) and mean angle (MA) at 45° range of motion, recorded for all active neck movement tasks. The four repeated measures across time are defined as (time 1) at baseline or before eccentric exercise, (time 2) immediately after eccentric exercise, (time 3) 24 h after and (time 4) 48 h after eccentric exercise.

Parameter	MD (cm)				MA (°)			
Time	T0	T1	T2	T3	T0	T1	T2	T3
Movement	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]	Mean (SD) [95% CI]
Flex/Ext natural	2.99 (0.67) [2.72, 3.19]	2.85 (0.63) [2.60, 3.06]	2.85 (0.72) [2.56, 2.98]	2.75 (0.47) [2.55, 2.88]	4.38 (0.91) [4.11, 4.78]	4.53 (0.83) [4.26, 4.89]	4.24 (0.68) [3.99, 4.52]	4.21 (0.70) [3.99, 4.52]
Flex/Ext slow	2.8 (0.61) [2.56, 2.97]	2.92 (0.65) [2.64, 3.13]	2.85 (0.68) [2.57, 3.01]	2.73 (0.48) [2.54, 2.90]	4.28 (0.95) [3.96, 4.68]	4.55 (0.95) [4.27, 4.97]	4.45 (0.64) [4.23, 4.72]	4.32 (0.72) [4.10, 4.64]
Flex/Ext fast	3.18 (0.74) [2.88, 3.39]	3.05 (0.72) [2.75, 3.21]	3.01 (0.91) [2.67, 3.06]	3.06 (0.6) [2.82, 3.23]	3.93 (0.69) [3.69, 4.22]	4.04 (0.72) [3.80, 4.35]	4.1 (0.7) [3.86, 4.39]	3.89 (0.64) [3.65, 4.15]
LatFlex natural	2.25 (0.43) [2.09, 2.42]	2.46 (0.59) [2.23, 2.66]	2.27 (0.54) [2.07, 2.48]	2.22 (0.54) [2.01, 2.40]	9.25 (2.63) [8.21, 9.42]	9.11 (1.56) [8.49, 9.68]	8.59 (1.93) [7.80, 9.28]	8.07 (1.76) [7.30, 8.43]
LatFlex slow	2.19 (0.55) [2.05, 2.42]	2.38 (0.65) [2.17, 2.64]	2.28 (0.64) [2.06, 2.54]	2.28 (0.53) [2.12, 2.50]	8.68 (1.7) [8.07, 9.35]	8.68 (1.72) [8.16, 9.40]	8.55 (1.41) [8.02, 9.08]	8.23 (1.31) [7.75, 8.74]
LatFlex fast	2.2 (0.47) [2.02, 2.38]	2.4 (0.75) [2.13, 2.50]	2.3 (0.5) [2.12, 2.50]	2.28 (0.63) [2.03, 2.44]	9.15 (2.08) [8.20, 9.52]	8.72 (2.21) [7.72, 9.22]	8.66 (1.83) [7.85, 9.19]	8.03 (1.92) [7.24, 8.38]
Rotation natural	1.97 (0.41) [1.81, 2.12]	2.09 (0.46) [1.91, 2.26]	2.03 (0.43) [1.87, 2.20]	2.07 (0.42) [1.91, 2.23]	4.06 (0.83) [3.78, 4.40]	4.25 (1.02) [3.87, 4.64]	4.15 (0.98) [3.80, 4.54]	4.00 (0.95) [3.66, 4.38]
Rotation slow	1.96 (0.39) [1.81, 2.11]	2.06 (0.49) [1.86, 2.24]	2.08 (0.37) [1.93, 2.21]	2.14 (0.47) [1.96, 2.32]	4.02 (0.81) [3.75, 4.36]	4.19 (0.96) [3.87, 4.60]	4.35 (0.87) [4.08, 4.73]	4.28 (0.98) [3.96, 4.70]
Rotation fast	2.02 (0.4) [1.85, 2.15]	2.1 (0.48) [1.90, 2.27]	2.11 (0.46) [1.92, 2.27]	2.11 (0.51) [1.89, 2.27]	4.09 (0.79) [3.83, 4.42]	3.99 (1.17) [3.60, 4.48]	4.18 (0.85) [3.85, 4.51]	3.91 (0.85) [3.60, 4.25]

of different muscle groups including the elbow flexors (Lau et al., 2013) and knee extensors (Hedayatpour et al., 2008; Hedayatpour and Falla, 2014), confirming the appropriateness of our model to induce DOMS.

4.2. Variability of active neck movements

Earlier work observed reduced movement variability in people with chronic neck pain as compared to healthy individuals (Alsultan et al., 2019). Additionally, reduced RoM of the neck is a common finding in people with chronic or acute neck pain (Woodhouse and Vasseljen, 2008; Puglisi et al., 2004; Fernández-Pérez et al., 2012; Sterling et al., 2003). Our findings uniquely demonstrate that both the quality and quantity of neck movement can change rapidly in the presence of neck muscle fatigue and soreness. Specifically, we observed reduced movement variability 24 h and 48 h post-eccentric exercise revealed through measures of the MD and MA, regardless of the movement direction or speed. Notably, the observed MA changes during the active neck movements clearly exceed the standard error of the measurement as

well as the minimal detectable change reported in a recent study (Barbero et al., 2017). This indicates good response stability, and indicates that the changes could be related to the participant's condition. Likewise, RoM was significantly reduced post-eccentric exercise when DOMS was present. Even though there may be multiple mechanisms contributing to impaired movement control in people with acute neck pain, the current findings suggest soreness and muscle fatigue can induce rapid changes in both the quality and quantity of neck movement.

Importantly, the MD and MA values recorded in this study had approximately similar means, regardless of the movement direction or speed, as compared to a previous study examining active neck movements in people with and without chronic neck pain (Alsultan et al., 2019). The mean difference of the MD varied up to 0.24 cm between the healthy participants and those with chronic neck pain in a previous study (Alsultan et al., 2019). In the current study, the mean difference of the MD between baseline and immediately after eccentric exercise ranged between 0.08 and 0.21 cm and when measured at 24 h and 48 h post exercise when soreness was present, the mean of difference of MD values relative to baseline ranged between 0.02 and 0.24 cm. Similarly, in the study examining active neck movements in people with and without chronic neck pain (Alsultan et al., 2019), the mean difference of the MA varied up to 1.01° between the healthy participants and those with chronic neck pain (Alsultan et al., 2019). In the current study, the mean difference of the MA between baseline and immediately after eccentric exercise was up to 0.43° and when measured at 24 h and 48 h post exercise when soreness was present, the mean of difference of MA values relative to baseline was up to 1.18°. A similar reduction of the helical axis parameters in people with chronic neck pain and following eccentric exercise induced neck muscle soreness is relevant when attempting to understand factors underlying impaired movement quality in people with pain. Although speculative, the reduced variability of neck movement may reflect a strategy to reduce or avoid pain during repeated neck movement (Arendt-Nielsen and Falla, 2009). Future studies should investigate neck muscle activation concurrently with measures of neck movement quality.

4.3. Methodological considerations

The participant sample in this study was a convenience sample, which is likely to reduce the generalisability of results. In addition, we used a 3D motion capture system to collect data on the quality and quantity of movement, which might not be accessible for use in clinics. Nevertheless, both the quality and quantity of movement could be assessed using portable virtual reality based devices and 3D motion–tracking systems, which have been validated (Kiper et al., 2020).

5. Conclusion

Using a novel approach to induce acute neck pain, changes in neck movement variability were observed immediately after, 24 h after and 48 h after eccentric exercise, indicating that the presence of fatigue and DOMS affects the quality of neck movement. These findings indicate the importance of examining the quality of neck movement in addition to the quantity of movement in order to better characterise movement dysfunction in people with painful neck disorders, including during the acute stage.

Declaration of Competing Interest

The researchers report no conflict of interest regarding this study.

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Appendix 4 – Ethical Review, Ethical Amendments, Consent forms and Patient Information Sheets for *Chapter Two* and *Chapter Three*

School of Sport, Exercise & Rehabilitation Sciences

Safety and Ethics Subcommittee

Investigation of Human Subjects

Application Form

2016/17

Note: Studies involving NHS patients/staff/facilities, participants with mental incapacity, storage of human tissue, clinical trials, etc are very likely to require ethical approval via National Research Ethics Service (NRES) through submission of an IRAS NHS REC form. Also, trials of drugs or nutritional supplements, even if carried out on normal subjects, may count as "Clinical Trials" from the point of view of the University's insurance and may therefore also need ethical approval through NRES. If in any doubt as to whether such approval is needed, it is the Principal Investigator's responsibility to check this with the University Ethical Review Committee (see https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-of-Research.aspx).

Please submit the completed application electronically to both the ***relevant RTG ethics lead*** and ***Andy Benham*** ( )

Has a similar study protocol already been approved by the School's Safety and Ethics Subcommittee (please tick relevant box)?

Yes X

☐
No

If yes then please give:

Project Identification Number: **CM06/03/17-1**

Related Document Versions (e.g., Application V4, Questionnaire V3 etc): Main document + Participant Information sheet (control + whiplash subjects) + Recruitment poster (control + whiplash subjects)

Principal Investigator: Alessandro M De Nunzio

Date of Approval: 31.03.17

Please clearly indicate in which way(s) the present protocol differs from that which was approved previously.

Payment to participants

This section has changed as we will provide a fixed amount as reimbursement for participation of 15£.

Inclusion Criteria

Subjects suffering from chronic neck pain (neck pain intensity > 3 during the last 4 weeks, on a Numerical rating scale (NRS) with 2 anchor points, 0 = no pain and 10 = worst pain imaginable), with a history of chronic neck pain longer than 3 months.

Pre-Application Checklist

The following checklist should be worked through by the applicant before the application is submitted. By submitting the application you are confirming this has been completed.

- ✓ The application and all accompanying documents have all been thoroughly checked and proof read by the applicant (i.e., The Principle Investigator)
- ✓ The study detailed in the application is ethically sound to the best of the applicant's knowledge
- ✓ Copies of all consent forms referred to in the application are attached
- ✓ Copies of all information sheets referred to in the application are attached
- ✓ Copies of all other documentation (e.g., interview scripts, questionnaires) referred to in the application are attached
- ✓ Specific details of opportunities for participant withdrawal (including process, deadline and any implications for compensation) are included in the application, consent form/s and information sheet/s
- ✓ Details relating to participant autonomy/confidentiality are clear and consistent in both the application and information sheet/s
- ✓ All relevant University of Birmingham data protection procedures (see (http://www.birmingham.ac.uk/Documents/university/legal/data-prot-policy.pdf) will be followed and relevant aspects (e.g., data storage procedures and length of storage) are included in the application and consent form/s
- ✓ Sufficient detail of relevant background literature is included so the reviewer can understand the primary academic rationale for the proposed study
- ✓ All relevant inclusion and exclusion criteria for the proposed sample are included in the application and information sheet/s
- ✓ The application is not for a PhD or MRes student led study
- ✓ A completed Hazard and Risk Assessment Summary form is attached (it is the applicant's responsibility to ensure Andy Benham approves the Health and Safety aspects of the study before the study commences)
- ✓ The approximate time involvement and location of data collection/s for all participants are included in the application and information sheet

Main Application

1. Title of Project

Evaluation of trunk and neck muscle control during postural and walking activities in people with chronic whiplash.

2. Investigators

Using the table below, please list all involved including those from outside the School: also indicate their qualifications and roles in the project, either here or when outlining the protocol (5 & 6 below).

Name	Qualification	Role	Institution
Ross Whalley	MSc Physio (pre-reg) student	Investigator	University of Birmingham
Syed Ali Ahmad	MSc Physio (pre-reg) student	Investigator	University of Birmingham
Feras Alsultan	PhD student	Investigator	University of Birmingham
Nicola Heneghan	PhD	Investigator	University of Birmingham
Deborah Falla	PhD	Investigator	University of Birmingham
Alessandro M De Nunzio	PhD	Project Supervisor	University of Birmingham

3. Purpose of the Research

Provide sufficient detail so that the Subcommittee can form an opinion as to the "value" of the project. Although the length of this section will depend on the specific nature of the study, include sufficient background (including relevant literature) to make the rationale for the study clear to the reviewer. Include all research questions/hypotheses as appropriate.

Whiplash Associated Disorder (WAD), a disorder caused by acceleration and deceleration mechanism of energy transferred to the neck, after e.g. traffic collisions, affects many people and its cumulative incidence has increased dramatically during the last years (Holm et al. 2009). A 1983–1984 hospital-based study from the UK (including patients seeing hospital healthcare for evaluation of WAD symptoms) reported an annual incidence of WAD of 27.8 per 100,000 inhabitants (Otremski et al. 1989). Following injury, individuals experience a range of clinical manifestations including neck pain, fatigue, nausea, low self-reported physical and mental health, cognitive problems and pain in multiple body parts (Johansson et al. 2015). WAD can be classified as grades 0-IV, depending on the severity of symptoms (Sterling 2004). Patients with WADII represent the most common group of patients (93.4%) experiencing neck pain along with stiffness or tenderness, and musculoskeletal signs (Sterling 2004).

Previous studies have identified risk factors for poor prognosis (Williamson et al. 2015), however we still do not know exactly why disability and pain persist beyond the normal tissue healing times for all patients. With 40–60% patients progressing to experience a chronic whiplash associated disorder (CWAD) and estimated

costs of €10 billion in Europe associated with management and time off work (Eck et al. 2001; Lovell and Galasko 2002) further research is needed to better understand the impact of this trauma on motor abilities during functional tasks, focusing our interest not only on the neck region but on the entire spine. This may perhaps explain why there is inconclusive evidence for the effectiveness of physiotherapy management for WAD, where interventions targeted a primary complaint of neck pain (Rushton et al. 2011). Although previous studies have focused on the primary complaint of neck pain (Bortsov et al. 2014), symptoms may also include stiffness (Sterling 2004) and pain in other regions including the head, upper and lower limbs,chest and abdomen (Hincapie et al. 2010).

While previous studies have estimated that the mid-spine contributes up to 33% and 21% of the movement occurring during neck flexion and rotation respectively (Tsang et al. 2013) little is known about the impact of WAD on the thoracic and lumbar spine (Heneghan and Rushton 2016) and how possibly impaired stability at the spinal level could influence functional motor tasks, e.g. upright posture and walking. The upper body accounts for a large percentage of the entire body mass. Therefore, trunk yaw and roll motion control could be considered fundamental skills to execute basic motor tasks of daily living.

The main objective of this project is to evaluate, at the kinematic, kinetic and muscular level, the biomechanical impairment induced in people with WADII during different tasks mimicking daily life activities and mainly involving control of posture during dynamic conditions and walking along rectilinear and curvilinear directions. The secondary objective of this study is to evaluate possible correlation between trunk biomechanical instability and reported dizziness, which represents a common main symptom in people with WAD (Oka et al. 2015). A Multifactorial evaluation of risk of falls will be executed to study the correlation of fall projected incidence and WAD as a higher risk of fall could be envisaged where poorer trunk and neck control is present (Granacher et al. 2013).

Finally, knowledge of trunk impairment in controlling functional motor tasks may be used to inform future clinical trials of novel interventions targeting the thoracic spine in WAD subjects.

4. Sample Characteristics

Describe the nature of the target sample (age, sex, level of fitness, etc.), including the estimated sample size, methods of recruitment and the inclusion/exclusion criteria to be applied.

Participants with WAD (40 subjects) and asymptomatic Control subjects (40 age and gender matched subjects) will be recruited from the population of staff and students at the University of Birmingham and data collection will take place in a laboratory in the School of Sport, Exercise and Rehabilitation Sciences.

Inclusion criteria

WAD Group: Chronic WAD Grade II based on Quebec Task Force Classification (neck complain, reduced range of movement and point tenderness) (>6 months), and subjects with a history of more than 3 months of suffering from chronic neck pain, with neck pain intensity > 3 during the last 4 weeks (evaluated using a Numerical rating scale (NRS) with 2 anchor points, 0 = no pain and 10 = worst pain imaginable), can speak English.

- **Control Group:** no history of a neck injury, no history of neck pain in the last 2 years that warranted evaluation from a health care practitioner and can speak English.

Exclusion criteria

WAD Group:

- Currently receiving active management, e.g. physiotherapy or ongoing care by a GP, for a neck or spinal complaint.
- Neck injury that resulted in a spinal fracture.
- Previous spinal surgery.
- Rheumatologic condition e.g. ankylosing spondylitis.
- Current or chronic respiratory condition.
- Have a compensation claim ongoing as part of an injury.

Control Group:

- Current or chronic respiratory condition.
- Have a compensation claim ongoing as part of an injury.

5. Design of the Study

Outline the research design to be adopted in the proposed study, including the overall duration of the project and the time over which individual participants will be involved. You should also specify where the study will take place.

An observational case-control study will be conducted in line with guidelines and reported in line with STROBE (von Elm et al. 2014).

Following screening for eligibility participants will have a number of measurements taken by the Investigator during a single visit assessment. It is estimated that the complete assessment will take no more than 90 minutes.

6. Specific Procedures

Please identify all specific procedures that will be used in the study. Where these are not covered by the School Standard Operating Procedures, this should be explicitly stated and a full description given of any equipment involved, how it will be used, and any discomfort participants may experience.

All the measurements will be conducted in the human movement laboratory (room G64) of the School of Sport, Exercise and Rehabilitation Sciences.

Participants will attend a single laboratory session. All measurements will be done as follows:

Active neck movements

Whilst seated, all participants will be instructed to perform the following active movements of the cervical spine with their eyes open: axial rotation, flexion/extension and lateral bending. Each single movement will be executed reaching full range and repeated 10 times, which will constitute a movement cycle. Movement cycles

will be performed at a natural, slow (30 bpm) and fast (60bpm) speed. These movements will then be repeated with the eyes closed. The participants will be instructed to maintain contact between their spine and the back of the chair, to avoid shoulder movements. First, each movement will be performed a few times to familiarize the participants with the requested tasks.

Postural control in normal and challenged conditions

Postural assessment will be performed using two Force Platforms (BTS Bioengineering, Italy) embedded in the floor and positioned at floor level to avoid vivid edges. The quiet upright posture assessment will be performed in order to detect the instant position of the Center of Pressure (CoP). Participants will be asked to stand barefoot, for 30 seconds, on the force platform with arms at their sides. In order to ensure accuracy and reiteration across trials, foot positioning will be marked on the platform. During the challenged condition trials the participants:

1. will be asked to lean forward or backward as far as possible. Inclinations will be accomplished without lifting toes or heels and within minimal bending at the hip or knees, and keeping the trunk as straight as possible.

To assure safety, an investigator will stand close to the participant preventing any possible fall, which in any case would be very unlikely.

Eyes-open (EO), and eyes-closed (EC) conditions will be recorded, and six consecutive trials (Pinsault and Vuillerme 2009) (3 EO, 3 EC randomly assigned) will be collected. In order to avoid possible fatigue, a 1-minute rest will be given between trials.

The CoP displacement will be analysed off-line from the unfiltered platform signal by using two different parameterisations techniques (Baratto et al. 2002): i) global parameterisation which numerically expresses the overall size of the sway patterns, in time and frequency domains; and ii) structural parameterisation which identifies subunits of posturographic data related to the underlying motor control process.

Head rotation during walking & Walking along curvilinear path

The participants will undergo a kinematic evaluation of walking with an infrared camera based optoelectronic system (BTS Bioengineering, Italy). Participants, starting with their feet on the force platforms, will be asked:

1. to walk barefoot at their usual cadence, along a 6-m rectilinear walkway and moving the head along the vertical axis (rotation) of 45° on each side. The timing of the movements will be fixed using a metronome.
2. making a continuous turn, following a curvilinear path with 100 cm radius of gyration and walk back to the starting point.

To assure safety, an investigator will stand close to the participant preventing any possible fall, which in any case would be very unlikely.

A set of at least three repetitions will be acquired. A 2 minutes rest between walking trials will be given to avoid participant exhaustion.

Anthropometric measurements will be taken which include the participant's height, weight and leg length. Data used for the estimation of the joint center locations will be collected, i.e. the knee and ankle widths (as seen in the coronal plane of the limb), the distance between right and left pelvic anterior superior iliac spine (ASIS) and the vertical distance in the sagittal plane of the supine participant between ASIS and the greater trochanter (with the femur rotated such that the greater trochanter is oriented as lateral as possible).

The optoelectronic system consists of 8 infrared cameras (100 Hz sampling rate) that track the 3D motion of passive retroreflective markers. All data will be acquired using BTS SMART Capture software and saved to disk for off-line analysis.

The retroreflective 22 marker set used in the lab will be placed according to the protocol described in Davis et al. (Davis et al. 1991).

Electromyographic (EMG) assessment

Surface EMG measurements will be acquired, synchronised with kinematic and kinetic (force) data. Surface electrodes for EMG measurements will be located and placed on the participant following a standard guideline provided by the SENIAM project (www.seniam.org). The SENIAM (Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles) is a concerted European action in the Biomedical Health and Research Program (BIOMED II) of the European Union.

Bipolar Ag-AgCl surface electrodes will be used to record EMG bilaterally from:

- Erector Spinae (ES),

- Sternocleidomastoid (Ster),

- Splenius capitis (SpC)

A completely wireless EMG acquisition system will be used (BTS Bioengineering, Italy). Each skin site will be cleaned with slightly abrasive paste (NuPrep) before electrode placement (Perotto 1994; Hermens et al. 1999). All data will be acquired at 1,000 Hz using BTS EMG Analyser software and saved to disk for off-line analysis.

Biomechanics data reduction and analysis

Synchronised kinematics and EMG acquisition and data processing will be performed using Analyser software (BTS S.p.a.) and custom-written routines in LabView National Instruments software. Correlations between kinematics (head and trunk movements), kinetics (CoP movement and force distribution), EMG and dizziness, pain, multifactorial fall risk will be assessed.

Kinematics

After the walk is complete and all camera information is collected, the two-dimensional coordinates of the centroid of each marker image will be determined for each frame of optoelectronic camera data. Three-dimensional marker coordinates will be computed stereometrically from the two-dimensional camera data. The instantaneous orientation of an orthogonal, marker-based, embedded coordinate system will be determined for the neck, trunk and pelvis segments. Three-dimensional body segments rotation angles will be calculated from the embedded coordinate system information.

EMG

The EMG signals will be off-line band-pass filtered (fourth-order zero-lag Butterworth digital filter, bandwidth 20 – 400 Hz) to attenuate DC offset, motion artefacts, and high-frequency noise (Hermens et al. 1999). The filtered signals will be full-wave rectified and low-pass filtered (fourth-order zero-lag Butterworth digital filter, cut-off frequency 10 Hz) to obtain the muscle activation patterns. To facilitate comparisons between participants and among different walking speeds, the EMG from each muscle will be normalised to its peak value from self-selected walking (Clark et al. 2010).

Healthy Controls
Questionnaire data as described below will be obtained from the controls:

- International Physical Activity Questionnaires (IPAQ) to measure physical activity of participants (Booth 2000)

WAD participants
Questionnaire data as described below will be obtained from the participants:

- Numerical rating scale (NRS) of average, worst and least neck pain intensity over the last 4 weeks ((0–10, 0 = no pain and 10 = worst pain imaginable))
- International Physical Activity Questionnaires (IPAQ) to measure physical activity of participants (Booth 2000)
- Neck Disability Index (Vernon and Mior 1991; MacDermid et al. 2009)
- Whiplash Disability Questionnaire (Pinfold et al. 2004)
- Self-reported dizziness intensity at rest and during movement or activity measured with NRS (0–10 = no symptoms and 10 = worst symptoms) (Carlsson 1983; Kammerlind et al. 2005).
- Self-reported dizziness with the Dizziness Handicap Inventory (Jacobson and Newman 1990)

Multifactorial fall risk assessment will be realised using the following tools:

- Timed Up and Go test (TUG) (Okubo et al. 2016)
- Activities-specific Balance Confidence (ABC) Scale (Lajoie and Gallagher 2004)
- Tinetti Falls Efficacy Scale as measure of fear of falling (Tinetti et al. 1990; Hauer et al. 2010).

7. Risk Assessment

Please specify the type and level of risk (please tick as appropriate):

Level and type of risk	Relevant (Yes/No)
Normal hazards of laboratory or field work that are covered by the School Code of Practice, together with any local rules that have been approved by the Head of School	Yes
Special physical hazards arising, for instance, from radiation, high voltage equipment, ultrasonics, lasers etc.	No
Hazards of fire and/or explosion	No
Toxic hazards arising, for example, from known toxic or carcinogenic compounds.	No
Biohazards arising from viruses, micro-organisms, animals or human tissue or the manipulation of genetic material.	No

If the risks come under any other than the first category in the above table, please identify the possible risks to health, the measures taken to minimise these risks and the procedures to be adopted in the event of a mishap in the space below.

Hazard and Risk Assessment Summary provided as a separate file.

8. Drugs and Diet

Are any drugs to be administered or will the diet be modified?

N/A

9. Finance

Provide details of any outside sponsorship, either Research Council, charity or commercial organisation. If the study has been sponsored by an outside body have arrangements for insurance liability been discussed and agreed with the University's Legal and Insurance departments?

N/A

10. Payment to participants

Detail all payments (or other inducements) to be made to subjects. Distinguish between reimbursement of expenses and payments for participation.

A fixed payment of 15£ will be provided to participants as reimbursement for the participation to the study.

11. Withdrawal

Include details of when the deadline for participant withdrawal will be, how this will be communicated to participants, and if withdrawal has any implications for any payments indicated in section 10.

Participants will be offered the right to withdraw at any time up to 2 weeks following data collection without giving reason. This will be included within the participant information sheet and consent form. They will be advised their data will be used as part of the analysis.

12. Participant Information Sheet

Include a copy of the Information Sheet to be given to subjects when they are first approached and any further information together with the feedback to be given to the subjects at the end of the study.

Provided as a separate file.

13. Participant Consent form

Include a copy of the consent form to be signed by subjects before any investigation begins.

Provided as a separate file.

14. Planned Start Date: 13/03/2017

15. End Date: 12/03/2018

I declare that the questions above have been ***answered truthfully*** and to the ***best of my knowledge*** and belief, and that ***I take full responsibility*** for these responses. I undertake to ***observe ethical principles throughout the research*** project and to report any changes that affect the ethics of the project to the School Ethical Review Committee for review. ***I have read and undertake to abide by*** the University's Code of Practice for Research (http://www.birmingham.ac.uk/Documents/university/legal/research.pdf).

Signed: 

Date: 16/05/2017

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UNIVERSITY OF BIRMINGHAM

School of Sport and Exercise Sciences

MEMORANDUM

To: Dr Alessandro De Nunzio

From: Dr Craig McAllister

Chair, School Ethics/Health and Safety Committee

Date: 25.05.17

CM06/03/17-1 Evaluation of trunk and neck muscle control during postural and walking activities in people with chronic whiplash

The School Ethics/Health and Safety Committee have reviewed the amendment to this application and hereby grant full ethical approval for your study.

The University of Birmingham
School of Sport, Exercise and Rehabilitation Sciences

Participant Identification number:

CONSENT FORM

Title of Project:

Evaluation of trunk and neck muscle control during postural and walking activities in people with chronic neck pain.

Name of Researchers: Ross Whalley, Syed Ali Ahmad, Feras Alsultan, Nicola Heneghan, Deborah Falla, Alessandro M De Nunzio

Please initial box

1. I confirm that I have **read** and **understand** the information sheet for this study ☐
2. I have had the opportunity to ask any questions and that my questions have been answered to my satisfaction. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☐
4. I am aware that my personal data will be processed for the purposes detailed above, in accordance with the Data Protection Act 1998. ☐
5. I agree to take part in the above study ☐

_____	_____	
Name of Participant	Date	Signature
_____	_____	
Name of Researcher	Date	Signature

(Copies of consent for: participant and researcher)

All information collected will be stored in accordance with the Data Protection Act 1998.

The University of Birmingham

School of Sport, Exercise and Rehabilitation Sciences

Participant Information Form

Study title

Evaluation of trunk and neck muscle control during postural and walking activities in people with chronic whiplash.

Investigators: Ross Whalley, Syed Ali Ahmad, Feras Alsultan, Nicola Heneghan, Deborah Falla, Alessandro M De Nunzio

1. Invitation

You are being invited to take part in a research study. Before you decide to participant it is important you understand why the research is being done and what it will involve. Please take time to read the following information sheet carefully and discuss it with the researcher or others if you wish.

2. What is the purpose of the study?

Chronic neck pain and whiplash associated disorders (WAD) may follow road traffic accidents, fall and sporting injuries. Individuals often complain of neck and back pain, with symptoms (discomfort and stiffness) often lasting longer than the usual soft tissue healing time. Whilst Physiotherapy is offered to some individuals following a WAD, the treatments often target symptoms in the neck and arms. Research suggests individuals experience symptoms in other parts of the spine, which suggests that the impact of WAD goes beyond the neck, including the mid-spine; a region which has received little research attention. Despite this, there is a small body of evidence that has identified evidence of dysfunction in the mid-spine, such as changes in the muscles. However to date no research has been done to investigate mid-spine posture and mobility following WAD, despite extensive evidence of these changes in the neck. With the mid-spine contributing to posture and movement occurring in the neck this research could inform future studies of interventions targeting the mid-spine in individuals following WAD.

3. Why have I been chosen?

You have been chosen because we understand that you, as healthy and physically active subject could represent a normal reference in this study. The only inclusion criteria, to take part to the study is the absence of history of a neck sprain.

4. Do I have to take part?

You are free to decide whether you participate or not. You will be given an information sheet to keep, and you will be asked to complete a brief screening questionnaire and answer some questions. Should you meet the inclusion criteria at that stage, you will be invited to sign a consent form before taking part in the study. If you agree to take part you are free to withdraw at any time up to 2 weeks following data collection and without giving a reason. Any decision to withdraw will not in any way affect any future care with the health service. If you withdraw from the study we will use the data collected up to your withdrawal.

5. What do I have to do?

You will be asked to visit the laboratory in the School of Sport, Exercise and Rehabilitation Sciences for approximately 90minutes. During this time you will be asked to do the following

- Complete a brief screening and questionnaires
- Perform a range of simple motor tasks e.g. standing still, rotating your head, walking, to measure your movement of your spine and activity of your spinal muscles. Light-weight wireless sensors (5 grams) will be placed over muscles and small plastic spheres (passive markers) placed on bony landmarks, on your head, hip and trunk. This will allow us to measure your neck and mid-spine movements.

During the test you should wear socks (no shoes), shorts, and a vest. You can request to have an investigator of your gender for positioning markers and sensors. The tests will be completely safe as there will be always an investigator close to you to avoid any remote possibility to experience an undesired event like a fall. No possibility of induced fatigue, pain or other postural problems is envisaged. However, in the remove case of feeling fatigued or slightly dizzy you should just report these feelings to your investigator which will immediately stop the evaluation and provide you with the necessary help.

6. Will my taking part in this study be kept confidential?

All information collected on you will be kept strictly confidential. Personal information will be retained, but only available to the researchers using password protected files. Data will be kept for 10 years in accordance with the University Regulations. All data for presentation will be anonymised and aggregated, so your identity will not be revealed in any way.

7. What will happen to the results of the research study?

The findings from this study will be presented will be shared with other researchers in the form of presentations and scientific papers as appropriate. These will be used to help inform the development of new approaches for managing individuals who have previously experienced a WAD.

8. Who is organising and funding the research?

The study has been designed and organised by Dr Alessandro M De Nunzio and supported by investigators from the School of Sport, Exercise and Rehabilitation Sciences. No funding has been given towards this study.

9. Reward

Participants will be reimbursed with a fixed amount of £ 10 for participating in the experiment.

10. Contact for further information

Investigators:

Ross Whalley, [redacted]

Syed Ali Ahmad, [redacted]

Feras Alsultan, [redacted]

Dr Nicola Heneghan, n.heneghan@bham.ac.uk

Professor Deborah Falla, d.falla@bham.ac.uk

Dr Alessandro Marco De Nunzio, [redacted]

Thank you for taking time to read this and considering taking part in the study.

The University of Birmingham

School of Sport, Exercise and Rehabilitation Sciences

Participant Information Form

Study title

Evaluation of trunk and neck muscle control during postural and walking activities in people with chronic whiplash.

Investigators: Ross Whalley, Syed Ali Ahmad, Feras Alsultan, Nicola Heneghan, Deborah Falla, Alessandro M De Nunzio

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You are being invited to take part in a research study. Before you decide to participant it is important you understand why the research is being done and what it will involve. Please take time to read the following information sheet carefully and discuss it with the researcher or others if you wish.

11. What is the purpose of the study?

Chronic neck pain and whiplash associated disorders (WAD) may follow road traffic accidents, fall and sporting injuries. Individuals often complain of neck and back pain, with symptoms (discomfort and stiffness) often lasting longer than the usual soft tissue healing time. Whilst Physiotherapy is offered to some individuals following a WAD, the treatments often target symptoms in the neck and arms. Research suggests individuals experience symptoms in other parts of the spine, which suggests that the impact of WAD goes beyond the neck, including the mid-spine; a region which has received little research attention. Despite this, there is a small body of evidence that has identified evidence of dysfunction in the mid-spine, such as changes in the muscles. However to date no research has been done to investigate mid-spine posture and mobility following WAD, despite extensive evidence of these changes in the neck. With the mid-spine contributing to posture and movement occurring in the neck this research could inform future studies of interventions targeting the mid-spine in individuals following WAD.

12. Why have I been chosen?

You have been chosen because we understand you have previously experienced a neck sprain (neck complaint, reduced range of movement and point tenderness) although are not currently receiving active care e.g. physiotherapy. Other exclusion criteria include, neck injury that resulted in a spinal fracture; previous spinal surgery; rheumatologic condition e.g. Ankylosing spondylitis; current or chronic respiratory condition or have a compensation claim ongoing as part of an injury

13. Do I have to take part?

You are free to decide whether you participate or not. You will be given an information sheet to keep, and you will be asked to complete a brief screening questionnaire and answer some questions. Should you meet the inclusion criteria at that stage, you will be invited to sign a consent form before taking part in the study. If you agree to take part you are free to withdraw at any time up to 2 weeks following data collection and without giving a reason. Any decision to withdraw will not in any way affect any future care with the health service. If you withdraw from the study we will use the data collected up to your withdrawal.

14. What do I have to do?

You will be asked to visit the laboratory in the School of Sport, Exercise and Rehabilitation Sciences for approximately 90minutes. During this time you will be asked to do the following

- Complete a brief screening and questionnaires
- Perform a range of simple motor tasks e.g. standing still, rotating your head, walking, to measure movement of your spine and activity of your spinal muscles. Light-weight wireless sensors (5 grams) will be placed over muscles and small plastic spheres (passive markers) placed on bony landmarks, on your head, hip and trunk. This will allow us to measure your neck and mid-spine movements.

During the test you should wear socks (no shoes), shorts, and a vest. You can request to have an investigator of your gender for positioning markers and sensors. The tests will be completely safe as there will be always an investigator close to you to avoid any remote possibility to experience an undesired event like a fall. No possibility of induced fatigue, pain or other postural problems is envisaged. However, in the remove case of feeling fatigued or slightly dizzy you should just report these feelings to your investigator which will immediately stop the evaluation and provide you with the necessary help.

15. Will my taking part in this study be kept confidential?

All information collected on you will be kept strictly confidential. Personal information will be retained, but only available to the researchers using password protected files. Data will be kept for 10 years in accordance with the University Regulations. All data for presentation will be anonymised and aggregated, so your identity will not be revealed in any way.

16. What will happen to the results of the research study?

The findings from this study will be presented will be shared with other researchers in the form of presentations and scientific papers as appropriate. These will be used to help inform the development of new approaches for managing individuals who have previously experienced a WAD.

17. Who is organising and funding the research?

The study has been designed and organised by Dr Alessandro M De Nunzio and supported by investigators from the School of Sport, Exercise and Rehabilitation Sciences. No funding has been given towards this study.

18. Reward

Participants will be reimbursed with a fixed amount of £ 15 for participating in the experiment.

10. Contact for further information

Investigators:

Ross Whalley,

Syed Ali Ahmad,

Feras Alsultan,

Dr Nicola Heneghan, n.heneghan@bham.ac.uk

Professor Deborah Falla, d.falla@bham.ac.uk

Dr Alessandro Marco De Nunzio,

Thank you for taking time to read this and considering taking part in the study.

Appendix 5 – STROBE Checklist for *Chapter Two*

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

Chapter Two	**Item No**	**Recommendation**	**Reported on page #**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	22
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	24
Objectives	3	State specific objectives, including any prespecified hypotheses	24
Methods			
Study design	4	Present key elements of study design early in the paper	25
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	25
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	25
		(*b*) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	31
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	31
Bias	9	Describe any efforts to address potential sources of bias	28
Study size	10	Explain how the study size was arrived at	25
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	31

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	32
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	33
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	34
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	35
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	33
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	42

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	45
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	42
Generalisability	21	Discuss the generalisability (external validity) of the study results	45
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 6 – STROBE Checklist for *Chapter Three*

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

Chapter Three	**Item No**	**Recommendation**	**Reported on page #**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	49
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	50
Objectives	3	State specific objectives, including any prespecified hypotheses	51
Methods			
Study design	4	Present key elements of study design early in the paper	51
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	51
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	51
		(*b*) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	54
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	54
Bias	9	Describe any efforts to address potential sources of bias	54
Study size	10	Explain how the study size was arrived at	52
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	54

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	55
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	56
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	56
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	59
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	56
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	61

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	64
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	63
Generalisability	21	Discuss the generalisability (external validity) of the study results	63
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 7 – Ethical Review, Ethical Amendments, Consent Forms and Patient Information Sheets for *Chapter Four*

UNIVERSITY OF BIRMINGHAM

APPLICATION FOR ETHICAL REVIEW

Who should use this form:

This form is to be completed by PIs or supervisors (for PGR student research) who have completed the University of Birmingham's Ethical Review of Research Self Assessment Form (SAF) and have decided that further ethical review and approval is required before the commencement of a given Research Project.

Please be aware that all new research projects undertaken by postgraduate research (PGR) students first registered as from 1st September 2008 will be subject to the University's Ethical Review Process. PGR students first registered before 1st September 2008 should refer to their Department/School/College for further advice.

Researchers in the following categories are to use this form:

1. The project is to be conducted by:
    - Staff of the University of Birmingham; or
    - Postgraduate research (PGR) students enrolled at the University of Birmingham (to be completed by the student's supervisor);
2. The project is to be conducted at the University of Birmingham by visiting researchers.

Students undertaking undergraduate projects and taught postgraduate (PGT) students should refer to their Department/School for advice.

NOTES:

- An electronic version of the completed form should be submitted to the Research Ethics Officer, at the following email address: aer-ethics@contacts.bham.ac.uk. Please **do not** submit paper copies.

- If, in any section, you find that you have insufficient space, or you wish to supply additional material not specifically requested by the form, please it in a separate file, clearly marked and attached to the submission email.
- If you have any queries about the form, please address them to the Research Ethics Team.

☒ **Before submitting, please tick this box to confirm that you have consulted and understood the following information and guidance and that you have taken it into account when completing your application:**

- **The information and guidance provided on the University's ethics webpages (https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-of-Research.aspx)**
- **The University's Code of Practice for Research (http://www.as.bham.ac.uk/legislation/docs/COP_Research.pdf)**

UNIVERSITY OF BIRMINGHAM **APPLICATION FOR ETHICAL REVIEW**	*OFFICE USE ONLY:* Application No: Date Received:

1. TITLE OF PROJECT

Evaluation of neck movement variability after eccentric exercise

2. THIS PROJECT IS:

University of Birmingham Staff Research project ☐
University of Birmingham Postgraduate Research (PGR) Student project ☒
Other ☐ (Please specify):

3. INVESTIGATORS

a) PLEASE GIVE DETAILS OF THE PRINCIPAL INVESTIGATORS OR SUPERVISORS (FOR PGR STUDENT PROJECTS)

Name: Title / first name / family name	Professor Deborah Falla
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	+44121 41 47253
Email address:	d.falla@bham.ac.uk

b) PLEASE GIVE DETAILS OF ANY CO-INVESTIGATORS OR CO-SUPERVISORS (FOR PGR STUDENT PROJECTS)

Name: Title / first name / family name	Dr Alison Rushton
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	[redacted]
Email address:	[redacted]

Name: Title / first name / family name	Dr Nicola R Heneghan
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	+44121 415 8367
Email address:	n.heneghan@bham.ac.uk

c) In the case of PGR student projects, please give details of the student

Name of student:	Feras Alsultan	Student No:	
Course of study:	PhD physiotherapy	Email	
Principal	Professor Deborah Falla		

4. ESTIMATED START OF PROJECT Date: Nov 2018

ESTIMATED END OF PROJECT Date: Nov 2019

5. FUNDING

List the funding sources (including internal sources) and give the status of each source.

Funding Body	*Approved/Pending /To be submitted*
Qassim University in Saudi Arabia and the Saudi Cultural Bureau in Britain (SACB)	Approved

If you are requesting a quick turnaround on your application, please explain the reasons below (including funding-related deadlines). You should be aware that whilst effort will be made in cases of genuine urgency, it will not always be possible for the Ethics Committees to meet such requests.

6. SUMMARY OF PROJECT

Describe the purpose, background rationale for the proposed project, as well as the hypotheses/research questions to be examined and expected outcomes. This description should be in everyday language that is free from jargon. Please explain any technical terms or discipline-specific phrases.

Background rationale

Movement variability is the normal variations that happen when a person performs a repeated movement or task (Stergiou et al., 2006). For example, if someone tries to copy a movement that they see, there may be some differences between movements no matter how familiar it is (Preatoni et al., 2013, Stergiou and Decker, 2011). Some theories suggest that movement variability is largely random, while others suggest that movement variability is often not random, and may therefore provide important information (Stergiou et al., 2006). A number of studies support the second concept, suggesting that movement variability may be determined by factors like previous experience of pain (Harbourne et al., 2009, Stergiou and Decker, 2011).

It is thought that optimal movement variability indicates greater adaptability of the underlying movement control system (Stergiou and Decker, 2011). Reduced movement variability is usually related to expected behaviour, and increased variability indicates unpredictable behaviour. Both higher and lower levels of movement variability can result in decreased ability to adapt when movements are disturbed, and can be a sign of physical function problems (Niederer et al., 2017, Stergiou and Decker, 2011). Our recent study showed that people with chronic neck pain move their neck with significantly less variability compared to asymptomatic individuals when moving the head up and down, and right and left. We also found significantly less variability with faster movements. Our findings showed the importance of evaluating neck movements in terms of movement variability, and the potential this examination has for providing clinicians with further insight into active neck movement behavior in people with chronic neck pain.

In daily life, physical activity includes the active lengthening of muscles called eccentric exercise (Madeleine et al., 2011, Dartnall et al., 2009). Eccentric exercise could have an impact on muscle function and performance (Madeleine et al., 2011), for example muscle fatigue, muscle pain, or both (Lee et al., 2017). Several studies have focused on examining muscle characteristics after eccentric exercise (Kawczyński et al., 2007), but with little attention to movement quality. In particular, the amount of variability while performing repetitive movements could be an indicator of how pain, or fatigue affect how the neuromuscular system functions, and may provide important knowledge regarding neck movement behaviour (Niederer et al., 2017, Barbero et al., 2017).

Objectives

1] To evaluate, in healthy volunteers, the variability of active neck movements before and after (immediately after, 24 hours and 48 hours after) eccentric exercise, and to measure the effects of delayed onset muscle soreness which typically occurs following eccentric exercise. [Active neck movements will be performed at different speeds, and with the eyes open and closed. Flexion-extension, lateral bending and rotation movements will be tested].

2] To assess the relationship between measures of movement variability and levels of physical activity, muscle soreness, and muscle fatigue.

Expected outcomes

We expect that this study will provide new insights into how neck movement behaviour is modified with fatigue and soreness, which may provide new insights into maladaptive movement behaviours in people with cervical spine disorders.

7. CONDUCT OF PROJECT

Please give a description of the research methodology that will be used

Design: Experimental single group design

Setting:

All the measurements will be collected within the laboratories of the Centre of Precision Rehabilitation for Spinal Pain; School of Sport, Exercise and Rehabilitation Sciences.

Procedure:

First, anthropometric measurements, including the participant's height and weight, will be taken at session 1.

Participants will be asked to perform active neck movement tasks before, immediately after, 24 hours (session 2) and 48 hours (session 3) after eccentric exercise in three sessions. All measurements will be conducted as follows:

Active neck movements (Sessions 1, 2 and 3)

The participant will be seated on a chair, and instructed to avoid shoulder movements, relax their arms, and perform the following neck movements: flexion-extension (up and down), bilateral lateral flexion (bring ear to shoulder), and bilateral rotation (turning right and left). Each single movement will be repeated continuously 10 times, at full and 45° range of motions.Each movement direction will be performed at a natural, self-selected speed, a slow speed and a fast speed, all with the eyes open. Then participants will be asked to perform two movements—bilateral rotation at a natural and then a fast speed—both with the eyes closed. The participants will initially perform each movement a few times to familiarise themselves with the required movements.

A three-dimensional motion capture system (BTS Bioengineering, Italy) will be used to record the neck movements following system calibration. The movement data will be acquired at a standard frequency of 250fps. This system consists of eight infrared cameras with a full resolution of 2,2 Mpixels (2048x1088pxs). These cameras will track the 3D motion of retroreflective markers attached to the subject's skin. The 9 retroreflective markers used in the lab will be attached based on the protocol described in Davis et al. (Davis et al. 1991).

These movements will be completed twice in Session 1 (before and then after eccentric exercise) and once in Sessions 2 and 3.

Maximum contractions

The Multi-Cervical Unit (MCU) (BTE Technologies, Hanover, MD), a reliable and valid device, will be used to determine the maximal voluntary contraction (MVC) force (Chiu and Lo, 2002). Participants will be briefed on the procedure, seated in the MCU, and a belt applied over the waist and shoulders. A head brace will be placed just above the forehead. Participants will perform three isometric neck contractions and will be instructed to "push as hard as you can." The MCU will notify the participant when to start and end the isometric contraction (Giggey and Tepe, 2009). For each participant, MVC will be first determined by averaging the highest force values produced during three isometric contractions lasting 5 seconds each (Hedayatpour and Falla, 2014). During MVC, standardised verbal encouragements will be given. The MVCs will be used as a measure before and after the eccentric exercise to confirm the effectiveness of the eccentric exercise (Sewright et al., 2008).

Additionally three maximum contractions will be completed at Session 2 and 3 to evaluate whether changes in neck muscle strength when delayed onset muscle soreness is present.

Eccentric exercise (Session 1 only)

Once the MVC has been determined, participants will perform eccentric contractions of the neck extensors by performing neck extension contractions (from 45° to 0°) consisting of 3 sets of 15 repetitions against a load of 30% MVC, as based on piloting testings . The participant will be asked to push their head against the head brace to perform the eccentric contractions. There will be no time restriction for completing the contractions, and rest time of 60 seconds will be given after every set. One of the eccentric contractions will be performed to familiarise the participants with the procedure before starting recording. During the eccentric exercise, standardised verbal encouragements will be given.

Questionnaires (Session 1)

Participants will be asked to complete the International Physical Activity Questionnaire (IPAQ), which will be used to describe the sample with respect to their physical activity level (Craig, et al., 2003). Also, participants will be asked to rate their perceived fatigue after the movement tasks and eccentric exercise using Borg's CR-10 scale, which is for measuring neck muscle fatigue (Thuresson et al., 2005, Ang, 2008). The scale ranges from 0 to 10, where 0 means no fatigue and 10 means maximal fatigue (Borg, 1982). A visual analogue scale (VAS) will be used to evaluate each participant's muscle soreness before and immediately after eccentric exercise and the movement tasks. The 100-mm horizontal line of the VAS includes ''no soreness'' at the beginning and ''extreme soreness'' at end of the line. Participants will be asked to make point marks on the line for determining the level of muscle soreness (Baroni et al., 2010).

Questionnaires (Session 2 and 3)

VAS will be used to evaluate each participant's muscle soreness 24 and 48 hours after eccentric exercise. Participants will be asked to complete the McGill pain questionnaire, which assesses pain quality and includes 15 elements (Nie et al., 2005, Melzack, 1987). Also, participants' perceived neck disability will be evaluated using the Neck Disability Index (NDI), with a possible score range of 0–50 (Vernon, 2008, Vernon and Mior, 1991). Additionally the participants will be asked to draw any perceived pain on a digital body chart. Participants will be asked to complete the McGill and NDI questionnaires and pain drawing at 24 and 48 hours after eccentric exercise.

Pressure pain threshold (PPT) testing (Sessions 1,2,3)

PPT will be assessed using a pressure algometer at an application rate of 40 kPa/s (Somedic Algometer, Sollentuna, Sweden) at predetermined locations over the posterior neck region. The PPT will be defined as the minimum pressure (kPa) that induced pain. The algometer consists of a 1-cm2 rubber tip plunger, mounted on a force transducer. On each day, measurements of PPT will be performed twice for each location in random order and averaged for data analysis. In addition, the percent difference in PPT in day 2 and day 3 with respect to day 1 will be calculated to compare changes across days.

8. DOES THE PROJECT INVOLVE PARTICIPATION OF PEOPLE OTHER THAN THE RESEARCHERS AND SUPERVISORS?

Yes ☒ No ☐

Note: 'Participation' includes both active participation (such as when participants take part in an interview) and cases where participants take part in the study without their knowledge and consent at the time (for example, in crowd behaviour research).

If you have answered NO please go to Section 18. If you have answered YES to this question

please complete all the following sections.

9. PARTICIPANTS AS THE SUBJECTS OF THE RESEARCH

Describe the number of participants and important characteristics (such as age, gender, location, affiliation, level of fitness, intellectual ability etc.). Specify any inclusion/exclusion criteria to be used.

Sample size

The sample size was estimated with the program G*Power 3.1 for MacOS. The sample size calculation was considered as a power calculation to detect within-group differences in the primary outcome measure of the movement variability measures extracted from the movement data during neck rotation at natural speed. We considered one group and three measurements for the primary outcome to obtain 80% statistical power (1-β error probability) with an α error level probability of 0.05. To do so, we used analysis of variance (ANOVA) of repeated measures, within-factors, and a medium effect size of 0.24. The effect size was based on our previous data on the difference between the means (0.23) of two groups, people with chronic neck pain and healthy individuals, divided on their standard division (0.94). The correlation among repeated measures, 0.67, was identified previously by Barbero et al. (2017). The nonsphericity correction ε is 0.5. This generated a sample size of 32 participants. To allow for a potential drop-out rate of around 10%, a total sample size of 35 participants will be recruited for this study.

Inclusion and exclusion criteria

Healthy participants (males and females aged between 18 to 55 years old) will be included in the study if they do not have a history of neck injury or neck pain in the last five years that required treatment from a health care practitioner (Vangsgaard et al., 2013, Goode et al., 2010). Participants will be excluded if they present with any of the following: previous spinal surgery, pregnancy, rheumatic condition, current or chronic respiratory condition, or having an ongoing compensation claim related to an injury.

10. RECRUITMENT

Please state clearly how the participants will be identified, approached and recruited. Include any relationship between the investigator(s) and participant(s) (e.g. instructor-student).

Note: Attach a copy of any poster(s), advertisement(s) or letter(s) to be used for recruitment.

Participants will be recruited from the community in Birmingham, including University of Birmingham students and staff who meet the criteria. Recruitment methods will include contacting participants within the CPR Spine Register, word of mouth, printed hard copy advertisements posted throughout the University of Birmingham campus and local public shopping areas, an identical soft-copy advertisement disseminated using the University's intranet and email system, and also distributed via social media platforms such as Facebook and Twitter.

11. CONSENT

a) Describe the process that the investigator(s) will be using to obtain valid consent. If consent is not to be obtained explain why**.** If the participants are minors or for other reasons are not competent to consent, describe the proposed alternate source of consent, including any permission / information letter to be provided to the person(s) providing the consent.

Participants will be provided with a participant information sheet that includes the purpose of the study and the requirements. Also, an investigator will introduce and explain all procedures of the study to participants before obtaining consent and starting data collection. If they agree to participate in the study, they will need to sign a written informed consent form. Please see attached Participant Information Sheet and Consent Form.
The information sheet includes information about data storage and that data will only be used for the purpose of research, statistical and audit purposes by the University of Birmingham in accordance with the General Data Protection Regulation (GDPR) 2018 and the University of Birmingham Research guidelines.

Note: Attach a copy of the Participant Information Sheet (if applicable), the Consent Form (if applicable), the content of any telephone script (if applicable) and any other material that will be used in the consent process.

b) Will the participants be deceived in any way about the purpose of the study? **Yes** ☐ **No** ☒

If yes, please describe the nature and extent of the deception involved. Include how and when the deception will be revealed, and who will administer this feedback.

12. PARTICIPANT FEEDBACK

Explain what feedback/ information will be provided to the participants after participation in the research. (For example, a more complete description of the purpose of the research, or access to the results of the research).

Participants will be offered the opportunity to receive a summary report of the research findings by email should they wish.

13. PARTICIPANT WITHDRAWAL

a) Describe how the participants will be informed of their right to withdraw from the project.

Participants will be offered the right to withdraw at any time up to two weeks following data collection without giving a reason. Notice of this right is included within the participant information sheet and consent form. They will be advised that any data already collected will be kept and

b) Explain any consequences for the participant of withdrawing from the study and indicate what will be done with the participant's data if they withdraw.

There will be no consequences if a participant chooses to withdraw from the study. Participants will be informed that all data collected up to point of withdrawal will be included in data analyses.

14. COMPENSATION

Will participants receive compensation for participation?

i) Financial **Yes** ☒ **No** ☐

ii) Non-financial **Yes** ☒ **No** ☐

If **Yes** to **either** i) or ii) above, please provide details.

Participants will be compensated with an amount of £30 or 3 research hours, based on personal preferences, for participating in the full experiment. If participants elect to receive research hours they will not receive financial compensation as well. The full experiment is comprised of 3 sessions of approximately 1 hour in duration each. If they opt for financial compensation, participants will receive a total of £30 compensation for completing this study, or a £10 fixed rate for each session of the study which they complete.

If participants choose to withdraw, how will you deal with compensation?

Participants will choose either having research hours or receiving financial compensation. If they attend and complete part of the study, they will be compensated as follows: • Decided to withdraw in the first one-hour session (1 research hour) or (£10) • Decided to withdraw in the second 30-minute session (2 research hours) or (£20). • Decided to withdraw in the third 30-minute session (3 research hours) or (£30).

15. CONFIDENTIALITY

a) Will all participants be anonymous? **Yes** ☐ **No** ☒

b) Will all data be treated as confidential? **Yes** ☒ **No** ☐

Note: Participants' identity/data will be confidential if an assigned ID code or number is used, but it will not be anonymous. Anonymous data cannot be traced back to an individual participant.

Describe the procedures to be used to ensure anonymity of participants and/or confidentiality of data both during the conduct of the research and in the release of its findings.

All participants will be allocated an ID number to enable pseudo-anonymisation. Only necessary personal data will be collected during the study, including name, contact telephone number and email address. This information will be collected on the consent form for the study, which will be securely stored in Prof. Falla's Office.

All electronic data will be saved on a secure University of Birmingham server for and remains strictly confidential throughout. The data will only be shared with the participant, investigator and research team. It will not be given to a third party, and it will be stored for 10 years in line with University of Birmingham Research Governance guidelines. All data will be collected and stored under the identification number allocated at the point of recruitment.

If participant anonymity or confidentiality is not appropriate to this research project, explain, providing details of how all participants will be advised of the fact that data will not be anonymous or confidential.

16. STORAGE, ACCESS AND DISPOSAL OF DATA

Describe what research data will be stored, where, for what period of time, the measures that will be put in place to ensure security of the data, who will have access to the data, and the method and timing of disposal of the data.

All data will be stored securely in electronic format on a secure University of Birmingham server. Access to data will require a password and all data will be managed in accordance with the GDPR 2018. The investigators will have access to the pseudo-anonymised data.
Following the completion of data collection, all consent forms containing personal data will be securely stored in a locked filing cabinet in Prof. Falla's office and can only be accessed by the investigators.
Data will be kept for 10 years under the University's Code of Practice for Research.

17. OTHER APPROVALS REQUIRED? e.g. Criminal Records Bureau (CRB) checks or NHS R&D approvals.

☐ YES ☐ NO ☒ NOT APPLICABLE

If yes, please specify.

18. SIGNIFICANCE/BENEFITS

Outline the potential significance and/or benefits of the research

This study is the first to evaluate the movement variability of active neck movement following eccentric exercise. We expect that this study will provide new insights into how neck movement behaviour is modified with fatigue and soreness, which may provide new insights into maladaptive movement behaviours in people with cervical spine disorders.

19. RISKS

a) Outline any potential risks to **INDIVIDUALS**, including research staff, research participants, other individuals not involved in the research and the measures that will be taken to minimise any risks and the procedures to be adopted in the event of mishap

Participants will be informed that they may experience some mild discomfort while performing the tests. Appropriate rest time will be provided throughout the experimental trials. Also, participants will be informed that they can take an extra rest period any time they need to. Participants' response to the tests will be monitored during the trials, and extra rest periods will be offered if needed.

Participants will also have the option to stop and withdraw from the study at any time and up to two weeks after the completed data collection.

Participants with also be advised that eccentric exercise typically leads to delayed onset muscle soreness which usually is experienced within 24 hours after the exercise but lasts usually no longer than 72 hours. The analogy of going to the gym and performing unaccustomed exercise will be used to explain this to the participants, where discomfort is usually felt in the muscle/s the day after but resolves after a couple of days. This is a normal response to eccentric exercise and is not expected to produce any long lasting effects.

b) Outline any potential risks to **THE ENVIRONMENT and/or SOCIETY** and the measures that will be taken to minimise any risks and the procedures to be adopted in the event of mishap.

Not applicable

20. ARE THERE ANY OTHER ETHICAL ISSUES RAISED BY THE RESEARCH?

Yes ☐ **No** ☒

If yes, please specify

21. EXPERT REVIEWER/OPINION

You may be asked to nominate an expert reviewer for certain types of project, including those of an interventional nature or those involving significant risks. If you anticipate that this may apply to your work and you would like to nominate an expert reviewer at this stage, please provide details below.

Name
Contact details (including email address)
Brief explanation of reasons for nominating and/or nominee's suitability

22. CHECKLIST

Please mark if the study involves any of the following:

- Vulnerable groups, such as children and young people aged under 18 years, those with learning disability, or cognitive impairments ☐
- Research that induces or results in or causes anxiety, stress, pain or physical discomfort, or poses a risk of harm to participants (which is more than is expected from everyday life) ☒
- Risk to the personal safety of the researcher ☐
- Deception or research that is conducted without full and informed consent of the participants at time study is carried out ☐
- Administration of a chemical agent or vaccines or other substances (including vitamins or food substances) to human participants. ☐
- Production and/or use of genetically modified plants or microbes ☐
- Results that may have an adverse impact on the environment or food safety ☐
- Results that may be used to develop chemical or biological weapons ☐

Please check that the following documents are attached to your application.

	ATTACHED	NOT APPLICABLE
Recruitment advertisement	☒	
Participant information sheet	☒	
Consent form	☒	
Questionnaire	☒	
Interview Schedule		☒

23. DECLARATION BY APPLICANTS

I submit this application on the basis that the information it contains is confidential and will be used by the

University of Birmingham for the purposes of ethical review and monitoring of the research project described

herein, and to satisfy reporting requirements to regulatory bodies. The information will not be used for any

other purpose without my prior consent.

I declare that:

- The information in this form together with any accompanying information is complete and correct to the best of my knowledge and belief and I take full responsibility for it.
- I undertake to abide by University Code of Practice for Research (http://www.as.bham.ac.uk/legislation/docs/COP_Research.pdf) alongside any other relevant professional bodies' codes of conduct and/or ethical guidelines.
- I will report any changes affecting the ethical aspects of the project to the University of Birmingham Research Ethics Officer.
- I will report any adverse or unforeseen events which occur to the relevant Ethics Committee via the University of Birmingham Research Ethics Officer.

Name of principal investigator/project supervisor:	Deborah Falla
Date:	26/3/2019

Please now save your completed form, print a copy for your records, and then email a copy to the Research Ethics Officer, at aer-ethics@contacts.bham.ac.uk. As noted above, please do not submit a paper copy.

References

Ang, B. O. (2008) 'Impaired neck motor function and pronounced pain-related fear in helicopter pilots with neck pain - A clinical approach', *Journal of Electromyography and Kinesiology,* 18(4), pp. 538-549.

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UNIVERSITY OF BIRMINGHAM
APPLICATION FOR ETHICAL REVIEW –
REQUEST FOR AMENDMENTS

Who should use this form:

- This form is to be completed by PIs or supervisors (for PGR student research) who are requesting ethical approval for amendments to research projects that have previously received ethical approval from the University of Birmingham.

  Please be aware that all new research projects undertaken by postgraduate research (PGR) students first registered as from 1st September 2008 will be subject to the University's Ethical Review Process. PGR students first registered before 1st September 2008 should refer to their Department/School/College for further advice.

- What constitutes an amendment?

  Amendments requiring approval may include, but are not limited to, additions to the research protocol, study population, recruitment of participants, access to personal records, research instruments, or participant information and consent documentation. Amendments must be approved before they are implemented.

NOTES:

- Answers to questions must be entered in the space provided
- An electronic version of the completed form should be submitted to the Research Ethics Officer, at the following email address: aer-ethics@contacts.bham.ac.uk. Please **do not** submit paper copies.
- If, in any section, you find that you have insufficient space, or you wish to supply additional material not specifically requested by the form, please submit it in a separate file, clearly marked and attached to the submission email.
- If you have any queries about the form, please address them to the Research Ethics Team.

UNIVERSITY OF BIRMINGHAM APPLICATION FOR ETHICAL REVIEW - REQUEST FOR AMENDMENTS	*OFFICE USE ONLY:* Application No: Date Received:

1. **TITLE OF PROJECT**

Evaluation of neck movement variability after eccentric exercise

2. **APPROVAL DETAILS**
   What is the Ethical Review Number (ERN) for the project?

ERN_18-1273

3. **THIS PROJECT IS:**
   University of Birmingham Staff Research project ☐
   University of Birmingham Postgraduate Research (PGR) student project ☒
   Other ☐ (Please specify):

4. **INVESTIGATORS**

d) PLEASE GIVE DETAILS OF THE PRINCIPAL INVESTIGATORS OR SUPERVISORS (FOR PGR STUDENT PROJECTS)

Name: Title / first name / family name	Professor Deborah Falla
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	+44121 41 47253
Email address:	d.falla@bham.ac.uk

Name: Title / first name / family name	Dr Alison Rushton
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	
Email address:	

Name: Title / first name / family name	Dr Nicola R Heneghan
Highest qualification & position held:	PhD
School/Department	Sports, Exercise, and Rehabilitation Sciences
Telephone:	+44121 415 8367
Email address:	n.heneghan@bham.ac.uk

e) PLEASE GIVE DETAILS OF ANY CO-INVESTIGATORS OR CO-SUPERVISORS (FOR PGR STUDENT PROJECTS)

Name: Title / first name / family name	
Highest qualification & position held:	
School/Department	
Telephone:	
Email address:	

f) In the case of PGR student projects, please give details of the student

Name of student:	Feras Alsultan	Student No:	
Course of study:	PhD physiotherapy		
Principal supervisor:	Professor Deborah Falla		

5. **ESTIMATED START OF PROJECT** **Date:** **Nov 2018**

ESTIMATED END OF PROJECT **Date:** **Mar 2019**

6. **ORIGINAL APPLICATION FOR ETHICAL REVIEW AND ANY SUBSEQUENT APPROVED AMENDMENTS:**

Please complete the table below for the original application and any subsequent amendments submitted

Title and reference number of application or amendment	**Key points of application and/or changes made by amendment (include: aims of study, participant details, how participants were recruited and methodology)**	**Ethical considerations arising from these key points (e.g. gaining consent, risks to participants and/or researcher, points raised by Ethical Review Committee during review)**	**How were the ethical considerations addressed? (e.g. consent form, participant information, adhering to relevant procedures/clearance required)**
Original application	Aims: 1. To evaluate the variability of active neck movements before and after (immediately after, 24 hours and 48 hours after) eccentric exercise, and to also measure the effects of delayed onset muscle soreness, which typically occurs following eccentric exercise. 2. To assess the relationship between measures of movement variability and levels of physical activity, muscle soreness and muscle fatigue. Participants: Healthy participants (males and females aged between 18 to 55 years old) will be	Consent: Participants will be provided with a participant information sheet that includes the purpose of the study and what is required of participants. Also, an investigator will introduce and explain all study procedures to participants before obtaining consent and starting data collection. If a participant agrees to take part in the study, they will need to sign a written informed consent form. Risks: 1. Calibration of the Multi-Cervical Unit (MCU) requires moving some weights. That could lead to an injury to the	1] The forms and participant information sheet have been corrected according to the points received from the committee, including PI status, data storage location and adherence to the GCPR 2018. 2] A copy of the IPAQ was provide

	included in the study if they do not have a history of neck injury or neck pain in the last five years that required treatment from a health care practitioner. Participants will be recruited from the community in Birmingham, including University of Birmingham students and staff who meet the criteria. Recruitment methods will include contacting participants within the CPR Spine Register, word of mouth, printed hard copy advertisements posted throughout the University of Birmingham campus and local public shopping areas, and an identical soft-copy advertisement disseminated using the University's intranet and email system, which will also be distributed via social media platforms such as Facebook and Twitter Methods: - Participants will be asked to perform active neck movement tasks before, immediately after, 24 hours after (session 2) and 48 hours (session 3) after eccentric exercise in three sessions.	investigator or technician. However, colleagues will be called if is needed 2. Use of the head brace, waist strap and shoulder straps may cause discomfort or even slight pain if improperly fitted. However, participants will be monitored and asked to inform the investigator if they feel uncomfortable. If this occurs, the test will be stopped immediately. Care will be taken to ensure correct use for participant comfort. Committee points: 1. The student will not be considered the PI on this project: the supervisors will instead be considered as the PIs. 2] Update all references to data protection, to now mention GDPR 2018. 3] Provide a copy of the IPAQ. 4] Amend the participant information sheet 5] Confirm where the electronic data will be stored	

7. **DETAILS OF PROPOSED NEW AMENDMENT**
Provide details of the proposed new amendment, and clearly and explicitly state how the proposed new amendment will differ from the details of the study as already approved (see Q6 above).

This amendment will provide more information regarding the neck movements and objective confirmation of performance of the exercise by participants. Minor changes in the methods section will be made as follows:

1. Participants will perform active neck movements at full and 45° range of motion. However, in the approved original application participants were to perform active neck movements at 45° range of motion only. After initial tests we deemed it relevant to also evaluate how eccentric exercise could affect their full range of neck movement.
2. Maximal voluntary contraction (MVC) will now be repeated after the eccentric exercise to confirm the presence of muscle fatigue. Additionally, the MVCs will be performed on session 2 and 3 to evaluate the effect of eccentric exercise on muscle performance. Initially the MVCs were only to be performed once in the first session.
3. Participants will perform eccentric contractions (the eccentric exercise) of the neck extensors by performing contractions (from 45° to 0°) consisting of 3 sets of 15 repetitions against a load of 30% MVC, based on pilot results. Rest time of 60 seconds will be given after every set. Originally, participants were to perform eccentric contractions by performing neck contractions (from 45° to 0°) consisting of 6 sets of 3 repetitions against a much higher load of 75% MVC in the approved original application. In addition, rest time of 30 seconds will now be given after every set. We have had to make this adjustment after pilot testing when we gained ethical approval as we found the load was too high but the number of repetitions was not sufficient to induce soreness 24h later.
4. Participants will be asked to complete the Borg's CR-10 scale and VAS questionnaires after performing the second MVC. These questionnaires have been added, along with the second MVC after the eccentric exercise. This simply provides an indication of the patients pain and fatigue which we will monitor throughout.
5. Pressure pain threshold testing has been added which was not initially included in the application. We have added this in as a further measure to confirm the effectiveness of the eccentric exercise protocol.

8. **JUSTIFICATION FOR PROPOSED NEW AMENDMENT**

The justification was written for each proposed new amendment as follows:

1. The measurements at full range of motion could show differences in active neck movements before and after the eccentric exercise.
2. MVC will be used as a measure before and after the eccentric exercise and 24h and 48h later to confirm the effectiveness of the eccentric exercise (Sewright et al., 2008).
3. After performing several tests for the eccentric exercise protocol, it has been determined that this mew amendment protocol will be more effective for this experiment and more compatible with the loads available for the Multi-Cervical Unit.
4. These questionnaire results will be compared with the questionnaire results obtained before the eccentric exercise (Sewright et al., 2008) again to confirm the appropriateness of the eccentric exercise protocol
5. Pressure pain thresholds have added as a further measure to confirm the effectiveness of the eccentric exercise protocol.

9. **ETHICAL CONSIDERATIONS**

What ethical considerations, if any, are raised by the proposed new amendment?

No additional risks are present other than those described in the initial application.

10. **DECLARATION BY APPLICANTS**

I make this application on the basis that the information it contains is confidential and will be used by the

University of Birmingham for the purposes of ethical review and monitoring of the research project described

herein, and to satisfy reporting requirements to regulatory bodies. The information will not be used for any

other purpose without my prior consent.

I declare that:

- The information in this form together with any accompanying information is complete and correct to the best of my knowledge and belief and I take full responsibility for it.
- I undertake to abide by University Code of Conduct for Research (http://www.birmingham.ac.uk/Documents/university/legal/research.pdf) alongside any other relevant professional bodies' codes of conduct and/or ethical guidelines.
- I will report any changes affecting the ethical aspects of the project to the University of Birmingham Research Ethics Officer.
- I will report any adverse or unforeseen events which occur to the relevant Ethics Committee project to the University of Birmingham Research Ethics Officer.

Signature of Principal investigator/project supervisor:	Deborah Falla
Date:	26/3/2019

Reference

Sewright, K. A., Hubal, M. J., Kearns, A., Holbrook, M. T. and Clarkson, P. M. (2008) 'Sex differences in response to maximal eccentric exercise', *Medicine and Science in Sports and Exercise,* 40(2), pp. 242-251.

Reply all | Delete Junk | •••

Application for amendment ERN_18-1273A

Samantha Waldron (Research Support Group) Reply all |
Wed 10/04/2019, 09:45
Deborah Falla (School of Sport Exercise and Rehabilitation Sciences); Alison Ru:

Inbox

Flag for follow up.

Action Items

Dear Professor Deborah Falla, Dr Alison Rushton & Dr Nicola R Heneghan,

Re: "Evaluation of neck movement variability after eccentric exercise"
Application for amendment ERN_18-1273A

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

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

I would like to remind you that any substantive changes to the nature of the study as now amended, 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. A revised amendment application form is now available at https://intranet.birmingham.ac.uk/finance/accounting/Research-Support-Group/Research-Ethics/Ethical-Review-Forms.aspx . Please ensure this form is submitted for any further amendments.

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.

If you require a hard copy of this correspondence, please let me know.

Kind regards,

Ms Sam Waldron
Deputy Research Ethics Officer
Research Support Group
C Block Dome (room 132)
Aston Webb Building

The University of Birmingham
School of Sport, Exercise and Rehabilitation Sciences

Participant Identification number:

CONSENT FORM

Title of Project: Evaluation of neck movement variability after eccentric exercise

Name of Researchers: Deborah Falla, Alison Rushton, Nicola R Heneghan, Feras Alsultan

Please initial box

6. I confirm that I have **read** and **understand** the information sheet for this study. ☐
7. I have had the opportunity to ask any questions and that my questions have been answered to my satisfaction. ☐
8. I understand that my participation is voluntary and that I am free to withdraw at any time up to two weeks following data collection, without giving any reason. ☐
9. I am aware that my personal data will be processed for the purposes detailed above, in accordance with the EU General Data Protection Regulation 2018. ☐
10. I agree to take part in the above study. ☐

_____	_____	
Name of Participant	Date	Signature
_____	_____	
Name of Researcher	Date	Signature

(Copies of consent for: participant and researcher)

The University of Birmingham

School of Sport, Exercise and Rehabilitation Sciences

Participant Information Form

Study title: Evaluation of neck movement variability after eccentric exercise

Investigators: Deborah Falla, Alison Rushton, Nicola R Heneghan, Feras Alsultan

You are being invited to take part in a research study. Before you decide to participate, it is important to know why the research is being done and what it will involve. Please take time to read the following information sheet carefully.

WHAT IS THE PURPOSE OF THE STUDY?

This study will evaluate the effects of a specific type of exercise called “eccentric exercise” which is an exercise involving lengthening of the muscle. This type of exercise typically leads to soreness within the muscle which usually appears within 24 hours and lasts 48-72 hours. It is the type of soreness that you may have experienced after going to the gym and performing new exercises. In this study we are interested in understanding how eccentric exercise of the neck muscles affects neck movement in healthy individuals. This research could help us to understand and interpret changes in movement in people with neck pain and could help develop new examination and management approaches for people with neck problems.

CAN I PARTICIPATE?

You **can** participate in this study if you are between 18 to 55 years old and do not have a history of neck injury or neck pain in the last five years that required treatment from a health care practitioner. You **cannot** participate if you have any of the following: previous spinal surgery, pregnancy, rheumatic condition, current or chronic respiratory condition, or having an ongoing compensation claim related to an injury.

WHAT WILL I HAVE TO DO IF I PARTICIPATE?

We will ask you to attend 3 sessions on consecutive days lasting approximately 1 hour each session. Each session will take place within the laboratories of the Centre of Precision Rehabilitation for Spinal Pain in the School of Sport, Exercise and Rehabilitation Sciences at the University of Birmingham. During this time you will be asked to do the following:

- Complete some questionnaires
- Perform maximum contractions to test the strength of the muscles. This will be done during each of the three sessions.
- Perform some neck movements, such as rotating your head and moving head up and down, to measure your neck movement. Small plastic markers will be placed on your head and upper body. These markers will help us to measure your neck and upper back movements exactly.
- Perform an exercise protocol (*session one only*) which will involve performing 3 sets of 15 repetitions against a load of 30% of your maximum neck muscle strength.
- A hand-held probe (algometer) will be pushed on the skin over the back of your neck and you will be asked to push a button when the pressure turns into pain. This will be tested at different sites over the back of your neck during each of the three sessions.

During the test you should wear a vest/T-shirt. You can ask to have an investigator of your own gender for positioning markers if you prefer.

HOW MUCH TIME WILL I HAVE TO SPEND IN TOTAL?

Data collection in the lab will last approximately 1 hour per session, totalling 3 hours across the 3 sessions.

ARE THERE ANY BENEFITS FOR ME IF I TAKE PART?

There is no specific benefit for you by taking part in this study. However, this research could help to understand and interpret changes in movement in people with neck pain disorders and could help develop new examination and management approaches for people with neck disorders.

ARE THERE ANY RISKS FOR ME IF I TAKE PART?

The risks are low, as all procedures are carried out by experienced professionals and you will be thoroughly screened to ensure that it is safe for you to take part. All tests performed are non-invasive. You are free to stop the experiment and should you wish, you can withdraw from the study at any time. You may experience some mild discomfort while performing the muscle tests. Appropriate rest time will be provided throughout the measurements and additional rest periods will be given if needed.

The eccentric exercise typically leads to a sensation of soreness within your muscles which usually is experienced within 24 hours after the exercise but lasts usually no longer than 72 hours. It is the same type of feeling as going to the gym and performing exercises that you are not used to – where you feel discomfort in your muscles the day after but this resolves after a couple of days. This is a normal response to eccentric exercise and is not expected to produce any long-lasting effects. However, if you still experience discomfort after four (4) days (beyond 96 hours), you should contact an investigator.

In the event of a complaint/concern with the project then contact: Susan Cottam (Research Ethics Officer), Tel: 0121 414 8825, Email: s.l.cottam@bham.ac.uk

ARE THERE ANY COST OR REIMBURSEMENTS FOR ME?

There is no cost for this study to you. You will be compensated £10 per session for your time, to a total of £30 for completing all sessions. Alternatively, you can claim up to 3 research hours for participating in this study.

DO I HAVE TO TAKE PART?

No, participation is entirely voluntary. If you decide to take part but you change your mind, you can withdraw from the study at any time up to two weeks following the study sessions, without having to give a reason.

WILL MY DATA BE KEPT CONFIDENTIAL?

All information collected on you will be kept strictly confidential. The consent form containing your allocated ID will never be present in electronic form, and will be securely stored within CPR Spine and only available to the researchers. All data will be stored on a secure University of Birmingham server for 10 years, managed in accordance with the EU General Data Protection Regulation 2018 and the University of Birmingham Research Guidelines.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

All data for presentation will be anonymised, that means your identity will not be revealed in any way. The findings from this study will be presented or shared with other researchers in the form of presentations and scientific papers as appropriate.

DOES THE STUDY FOLLOW ETHICS PROCEDURES?

This study underwent the ethical review processes of the University of Birmingham and received official approval from the University Ethics Committee.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The study has been designed and organised by Professor Deborah Falla, Chair in Rehabilitation Science and Physiotherapy (d.falla@bham.ac.uk or 0121 41 47253)

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Thank you for taking the time to read this and considering taking part in the study!

Appendix 8 – STROBE Checklist for *Chapter Four*

STROBE Statement—Checklist of items that should be included in reports of ***case-control studies***

Chapter Four	**Item No**	**Recommendation**	**Reported on page #**
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	66
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	68
Objectives	3	State specific objectives, including any prespecified hypotheses	68
Methods			
Study design	4	Present key elements of study design early in the paper	69
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	69
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	69
		(*b*) For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	71
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	71
Bias	9	Describe any efforts to address potential sources of bias	72
Study size	10	Explain how the study size was arrived at	69
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	71

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	75
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how matching of cases and controls was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	76
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	77
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	78
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	80
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	84

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	86
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	84
Generalisability	21	Discuss the generalisability (external validity) of the study results	86
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for cases and controls.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Appendix 9– PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	88
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	89
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	90
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	91
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	91
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	91
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	93
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	93
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	94
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	94
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	95
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	95
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	100

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	100
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	101
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	105
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	112
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	115
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	118
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	123
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	127
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	128
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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