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Ingebrigt Meisingset

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Bevegelse, motorisk kontroll og psykologiske faktorer ved nakkesmerte

Sammendrag

Hovedformålet med denne avhandlingen var å undersøke bevegelse og motorisk kontroll hos pasienter med nakkesmerte og om dette hadde sammenheng med faktorer som smerte, funksjon, frykt for bevegelse og selvopplevd bedring gjennom et behandlingsforløp.

Nakkesmerte er globalt rangert som den fjerde viktigste årsaken for redusert funksjon. Effekten av ulike behandlinger er moderat med liten forskjell mellom ulike behandlingsmetoder. Pasienter med nakkesmerte utgjør ei heterogen gruppe, der årsaken til nakkesmerte oftest er ukjent. Tidligere studier viser at pasienter med nakkesmerte kan ha dårligere bevegelse og motorisk kontroll i nakken, men vi vet lite om hvorvidt dette har betydning for om de blir bedre eller ikke av behandling, eller om det er andre faktorer som virker inn. Noen studier har vist at tanker knyttet til frykt for bevegelse, katastrofetenkning og mestringstro kan virke inn på bevegelse av nakke/hodet, og om man blir bedre etter endt behandling. Men ingen studier har sett på forholdet mellom disse faktorene samlet gjennom et behandlingsforløp.

Vi målte ulike aspekter av bevegelse og motorisk kontroll hos pasienter med uspesifikke nakkesmerter før oppstart av fysioterapibehandling, og etter 2 uker og 2 måneder. I tillegg brukte vi spørreskjema for å kartlegge smerte, funksjon, oppfatninger og tanker knyttet til frykt for bevegelse og mestringstro. Studie 1 og 2 viste at pasienter er preget av en generelt stivere bevegelse og kontroll av nakke sammenlignet med personer uten nakkesmerte. Studie 2 viste også at det stivere bevegelsesmønsteret befinner seg innenfor det man kan anta er styrt av viljemessige prosesser og ikke refleksstyrte. Frykt for bevegelse hadde liten eller ingen sammenheng med bevegelse av nakken i disse studiene. I løpet av 2 måneder med behandling fant vi kun små endringer på bevegelse og motorisk kontroll hos pasientene (studie 3). Økt bevegelsesutslag i nakken og forbedret finmotorisk kontroll viste seg å ha størst sammenheng med redusert smerte og forbedret funksjon. De samme aspektene av bevegelse og motorisk kontroll, i tillegg til smerteintensitet/-varighet og funksjon, predikerte pasientenes globale oppfatning av bedring etter 2 måneder. Oppfatninger og tanker ved oppstart av behandling, slik som frykt for bevegelse, katastrofetanker og mestringstro kunne ikke predikere bedring ved 2 måneder. Redusert frykt for bevegelse og katastrofetanker og økt mestringstro hadde derimot sammenheng med pasientenes opplevelse av global bedring, i tillegg til redusert smerte og økt funksjon (studie 4).

Contents

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List of papers

1. Ingebrigt Meisingset, Astrid Woodhouse, Ann- Katrin Stensdotter, Øyvind Stavdahl, Håvard Lorås, Sigmund Gismervik, Hege Andresen, Kristian Austreim, Ottar Vasseljen
   Evidence for a general stiffening motor control pattern in neck pain: A cross sectional study. BMC. Musculoskeletal Disorders, (2015);16:56.

2. Ann-Katrin Stensdotter, Ingebrigt Meisingset, Morten Dinhoff Pedersen, Ottar Vasseljen Øyvind Stavdahl
   Head steadiness in response to unpredictable perturbations in patients with insidious neck pain. Submitted

3. Ingebrigt Meisingset, Ann-Katrin Stensdotter, Astrid Woodhouse, Ottar Vasseljen
   Neck motion, motor control, pain and disability: A longitudinal study of associations in neck pain patients in physiotherapy treatment. Manual Therapy: Article in Press

4. Ingebrigt Meisingset, Ann-Katrin Stensdotter, Astrid Woodhouse, Ottar Vasseljen.
   Predictors for global perceived effect after physiotherapy treatment in patients with neck pain: An observational study. Submitted

1 Introduction

Severe neck pain is reported to influence activities of daily living, ability to work, and social life (Andelic et al., 2012). The etiology of neck pain is unknown and no underlying mechanisms have been shown to explain why people develop this long term disability. Neck pain has thus been classified as non- specific for patients with no evidence of serious pathological cause or systemic disease.

Investigations into possible underlying mechanisms for the chronicity of neck pain are important in order to develop effective treatment and prevention strategies, since current therapies have shown similar and moderate effect across a wide range of reported interventions (Hurwitz et al., 2008). Within a biopsychosocial model of understanding neck pain, a range of factors may affect the degree of pain and disability in neck pain patients. It is widely accepted that psychological factors like fear avoidance and kinesiophobia are associated with neck pain, but studies have not shown a superior treatment effect for interventions aimed at reducing fear avoidance (Monticone et al., 2015a). Research in the last decade has provided evidence for deficits in neck motion and motor control in neck pain. (Falla, 2004, Falla and Farina, 2007, Treleaven, 2008a). Motor control may be viewed as the result or output of all peripheral and central nervous processes involved in executing a movement, and studies show that subjects move differently when experiencing pain (Hodges and Tucker, 2011).

This thesis aims to contribute to the knowledge regarding pain, disability and favorable treatment outcome in neck pain, with emphasis on neck motion and motor control and psychological factors. The background to the research presented in this thesis is provided in the next section.

2 Background

Neck pain is associated with restriction of activity in the working population, as well as in the general population (Hogg-Johnson et al., 2008, Cote et al., 2008). The Global Burden of Disease Study 2010 found that the global point prevalence of neck pain is estimated to be 4.9 %, and that neck pain is ranked as the 4th most disabling condition (Hoy et al., 2014, Vos et al., 2013). Women have a slightly higher prevalence than men, while prevalence is similar across different geographical regions (Hoy et al., 2014). The annual prevalence of neck pain varies from 30 to 50% and exerts significants effects on both the individual and the society through decreased quality of life, health care expenditure, and sick leave (Hogg-Johnson et al., 2008, Kinge et al., 2015). A considerable gap exists between the burden of neck pain and the number of research trials aimed at developing effective treatments, compared with other disabling conditions such as osteoarthritis and diabetes (Emdin et al., 2015). For example, only 1 % of total grant funding for clinical trials in Australia is allocated to spinal disorders (Maher, 2013). The burden of neck pain calls for more research into its causative factors in order to develop effective prevention and treatment programs, as the current treatment outcome have been shown to be moderate at best and similar across a wide range of reported interventions (Hurwitz et al., 2008).

2.1 Classification of neck pain

In physiotherapy and medicine, the classification and diagnosis of disease or illness is based on the signs and symptoms observed in a clinical examination and, when indicated, from additional procedures such as radiography or MRI. In most cases, unfortunately, imaging cannot produce objective findings to explain the origin of pain in neck pain conditions, and is therefore not recommended without a clear indication of serious pathology (Nordin et al., 2008, Nykanen et al., 2007). Due to a lack of causal mechanisms, most cases of neck pain are therefore classified as non- specific.

The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders presented a classification system for neck pain that was independent of neck pain type (for example, whiplash versus non- specific pain) and professional background of the clinician (Guzman et al., 2008). They proposed four different grades according to severity and functional deficits:

- Grade I: No signs or symptoms of major structural pathology and minor interference with activities of daily living.

- Grade II: No signs or symptoms of major structural pathology, but major interference with activities of daily living.
- Grade III: No signs or symptoms of major structural pathology, but presence of neurologic signs such as decreased deep tendon reflexes, weakness, or sensory deficits.
- Grade IV: Signs or symptoms of major pathology.

However, the clinical utility of this classification system is unknown. A recent study evaluated the prognostic value of the Quebec Task Force Classification system (which shares similarities with the abovementioned system) in chronic neck pain patients and found small differences in the clinical course between the subgroups (Rasmussen et al., 2015). The clinical utility of the classifications system described above are therefore questionable. The complexity of neck pain suggests that a classification system should incorporate a wider range of variables in order to predict outcome and facilitate treatment decision making. Identification of subgroups to guide treatment initiation and stratification of patients to targeted treatments is important in future research into neck pain, given that this is a heterogeneous group of patients. In addition, such strategies have produced promising results in low back pain patients using the StartBack screening tool (Hill et al., 2011).

The International Classification of Functioning (ICF) presented by the World Health Organization (WHO) is a model that can be used to categorize the impact on function of conditions such as neck pain. The model is divided into different domains, reflecting the biopsychosocial perspective of health conditions. These domains are 1) body functions and structure, 2) activity, 3) participation, and the contextual factors defined as environmental- and personal factors (WHO, 2015). The ICF model can be used to classify findings from the clinical examination into different categories, and thus allowing clinicians to prioritize the factors that are important to increase function and reduce disability. This model is implemented in the education of physiotherapists in Norway (HiOA, 2015) and provides a framework for assessing neck pain patients as well as all patient groups and conditions across different health care providers, as it is not disease specific. Andelic and colleagues categorized the functional limitations reported by patients with neck pain according to the ICF. They found that neck pain patients reported functional problems related to all the ICF domains, suggesting that researchers should consider all potential factors related to the experience of neck pain (Andelic et al., 2012).

2.2 Course and prognostic factors

Knowledge of the different courses involved in neck pain may help clinicians with treatment planning. The natural course of neck pain describes whether individuals recover or not from an incident neck pain episode, ideally without receiving treatment, while the clinical course of neck pain is studied in settings where patients receive treatment. The clinical course thus constitutes the additive effect of treatment on the natural course. Some patients may recover with advice and self-care, while others with a less favorable prognosis may need a more comprehensive treatment approach.

Natural course

In the general population, most subjects with non- specific acute neck pain are characterized by a rapid decline in neck pain in the first months after the pain initiates, with small improvements over the next 12 months. However, patients with equally intense pain in the low back or with four or more pain sites experienced little change in the follow- up year (Vasseljen et al., 2013).

Although most reported recurrence of symptoms, the subjects in the abovementioned study were characterized by acute pain, as subjects were included in the trial if the neck pain symptoms started in the month prior to inclusion. However, the natural course of chronic neck pain may differ from acute/ sub-acute neck pain. A systematic review argued that the outcome of control groups in clinical trials of non- specific neck pain could be used to study the natural history of chronic neck pain, since participants did not receive any treatment (Vernon et al., 2006). Compared to the general population study of Vasseljen et al, only minor differences in pain trajectories were observed during a follow up period of 1 year in patients with chronic neck pain.

Clinical course

Non- specific neck pain patients are characterized by different short term clinical trajectories, whereby some patients show small improvements during the first month while others show a more stable trajectory of neck pain (Walton et al., 2013b), consistent with the natural course of neck pain described above. There is a lack of studies on the clinical course of patients with non-specific neck pain who receive physiotherapy, as studies have investigated general practice (Vos et al., 2008), included acute or sub- acute neck pain patients (Vos et al., 2008, Pool et al., 2010), or have several methodological flaws leading to inconsistent evidence across studies (Bruls et al., 2015, Walton et al., 2013a).

Knowledge of risk factors and prognostic factors are important for clinicians to prevent and reduce the disability and pain associated with neck pain conditions. A recent study investigated risk factors for onset of a new episode of neck pain in healthy office workers, and found that the development of chronic neck pain was predicted by depressed mood, poor cervical muscle endurance, and impaired endogenous pain inhibition (Shahidi et al., 2015). A study of female healthy workers found that cervical mobility and cervical isometric muscle strength were not risk factors for future neck pain. (Salo et al., 2012). A review study found that risk factors for neck pain were high employment demands, low social/work support, being an ex- smoker, and a history of low back or neck pain (McLean et al., 2010). These studies show that risk factors for neck pain are multifactorial and related to a biopsychosocial model for understanding development of neck pain.

The most consistent prognostic factors for non-recovery or unfavorable treatment outcome in the short term (i.e. < 6 months) across studies seem to be a longer duration of symptoms, a higher symptom severity, use of specific coping mechanisms, and more functional limitations at baseline (Bruls et al., 2015). For long term follow up (i.e. ≥ 6 months), only a longer duration of symptoms at baseline had strong evidence for a poor outcome. The prognostic value of other relevant modifiable factors within a biopsychosocial framework will be discussed in the following sections.

2.3 Biopsychosocial factors

The biopsychosocial model has become the most widely accepted model in understanding chronic pain (Engel, 1977). The relationship and interaction between biological, psychological and social factors in understanding and treating neck pain is complex (Gatchel, 2004), as illustrated in Figure 1. This model implies that research on neck pain, and chronic pain conditions in general, should emphasize a broad spectrum of variables, especially since no single intervention has shown a clear superior effect in treating neck pain (Driessen et al., 2012, Hurwitz et al., 2008). A criticism against research has been that studies have relied too much on psychological and self-report measures, compared with the biological and more objective parts of the model (Jull and Sterling, 2009, Weiner, 2008, Gatchel and Turk, 2008). However, the model implies an interaction between these factors, instead of a neither/-nor relationship, where the strength or meaning of each factor may vary between individuals. The interaction between factors may also differ across diagnoses. Patients with neck pain report more functional problems related to the biological part of the model than patients with pain in other body regions (Fairbairn et al., 2012). Furthermore, a prospective cohort study of patients with either neck pain or low back pain found a weaker relationship between psychological factors (fear avoidance) and disability in patients with neck pain, compared with patients with low back pain (George et al., 2001), suggesting caution when extrapolating studies on low back pain patients to neck pain patients. This thesis focus on the bio- and psychological part, but will also include variables covering the social domain.

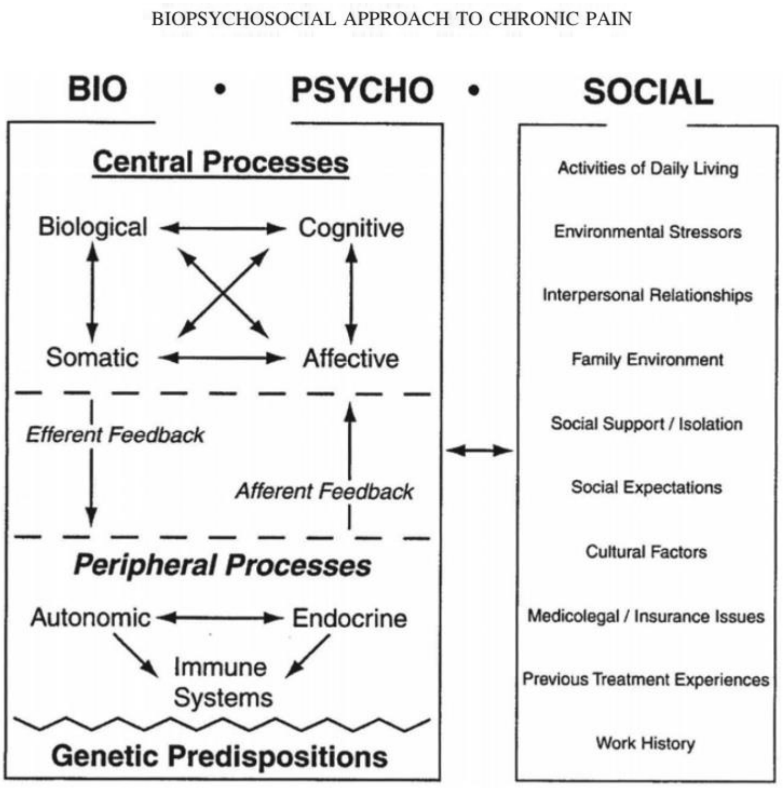

Figure 1 The biopsychosocial model. Reproduced from “Comorbidity of Chronic Mental and Physical Health Conditions: The Biopsychosocial Perspective,” by R.J.Gatchel, Americal Psychologist,59,792-805. Copyright 2004 by the American Psychological Association (Gatchel, 2004).

2.3.1 Psychological factors

The term psychological factors will in this thesis be used as an umbrella-term for kinesiophobia, catastrophizing, and pain-self-efficacy. It is however important to acknowledge that other psychological factors such as anxiety, depression and optimism, are possible important psychological aspects in chronic pain conditions.

In spinal pain, the fear avoidance model (FAM) has gained interest among researchers and clinicians, and was developed in order to explain why some people with acute low back pain develop chronic pain while other recover (Lethem et al., 1983). The model emphasizes a cyclical relationship between pain catastrophizing, pain- related fear, avoidance behavior, disuse and disability (Vlaeyen and Linton, 2012, Vlaeyen and Linton, 2000). The cyclical relationship is appealing to clinicians as it provides a causal model to explain why some individuals develop chronic pain while others, with lower fear avoidance beliefs, recover from the initial painful condition. A recent study showed promising results for adding a cognitive-behavioral intervention, aimed at reducing catastrophizing and pain related fear, to a neck exercise program for chronic neck pain subjects (Thompson et al., 2015). However, the authors did not find a superior effect on the primary outcome (disability) when compared to with patients receiving the neck exercise program alone, an observation corroborated by a recent review that found no superior effect of cognitive behavioral treatment when compared to other treatments (Monticone et al., 2015b).

Psychological factors may be associated with how people move their head, i.e. the interaction between biological and psychological factors illustrated in Figure 1. A cross- sectional study found moderate correlations (r = 0.4–0.6) between kinesiophobia and head and neck kinematics, such as peak velocity, range of motion (ROM), and movement smoothness, while correlations with kinematic measures were lower for pain and disability (Sarig Bahat et al., 2013). This finding underlines the validity of the FAM in neck pain, though the causality between kinesiophobia and kinematic measures remains unknown (Hudes, 2011). Catastrophizing is correlated to pain level and disability and may modify treatment outcomes in neck pain patients (Verhagen et al., 2010, Thompson et al., 2010). A study of sub- acute neck pain patients found an inconsistent relationship between psychological factors and pain, with fear avoidance as the most consistent variable (Pool et al., 2010), while other evidence indicates that deficits in motor control are more important than psychological factors when explaining variations in pain levels among office workers with neck pain (Johnston et al., 2009). More research is thus needed on the relative importance of psychological factors in neck pain.

Self-efficacy is a part of the social cognitive theory developed by Bandura, which describes the relationship between self-efficacy, outcome expectancies, intentions and behavior (Bandura, 1977). It has been suggested that pain must be taken into account when measuring self-efficacy in subjects with chronic pain (Nicholas, 2007). Nicholas defines pain self-efficacy as a subject`s confidence in performing an activity, despite experiencing pain. Studies of low back pain patients suggest that self-efficacy is an important mediator of the relationship between pain and long term disability (Costa Lda et al., 2011), and a strong predictor for recovery (Foster et al., 2010). A mediator (for example, self-efficacy) is a variable in the causal pathway between an exposure (for example, pain) and the outcome (for example, disability), and describes the indirect effect of pain on disability through self-efficacy (Hill and Fritz, 2011). The influence of pain self- efficacy in neck pain is unknown.

2.3.2 Structure and function of cervical muscles in neck pain

Mobility and stability are the main functions of the cervical spine, as it supports and orients the head relative to the trunk. A large proportion of stability is maintained by the cervical muscles (Panjabi et al., 1998), which are commonly divided into deep and superficial muscles according to their function and anatomic insertion to the cervical spine, the occiput, as well as the clavicle and scapulae. Superficial muscles (for example, splenius capitis, semispinalis capitis, sternocleidomastoideus, trapezius, and anterior scalene) exert greater torque than the deep cervical muscles, due to their larger lever-arms and cross- sectional areas. The deep cervical muscles (longus colli, longus capitis, semispinalis cervicis, and multifidus) have a large muscle spindle density, segmental attachments, and high proportion of slow twitch fibers, and the main function is to guide and support vertebral motion segments (Jull et al., 2008a, Boyd-Clark et al., 2001). The large density of muscle spindles in the cervical muscles especially in the craniocervical region provides sensory information through connections with the visual, vestibular, and postural control systems (Treleaven, 2008b, Boyd-Clark et al., 2002, Kulkarni et al., 2001).

The interaction between the deep and superficial muscles is considered to be important for cervical function. In research and clinical settings, use of the craniocervical flexion test (CCF) has become popular as it evaluates the function of the deep cervical flexors, longus colli and longus capitis (Jull et al., 2008b). Studies have also described a more global isometric neck flexion test to evaluate neck function (Vitti et al., 1973, Grimmer, 1994, Cleland et al., 2006). Figure 2 summarizes the findings of the deficits in cervical neck flexors. More recent studies have also found alterations in the deep and superficial muscles of the neck extensor. Compared with healthy controls, neck pain subjects have reduced activation of the deep neck extensors (semispinalis cervicis and multifidus) during an isometric neck extension task (O'Leary et al., 2011), increased coactivation and activity of superficial neck extensors during a neck flexion task (Lindstrom et al., 2011), and reduced cross sectional area of the deep cervical extensors. Studies investigating the structure and function of the neck extensors have also found that neck pain patients may have reduced neck extensor muscle strength (Cagnie et al., 2007), , reduced relaxation of the neck extensors after activity (Johnston et al., 2008), altered flexion- relaxation ratio (Murphy et al., 2010), reduced directional specificity of the semispinalis cervicis (Schomacher et al., 2013) and the superficial muscle splenius capitis (Lindstrom et al., 2011), (Elliott et al., 2014). Recent studies show that the activation of the deep neck extensors relative to the superficial neck extensors may be modified by specific exercises (Schomacher et al., 2012, Schomacher et al., 2015). Preliminary evidence suggests that exercise induce changes in cervical extensor muscle morphology in whiplash patients that correlate with increased muscle strength and reduced disability (O'Leary et al., 2015). More research is required to investigate whether normalization of these alterations is associated with recovery from non- specific neck pain.

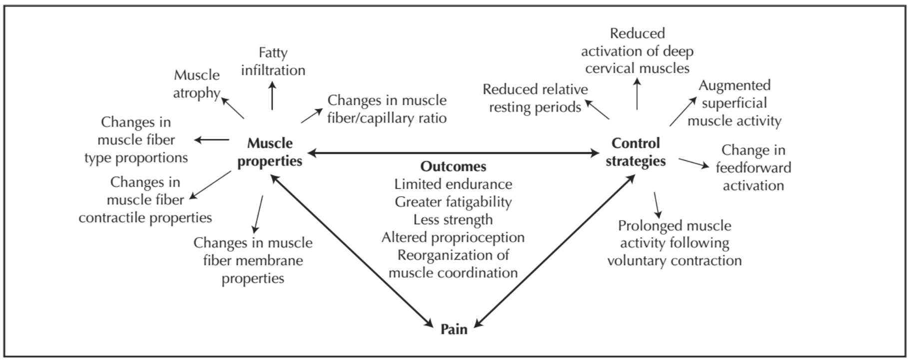

Figure 2. Inter-relationships between pain, altered control strategies, and peripheral changes of the cervical muscles. With kind permission from Springer Science: Current Rheumatology Reports (2007) 9:497-502. Figure 1 page 498. Neural and muscular factors associated with motor impairments in neck pain. Falla, D. Farina, D.

2.3.3 Motor control and neck motion

The broad definition of motor control, as adopted in this thesis, is the “ability to regulate or direct the mechanisms essential to movement” and thus involves all aspects from the processes in the central nervous system via the motor units in the muscles, to the final output which is the specific movement performed (Shumway-Cook and Wollacott, 2001). Head and neck motor control is complex due to the connections between the visual, vestibular, and proprioceptive senses. The neck reflexes, the cervicococollic reflex (CCR) and vestibulocollic reflex (VCR), and voluntary control of the head and neck interact and contribute to 1) stabilize the head on the trunk 2) to guide and control the gaze in the surrounding environment 3) and postural control (Peterson, 2004). The complexity of these relationships is further illuminated by the biomechanics and anatomy of the head and neck plant, also keeping in mind the influence of psychological factors. The head is, in contrast to the lumbar spine, an unstable system with a relatively small base of support where the muscles contribute to approximately 80 % of the stability of the cervical spine (Panjabi et al., 1998). The large number of muscles in the cervical region, whereby approximately 20 pairs of muscles contribute to head movement (Kamibayashi and Richmond, 1998), indicate that a specific head movement can be accomplished by several different motor commands or muscle activation patterns (Peterson, 2004). For example, unique patterns of muscle activation were not observed when subjects were asked to stabilize their heads against load, or when they had to perform a trajectory task (Keshner and Peterson, 1988, Keshner et al., 1989). A recent study showed that healthy subjects exposed to experimentally induced neck pain performed a kinematic task in a similar way as in the non-painful condition, but with altered neck muscle activation patterns (Gizzi et al., 2015). These findings underline the complexity of motor control adaptations in neck pain. Several theories have been proposed to explain the impact of pain on motor control. These will be discussed in the following section.

2.3.3.1 Pain and motor control theories.

Several theories have been developed to explain the changes in motor control observed in pain conditions like neck pain and low back pain. The “vicious cycle” theory hypothesized that pain may lead to a stereotypical increase in muscle activity both during activity and rest, in turn leading to ischemic processes that cause activation of nociceptive afferents and increased muscle activity (Travell et al., 1942). However, this vicious cycle of pain does not explain the various muscle activation patterns observed in neck pain patients, such as decreased deep neck flexor activity (Falla, 2004). The pain adaptation model was developed by Lund et al. (1991) due to the limitations of the vicious cycle theory. This model suggested that pain causes reduced force production, and reduced range and velocity of movement of the affected body part through muscle inhibition when acting as an agonist and increased muscle activity when acting as an antagonist. This adaptation was therefore considered to be a protective adaptation of the body to prevent further damage or pain. A study of healthy subjects found that experimental muscle pain induced by injection of hypertonic saline into the sternocleidomastoid or the splenius capitis led to an increase in agonist activity and an inhibition of antagonist activity (Falla et al., 2007). However, other findings from these researchers do not support the pain adaptation model. Falla et al. (2010) measured the activation of the sternocleidomastoid during a multidirectional isometric task in chronic neck pain patients, and found increased muscle activity aross all movement directions, thus, supporting the vicious cycle theory (Falla et al., 2010).

A pathophysiological model was developed by Johansson and Sojka to explain the contribution of muscle spindles to work related muscle tension and pain. According to this model, metabolites produced in the muscles during repetitive or sustained static muscle contractions activate chemosensitive group III and group IV afferents that increase activity in the muscle spindles and thereby increase muscle stiffness (Johansson and Sojka, 1991). Thus, a positive feedback loop is created as increased muscle stiffness causes increased production of metabolites (Johansson et al., 1999). The recent finding of direct sympathetic innervation of the muscle spindles supports this model, and provides an explanation for the deficits in proprioception and other aspects of motor control observed in neck pain conditions (Radovanovic et al., 2015).

The partly contradicting evidence for different theories suggests a wide variety of individual adaptations of motor control and that new theories are required to explain the multiple alterations in motor control observed in chronic neck pain (Hodges and Tucker, 2011, Hodges and Smeets, 2015). Due to this complexity, neck motor control and motion and associations with clinical symptoms will further be described by division into different constructs. These conceptually different constructs have been applied in the methodology of this thesis.

2.3.3.2 Constructs of neck motion and motor control

Neck flexibility

In this thesis, neck flexibility refers to ROM in the three movement planes of the cervical spine:1) flexion/extension in the sagittal plane; 2) rotation in the horizontal plane and; 3) lateral flexion in the coronal plane. Conjunct motion (CM), a measure of the stiffness of the movement, and movement velocity are also included in this construct in order to describe the head and neck kinematics during movement in the three planes.

Cervical ROM is routinely assessed in clinical practice (Walton et al., 2013c) and widely used in neck pain studies. Chronic neck pain patients have less cervical ROM compared with healthy controls (Woodhouse and Vasseljen, 2008, Guo et al., 2012, Vogt et al., 2007, Johnston et al., 2008, Rudolfsson et al., 2012, Hagen et al., 1997, Meisingset et al., 2015). Rudolfsson et al. used a three segmental model of the thorax, cervical spine, and head in order to investigate ROM in the upper and lower cervical spine. Compared with healthy controls, subjects with neck pain had less movement in the lower cervical spine when performing flexion and less movement in the upper cervical spine when performing extension (Rudolfsson et al., 2012). This procedure thus provides specific information on the impairments observed in the different structural and functional regions of the cervical spine. Despite the large volume of evidence for impaired neck motion the prognostic value of cervical ROM is unclear, and moderate to weak associations (Pearsons's $r < 0.7$) are shown with clinical characteristics like pain and disability (Howell, 2011, Walton et al., 2013a, Chiu et al., 2005, Hagen et al., 1997, Snodgrass et al., 2014, Rudolfsson et al., 2012).

Conjunct motion is, in this thesis, defined as motion in the accessory planes during a test of cervical ROM in the cardinal planes. Woodhouse and Vasseljen found that neck pain patients have reduced CM compared with healthy controls when performing flexion/extension and rotation in the horizontal plane (Woodhouse and Vasseljen, 2008). A study of fast cervical rotations calculated CM as a change in the direction of the rotational axis and found smaller deviations in the axis of rotation in chronic neck pain patients compared with healthy controls (Roijezon et al., 2010). These findings suggest a stiffer movement pattern in neck pain patients compared with healthy controls.

Recent evidence emphasizes the importance of measuring movement velocity in neck pain due to the diagnostic value of this variable; patients with neck pain move their head slower than healthy controls (Sarig Bahat et al., 2013, Sarig Bahat et al., 2010, Sarig Bahat et al., 2014, Tsang et al., 2013b, Tsang et al., 2013a). Quick and precise head movements are an important daily function, as we are required to respond to stimuli from the surrounding environment (Roijezon et al., 2010). Movement velocity is often measured as peak velocity and has been shown to better discriminate neck pain individuals from healthy controls than cervical ROM (Roijezon et al., 2010). Peak velocity correlates with clinical features like pain intensity, disability, and fear avoidance suggesting that the management of neck pain may include increasing movement velocity (Sarig Bahat et al., 2013). The causal relationship between reduced peak velocity and clinical features are unknown, however.

Proprioception

Proprioception involves afferent information from receptors located in the skin, muscles, and joints that contribute to conscious or unconscious awareness of joint position, movement, and sensation of force, effort and heaviness (Riemann and Lephart, 2002). Receptors located in the muscles, the muscle spindle system, seem to be most important for sensing position and movement (Goodwin et al., 1972), while joint receptors are mainly regarded as limit detectors (Proske and Gandevia, 2009). The muscle spindles provide information to the central nervous system about the degree and speed of change in muscle length, and may thus contribute to both position and movement sensing (Proske and Gandevia, 2009). Proprioception is thus an overlying dimension of the other constructs applied in this thesis. Movement sense is described below, in the paragraph titled “trajectory movement control”. Due to the connections between mechanoreceptors (muscle spindles), vision, and the vestibular system, altered afferent information from the mechanoreceptors in neck pain conditions may cause mismatch between afferent signals and thus lead to disturbances in neck motor control and sensorimotor dysfunctions like dizziness, visual disturbances and altered postural control (Treleaven and Takasaki, 2014, Treleaven, 2008a). Proprioceptive information is important for head motor control (Shaikh et al., 2013), and pain may alter this information through activation of the sympathetic nervous system in addition to altering nociceptive information (Passatore and Roatta, 2006, Radovanovic et al., 2015). Subjects with chronic neck pain may exhibit alterations in sympathetic activity in response to physical activity compared with healthy controls (Hallman et al., 2015), underlining that neck pain is associated with a dysregulation in central processes. Recent evidence has shown that pain may also influence proprioception through reorganization of the somatosensory cortex (Moseley and Flor, 2012).

In neck pain, proprioception has traditionally been assessed using tests for joint position sense and measuring the repositioning error following active neck motion. Studies have shown that neck pain patients may have altered joint position sense (Chen and Treleaven, 2013, Revel et al., 1991, Stanton et al., 2015, Treleaven, 2008a). However, a recent meta- analysis revealed only a moderate difference (standardized mean difference of 0.44; 95% CI: 0.25 to 0.63) in joint position sense between neck pain patients and healthy controls, suggesting that other aspects of neck motor control should be evaluated in conjunction with joint position sense (Stanton et al., 2015). In general, proprioceptive training may induce reorganizing of the somatosensory cortex and improve sensorimotor function (Aman et al., 2014), but studies have shown no additional effect of adding proprioceptive exercises during neck pain rehabilitation (McCaskey et al., 2014).

Trajectory movement control

The ability to track a pattern, visible or invisible, by movement of the head is termed trajectory movement control. The term kinesthesia, first described in 1888, is used in studies involving trajectory movement control (Bastian, 1888, Kristjansson et al., 2004) and encompasses both the position sense and the movement sense. Although muscle spindles are the main sensory receptors for both position sense and movement sense, they should be viewed as two distinct senses, as evidence indicates that their central processing is performed separately (Proske and Gandevia, 2009). Application of both trajectory movement control and tests for joint position sense may thus complement and strengthen the evaluation of motor control deficits in neck pain.

The Fly test and figure-of-eight (FOE) are two tests used to assess trajectory movement control. These tests are considered as more complex than tests for joint position sense, due to the dynamic properties requiring continuous matching between visual and kinesthetic input. In the Fly test, subjects are required to track a cursor displayed on a screen (the Fly) with movement of the head (Kristjansson and Oddsdottir, 2010). The pattern in the Fly test is invisible and unpredictable for the subjects, in contrast to the FOE test where the subjects are instructed to track a cursor moving along the line of the figure as accurately as possible by moving their head (Woodhouse et al., 2010b). It can thus be hypothesized that the Fly test relies more on feedback control than the FOE test due to the invisible pattern. The Fly test has been shown to discriminate patients with non-specific neck pain from healthy controls and whiplash patients from healthy controls, and can also discriminate between the two patient groups (Kristjansson and Oddsdottir, 2010). Tests of trajectory movement control have also assessed smoothness or movement irregularities and found that neck pain is associated with jerkier head movements and movement irregularities (Oddsdottir et al., 2015, Woodhouse et al., 2010b). Movement irregularities were found only in whiplash patients and not in non-traumatic neck pain patients (Woodhouse et al., 2010b). These movement irregularities, characterized by increased angular velocity in the frequency bands 3-4 Hz and 4-5 Hz were related to severe pain and dizziness in the whiplash patients. Sjolander and colleagues found that non-traumatic neck pain patients displayed a jerky movement pattern during fast head rotation in the horizontal plane (Sjolander et al., 2008). By contrast, evidence suggest that jerky and irregular movement patterns in unconstrained head movements are not a feature of altered motor control, but are related to differences in movement velocity and movement displacement between neck pain and healthy subjects during the performance of these tests (Vikne et al., 2013b, Vikne et al., 2013a). The prognostic value of tests for trajectory movement control is unknown. A study of whiplash patients showed two different courses for performance in the Fly test during a follow- up period of one year, but they were not related to subjective clinical characteristics (Oddsdottir and Kristjansson, 2012). More research is needed to evaluate the clinical application of tests for trajectory movement control, especially as these tests require expensive equipment to assess different aspects of performance.

Visual control

Trajectory movement control is highly dependent on eye- head movement control, and a short description is therefore given below. Cervical afferents contribute to information for the eye-head coordination and reflex responses for stabilization of gaze when moving the head (Treleaven et al., 2011b, Jurgens and Mergner, 1989). The cervico-ocular reflex (COR) reacts to stretching of the cervical muscles and is thus thought to be most relevant during fast head movements to stabilize and reorient gaze (Jurgens and Mergner, 1989). The vestibuloocular and optokinetic reflexes assist the COR in optimizing clear vision during movement (Mergner et al., 1998). Proprioceptive information from the cervical muscle spindles and visual control is therefore closely linked, and is important for function in daily living (Pettorossi and Schieppati, 2014).

Visual disturbances have been observed in both non-specific neck pain and whiplash patients (Della Casa et al., 2014) , although the deficits seem to be more prevalent and severe in whiplash associated disorders which exhibit higher pain levels and increased dizziness (Treleaven and Takasaki, 2014, Treleaven et al., 2011a). Commonly reported visual disturbances among patients with non-specific neck pain are “need to concentrate to read, sensitivity to light, visual fatigue, and eye strain” (Treleaven and Takasaki, 2014).

Head steadiness

The ability to keep the head steady relative to the trunk or to the environment in response to external perturbations or to gravity, is essential in daily activities as the head controls the direction of gaze and provides a base for vestibular input (Peterson, 2004). As a number of studies show deficits in neck muscle structure and function in neck pain, the question arises as to whether these deficits alter the ability to keep the head steady, and the extent to which the function of the neck is influenced by alterations in the neuromuscular system (Turker, 2010). Head stabilization is mainly achieved by regulating muscle stiffness, which is controlled by voluntary and/or reflex mechanisms (Peterson, 2004). The vestibular reflex, VCR, stabilizes the head in space by activating neck muscles to produce compensatory head movements in the opposite direction and inhibiting muscles that produce forces in the same direction, relative to the perturbation force (Wilson and Schor, 1999). The cervicocollic reflex (CCR) keeps the head stable, relative to the trunk, by means of proprioceptive input from the muscle spindles in the cervical spine.

Studies of investigating head steadiness have measured both static and dynamic steadiness. A study by Keshner in 1995 provided a model for studying the contribution of voluntary and reflex control for dynamic head steadiness in healthy subjects. Subjects were exposed to whole body random perturbations in the horizontal plane using an actuated chair while seated with the trunk in a fixed position and the head allowed to move freely. The perturbations were in the frequency range of 0.185 to 4.11. The instruction given was to keep the head facing forward during performance of three different conditions; with vision, without vision, and a mental arithmetic task in combination with no vision. Results showed that voluntary and reflex controls were frequency-dependent, where voluntary control was seen for frequencies below 1 Hz and reflex control was most apparent between 1-2 Hz. At frequencies above 3 Hz, mechanical resonance occurred and neither voluntary or reflex systems were able to control the head position (Keshner and Peterson, 1995). However, the contribution of voluntary and reflex control mechanisms in neck pain, and whether alterations in the two different regulatory systems are important for the perpetuation and recurrence of neck pain symptoms, remains unknown.

Head steadiness is mostly assessed using different forms of static tests (Woodhouse et al., 2010a, Harris et al., 2005, Edmondston et al., 2008, Grimmer, 1994). Neck pain patients have reduced holding time and endurance during isometric neck flexion (Harris et al., 2005), with some studies showing conflicting results (Edmondston et al., 2011, Juul et al., 2013). Woodhouse et al. evaluated the ability to keep the head steady during isometric neck flexion in a supine position and when seated in a recumbent position of 60 degrees. Patients with non-traumatic neck pain performed similarly to healthy controls; although a trend towards lower head angular velocity was observed. By contrast, whiplash patients showed a significantly higher head angular velocity compared with healthy controls, indicating different motor control strategies in non-traumatic neck pain compared with whiplash patients, or it may reflect different endurance capacity (Woodhouse et al., 2010a). No studies to date have evaluated the prognostic value of tests for head steadiness in patients with non-traumatic neck pain, or whether changes in head steadiness are related to changes in clinical characteristics.

Postural sway

Assessment of postural sway and other variables of postural control is important when evaluating motor control in neck pain patients, due to the role of cervical neural connections between proprioceptive, visual, and vestibular systems in controlling posture (Treleaven, 2008a). The abundance of mechanoreceptors in the cervical spine is important for maintaining postural control (Boyd-Clark et al., 2002), and altered proprioceptive input to reflex and/or voluntary control is thus a potential mechanism for disturbed postural control (Treleaven, 2008a, Wrisley et al., 2000). Neck pain is associated with impaired postural control characterized by greater postural sway and postural instability (Ruhe et al., 2011, Field et al., 2008, Jorgensen et al., 2011, Cheng et al., 2015a). Evidence indicates that alterations in postural sway are more evident in traumatic neck pain compared with non-traumatic neck pain (Ruhe et al., 2011). Altered postural sway may be related to muscle fatigue reported by individuals with neck pain (Schieppati et al., 2003, Liang et al., 2014, Allen and Proske, 2006). Experimental studies have shown conflicting results in postural control responses to painful stimuli. Postural sway decreased when healthy subjects were exposed to a painful stimuli, suggesting a postural stiffening strategy (Huntley et al., 2015). The same rigid strategy was observed when subjects with chronic neck pain and healthy controls were exposed to perturbations after undergoing a fatiguing neck flexor task (Cheng et al., 2015a). The authors concluded that the stiffening strategy was related to neck muscle fatigue and not to neck pain, as neck pain subjects and healthy controls used the same strategy. The lack of correlation between neck pain and altered postural control strategy in the latter study is corroborated by a review that found limited or conflicting results for the associations between postural control and clinical characteristics such as pain and disability (Ruhe et al., 2011). Furthermore, limited evidence exists to support a specific intervention in achieving changes in postural control parameters (Ruhe et al., 2013, Rudolfsson et al., 2014), suggesting that more research is needed to evaluate the clinical value of postural control interventions.

2.4 Effect of interventions

Physiotherapists apply a wide range of different modalities to the treatment of neck pain, either in combination or as a single treatment choice. However, the choice of treatment is, traditionally, more based on the interests, cultural beliefs and specialty of the therapist than on evidence from systematic reviews and the patient`s prognosis (Walton et al., 2013c). The Task Force on Neck Pain and Its Associated Disorders 2008 concluded that treatments involving manual therapy and exercise are more effective than other treatments for whiplash patients, but no treatment showed superiority for non-specific neck pain (Hurwitz et al., 2008). Table 1 provides current evidence for different physical therapy interventions in neck pain.

Table 1 Overview of systematic reviews for the effect of different physical therapy interventions.

Little to moderate effect	**No effect (or uncertain)**
Manipulation/mobilization (Gross et al., 2015b)	Electrotherapy (Kroeling et al., 2013)
Physical modalities (Graham et al., 2013)	Massage (Patel et al., 2012)
Therapeutic exercise (Cheng et al., 2015b, Bertozzi et al., 2013, Kay et al., 2012, Gross et al., 2015a)	Patient education (Gross et al., 2012)
Dry needling (Cagnie et al., 2015)	Kinesio taping (Parreira Pdo et al., 2014)
Cognitive behavioral treatment (Monticone et al., 2015b)	

Current guidelines and evidence recommend the inclusion of active exercise, consisting of strengthening exercises, in the management of chronic neck pain (O'Riordan et al., 2014, Childs et al., 2008).

2.5 Underlying mechanisms and modifiable factors

Identification of patients that will respond to a particular treatment or patients with a good or poor prognosis has received increasing attention in research on neck and low back pain. Subgrouping of patients based on differences in underlying mechanisms, effect modifiers or prognostic factors may potentially improve diagnostic and treatment efficacy in neck pain patients as shown in low back pain patients (Hill et al., 2011). It has been reported, however, that subgrouping of neck patients based on a clinical prediction rule to a specific treatment did not improve treatment efficacy in the short term (1-4 weeks) or long term (6 months) (Cleland et al., 2010). Further research into possible underlying mechanisms and modifiable factors are warranted in order to develop effective interventions to reduce the burden of neck pain. The background for this thesis, as outlined above, provides the rationale for the studies in this thesis. Figure 3 illustrates the possible relationship between the different factors described in the background. According to the figure, motor control can be viewed as the sum of multiple factors related to peripheral and central nervous system processing. Subject characteristics, such as age and gender, are viewed as covariates for all factors.

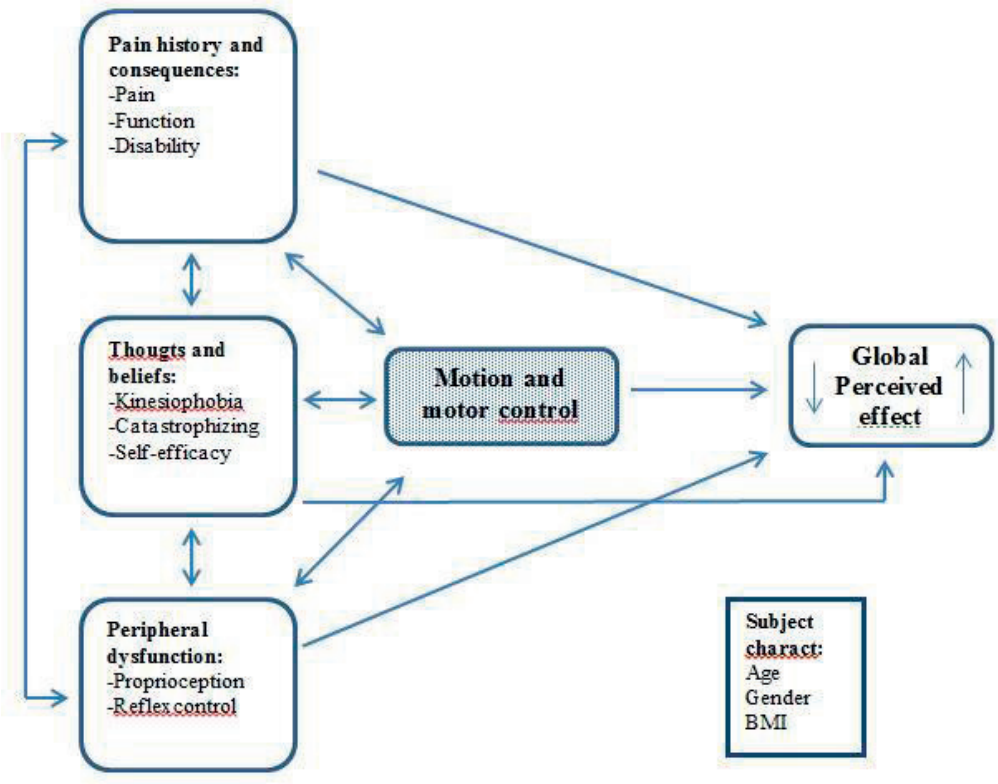

Figure 3 Overview and relationship between the background factors for this thesis. Double arrows indicate associations between the variables, while single arrows indicate one direction of the relationship. Subject characteristics are possible covariates for all factors.

3 Aims

3.1 Overall aim

The overall aim of this thesis was to investigate motor control and neck motion in neck pain patients receiving standard physiotherapy treatment, and their relationship with clinical features such as somatic symptoms, disability, psychological factors and global improvement in a longitudinal study design. Thus, we investigated factors within a biopsychosocial framework in order to explore possible mechanisms, modifiable treatment variables, and prognostic factors in longstanding neck pain.

3.2 Specific aims of the thesis

Study 1

The primary aim of this study was to evaluate neck motion and motor control in neck pain patients compared with healthy controls. The secondary aim was to evaluate the association between clinical features like pain intensity and duration, disability, and kinesiophobia, with neck motion and motor control.

Study 2

The aim of this study was 1) to investigate whether deficits exist in motor control of the head and neck in individuals with neck pain compared with healthy controls when exposed to random perturbations, and 2) whether these deficits reside in the reflex systems or arise from impaired voluntary control, or both.

Study 3

The aim of this study was 1) to investigate changes in motor control and neck motion and 2) to evaluate whether these changes were associated with self-reported neck pain and disability over a clinical course of 2 months.

Study 4

The primary aim of this study was to investigate the contribution of neck motion and motor control, and somatic and psychological factors as prognostic factors for improvement after treatment. The secondary aim was to investigate whether changes in these factors were associated with improvement.

4 Methods

4.1.1.1 Design and data collection

An overview of the studies included in this thesis is presented in Table 2. The same cohort of neck pain patients was used in studies 1-4, but the sample size of the neck pain group differed in the studies due to the following reason: the recruitment of patients to study 1 (n=75) was stopped in February 2014, but recruitment of patients to studies 2, 3, and 4 (n= 81) continued until May 2014 to include a further six subjects. Studies 1 and 2 were cross-sectional, comparative, case-control studies of people with neck pain and healthy controls. For the HC groups in studies 1 and 2, two independent data collections were conducted, since the necessary laboratory equipment was still preparation when the data collection for the HC group in study 1 commenced. Studies 3 and 4 were prospective cohort studies, using the same sample of neck pain patients.

Table 2 Overview of study design, sample size, and outcome variables in the different studies

	Study 1 N=166 (75 NP, 91 HC)	**Study 2** n= 88 (71 NP, 17 HC)	**Study 3** n= 71 (NP)	**Study 4** n= 70 (NP)
Design				
Cross-sectional	x	x		
Prospective cohort			x	x
Neck motion and motor control	x	x	x	x
Psychological factors				
TSK	x	x	x	x
PCS			x	x
PSES			x	x
Clinical features				
Pain characteristics	x		x	x
Disability	x		x	x
Function				x
Global perceived effect				x
Physical activity				x

NP: neck pain patients; HC: healthy controls;TSK: Tampa scale of kinesiophobia; PCS: Pain catastrophizing scale; PSES: Pain self-efficacy scale

The examiners were not blinded to the subjects' group allocations. In study 1, the data from the HC group were collected by a nurse and a physiotherapist, while the data from the neck pain group were collected by a second physiotherapist. The same physiotherapist performed the data collection at 2 weeks and 2 months (studies 3 and 4) in addition to data collection from the HC group in study 2. The examiners were equally and trained in the test procedures, and standardized instructions were used for all tests. In addition, the physiotherapist who performed the data collection for the neck pain group observed the data collection in the HC group to avoid discrepancies in the procedures. All subjects provided written informed consent and the study was conducted in accordance with the Declaration of Helsinki and approved by the Regional Committee for Medical and Health Research Ethics, REC Central (2011/2522/REC Central).

4.2 Subjects

4.2.1 Inclusion and exclusion criteria

Healthy controls

Men and women aged between 18–67 years with no neck pain were included in the healthy control (HC) group in study 1 (August 2012 to December 2012) and in study 2 (September 2014 to December 2014). The subjects were recruited by inviting friends and colleagues from the local university and university hospital to participate. Exclusion criteria were episode of neck pain within the last 3 months, markedly reduced or uncorrected vision, history of neck trauma, diagnosis of any neurological, vestibular or orthopedic condition that could affect motor control, positive Spurling's test for neurological radiating arm pain, pregnancy, and insufficient comprehension of Norwegian.

Neck pain patients

Neck pain patients were recruited consecutively from private physiotherapy clinics in primary health care and from a specialized neck and back pain clinic at the university hospital in the period January 2013 to May 2014. Patients were initially screened for eligibility by telephone. Upon later examination, inclusion criteria were non-specific neck pain as the main medical condition with a score of 3 or more on a numerical rating scale (NRS; 0–10) on the day of testing, and the current neck pain episode lasting >2 weeks. Exclusion criteria were the same as for the control group, except for the criterion of neck pain.

4.2.2 Subject characteristics

The flow of subjects in studies 3 and 4 is shown in Figure 4. Subject characteristics in study 1 are shown in Table 3. The subject characteristics did not vary significantly across the different studies, except with respect to the HC group in study 2. Detailed information on the subjects can be found in the specific papers in this thesis.

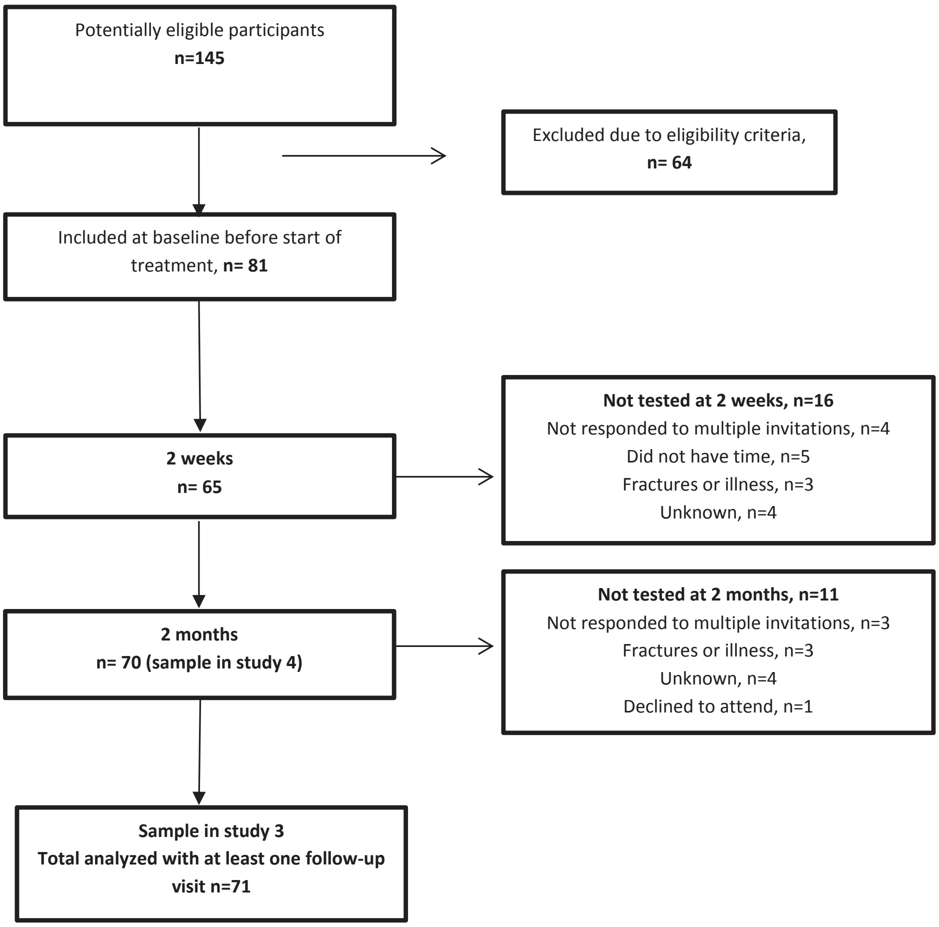

Figure 4 Flow chart of subjects in studies 3 and 4.

Table 3 Subject characteristics and clinical features. Studies 2, 3, and 4 consisted of approximately the same group of neck pain patients as described in study 1.

	Neck pain patients	**Healthy controls**
Study 1		
Sample size (n)	75	91
Age	43.1 (12.9)	40.8 (13.8)
Gender (male/female)	20/55	43/48
Body mass index	24.9 (4.7)	25.0 (3.5)
Current neck pain (NRS: 0-10)	4.6 (1.4)	
Duration of neck pain, n (%)		
< 3 months	7 (9%)	
3-12 months	24 (32%)	
>12 months	44 (59%)	
Neck Disability Index (0-100)	31.2 (11.6)	
Patient-specific functional scale (0-10)	6.5 (2.1)	
TSK (13-52)	24.4 (4.3)	
PCS (0-52)	12.9 (8.5)	
PSES (0-60)	44.3 (10.0)	
Concurrent low back pain, n (%)	20 (27%)	
≥2 additional pain sites, n (%)	39 (52%)	
Neck pain recurrence, n (%)		
First episode	12 (16%)	
1-3 episodes/year	21 (28%)	
>3 episodes/year	42 (56%)	
Study 2		
Sample size	71	17
Age	44.0 (12.9)	31.5
Gender (male/female)	25/50	8/9
Body mass index	24.2 (3.7)	23.7 (2.9)

TSK: Tampa scale of kinesiophiobia; PCS: Pain catastrophizing scale; PSES: Pain self-efficacy scale

4.3 Quantification of neck motion and motor control

4.3.1 Instrumentation

Motion data for cervical and postural sway measurements were acquired using three bodily-worn sensors and the Liberty electromagnetic motion tracker system (Polhemus, Inc, Colchester, Vermont, USA) with a sampling rate of 240 Hz. The system creates an electromagnetic field where the magnetic sensors attached to the body are monitored. Position and orientation in six degrees of freedom are measured, rotation about and translation along three axis relative to the transmitter of the system (TX). Detailed information on the Liberty motion tracker system can be found on the manufacturers' homepage (http://polhemus.com/_assets/img/LIBERTY_Brochure.pdf). Sensor 1 (S1) was placed on the subject's forehead, 1 cm above the arcus superciliaris, and the second sensor (S2) was placed on the spinous process of Th2, while a third sensor (S3) was placed in the area of the spinous processes of L4-L5. In study 2 S3 was placed on a rotating chair in order to validate movement of the trunk relative to the chair. Tight elastic bands were used to hold the sensors in position. The electromagnetic transmitter (TX) was positioned at a distance of 10–50 cm above the head during all measurements. For S1 and S2, raw data were low pass filtered at 20 Hz using a second order Butterworth filter, while raw data for S3 were low pass filtered at 5 Hz for postural sway measurements.

In study 2, dynamic head steadiness was evaluated during unpredictable perturbations to the trunk induced by means of an actuated chair. The main structure of the chair, including casings and main bearing, was custom-made using non-metallic materials to minimize their influence on the electromagnetic motion tracker system. For the same reason, the motor and gear were placed close to the floor, and power electronics were placed at a 2 m horizontal distance from the base of the chair. The rotation around the vertical axis of the chair, which coincided approximately with the axis of the cervical spine, was driven by a brushed DC motor with a 1:308 gear ratio (Maxon Motor, Sachseln, Switzerland, part no. 353295), controlled by a LabVIEW program via a NI 9505 DC Brushed Servo Drive (both of National Instruments Corporation, Austin, TX, USA).

The perturbation signal to the chair provided pseudorandom perturbations in a non-repetitious pattern, selected to prohibit any anticipatory preparation in the subjects or contamination between the resulting frequencies, which ranged from 0.185 to 4.117 Hz. Chair velocity amplitudes were decreased as frequency increased: 20°/s from 0.185 to 0.355 Hz, 19°/s from 0.505 to 1.055 Hz, 16°/s from 1.475 to 2.095 Hz, 15°/s at 2.945 Hz, and 13°/s at 4.115 Hz, with the maximum excursion ±17° occurring at the lowest frequency (in practice, however, being somewhat larger due to superposition of all harmonics). The same waveform was used for all participants.

A software tool based on Matlab (The MathWorks, Inc., Natick, MA, USA) was developed (SINTEF ICT, Applied Cybernetics and Dept. of Engineering Cybernetics, NTNU, Norway) to record and analyze motion data. Furthermore, the software allowed real-time viewing of the motion trace. The coordinate system defined by the TX was used for calculating all variables except cervical ROM. For this variable, a new coordinate system was calibrated for each subject to adjust the coordinate axes to the individually preferred axes of cervical motion. A detailed description of the calibration process is available online in the appendix of study 1.

4.3.2 Test procedures and outcome variables for the kinematic measures.

The description of tests of motor control and the calculated variables is summarized in Table 4. We adopted five constructs of motor control and neck motion to group the different tests used in this thesis. The tests were performed in the order listed in Table 3. The same order was used for the HC and the neck pain groups, and for the follow-up visits at 2 weeks and 2 months. The test procedures and calculation of the outcome variables in the different constructs of neck motor control and motion are described below.

Table 4 Description of the motor control and cervical motion variables. The column "test" lists the order of the tests in the data collection in studies 1, 3, and 4.

Construct	Test	Assessment	Unit of measure	Sensors	Reps per test	Analyzed	Comments
Neck flexibility	Active neck movements in flexion/extension, rotation and lateral flexion	Cervical ROM in flexion/extension, rotation, and, lateral flexion	deg	S1 vs S2	3	Avg	Full cycle cervical ROM
		Conjunct motion in the two associated movement planes	deg			Avg	
		Peak velocity in flexion/extension, rotation and lateral flexion	deg/s			Avg	3 D angular velocity
Proprioception	Joint position error in left and right head rotation	3D repositioning error in left and right rotation	deg	S1 vs S2	6	Avg	3 repetitions in each direction
Trajectory movement control	FOE slow speed	Average point deviation (PD)	cm	S1 vs TX	1	Single	30 sec duration
	FOE fast speed				1		20 sec duration
	FOE in standing, slow speed				1		30 sec duration.
	The Fly test, 1A	Average point deviation (PD)	cm	S1 vs TX	1	Single	30 sec duration for all of the Fly tests. Adapted from Kristjansson et al. (2010)
	The Fly test, 2B				1		
	The Fly test, 1B				1		
	The Fly test, 2A				1		
Head steadiness	Isometric neck flexion, low load	Average 3 D angular velocity	deg/s	S1 vs S2	1	Single	60 sec duration 60° recumbent position
	Isometric neck flexion, high load	Average 3 D angular velocity Holding time	deg/s sec		1		30 sec duration Supine position
Postural sway	FOE in standing	Sway area (95 % confidence area)	cm^2	S3 vs TX	1	Single	30 sec duration
	Standing balance EO				1		60 sec duration for the tests of standing balance.
	Standing balance EC				1		
	Standing balance EOB				1		

ROM=range of motion. CM= conjunct motion. Deg= degrees. 3D= 3 dimensional. PD= point deviation. FOE= figure of eight. EO= eyes open. EC= eyes closed. EOB= eyes open balance pad. S1= forehead sensor. S2= spinous process of T2. S3= spinous process of L4-L5. TX= transmitter on Liberty. 1A= easy pattern, small ROM. 1B= easy pattern, large ROM. 2A= difficult pattern, small ROM. 2B= difficult pattern, large ROM.

Neck flexibility

Maximal cervical ROM was measured with the subjects seated on a wooden bench with a backrest in an 80º recumbent position, and with shoulders fixed using nonflexible shoulder straps to avoid movement of the thorax (Figure 5). The subjects were asked to move as far as possible in all three primary movement planes (flexion/extension, rotation in the horizontal plane and lateral flexion) with a self-selected velocity. Start and stop of the recording was manually set by the examiner before and after each movement. Maximal cervical ROM was calculated as the mean of three trials for each primary movement plane. During each primary plane ROM test, neck flexibility was also assessed by the degree of motion in accessory planes, i.e., conjunct motion (CM), which was calculated as the maximum ROM in the two associated movement planes. Peak velocity in the three tests of maximal cervical ROM was computed to assess movement velocity as the peak 3D angular velocity and expressed as mean of three trials. Here, 3 D velocity was calculated as the rotation velocity at the movement`s instantaneous helical axis. ROM variability was calculated as the standard deviation of three trials (SD_{mean}) in each primary neck movement plane (non-published data).

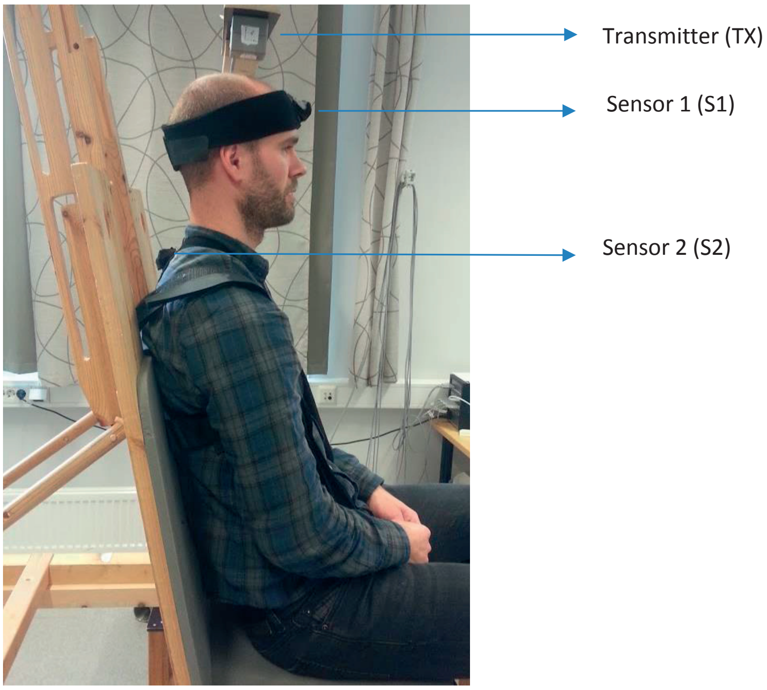

Figure 5 Starting position for tests of neck flexibility and trajectory movement control

Proprioception

Joint position error (JPE) after left and right cervical rotation in the horizontal plane was used to assess proprioception. The subjects were blind-folded and instructed to start with the head in a preferred neutral position, and then to rotate the head as far as possible before returning back to the neutral position (Figure 6). The subjects performed three repetitions in each direction; first to the left (3x) and then to the right (3x). Subjects were asked to provide oral confirmation when they believed they had returned to the neutral position. The examiner did not reposition subjects' heads back to the initial neutral position, but used the end position of the previous trial as the starting position for the next repetition.

Figure 6 Test of joint position error. Starting position blindfolded in neutral position (A). Maximum rotation to left and back to neutral (3x), and to right and back to neutral (3x) (B).

Joint position error was calculated as follows: the absolute angular difference (in degrees) between the start and end position of the left and right head rotations was summed over the three cardinal planes of rotation. The mean of the results from six trials (three to the left and three to the right) was used to express the repositioning error. We also calculated JPE variability (VE) (unpublished data) since this variable has previously been shown to discriminate between neck pain groups and healthy controls (Sjolander et al., 2008). JPE variability was calculated as the standard deviation of six trials in the primary plane rotation

Trajectory movement control

Two head tracking tasks were performed in order to assess trajectory movement control; a figure-of-eight test (FOE) (adapted from the study of Woodhouse et al. 2010b) and a "Fly test" (adapted from Kristjannson et al. 2010). The tests were performed in a seated position as shown in Figure 5, but shoulder straps were not used. For the FOE test, a horizontal figure-of-eight (Figure 7) was displayed on a screen in front of the subject at a distance of 250 cm. Subjects were instructed to follow a white cursor moving along the line of the figure as accurately as possible by moving their head. The speed of tracking was set by the movement of the white cursor. The movement of the head was projected onto the screen as a red cursor. Two different tracking velocities, slow and fast, were used to investigate possible differences in the speed-accuracy trade-off between neck pain subjects and HC subjects (Fitts, 1954). The test with low velocity was also repeated in a standing position. The HC and neck pain subjects were familiarized with the test by performing one test session with high velocity.

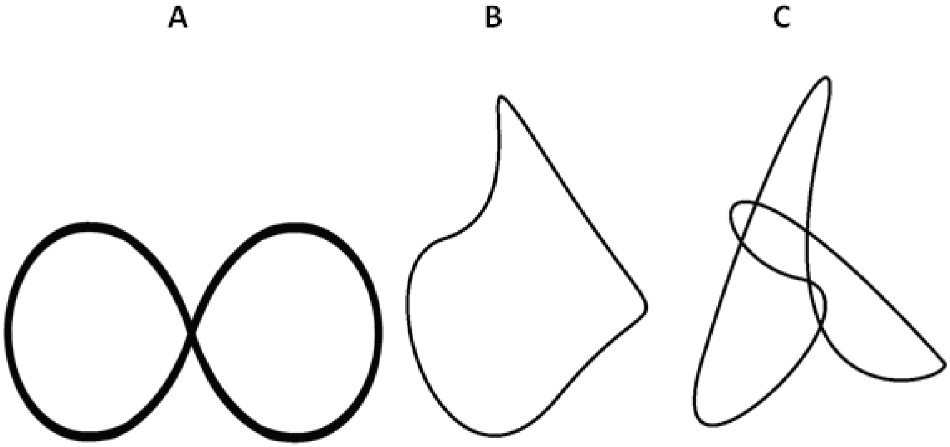

Figure 7 The movement patterns of the figure of eight (FOE) and "the Fly" tests for assessment of trajectory movement control. A: FOE. B: Movement pattern 1A and 1B in the Fly test. C: Movement pattern 2A and 2B in the Fly test (modified from Kristjansson et al. (2010)). Mean cervical ROM in the performance of the FOE was 11° flexion/extension and 24° rotation in the horizontal plane. Mean cervical ROM in the Fly test was 14° flexion/extension and 10° rotation in the horizontal plane in movement pattern 1A, and 15° flexion/extension and 10° rotation in the horizontal plane in movement pattern 2A. Movement patterns 1B and 2B, which were the same patterns as 1A and 2A, respectively, exhibited twice as much cervical ROM (movement ratio head to cursor 2:1).

Two patterns of the Fly test were used in this study (Figure 7). Two different demands for head movement were applied for the two patterns during the Fly test, one with a head- to-projected-cursor movement ratio of 1:1 and another with a ratio of 2:1 , the latter requiring the head to move twice as far as in the first test to move the cursor on the screen. The 2:1 ratio was included to assess the demands of increased ROM on trajectory movement control. The tracking velocities for the Fly tests measurement of head motion velocity were in the range of 2–5°/s. The patterns were not visible to the subject, and were thus unpredictable. The setup was similar to that of the FOE test, and subjects were instructed to follow the white cursor ("the Fly") as closely as possible. The HC group was familiarized with the test by performing one of the Fly tests, and the neck pain group performed two of the tests. Point deviation (PD), a measure of movement accuracy, was calculated as the mean absolute distance (in cm) between the red cursor and the white cursor during both the FOE and the Fly tests.

Head steadiness

Isometric neck flexion (INF) was used to investigate the ability to hold the head steady under two conditions, low load and high load (Figure 8). For the low load test, subjects were seated in a 60° recumbent position with a footrest and no shoulder straps and asked to slightly lift the head (1-2 cm) from the backrest and hold it as steady as possible in the same position for 1 minute. For the INF high load test, subjects were positioned supine and asked to perform craniocervical flexion while the head was positioned on the bench, and then to lift the head slightly from the bench and hold it as steady as possible in the same position for 30 s. The test was terminated if the subject touched the table with the back of the head, or if the subject chose to end the test due to fatigue or neck pain. Angular velocity of the head was calculated to assess the ability to hold the head steady during the INF test. Holding time during the high load INF test was used as a descriptive variable. Angular velocity (deg/s) was calculated as the point to point change in orientation of the forehead sensor (S1) over time, relative to the sensor placed on the spinous process of T2 (S2).

Figure 8 Isometric neck flexion with high (A) and low (B) load.

In study 2 we aimed to replicate a method previously described by Keshner, using a modified rotating chair (Figure 9) as described under instrumentations (Keshner and Peterson, 1995).

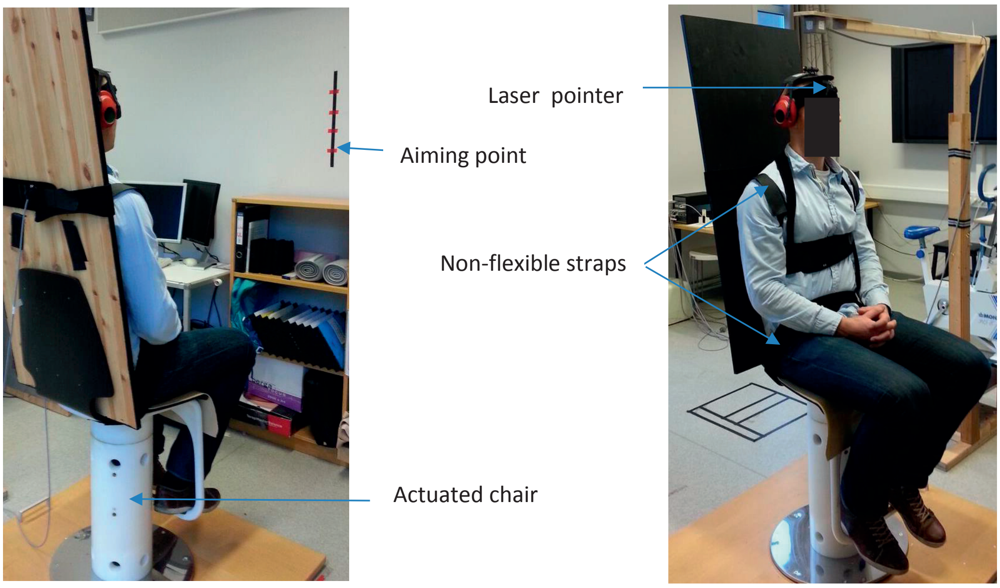

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Figure 9 The starting position for the tests in study 2.

The required task was to keep the head steady in space while the body was exposed to pseudorandom rotations in the horizontal plane. Each subject was exposed to one trial (of duration 200 s) under each of three conditions, in the following order: with vision (VS), without vision (NV), and without vision but with an additional mental task (counting backwards from 500 in steps of seven) (MA), the latter performed in order to divert the attention away from head position control. The first condition (VS) aimed to investigate voluntary control using an available visual reference to position provided by a laser pointer mounted in a rigid fixture on top of the head, aimed toward a vertical line on a white surface (distance 1.6 m) in front of the subject. The second condition (NV) challenged voluntary control without visual information. The purpose of the third condition (MA) was to investigate the contribution of reflex control. The subjects were familiarized with the task by performing approximately 60 s of the test using vision.

To evaluate the ability to keep the head steady in space, gain and phase shift were calculated using the kinematic data from the S1 and S2 sensor, according to the procedures described in study 2. Gain and phase are measures of the relative response between head-room and trunk room during perturbations induced by the rotating chair. Perfect spatial compensation for the head in response to the perturbations is shown as gain = 0, i.e., the head is kept stationary in space by rotations in the opposite direction relative to the trunk with the same amplitude. Perfect temporary compensation in response to perturbations is shown as a 0^o shift in phase angles. When the head is kept perfectly steady in space, gain and phase equal zero.

Detailed information regarding data management and outcome variables in study 2 can be found in the specific paper.

Postural sway

Postural sway during quiet standing was assessed over 70 s for each one of four conditions, where the first 10 s were not used in the analyses to exclude initial postural adjustments in the analyses. The first condition was a dual task where the FOE test with low tracking velocity was performed during quiet standing. In the second condition eyes open (EO), subjects were instructed to focus at a point on the wall 250 cm straight ahead. For the third condition, subjects were blindfolded (EC). The fourth and last condition was performed with eyes open, standing on a balance pad (EOB).

Unfortunately, postural sway during the FOE test iwhile standing was not recorded in 43 subjects in the HC, leaving only 48 subjects remaining in the HC group for this analysis. The same standing position was ensured for all conditions (feet parallel with 10 cm between the medial malleoli and arms held across the chest) and the order of presentation of conditions was the same for all subjects. The instructions given were to “stand still for one minute”. Sway was assessed from the antero-posterior and mediolateral position data from the sensor (S3) placed on the spinous process of L4-L5 and 95% confidence interval (CI) for sway area (cm^2) was calculated.

4.4 Self-reported data and questionnaires

At baseline and follow-up at 2 weeks and 2 months, all subjects completed a set of questionnaires before conducting tests of motor control and neck motion in the laboratory. Healthy controls did not complete questionnaires related to somatic symptoms and psychological factors. Neck pain subjects required approximately 15 minutes to complete the questionnaires.

Personal factors

Personal factors collected were age, gender, height, and weight. Age was used as a continuous variable for descriptive purposes, and dichotomized with 45 years as cut- off according to a previous prognostic study (Cote et al., 2004), when used as a prognostic factor in study 4. Body mass index was calculated based on height and weight. All personal factors were used as prognostic factors in study 4.

Neck pain characteristics

Neck pain intensity on the day of testing was measured on a 0-10 numerical rating scale (NRS). In study 3, the minimal clinically important change (MCIC) was used to evaluate changes in neck pain. We used the recommendation from IMMPACT for NRS that proposes a decrease of 2 or more on the NRS as the MCIC (Dworkin et al., 2008). In study 4, NRS for pain intensity was dichotomized as moderate (NRS= 3-5) or severe (NRS ≥ 6) when applied as baseline prognostic factor. Information regarding neck pain recurrence, number of additional pain sites, and neck pain duration was collected at baseline, and used for descriptive purposes (studies 1-4) and as prognostic factors (study 4).

Psychological factors

The Tampa Scale of Kinesiophobia (TSK; 13-52) with 13 items was used to assess fear of movement (Haugen et al., 2008), and the Pain Catastrophizing Scale (PCS; 0-60) was used to assess catastrophizing thoughts (Fernandes et al., 2012). Higher scores in TSK and PCS indicates increased kinesiophobia and catastrophizing thoughts, respectively. A Pain Self-Efficacy Scale (PSES; 0-60) was used to measure self-efficacy (Nicholas, 2007). Higher scores on PSES reflect a higher level of self-efficacy. In study 1, TSK was used to assess the correlation between fear of movement and motor control and neck motion. In study 4, psychological questionnaires were used as both baseline prognostic factors and as change scores from baseline to 2 months.

Disability, function, and physical activity

Neck disability was measured with the Neck Disability Index (NDI;0-100, lower scores= less disability) (Vernon and Mior, 1991). The NDI consists of 10 items (pain intensity, personal care, lifting, reading, headache, concentration, working, driving, sleeping, and leisure activities), covering all domains in the ICF. MCIC for NDI has been defined to 7 points (Pool et al., 2007). Function was measured using the Patient- Specific Functional Scale (PSFS; 0-10, where the original PSFS was reversed (Stratford et al., 1995), so that 0 indicated no problem with the activity and 10 indicated an inability to perform the activity due to neck pain. PSFS was used as a continuous variable, except in study 4, when used as a prognostic variable it was dichotomized. Since no established cut- off for PSFS exists we categorized PSFS as poor ($PSFS \geq 7$) or moderate ($PSFS < 7$) using the median score as the cut-off in study 4. A physical activity index (PAI; 0-15), described by Kurtze et al., was calculated based on three questions to quantify the intensity and duration of activity, and number of sessions during one week, where a higher number indicated increased physical activity (Kurtze et al., 2008).

4.5 Treatment in studies 3 and 4.

Patients in private clinics received standard physiotherapy treatment, the duration and number of which was at the discretion of the physiotherapist. The treatment, as reported by the physiotherapists, consisted of a wide range of modalities (percentage of patients who received the specific modality given in parentheses): individually supervised exercises (52%), mobilization/manipulation (45%), massage (43%), advice and information (27%), dry needling (23%), cognitive therapy (14%); other therapies reported by less than 10% of physiotherapists were group exercise, prescribed home exercises, electrotherapy, and shock wave therapy. Certified manual therapists treated 50% of the patients, while general physiotherapists and psychomotor specialized physiotherapists treated 30% and 20% of the patients, respectively.

The patients in the specialized neck and back pain clinic received three weeks of multimodal treatment from a group of several health care professionals (physicians, physiotherapists, psychologists, and social workers). The first and third week of multimodal treatment consisted of four full days, including patient education, physical exercise and cognitive therapy, aimed at reducing fear avoidance/catastrophizing and increasing function, coping and self-management. The week in between (week 2) was dedicated to individually-prescribed home exercises.

4.6 **Outcome variables**

Study 1

Variables for neck motion and motor control are shown in Table 4. Correlation analyses were performed between these variables and the clinical characteristics pain intensity and duration, disability (measured with the NDI) and kinesiophobia (measured with the TSK).

Study 2

Gain and phase were used to evaluate the spatial and temporal response to the perturbations. Perfect spatial compensation for the head in response to the perturbations is shown as gain = 0, i.e., the head is kept stationary in space by rotations in the opposite direction relative to the trunk with the same amplitude. Perfect temporary compensation in response to perturbations is shown as 0^o shift for phase angles, where positive values indicate phase lead and negative values a phase lag. When the head is kept perfectly steady in space, gain and phase equal zero.

Study 3

Primary outcomes were 1) changes in neck motion and motor control from baseline to 2 weeks and 2 months, and 2) associations between changes in neck motion and motor control and the self-reported outcomes pain intensity (measured with the NRS) and disability (measured with the NDI).

Study 4

The primary outcome was the global perceived effect of change perceived by patients at 2 months, measured using the Global Perceived Effect Scale (GPE; 1-7: 1= very much improved, 2= much improved, 3= slightly improved, 4= no change, 5= slightly worsened, 6= much worsened, 7= very much worsened) (Dworkin et al., 2005).

4.7 Statistics

All statistical analyses were performed using STATA 13 (Stata Corp., College Station, TX, USA). The significance level was defined as $p<0.05$.

Outliers, meaning those who did not perform the test correctly or were exposed to technical problems were eliminated from the analyses of the kinematic data.

Study 1

The chi square test was used to analyze baseline group differences for categorical variables. Multiple regression was used to investigate group differences for cervical ROM, CM, peak velocity, and JPE. Multiple robust regression using Huber's method was used for the other variables, due to heteroskedasticity (Rabe- Hesketh and Skrondal, 2012). We adjusted for age and gender (model 1) in all analyses, as age has been shown to influence several of the variables measured (Lansade et al., 2009, Oddsdottir et al., 2013, Yoon et al., 2012) and gender was not equally distributed between the groups (Table 3). In the analyses of CM, we also adjusted for maximum ROM in the primary plane (model 2) and in the final model for both maximum ROM and peak velocity in the primary plane ROM test (model 3), since these covariates have been shown to influence smoothness of movement in previous studies (Vikne et al., 2013b). In the sole analysis of peak velocity and JPE, we adjusted for maximum ROM in the primary plane (Sjolander et al., 2008). All variables except for ROM and CM showed skewness of the data. Log- transformation of these variables gave acceptable normal distribution, but did not change the result of the regression analysis; thus, non-transformed data and p-values are reported for ease of interpretation. Effect size (ES) was calculated using the formula: $ES = \frac{HC_{mean} - NP_{mean}}{\sqrt{\frac{HC_{SD^2} + NP_{SD^2}}{2}}}$, where SD is the standard deviation (Fritz et al., 2012). The effect sizes were interpreted as low (0.2-0.5), medium (0.5- 0.8) or large (>0.8), as described by Cohen (Cohen, 1988).

Study 2

Normal distribution of gain and phase in each of the three conditions was confirmed with Q-Q and P-P plots. For gain and phase, separate general linear models were constructed for repeated measures with conditions as within subject factors (n=3, VS, NV, MA) with frequencies (n=10) as measures within each condition. Differences between groups (n=2: neck pain and control) were assessed with multivariate analysis across conditions with Bonferroni corrections for multiple comparisons. Sphericity was assumed according to Mauchly’s test. Post hoc linear regressions were used to assess group differences with 95% CI for separate measures within each condition. Due to differences between the groups, age and gender were used as covariates in the analyses. Unadjusted results were used to plot the data.

Study 3

Neck pain and disability, motor control, and neck motion at baseline were described using descriptive statistics, while data from the assessments at 2 weeks and 2 months were given as change scores from baseline with 95% CI. Changes from baseline to 2 weeks and 2 months were analyzed on a group level using a paired t- test for the normally distributed data. Variables for proprioception, head steadiness, trajectory movement control and postural sway showed non- normality. Log transformation was performed and gave acceptable normal distributed data. Log-transformed data gave similar results, thus, non- transformed data and statistics are presented to facilitate interpretation of the data. When evaluating changes in neck pain and disability on an individual level, it is important to consider the MCIC for these outcomes. We used the recommendation from IMMPACT for NRS that proposes a decrease of 2 or more on NRS as the MCIC (Dworkin et al., 2008). For NDI, the MCIC is considered to be 7 points (Pool et al., 2007). We performed a responder analysis based on these cutoff points for NRS and NDI, since group analysis does not indicate the number of patients that experienced a clinically important change in neck pain and disability.

Fixed effect univariate regression analysis, using the command ”xtreg, fe” in STATA, was used to investigate the association between the dependent variables, neck pain and neck disability, and motor control and neck motion as independent variables within individuals over time (Rabe- Hesketh and Skrondal, 2012). The analyses are thus controlled for subject time-invariant variables, like age, gender, and socioeconomic status. We used multiple linear regression with change score (between baseline and 2 months) for NRS and NDI as outcomes to investigat the degree of variance in changes in neck pain and neck disability that could be explained by changes in motor control and neck motion (given by r squared, R^2). Variables were selected based on the univariate association with the outcomes with a significance value of $p<0.1$, to avoid exclusion of possible important variables in the multivariable model. We used effect size, Hedges g, to compare the size of changes in the different constructs of motor control (Fritz et al., 2012).

Study 4

Global perceived effect at 2 months was used the primary outcome, dichotomized as “improved” (GPE score 1 and 2) and “not-improved” (GPE score 3-7) (Schellingerhout et al., 2008). We used univariable logistic regression analysis to estimate odds ratios with 95% CI for the baseline prognostic variables in relation to the primary outcome GPE. Baseline prognostic variables with $p<0.1$ in the univariable analysis were entered in a multivariable model. Only significant variables after stepwise backward selection ($p \leq 0.05$) were retained in the final multivariable model. For the secondary aim, we calculated change scores from baseline to 2 months, where positive change scores represent "improvement". In order to avoid multiple testing we reduced the number of neck motion and motor control variables in the analysis of change scores by including only those that significantly contributed to the final multivariable model for the baseline predictors. Change scores with $p<0.1$ in the univariable analysis were then entered in a multivariable model. Only variables significant after stepwise backward selection ($p \leq 0.05$) were retained in the final multivariable model. Age and gender were included as covariates in the multivariable analyses. The multivariable models were checked for multicollinearity. R^2 was used to assess the explained variance for the multivariable models.

5 Results

A summary of the main results related to the specific aims of the papers are presented in this section, while detailed results are reported in studies 1-4.

5.1 Study 1

Neck pain patients had significantly less total cervical ROM compared with the HC group, indicated by significantly less maximal cervical ROM in flexion/extension and rotation, while lateral flexion barely fell short of reaching significance (Table 5). Conjunct motion in accessory planes during all primary planes motion was significantly smaller in the neck pain patients compared to the HC group, independent of ROM in the primary plane (Table 5). When adjusted for peak velocity, CM in flexion/extension and rotation in the neck pain group was still significantly smaller compared with HC, but not for CM in lateral flexion. Peak velocity during all ROM tests was significantly lower in neck pain patients compared with HC, and remained significantly lower after adjustment for cervical ROM in the primary plane.

Proprioception, measured with the repositioning error following head rotation in the horizontal plane, did not differ between the groups (Table 5). Head steadiness showed the largest magnitude of effect (ES: 1.3 for low load and 2.0 for high load) for differences between neck pain patients and the HC group. In the low load and high load tests, neck pain patients had a markedly lower head angular velocity compared with HC (Table 6).

Trajectory movement control was assessed using two different tests, the FOE and a modified version of the Fly test. HC subjects departed more from the trajectory pattern in the FOE test than the neck pain subjects, indicated by the higher point deviation values. The differences were statistically significant for the high speed FOE test, with a mean group difference in PD of −0.8 cm (95% CI; −1.3 to −0.2; $p<0.01$) and the FOE test while standing (mean difference: −0.5 cm; 95% CI; −0.8 to −0.1; $p<0.05$). The HC group also showed increased departure from the trajectory (i.e. higher point deviation) in the Fly test 1A compared with the neck pain group. No other movement patterns in the Fly tests revealed any significant group differences in PD between the neck pain and HC groups (Table 6). The tests for trajectory movement control showed low effect sizes (ES < 0.5) for differences between neck pain patients and HC subjects.

Postural sway was quantified by measuring the sway area during quiet stance. Postural sway during quiet standing with eyes open and eyes closed did not differ significantly between the groups. The neck pain group had a significantly larger sway area for the EOB test compared with the HC group (mean difference: 2.9; 95% CI; 1.5 to 4.4; p>0.01). By contrast, the neck pain patients had less sway area during the FOE test, but this difference was not statistically significant (mean difference: −1.6; 95% CI; −3.5 to 0.3; p=0.09).

Table 5 Group comparisons of neck flexibility and proprioception. Given values are mean (95 % CI) adjusted for 3 different models of covariates.

	Neck pain (n=75)	**Healthy controls (n=91)**	**p**
Neck flexibility			
Flexion/extension (°)[1]	110.1 (105.7-114.5)	126.2 (122.3-130.2)	<0.01
CM (°)[1]	12.3 (11.3-13.3)	16.5 (15.6-17.4)	<0.01
CM (°)[2]	12.9 (11.9-14.0)	16.0 (15.1-16.9)	<0.01
CM (°)[3]	13.7 (12.4-15.0)	15.4 (14.4-16.3)	0.03
Peak velocity (°/s)[1]	70.6 (62.5-78.7)	115.6 (108.4-122.8)	<0.01
Peak velocity (°/s)[2]	75.0 (66.8- 83.1)	112.1 (104.9-119.4)	<0.01
Rotation (°)[1]	128.2 (124.3-132.2)	140.7 (137.2-144.2)	<0.01
CM (°)[1]	19.8 (18.0-21.6)	25.1 (23.5-26.7)	<0.01
CM (°)[2]	20.6 (18.7-22.4)	24.5 (22.8-26.1)	<0.01
CM (°)[3]	21.1 (19.2-23.1))	24.0 (22.3-25.7)	0.04
Peak velocity (°/s)[1]	109.3 (98.9-119.7)	158.9 (149.6-168.3)	<0.01
Peak velocity (°/s)[2]	114.3 (103.9-124.7)	154.9 (145.7-164.2)	<0.01
Lateral flexion (°)[1]	68.1 (64.7-71.6)	72.6 (69.5-75.7)	0.06
CM (°)[1]	45.7 (40.1-51.3)	62.5 (57.5-67.5)	<0.01
CM (°)[2]	44.9 (39.4- 50.5)	63.1 (58.1-68.0)	<0.01
CM (°)[3]	52.7 (47.6-57.7)	56.9 (52.4-61.4)	0.25
Peak velocity (°/s)[1]	57.9 (52.2-63.5)	85.7 (80.6-90.7)	<0.01
Peak velocity (°/s)[2]	58.6 (53.0- 64.2)	85.1 (80.1-90.1)	<0.01
Total cervical ROM (°)[1]	306.5 (296.5-316.5)	339.5 (330.6-348.5)	<0.01
Proprioception			
JPE (°)[2]	5.6 (5.2-6.1)	5.1 (4.6-5.5)	0.11

[1] Adjusted for age and gender (model 1)

[2] Adjusted for age, gender, and cervical ROM (model 2)

[3] Adjusted for age, gender, cervical ROM, and peak velocity (model 3)

[#] Un-published data

[¤] Variable error is calculated from error in the primary plane

p= p- value. ROM= range of motion. CM= conjunct motion in the two accessory movement planes. JPE= joint position error

Table 6 Group comparisons of head steadiness, trajectory movement control, and postural sway. Given values are mean (95 % CI) adjusted for age and gender (model 1).

	Neck pain	Healthy controls	n= NP/HC	p[1]
Head steadiness				
INF Low load				
Angular velocity (°/s)	1.3 (1.2-1.4)	1.7 (1.6-1.8)	75/90	<0.01
INF High Load				
Angular velocity (°/s)	2.8 (2.6-2.9)	4.5 (4.3-4.7)	73/91	<0.01
Trajectory movement control				
FOE Low speed				
Point deviation (cm)	3.4 (3.1-3.7)	3.8 (3.4-4.1)	75/89	0.17
FOE High speed				
Point deviation (cm)	4.4 (4.1-4.8)	5.2 (4.8-5.6)	75/91	<0.01
FOE Standing, low speed				
Point deviation (cm)	2.9 (2.6-3.1)	3.3 (3.0-3.6)	74/91	0.02
The Fly test				
PD test 1A (cm)	2.2 (2.0-2.4)	2.5 (2.3-2.7)	75/89	0.03
PD test 1B (cm)	2.1 (2.0-2.2)	2.1 (2.0-2.3)	75/89	0.63
PD test 2A (cm)	3.1 (2.9-3.3)	3.3 (3.1-3.5)	74/88	0.33
PD test 2B (cm)	2.8 (2.7-3.0)	2.8 (2.6-2.9)	75/83	0.64
Postural sway				
Sway area EO (cm^2)	3.0 (2.4-3.5)	2.7 (2.2-3.3)	72/90	0.53
Sway area EC (cm^2)	2.5 (2.0-3.1)	2.0 (1.7-2.3)	72/87	0.12
Sway area EOB (cm^2)	11.0 (9.7-12.3)	8.1 (7.4-8.7)	73/91	<0.01
Sway area FOE (cm^2)	4.3 (3.3-5.2)	5.9 (4.2-7.5)	73/48	0.09

[1] p value adjusted for age and gender (model 1)

NP= neck pain patients. HC= healthy controls. INF= isometric neck flexion. FOE= figure of eight. PD=point deviation. 1A= easy pattern, small ROM. 1B=easy pattern, large ROM. 2A= difficult pattern, small ROM. 2B= difficult pattern, large ROM. EO= eyes open. EC= eyes closed. EOB= eyes open balance pad

Neck flexibility was the only construct that showed a consistent significant association with neck pain intensity. Only peak velocity during flexion/extension was associated with fear of movement (Pearson's r = 0.23) (measured by the Tampa Scale of Kinesiophobia). The correlation between constructs of neck motion and motor control and clinical features (pain intensity, pain duration, and disability) were low (Pearson`s r < 0.4).

5.2 Study 2

This study assessed the ability to keep the head steady in space in response to unpredictable perturbations. The response to the perturbations was evaluated using gain and phase, were gain reflects the spatial and phase the temporal response. The unadjusted results for gain and phase are plotted in Figure 10, while results with adjustment for age and gender are provided below.

The perturbations induced by the chair produced a similar general pattern across groups and conditions with increasing gains as an effect of higher frequencies, however with significant effects of group and of condition. Multivariate tests showed a significant effect of group for at least one measure across conditions (p=0.009). Between 0.185-1.055 Hz, neck pain patients displayed significantly higher gains than controls in the VS condition. At frequencies above 1.055 Hz, no differences were observed between groups. In the NV condition, patients displayed significantly higher gains than controls between 0.245-0.715 Hz. In the MA condition higher gain was found in patients only at 0.505 Hz.

Phase

Similar to gain, the perturbations produced a similar general pattern across groups and conditions (Figure 10). A phase lead ($> 0^o$) was seen for lower frequencies, while an increasing phase lag ($< 0^o$) was seen with higher frequencies. Multivariate tests showed no significant effect of group across conditions (p=0.265). Group differences with 95% CI were calculated and can be found in the specific paper.

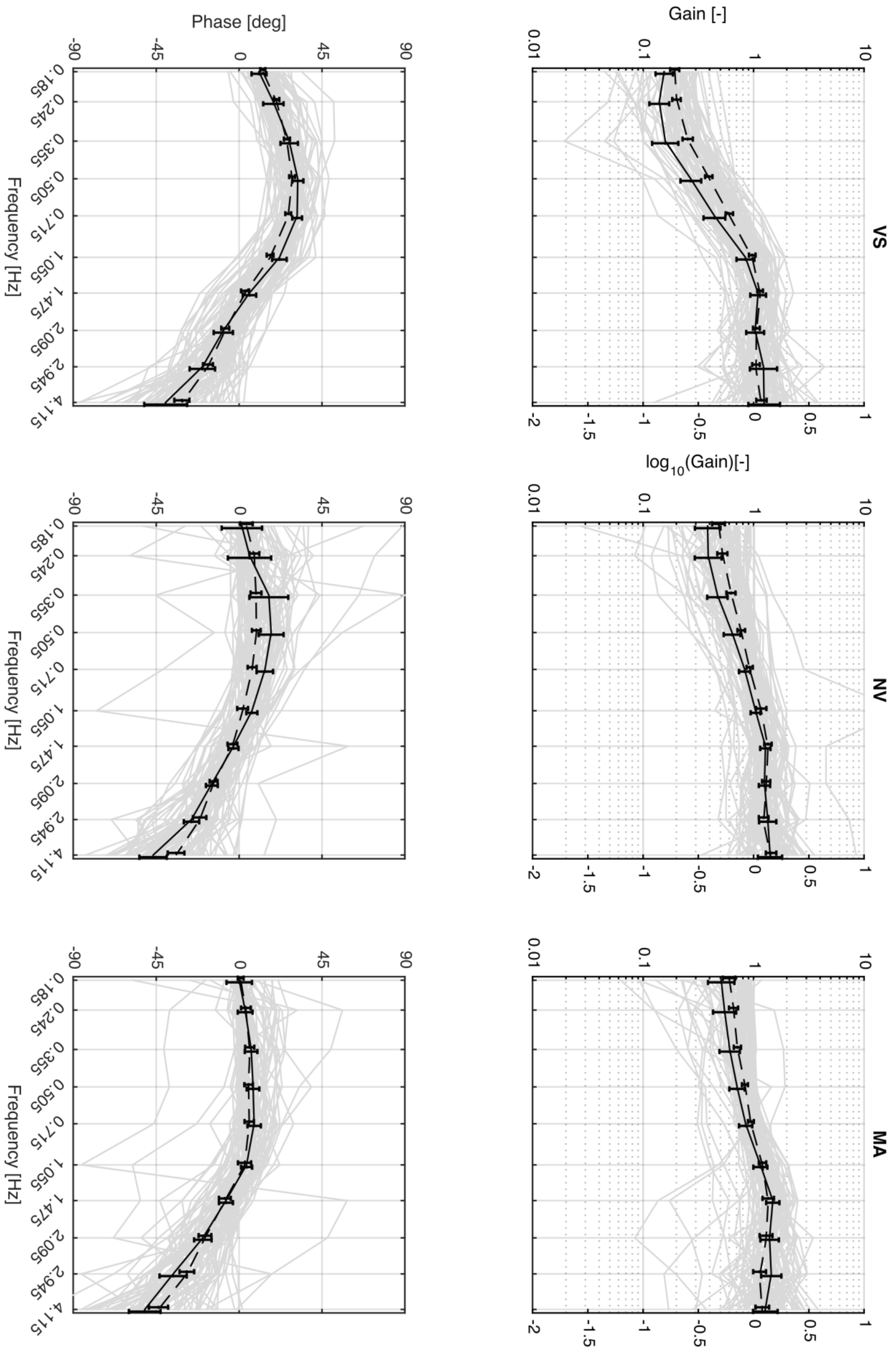

Figure 10 Bode diagrams of transfer functions for the three conditions with vision (VS), without vision (NV), and without vision with a cognitive task (MA), respectively. Gain indicate the spatial response, while phase the temporal response. Unadjusted means and 95% CI. Grey curves in the background show the individual responses. Solid line: healthy controls, dashed line: neck pain patients.

5.3 Study 3

The proportion of subjects with clinically significant changes in NRS for neck pain intensity and NDI were 35% and 40% at 2 weeks, respectively, and 63% and 68% at 2 months, respectively. At 2 months, the effect sizes for changes in neck pain and disability were 0.8 for both outcomes.

Changes in neck motor control and motion occurred mainly between baseline and two weeks in all constructs of motor control and neck motion (Figure 11). At two months, no significantly changes were found for proprioception, conjunct motion, high load INF, and sway area with eyes closed (see Table 2 in applicable paper). The largest effect sizes at two months following the start of treatment were found for neck flexibility and trajectory movement control (Figure 11).

Associations with neck pain

Associations with neck pain were found only for ROM in flexion-/extension (β=-0.04; 95%: -0.07 to -0.01) and sway area with eyes open (β=-0.16; 95% CI: -0.31 to -0.01). The results indicate that individuals had larger ROM in flexion/extension and more postural sway when they had lower levels of pain, compared to when they had higher pain levels.

Associations with neck disability

The Neck Disability Index showed a significant association only with variables within the constructs of neck flexibility and trajectory movement control. Decreased neck disability within a subject was associated with larger ROM in flexion/extension (β=-0.18; 95% CI: -0.32 to -0.04) and increased peak velocity in lateral flexion (β=-0.16; 95% CI: -0.30 to -0.02). For trajectory movement control, 3 out of 6 variables showed a significant association with neck disability, indicating that subjects departed less from the trajectories in two of the FOE tests and one of the Fly tests at times when they reported less neck disability.

At two months the, explained variance in neck pain and neck disability for the variables that were statistically significant in the univariate analysis were 25% (R^2= 0.25) and 19% (R^2=0.19), respectively.

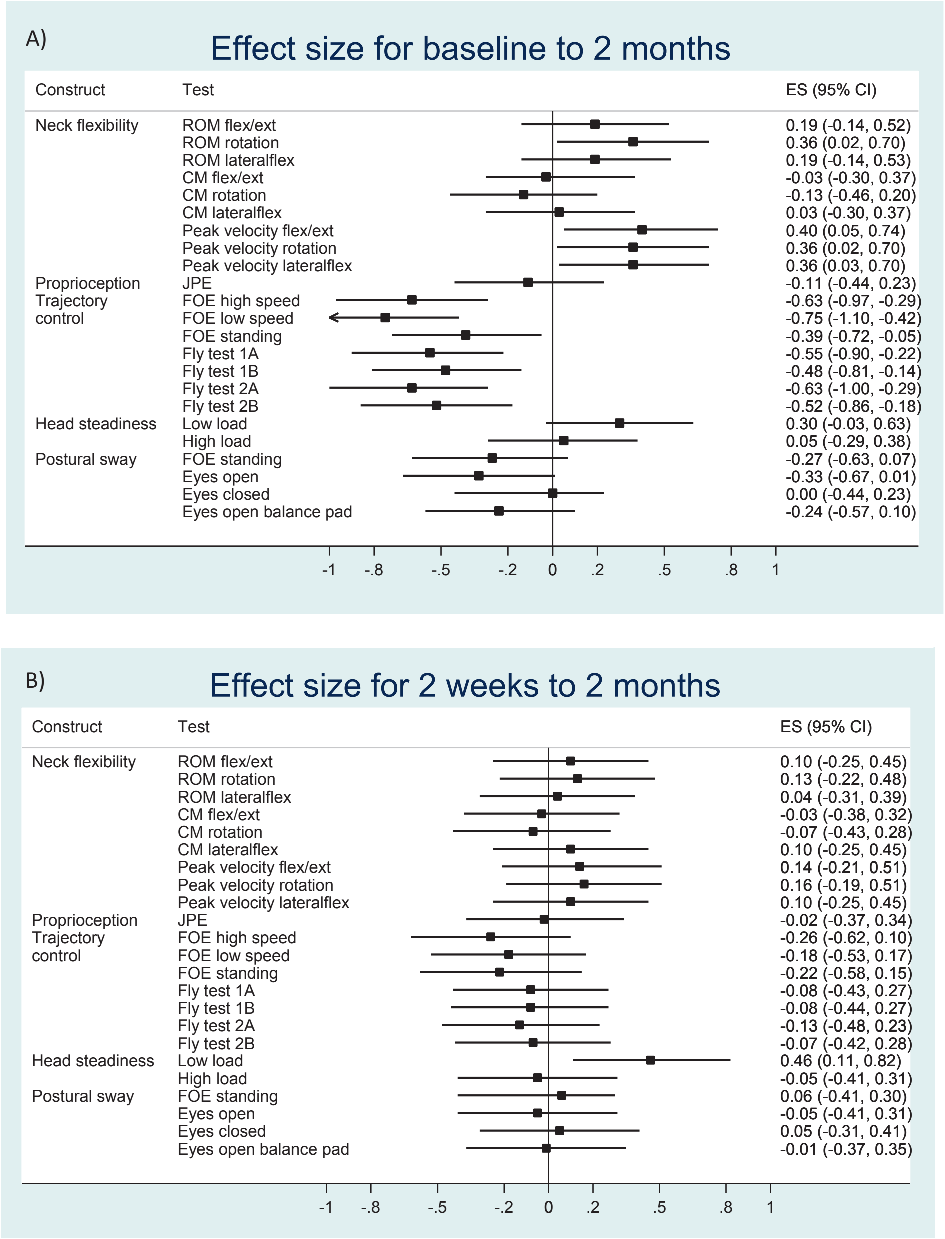

Figure 11 Effect sizes for changes in motor control and neck motion at 2 months after baseline (A) and between 2 weeks and 2 months (B). Positive effect sizes on the right side of the vertical line indicate increased values for follow- up tests, while negative values indicate decreased values. Interpretation of the effect size: High= <-0.8 or >0.8. Medium= -0.5 and 0.5. Low= <-0.2 or >0.2. Confidence intervals not overlapping 0 indicate statistically significant effect sizes (p<0.05).
ROM= range of motion.CM= conjunct motion. JPE= joint position error. PD= point deviation. FOE= figure-of-eight. 1A= easy pattern, small ROM. 1B= easy pattern, large ROM. 2A= medium pattern, small ROM. 2B= medium pattern, large ROM.

5.4 Study 4

Seventy patients completed the follow-up visit at 2 months (Figure 4). The patients lost to follow up from baseline (n=11) were similar in age, gender distribution, severity of neck pain, disability, and psychological features as patients included in the analyses.

Global perceived effect

Fifty percent of patients improved (i.e. GPE= 1; very much better and GPE=2; much better) 2 months after the start of treatment. Patients in the “improved” category reported lower levels of neck pain intensity (mean decrease: 2.1 points on NRS; 95% CI: 1.2-3.0), reduced level of disability (mean decrease: 11.4 points on NDI; 95% CI 6.3-16.5) and increased functioning (mean decrease: 1.6 points on PSFS; 95% CI: 0.5-2.6) compared with patients classified as “not improved”.

Baseline prognostic factors

Table 7 presents the associations between baseline prognostic factors and GPE at 2 months. In the univariable analyses, the baseline prognostic factors that were significantly associated with improvement at 2 months were lower neck pain intensity (NRS ≤ 6), higher functioning measured by the PSFS, larger ROM in rotation and lateral flexion, higher peak velocity in flexion/extension and lateral flexion in tests of ROM, and less deviation in two out of seven tests of trajectory movement control. Variables for proprioception, head steadiness, and postural sway were not associated with improvement at 2 months. Four variables were retained in the multivariable model: pain duration, PSFS, ROM in rotation and one test for trajectory movement control. The explained variance for GPE in the multivariable model was 28%.

Table 7 Univariable and multivariable analysis of baseline predictors for Global Perceived Effect (GPE) at 2 months after start of treatment. Statistical significant associations ($p<0.05$) are in bold.

	GPE 35 of 70 improved OR (95% CI)	P- value	Multivariable model GPE[2] OR (95% CI)	P-value
Patient self-reported outcomes				
Old age (≥45 years vs < 45 years)	0.44 (0.17; 1.16)	0.09		
Gender (female vs male)	0.74 (0.25; 2.18)	> 0.3		
Body mass index (per unit)	0.96 (0.87; 1.07)	> 0.3		
Pain duration (≥6 months versus < 6 months)	0.38 (0.13; 1.09)	0.07	**0.18 (0.04; 0.76)**	0.02
Multiple pain sites (≥2 additional sites vs < 2 sites)	0.63 (0.25; 1.62)	> 0.3		
Recurrence (>3 episodes/year vs ≤3 episodes/year)	0.56 (0.22; 1.45)	0.23		
Pain intensity: Moderate (NRS= 3-5)	ref			
Severe (NRS≥6)	**0.22 (0.07; 0.71)**	0.01		
Neck Disability Index, low (NDI<30)	0.98 (0.94; 1.01)	0.21		
Patient Specific Functional Scale, moderate (PSFS<7)	**0.72 (0.57; 0.93)**	0.01	**0.69 (0.50; 0.95)**	0.03
Psychological factors[1]				
Kinesiophobia (TSK:13-52)	1.06 (0.95; 1.19)	> 0.3		
Catastrophizing (PCS: 0-52)	1.03 (0.97; 1.09)	> 0.3		
Self-efficacy (PSES;0-60)	1.00 (0.95; 1.05)	> 0.3		
Physical activity index[1]	1.06 (0.86; 1.31)	> 0.3		
Neck motor control and motion				
Neck flexibility				
Flexion-/extension ROM	1.02 (1.00; 1.04)	0.09		
Peak velocity	**1.02 (1.00; 1.05)**	0.04		
Rotation ROM	**1.05 (1.01; 1.08)**	0.004	**1.04 (1.00; 1.08)**	0.03
Peak velocity	1.01 (1.00; 1.03)	0.13		
Lateral flexion ROM	**1.04 (1.00; 1.07)**	0.03		
Peak velocity	**1.04 (1.01; 1.08)**	0.01		
Trajectory movement control[3]				
figure-of-eight low speed	0.81 (0.55; 1.20)	0.29		
figure-of-eight high speed	0.77 (0.56; 1.05)	0.09		
Fly test 1A	0.62 (0.32; 1.17)	0.14		
Fly test 1B	**0.30 (0.12; 0.80)**	0.02		
Fly test 2A	**0.44 (0.23; 0.85)**	0.01	**0.39 (0.16; 0.94)**	0.04
Fly test 2B	0.97 (0.49; 1.91)	> 0.3		
figure-of eight low speed in standing	0.58 (0.32; 1.05)	0.07		
Postural sway				
Sway area standing figure-of-eight	0.92 (0.81; 1.04)	0.19		
Sway area eyes open	0.93 (0.79; 1.10)	> 0.3		
Sway area eyes closed	0.97 (0.81; 1.16)	> 0.3		
Sway area eyes open on balance pad	1.03 (0.95; 1.12)	> 0.3		

[1] OR estimates are based on unit increases in the independent variable.
[2] Variables with $p<0.1$ from the univariable analyses were included in the multivariable model. Age and gender were included as covariates.
[3] Outcome variables for tests of trajectory movement control was the deviation in the tracking tasks.

OR=odds ratio. Patient-Specific Functional Scale: 0= no problem at performing activity. 10= Inability to perform activity due to neck pain. NRS= numerical rating scale (0-10). Neck disability index (0= no disability, 100= 100 % disability). TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale. ROM= range of motion. 1A= easy pattern,small range of motion. 1B=easy pattern,large range of motion. 2A= medium pattern, small range of motion. 2B= medium pattern, large range of motion

Associations between change scores and GPE

Table 8 shows the univariable analyses of change scores. Reduced kinesiophobia (OR: 1.21; 95% CI: 1.07 to 1.37), reduced catastrophizing (OR: 1.09; 95% CI: 1.01 to 1.18), increased self- efficacy (OR: 1.12; 95% CI: 1.03 to 1.21), decreased neck pain intensity (OR: 1.86; 95% CI: 1.31 to 2.62), less disability (OR: 1.12; 95% CI: 1.05 to 1.20), and increased function (OR: 1.46; 95% CI: 1.11 to 1.92) all gave increased odds for improvement at 2 months. In the multivariable analysis for change scores, reduced pain intensity and less kinesiophobia were the only variables retained in the model and explained 28% of the variation in GPE.

Table 8 **Univariable and multivariable analysis of Global Perceived Effect (GPE) and association with change scores from baseline to 2 months.** Statistical significant associations ($p<0.05$) are in bold.

	GPE 35 of 70 improved OR (95% CI)	P-value	Multivariable model GPE[2] OR (95% CI)	P-value
Patient self- reported outcomes				
Pain intensity (NRS;0-10)	**1.86 (1.31;2.62))**	< 0.001	**1.88 (1.27; 2.78)**	0.002
Neck Disability Index (NDI;0-100)	**1.12 (1.05; 1.20)**	0.001		
Patient Specific Functional Scale (PSFS; 0-10)	**1.46 (1.11; 1.92)**	0.007		
Psychological factors				
Kinesiophobia (TSK:13-52)	**1.21 (1.07; 1.37)**	0.003	**1.21 (1.05; 1.39)**	0.01
Catastrophizing (PCS: 0-52)	**1.09 (1.01; 1.18)**	0.04		
Self-efficacy (PSES;0-60)	**1.12 (1.03; 1.21)**	0.009		
Physical activity. Index	1.05 (0.85; 1.30)	> 0.3		
Neck motor control and motion				
ROM cervical rotation	1.00 (0.96; 1.05)	> 0.3		
Fly test 2A	0.87 (0.44; 1.72)	> 0.3		

[1] Odds ratio estimates are based on unit increases in the independent variable.

[2] Age and gender were included as covariates

OR= odds ratio. PSFS: 0= no problem at performing activity. 10= Inability to perform activity due to neck pain. NRS= numerical rating scale (0-10). NDI: 0= no disability, 100= 100 % disability. TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale. ROM= range of motion. 2A= medium pattern, small range of motion

6 Discussion

6.1 Main findings of the thesis

This thesis has evaluated the influence of a wide range of bio-psychological factors in patients with neck pain, with emphasis on neck motion, motor control and psychological factors. Main findings are summarized in Figure 12. Subjects with neck pain are characterized by a generally stiffer neck motion and motor control pattern (study 1). Evidence suggests that these alterations are more likely within the voluntary control and not the reflex system (study 2). Standard physiotherapy treatment induced several, albeit small changes in neck motion and motor control, but these changes were associated with altered pain and disability to a lesser extent (study 3). At baseline, neck motion and motor control and not psychological factors predict global perceived effect at 2 months. However, changes in psychological factors in addition to changes in pain, disability, and function were all associated with global perceived effect (study 4).

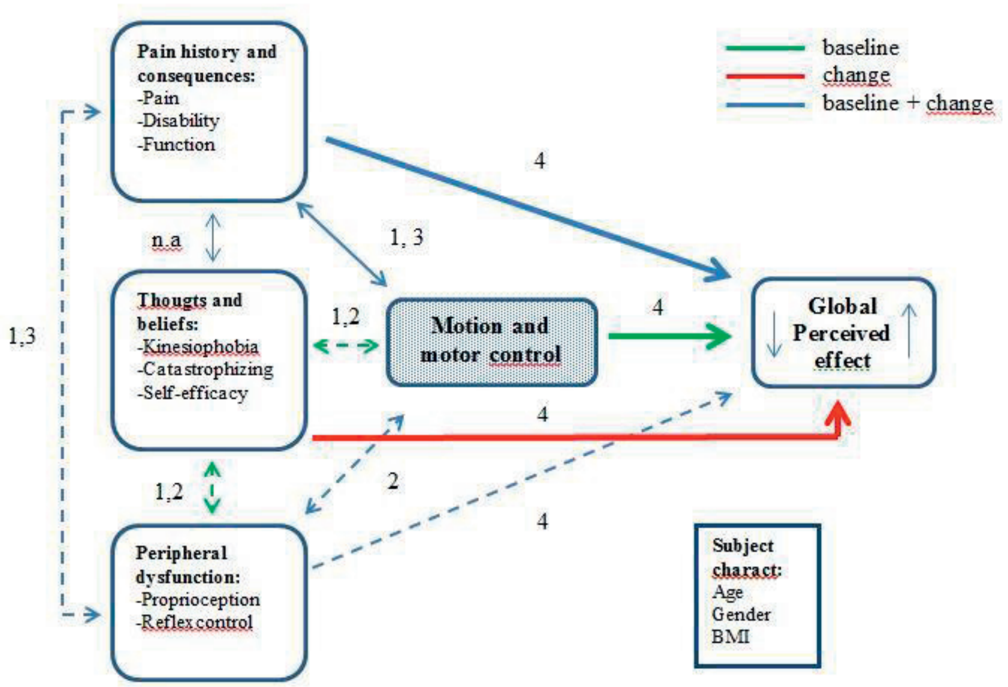

Figure 12 Overview of main results in studies 1 – 4, marked as numbers. Dashed line indicates no or little associations, while solid indicate significant associations between factors. Thin line between pain, disability and motor control indicate weak association. Subject characteristics are listed as covariates n.a= not applicable

The discussion aims to compile and elaborate on findings from the studies of relevance for clinical practice and future research in neck pain. In-depth discussions of the impairments in neck motion and motor control are presented in the papers. The focus of the discussion will thus be on the relevance of neck motion and motor control relative to psychological factors and clinical characteristics in the perpetuation and recurrence of neck pain, as illustrated in Figure 12.

6.2 Methodological considerations

Studies 1 and 2 were cross- sectional and thus provide evidence for motor control deficits in neck pain patients compared with HC, but not for causal relationships. This is showed as double arrows between the factors in Figure 12. Cohort studies, such as 3 and 4 can be used to investigate causal relationships, but cohort studies do not automatically solve the cause and effect relationship, (Mann, 2003), as the temporal relationship between cause and effect is unknown in this thesis. We do not know whether pain caused altered motor control or if deficits in altered motor control caused neck pain. This thesis, however, investigated if attenuation of neck pain, in a prospective longitudinal design, were associated with improved motor control, which is stronger than a cross-sectional design when evaluating associations between different factors (Mann, 2003).

The external validity refers to the generalizability of the results. Patients with pain scores below 3 on NRS were excluded due to the favorable natural course of these patients (Vasseljen et al., 2013), and because studies have showed correlations between pain intensity and deficits in neck motion and motor control, suggesting that patients with mild symptoms present with less impairments in neck motion and motor control (Sarig Bahat et al., 2013). The results of this thesis are therefore limited to patients with non-specific neck pain of pain intensity above 3 on NRS who are referred to physiotherapy in primary health care or treatment in a specialized neck and back pain clinic. Patients attending the neck and back pain clinic at the University Hospital had longer duration of neck pain symptoms and lower self-efficacy (mean difference PSES: 9.0; 95% CI: 4.1 to 14.0), but were similar in all variables for neck motion and motor control. As a sensitivity analysis, we therefore included treatment site as a covariate in the analyses of self-efficacy and pain duration (unpublished). The estimates for the prognostic variables and change scores did not change significantly, suggesting that the results are generalizable to both treatment groups.

Sample size was calculated a priori for the objective in study 1 and was based on previous studies investigating conjunct motion and deviation in the Fly test (Woodhouse and Vasseljen, 2008, Kristjansson and Oddsdottir, 2010). Sample size calculation was not performed in studies 2, 3 and 4.

Study 3 assessed the explained variance for pain and disability related to neck motion and motor control, while study 4 applied a range of biopsychosocial variables to explain the variation in global perceived effect, The explained variance in the different regression models was low: 19% for pain and 25% for disability in study 3, with the outcome global perceived effect in study 4 having an explained variance of 28% for prognostic factors and change scores, respectively. A possible reason for the low explained variance in study 4 is the small sample size, as some of the estimates (age, pain duration, pain intensity, NDI, and PSFS) showed insufficient precision to be included in the multivariable model. The high number of associations investigated in study 4 calls for caution, as the probability of spurious findings (type 1 errors) increases when multiple testing is performed.

6.3 Neck motion and motor control in neck pain

Neck motion and motor control are possible modifying factors for physiotherapy treatment, and a large proportion of clinicians assess different aspects of motor control and motion in neck pain patients. The results of the comprehensive assessment of neck motion and motor in this thesis will be discussed in relation to other studies, current pain theories, and the clinical relevance. Associations with self-reported outcomes will also be discussed, as outlined in Figure 12.

Findings from studies 1 and 2 provide consistent evidence for a generally stiffer neck motion and motor control pattern in neck pain, regardless of tasks. This conclusion is in line with previous studies that found decreased movement velocity (Tsang et al., 2013b, Tsang et al., 2013a, Sarig Bahat et al., 2013), decreased range of motion (Woodhouse and Vasseljen, 2008, Johnston et al., 2008, Rudolfsson et al., 2012, Hagen et al., 1997), deficits in direction specific force production and increased muscle co-activation (Lindstrom et al., 2011, Schomacher et al., 2013), and reduced freedom of movement (Roijezon et al., 2010, Woodhouse and Vasseljen, 2008). This suggests that patients use the same stiffening strategy when performing different tasks, and that this is possibly within the frequency range associated with voluntary control as shown in study 2. Furthermore, neck pain patients did not have any deficits nor changes in joint position error during the clinical course, suggesting that the afferent information from mechanoreceptors that are important for the reflex control of head and neck movement, was not altered. However, a recent systematic review concluded that non- specific neck pain is associated with a moderate deficit in joint position sense (ES: 0.44; 95% CI: 0.25 to 0.63) (Stanton et al., 2015); thus, our study cannot exclude the possibility that these patients have altered afferent information, as there are some weaknesses with the test used in our study (Chen and Treleaven, 2013). No studies to date have directly measured the contribution of voluntary control and reflex control in chronic neck pain patients, unabling comparison with other studies.

Several of the tests for neck motion and motor control involve interactions between visual control, head movement control, and postural control. Unfortunately, no assessment of visual control was included in the studies. A recent study found deficits in visual control in non-specific neck pain (Treleaven and Takasaki, 2014) and we cannot exclude the possibility that neck pain patients had such impairments in our study.

6.3.1 Findings related to current theories of motor control

The Pain Adaptation model and the vicious cycle theory are both partly supported by the finding of general neck stiffening in neck pain subjects (studies 1 and 2). However, study 2 indicates that the neck stiffening pattern is likely a voluntary mechanisms, at least partly. This means that subjects stiffen their neck in order to avoid painful stimuli. Joint position sense was not altered in study 1, which may reflect normal afferent information flow from the cervical spine to the central nervous system. Study 1 and 2 thus partly contradict the Vicious Cycle theory and the pathophysiological model proposed by Johansson and Sojka, which emphasizes altered muscle spindle activity leading to increased muscle activity (Johansson and Sojka, 1991). The pain adaptation model suggests that motor adaptations are needed in order to reduce movement amplitude and velocity and thus avoid painful stimuli. This is partly supported by our findings of reduced peak velocity and ROM. This thesis (and other recent studies) has highlighted the limitations of current theories in explaining the relationship between pain, disability, and impairments in motor control (Hodges and Tucker, 2011, Hodges and Smeets, 2015). Large individual variations in motor control adaptations exist, and existing theories do not account for this variability. The stiffness observed across different tasks in this thesis may be caused by increased co-contraction of cervical agonist-antagonists and/or generally increased muscle activity (Lindstrom et al., 2011, Cheng et al., 2014, Falla et al., 2010), but others have found no evidence of generally increased muscle activity in musculoskeletal pain conditions (Westgaard et al., 2001, Holte et al., 2003, Strom et al., 2009). As Hodges and Smeets have proposed, adaptations reflecting increased stiffness may be beneficial in the short term but may have long term consequences due to increased load on the neck and reduced movement variability (Hodges and Smeets, 2015). This thesis partly supports the pain adaptation model, but the model cannot explain the diversity of motor control adaptations observed in musculoskeletal pain conditions.

6.3.2 Reliability of neck motion and motor control

Currently, there are no clinically relevant thresholds for normal versus impaired neck motion and motor control. Evidence indicates that large intra- and interindividual variations exist in motor control impairment (Juul et al., 2013, Kristjansson and Oddsdottir, 2010), suggesting that it is difficult to be certain whether changes in motor control are clinically relevant (i.e., changes need to be larger than the measurement error). Measures of neck motion and motor control also need to be reliable and sensitive to change in order to detect impairments and changes after treatment. We conducted a test-retest study of the evaluations used in this thesis with 29 healthy subjects before the data collection in study 1 commenced (unpublished data, results shown in appendix). The smallest detectable difference (SDD) was calculated to reflect the size of the change required to be confident that the change reflects a true difference between two measurements (Weir, 2005). The number of subjects with change scores above the SDD at 2 months varied from 7 to 18 subjects for the tests of ROM, while almost no subjects (i.e. < 3 subjects at each test) had change scores above the SDD for peak velocity and tests for trajectory movement control at 2 months. These findings underline the difficulty in evaluating individual changes in neck motion and motor control, and in determining clinically relevant cut-offs for neck motion and motor control impairment.

6.3.3 Associations with clinical characteristics

Study 3 and 4 evaluated the longitudinal association between neck motion and motor control and clinical outcomes such as pain intensity, disability and global perceived effect. In addition to the different outcome measures, the main difference in these studies was the statistical analyses applied. In study 3, we used fixed effect linear regression, meaning that only the within subject variation was used. The subjects therefore serve as their own controls and time-invariant confounding factors (both measured and unmeasured) such as age, gender and socioeconomic factors are therefore controlled for. In study 3, the interpretation of the significant negative association between neck pain intensity and ROM in flexion/extension is as follows: Compared to time points when a patient had high pain intensity, the patient had larger ROM in flexion/extension when he/she had less neck pain. In study 4, the interpretation of a positive significant association between GPE and baseline ROM in rotation, is that patients with large ROM in rotation had increased odds for GPE compared to patients with less ROM in rotation at baseline.

Neck pain patients showed only minor improvements in neck motor control and motion from baseline to 2 months, with most changes appearing at 2 weeks (study 3). When investigating associations between changes in clinical characteristics and neck motion and motor control it is therefore not surprising that studies 3 and 4 found few associations between these variables. One may argue that associations could have been larger if standard treatment was aimed at improving motor control and neck motion, but a recent study suggested that specific motor control training was not superior to strength training or massage in improving aspects of neck motor control (Rudolfsson et al., 2014). On the other hand, ROM in rotation and trajectory movement control at baseline significantly predicted outcome at 2 months (study 4). Patients experiencing GPE at 2 months had values for ROM in rotation that were within the normal range for healthy controls in study 1, in contrast to patients not experiencing GPE that have ROM values comparable to the baseline values for the neck pain group. This thesis contributes with novel information on the relative role of impairment in cervical mobility, as a recent review study found a lack of evidence for the prognostic value of physical impairments in the perpetuation and recurrence of pain and disability in subjects with non-specific neck pain (Bruls et al., 2015). In light of our findings, assessment of cervical ROM may contribute to clinical decision making, as knowledge of the prognosis enables clinicians to decide which patients need a targeted (and possible multidisciplinary) intervention in which an intensive intervention is not required or recommended. Cervical ROM in flexion/extension, which was significantly associated with pain and disability in study 3, can be further divided into assessment of upper and lower cervical neck, as a recent study found reduced flexion in lower-, and reduced extension in upper cervical levels in neck pain patients compared to healthy controls (Rudolfsson et al., 2012).

Two of the Fly tests significantly predicted global perceived effect at 2 months (study 4). Neither the Fly test or the FOE test were associated with pain level, and only three out of six tests of trajectory movement control were associated with disability (study 3). This suggests that the different outcomes measure distinct aspects of recovery in neck pain subjects, in line with a study that found no associations between disability and the Fly test in whiplash patients (Oddsdottir and Kristjansson, 2012). The independent prognostic value of this test is promising (study 4), but the inconsistency between the different Fly tests and the lack of associations between changes in this test and global perceived effect warrants further research before the test is implemented in clinical practice. In conclusion, only variables for neck flexibility and trajectory movement control showed significant associations with clinical characteristics such as, pain, disability and GPE.

6.4 Biopsychosocial considerations

Figure 12 outlines the main results from the thesis and the complex relationship between the conceptually different factors studied. Motor control is central in the figure as it may reflect central nervous processes driven by multiple factors, for example patient's thoughts and beliefs reflected by the psychological variables applied in this thesis. Psychological factors have gained popularity in research into musculoskeletal pain and among clinicians, as the Fear Avoidance Model (FAM) provides a causal and sequential relationship between different psychological factors and pain and disability (Vlaeyen and Linton, 2000, Vlaeyen and Linton, 2012). Recent studies have questioned the sequential relationship between the factors in the FAM, as no clinical studies to date have provided evidence for the causal or mediating relationship between the factors in the model (Pincus et al., 2010, Wideman et al., 2013). In addition, a study of low back pain patients found a considerable overlap between the three psychological variables used in this thesis, and suggested that they reflect the same underlying construct, namely psychological emotional distress related to pain and disability (Campbell et al., 2013). The next section provides a discussion of the psychological factors applied in this thesis and the association with motion, motor control and clinical outcomes.

Association with motion and motor control

Kinesiophobia was not significantly correlated with neck stiffening during dynamic head steadiness (study 2), while peak velocity, as the only variable, was weakly correlated with neck motion and motor control in study 1. This thesis does thus not provide evidence for a link between adaptations in motor control and psychological factors (Figure 12). This is in line with Roijezon and coworkers that investigated fast cervical rotations, and found no correlation between lower peak velocity and kinesiophobia in non-specific neck pain patients (Roijezon et al., 2010). A previous study found stronger correlations for kinesiophobia and kinematic variables such as ROM, velocity, and smoothness of cervical motion (Sarig Bahat et al., 2013). The study population in the latter study consisted of both traumatic and non-traumatic neck pain patients, thus, the results may not be comparable. The individual scores of the psychological outcome measures were scrutinized to evaluate the severity of psychological distress in the neck pain patients in our study.

Severity of psychological distress

Neblett and coworkers (2015) suggested clinically relevant cut-off scores for the TSK-13 version (kinesiophobia), used in this thesis (Neblett et al., 2015). The neck pain patients in study 1 had a mean TSK of 24.4 (SD: 4.3), slightly lower than a comparable cohort of non-specific neck pain (TSK=27.1; SD: 7.7) (Cleland et al., 2008). According to Neblett et al. (2015), the patients in study 1 would be categorized as mild (TSK= 23-32). Only one patient was classified as moderate (TSK=33-42), while none had severe kinesiophobia (TSK= 43-52). Nicholas (2007) suggested a cut-off at 17 points for the Pain Self-Efficacy Scale (PSES: 0-60, higher scores indicate more self-efficacy) for patients that needed to change their self-efficacy beliefs before starting a targeted treatment. At baseline in study 1, none of the patients had a score below 19 and only two patients scored below 30, which indirectly indicates that this cohort had relatively good self-efficacy beliefs. The level of low level of kinesiophobia and relatively good self-efficacy beliefs for the patients in our study might explain why kinesiophobia could not predict treatment outcome in study 4, the low correlation with peak velocity in study 1 (r=-0.23), and that baseline PSES did not predict GPE in this cohort. However, studies of low back pain patients have shown a predictive value for pain self-efficacy with similar baseline values as used in this thesis (Costa Lda et al., 2011). To summarize, our study indicates that not all patients have pain related fear, corroborated by a previous study (Asmundson et al., 1997). This suggests that assessment of these factors is an important part of the clinical examination in order to reveal patients requiring a more targeted intervention.

Change in psychological factors

In contrast to several neck motion and motor control variables, baseline psychological factors did not predict GPE at 2 months, as described above. Previous studies have found conflicting results for psychological factors (Bruls et al., 2015, Pool et al., 2010, Walton et al., 2013a), indicating that the prognostic value of psychological factors in neck pain may be less than that observed in low back pain (George et al., 2001). On the other hand, changes in psychological factors, function, disability, and pain were associated with GPE. The use of change scores in study 4 is a method of investigating possible treatment modifying effects, although a different study design is required to conclude whether a variable is an effect mediator or not (Hill and Fritz, 2011). Reduced catastrophizing and kinesiophobia, and increased self-efficacy were associated with global perceived effect at 2 months, as illustrated in Figure 12. A recent study found that reduced fear avoidance during the first 4 months after start of treatment was associated with reduced disability and return to work one year after treatment initiation (Marchand et al., 2015). Other studies found have found that treatment aimed at reducing catastrophizing and fear avoidance, such as cognitive behavioral treatment (CBT), has shown no additional treatment effect when patients undertake exercise (Monticone et al., 2015b). In our study, treatment at the neck and back pain clinic, which focused on reducing fear avoidance and catastrophizing, showed similar improvement in the psychological factors at 2 months as for patients in primary health care. Physiotherapists in primary health care may also be aware of the importance of addressing psychological factors, and may therefore incorporate cognitive aspects in the usual treatment of patients with longstanding neck pain. Interestingly, physical activity seems to reduce catastrophizing similar to cognitive behavioral treatment (Smeets et al., 2006). In conclusion, the study by Marchand and coworkers (2015), and the significant association between change scores for psychological factors and GPE (study 4), support the relevance of psychological factors in the treatment of neck pain. This is corroborated by a recent meta-analysis indicating a robust association between pain-related fear and disability (Zale and Ditre, 2015).

The low explained variance for baseline prognostic factors and change scores (study 4) is in accordance with other studies that have investigated prognostic factors in neck pain (Hill et al., 2007, Schellingerhout et al., 2010, Pool et al., 2010, De Pauw et al., 2015). The question is therefore: What are we missing? The FAM and research into motor control in the past two decades has enhanced our understanding of neck pain and spinal pain in general. Still, the interventions aimed to target impairments in motor control and neck motion and the psychological aspects have not provided more than moderate effect sizes. Information is lacking on possible subgroups of patients who might have a superior response to targeted interventions directed towards impaired neck motion and motor control and/or pain-related psychological distress. The biopsychosocial model explicitly emphasizes the importance of having a broad perspective when evaluating disability and health. A main limitation of study 4, when investigating prognostic factors, was the lack of variables in the social part of the biopsychosocial model, which is reported to be important for recovery in neck pain (Walton et al., 2013d). However, the NDI contains items related to social life (items work and recreation), in addition to PSFS, which might cover functions related to social life and the participation domain of the ICF. Future studies in neck pain should incorporate variables reflecting the social domain and other factors that patients perceive as important in their lives

(Wiitavaara et al., 2016). Among these are poor sleep quality (Kovacs et al., 2014) , the therapist-patient relationship (Hall et al., 2010), expectations of treatment outcome (Skatteboe et al., 2014, Bialosky et al., 2010, Bishop et al., 2013), economic stress (Palmlof et al., 2012), parental history of musculoskeletal pain (Lier et al., 2014), genetics (Nyman et al., 2011), emotional distress (Johansen et al., 2013), and resilience factors (Sturgeon and Zautra, 2010). These factors clearly underline the complexity of chronic neck pain and other musculoskeletal pain conditions.

6.5 Clinical implications

Variables related to biomechanical performance (cervical ROM) and fine neck motor control (trajectory movement control) were associated with neck pain, disability and global perceived effect in the longitudinal studies. The assessment of neck motion and fine motor control in neck pain may help clinical decision-making, and to prioritize patients.

The clinical value of psychological factors depend on whether they are applied as baseline factors to predict treatment outcome or as change scores to evaluate treatment modifying effects. This suggest that physiotherapy treatment, although mainly focused on variables related to somatic health, may be mediated through effects on psychological factors such as kinesiophobia, catastrophizing and pain self- efficacy.

6.6 Future research

The studies in thesis provide evidence for an altered neck motion and motor control in neck pain patients. However, the relative importance of conceptually different constructs of motor control for reducing the chronicity and recurrence of neck pain requires studies with longer term follow-up than used in this study. Further studies are required to elaborate the contribution of voluntary and reflex control in neck pain, using electromyography and/or measures of the central nervous system.

Recent studies have shown promising results for prediction models in musculoskeletal conditions, such as low back pain (Hill et al., 2011). Such models can help clinical decision making and in selecting the patients who need a targeted (and possible multidisciplinary) treatment. Studies of neck pain have found conflicting evidence for prediction models in neck pain (Cleland et al., 2010, Schellingerhout et al., 2010); however, these models either lack the influence of biological factors (such as variables for neck motion and motor control described in this thesis) (Schellingerhout et al., 2010), or factors related to social life (Cleland et al., 2010). Studies with sufficient power, incorporating a range of known prognostic factors within a biopsychosocial framework, is therefore needed to improve prediction models and to uncover subgroups of patients who need a targeted treatment.

7 Conclusions

- Compared to healthy controls, neck pain patients displayed a generally stiffer neck motion and motor control patterns regardless of tasks. Our results indicate that these alterations are probably under voluntary control (studies 1 and 2)

- Small changes were observed in neck motion and motor control during a clinical course of 2 months, where only two out of five constructs (neck flexibility and trajectory movement control) showed significant associations with either pain or disability (study 3).

- The prognostic value of different variables depends on whether they are applied as baseline factors or as change scores from baseline to follow-up. Baseline factors that predicted a favorable treatment outcome were pain duration, pain intensity, patient-specific function, and variables for neck motion and motor control (cervical ROM in rotation and trajectory movement control). Change scores that were significantly associated with favorable treatment outcome were reduced pain intensity, reduced disability, increased patient-specific function, reduced kinesiophobia and catastrophizing, and increased self-efficacy.

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9 Appendix

Table 3: Test– retest reliability of cervical ROM, conjunct motion, joint position error, isometric neck flexion, figure of eight, the FLY test, and postural sway. Given values are mean (SD).

	n	Test 1	Test 2	Mean difference, (95% CI)	ICC^2	SDD^3
Neck flexibility						
Flexion/extension (°)	28	130.5 (19.3)	128.0 (19.2)	2.6 (-7.8, 12.9)	0.94	18.0
CM (°)		16.9 (5.2)	15.0 (5.2)	1.9 (-0.9, 4.7)	0.64	10.7
Peak velocity (°/s)		115.1 (44.2)	108.6 (35.9)	6.5 (-15.1, 28.0)	0.66	78.1
Rotation (°)	29	145.6 (15.6)	144.5 (15.7)	1.1 (-7.2, 9.3)	0.95	12.9
CM (°)		23.3 (9.6)	21.7 (7.6)	1.7 (-2.9, 6.2)	0.90	10.4
Peak velocity (°/s)		153.9 (53.0)	150.9 (45.4)	3.0 (-23.0, 29.0)	0.82	73.9
Lateral flexion (°)	29	76.6 (19.7)	76.0 (19.3)	0.6 (-9.7, 10.9)	0.98	10.3
CM (°)		62.7 (31.2)	57.3 (29.7)	5.5 (-10.5, 21.5)	0.92	34.3
Peak velocity (°/s)		84.3 (29.9)	81.0 (23.1)	3.3 (-10.8, 17.3)	0.87	35.5
Joint position error						
Left rotation (°)	29	5.2 (1.9)	4.5 (1.9)	0.7 (-0.3, 1.7)	0.58	4.2
Right rotation (°)	27	5.2 (2.0)	4.9 (2.3)	0.3 (-0.9, 1.5)	0.75	3.7
Head steadiness						
Low load						
Angular velocity (°/s)	29	1.8 (0.4)	1.7 (0.4)	0.1 (-0.1, 0.3)	0.66	0.59
High Load						
Angular velocity (°/s)	28	4.5 (0.9)	4.4 (0.9)	0.1 (-0.4, 0.6)	0.67	1.44
Figure of eight						
Low speed						
PD (cm)	27	3.6 (1.5)	2.7 (1.0)	0.9 (0.2, 1.6)	0.54	2.9
High speed						
PD (cm)	27	5.0 (1.7)	3.9 (1.3)	1.1 (0.3, 1.9)	0.40	3.8
Standing, low speed						
PD (cm)	29	3.2 (1.3)	3.0 (1.0)	0.2 (-0.4, 0.9)	0.40	2.7
Fly test						
PD Fly test 1A	28	2.5 (1.0)	2.0 (0.8)	0.4 (-0.1, 0.9)	0.74	2.3
PD Fly test 2A	26	2.8 (0.7)	2.6 (0.7)	0.3 (-0.1, 0.7)	0.71	1.1
PD Fly test 1B	28	2.0 (0.6)	1.8 (0.5)	0.2 (-0.05, 0.5)	0.66	1.5
PD Fly test 2B	29	3.4 (1.1)	2.9 (1.0)	0.5 (-0.05, 1.1)	0.83	2.9
Postural sway						
Sway area EO (cm^2)	28	2.2 (1.9)	2.1 (1.6)	0.04 (-0.9. 1.0)	0.52	3.4
Sway area EC (cm^2)	27	2.0 (1.3)	1.4 (0.7)	0.7 (0.1, 1.2)	0.16	2.9
Sway area EOB (cm^2)	29	8.4 (2.7)	9.0 (3.4)	-0.6 (-2.3, 1.0)	0.44	6.4

1) Difference between test 1 and test 2.

2) ICC= Intraclass correlation coefficient. ICC 3,k for tests with > one repetition. ICC 3,1 for single tests.

3) SDD= Smallest detectable difference

ROM= Range of motion. PD= Point deviation EO= Eyes open. EC= Eyes closed. EOB= Eyes open standing on a balance pad

n= Number of subjects analyzed in each test.

Paper I

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RESEARCH ARTICLE **Open Access**

Evidence for a general stiffening motor control pattern in neck pain: a cross sectional study

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Abstract

Background: Neck pain is associated with several alterations in neck motion and motor control. Previous studies have investigated single constructs of neck motor control, while few have applied a comprehensive set of tests to investigate cervical motor control. This comparative cross- sectional study aimed to investigate different motor control constructs in neck pain patients and healthy controls.

Methods: A total of 166 subjects participated in the study, 91 healthy controls (HC) and 75 neck pain patients (NP) with long-lasting moderate to severe neck pain. Neck flexibility, proprioception, head steadiness, trajectory movement control, and postural sway were assessed using a 3D motion tracking system (Liberty). The different constructs of neck motion and motor control were based on tests used in previous studies.

Results: Neck flexibility was lower in NP compared to HC, indicated by reduced cervical ROM and conjunct motion. Movement velocity was slower in NP compared to HC. Tests of head steadiness showed a stiffer movement pattern in NP compared to HC, indicated by lower head angular velocity. NP patients departed less from a predictable trajectory movement pattern (figure of eight) compared to healthy controls, but there was no difference for unpredictable movement patterns (the Fly test). No differences were found for postural sway in standing with eyes open and eyes closed. However, NP patients had significantly larger postural sway when standing on a balance pad. Proprioception did not differ between the groups. Largest effect sizes (ES) were found for neck flexibility (ES range: 0.2- 0.8) and head steadiness (ES range: 1.3- 2.0). Neck flexibility was the only construct that showed a significant association with current neck pain, while peak velocity was the only variable that showed a significant association with kinesiophobia.

Conclusions: NP patients showed an overall stiffer and more rigid neck motor control pattern compared to HC, indicated by lower neck flexibility, slower movement velocity, increased head steadiness and more rigid trajectory head motion patterns. Only neck flexibility showed a significant association with clinical features in NP patients.

Keywords: Neck, motor control, Neck flexibility, Proprioception, Head steadiness, Trajectory movement control, Postural sway, Clinical features

Background

Neck pain is common in the general population with one-year prevalence varying from 30% to 50% [1]. Globally, neck pain is the fourth leading cause of years lived with disability, which underlines the importance of research to develop effective prevention and treatment programs based on knowledge of underlying mechanisms of neck pain [2]. A recent paper indicates a close connection between alterations in motor control and pain processing in the brain [3].

Research over the last decade indicates several alterations in neck motor control and sensorimotor entities in subjects with neck pain compared to healthy subjects. Neck pain patients may have delayed onset of deep neck flexors [4], increased activation of superficial neck flexors [5], jerky movement patterns [6], decreased cervical flexor endurance [7], lower movement velocity [8-10], decreased cervical muscle strength [11], reduced trajectory movement control [12], irregular and stiffer movement patterns [13,14], increased postural sway

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[15,16], and reduced joint position sense[17-19]. However, no single parameter stands out as representing motor dysfunction in the neck and studies typically use a subset of variables that vary between studies [17,20].

Surprisingly, few studies have utilized a comprehensive set of neck movement and motor control tests to contrast patients and healthy subjects. Such comparisons may help identifying specific underlying neck movement or motor control constructs that differentiate patients from healthy subjects. Based on the previous research we decided to group different neck motion and motor control parameters within different constructs of tentative underlying neck motor dysfunction. The aim of this study was thus to compare neck motion and motor control in neck pain patients with moderate to severe neck pain and healthy subjects with tests representing five different constructs: neck flexibility, proprioception, trajectory movement control, head steadiness, and postural sway. Secondary aim was to evaluate the association between clinical features such as pain, disability, and kinesiophobia and the constructs of motor control and neck motion.

Methods

We conducted a comparative case–control study (n = 166) in the period August 2012 to February 2014. The data from healthy controls (n = 91) were collected by a nurse and a physiotherapist, while the neck pain patients (n = 75) data were collected by a second physiotherapist. The different examiners were equally and well trained in the test procedures. In addition the physiotherapist who performed the data collection for the NP group observed the data collection in the HC group to avoid discrepancies in the procedures. All subjects gave written and informed consent and the study was conducted in accordance with the Helsinki Declaration and approved by the Regional Committee for Medical and Health Research Ethics, REC Central (2011/2522/REC Central).

Healthy control group (HC)

Men and women between 18–67 years with no neck pain were included in the HC group. The subjects were recruited by inviting friends and colleagues at the local university and university hospital. Exclusion criteria were episode of neck pain within the last 3 months, markedly reduced or uncorrected vision, history of neck trauma, diagnosed with neurological or orthopedic conditions that could affect motor control, positive Spurling's test for neurological radiating arm pain, pregnancy, or insufficient comprehension of Norwegian.

Neck pain group (NP)

Neck pain patients were recruited from private physiotherapy clinics in primary health care (56 subjects) and from a specialized neck and back pain clinic at the university hospital (19 subjects). Patients were initially screened for eligibility by telephone. Upon later examination, inclusion criteria were non- traumatic neck pain as the main problem with a score of 3 or more on numerical rating scale (NRS; 0–10) , where 0 represent no pain and 10 worst imaginable pain, at the day of testing and the current neck pain episode lasting >2 weeks. Exclusion criteria were the same as for the control group, except the criteria for neck pain.

Questionnaire data

On the day of testing, both HC and NP patients first completed a questionnaire which consisted of biographical data (age, gender, height and weight), duration of current neck pain episode, neck pain intensity at the day of testing and average neck pain last month assessed by NRS. Further descriptive data were obtained by the Neck Disability Index (NDI; 0–100) [21], Tampa Scale of Kinesiophobia (TSK; 13–52) [22], Pain Catastrophizing Scale (PCS;0–52) [23], and Pain Self Efficacy Questionnaire (PSEQ;0–60) [24]. High values in TSK and PCS indicate more kinesiophobia and catastrophizing, respectively, while low values in PSEQ indicate low self efficacy.

Instrumentation and sensors

Motion data for the cervical and postural sway measurements were acquired with body worn sensors using the Liberty electromagnetic motion tracker system (Polhemus, Inc, Colchester, Vermont, USA) with a sampling rate of 240 Hz. Sensor 1 (S1) was placed on the subject's forehead 1 cm above arcus superciliaris, the second sensor (S2) was placed on the spinous process of Th2, and a third sensor (S3) was placed in the area of the spinous processes of L4-L5. Tight elastic bands were used to hold the sensors in position. The electromagnetic transmitter (TX) was positioned at a distance of 10–50 cm above the head during all the measurements. For S1 and S2 raw data were low pass filtered at 20 Hz using a 2nd order Butterworth filter, while raw data for S3 were low pass filtered at 5 Hz.

A software tool based on Matlab (The MathWorks, Inc., Natick, MA, USA) was developed (SINTEF ICT, Applied Cybernetics and Dept. of Engineering Cybernetics, NTNU, Norway) to record and analyze the motion data. Table 1 shows the sensors used for calculations of the different tests. The coordinate system defined by the TX was used for calculating all variables except cervical range of motion (ROM). For this variable, a new coordinate system was calibrated for each subject to adjust the coordinate axes to the individually preferred axes of

Table 1 Description of the motor control and cervical motion variables

Construct	Test	Assessment	Unit of measure	Sensors	Reps per test	Analyzed	Comments
Neck flexibility	Active neck movements in flexion/extension, rotation and lateral flexion	Cervical ROM in flexion/ extension, rotation, and, lateral flexion	deg	S1 vs S2	3	Avg	Full cycle cervical ROM
		Conjunct motion in the two associated movement planes	deg			Avg	According to Woodhouse et al. (2008)
		Peak velocity in flexion/ extension, rotation and lateral flexion	deg/s			Avg	3 D angular velocity
Proprioception	Joint position error in left and right head rotation	3D repositioning error in left and right rotation	deg	S1 vs S2	6	Avg	3 repetitions in each direction
Trajectory movement control	FOE slow speed	Average point deviation (PD)	cm	S1 vs TX	1	Single	30 sec duration
	FOE fast speed				1		20 sec duration
	FOE in standing, slow speed				1		30 sec duration.
	The Fly test, 1A	Average point deviation (PD)	cm	S1 vs TX	1	Single	30 sec duration for all of the Fly tests. Adopted from Kristjansson et al. (2010)
	The Fly test, 2B				1		
	The Fly test, 1B				1		
	The Fly test, 2A				1		
Head steadiness	Isometric neck flexion, low load	Average 3 D angular velocity	deg/s	S1 vs S2	1	Single	60 sec duration 60° recumbent position
	Isometric neck flexion, high load	Average 3 D angular velocity	deg/s		1		30 sec duration Supine position
		Holding time	sec				
Postural sway	Standing balance EO	Sway area (95 % confidence area)	cm^2	S3 vs TX	1	Single	60 sec duration for the tests of standing balance.
	Standing balance EC				1		
	Standing balance EOB				1		
	FOE in standing				1		30 sec duration

The column test lists the order of the tests in the data collection.
ROM = range of motion. CM = conjunct motion. Deg = degrees. 3D = 3 dimensional. FOE = figure of eight. EO = eyes open. EC = eyes closed. EOB = eyes open balance pad. S1 = forehead sensor. S2 = spinous process of T2. S3 = spinous process of L4-L5. TX = transmitter on Liberty. 1A = easy pattern, small ROM. 1B = easy pattern, large ROM. 2A = difficult pattern, small ROM. 2B = difficult pattern, large ROM.

cervical motion. Detailed description of the calibration is available in Additional file 1.

Outcome variables and testing procedures

The description of the tests of motor control and the calculated variables are summarized in Table 1. We adopted five constructs of motor control to group the different tests used in the study. Standardized instructions were used for all tests. The tests were performed in the order listed in Table 2.

Neck flexibility

Maximal cervical ROM was measured with the subjects seated on a wooden bench with backrest in 80^0 recumbent position and the shoulders fixed with nonflexible shoulder straps to avoid movement of the thorax. The subjects were asked to move as far as possible in all three primary movement planes (flexion/extension, rotation in the horizontal plane and lateral flexion) with a self- preferred velocity. Start and stop of the recording was manually set by the examiner before and after the movement. Maximal cervical ROM was calculated as the mean of three trials for each primary movement plane. During each primary plane ROM test neck flexibility was also assessed by the degree of motion in accessory planes, i.e., conjunct motion (CM), which was calculated as the maximum ROM in the two associated movement planes, adopted from Woodhouse et al. [14]. Peak velocity in the three tests of maximal cervical ROM was computed to assess movement velocity (see Additional file 1), since this variable has been shown to differentiate neck pain patients from healthy controls [8,10].

Proprioception

Joint position error (JPE) was used to assess proprioception and was recorded as the difference in head orientation at neutral position before and after cervical left and

Table 2 Subject characteristics and clinical features

	Neck pain patients n = 75	Healthy controls n = 91	p
Age	43.1 (12.9)	40.8 /13.8)	0.28
Gender (male/female	20/55	43/48	0.01
Body mass index	24.9 (4.7)	25.0 (3.5)	0.9
Current neck pain (NRS: 0-10)	4.6 (1.4)	N/A	
Worst neck pain last month (NRS: 0-10)	7.4 (1.5)	N/A	
Duration of neck pain, n (%)		N/A	
< 3 months	7 (9%)		
3-6 months	13 (17%)		
> 6 months	55 (74%)		
Neck Disability Index (0-100)	31.2 (11.6)	N/A	
TSK (13-52)	24.4 (4.3)	N/A	
PCS (0-52)	12.9 (8.5)	N/A	
PSEQ (0-60)	44.3 (10.0)	N/A	
Concurrent low back pain, n (%)	20 (27%)	N/A	
Self-rated general health, n (%)		N/A	
Poor	0 (0)		
Fair	36 (48%)		
Good	37 (49%)		
Very good	2 (3%)		
Frequency physical activity, n(%)		N/A	
< once per week	10 (12%)		
1-3 days per week	51 (68%)		
4-7 days per week	14 (19)		
Use of analgesica, n (%)	38 (51)	N/A	

Mean (SD), unless otherwise stated.
NRS = Numerical Rating Scale. TSK = Tampa Scale of Kinesiophobia. PCS = Pain Catastrophizing Scale. PSES = Pain Self Efficacy Questionnaire. N/A = Not applicable.

right head rotation (see Additional file 1). The subjects were blind- folded and instructed to start with their head in a preferred neutral position and then rotate the head as far as possible and back to the neutral position. The subjects performed three repetitions in each direction; first to the left and then to the right. Subjects were asked to respond orally when they believed they had returned to neutral position. The examiner did not reposition the subjects' head back to the initial neutral position, but used the end position of the previous trial as the starting position for the next repetition.

Trajectory movement control

Two head tracking tasks were performed in order to assess trajectory movement control; a figure-of-eight test (FOE) (adopted from the study of Woodhouse et al. [25]) and a "Fly test" (as described by Kristjannson et al. [12]). For the FOE test, a horizontal figure-of- eight was displayed on a screen in front of the subjects at a distance of 250 cm (Figure 1). The subjects were instructed to follow a white cursor moving along the line of the figure as accurately as possible by moving their head. The speed of the tracking was set by the movement of the white cursor. The movement of the head was projected on the screen as a red cursor. Two different tracking velocities, slow and fast, were used to investigate possible differences in the speed-accuracy trade-off between NP subjects and HC's [26]. For the slow and fast tracking velocity tests the speed of the white cursor displayed on the screen was approximately 10 cm/s and 15 cm/s, respectively. The head velocity required to track the FOE was approximately 3.0 °/s and 4.3°/s for the slow and fast tracking velocity, respectively. The test with low velocity was also repeated in standing. The HC and NP subjects were familiarized with the test by performing one test session with high velocity.

Two patterns of the Fly test (Figure 1) were used in this study corresponding to the easy (1A and 1B) and medium (2A and 2B) patterns described by Kristjanssons et al. [12]. Two different demands for head movement were applied during the Fly test, one with a head to projected cursor movement ratio of 1:1 (1A and 2A) and

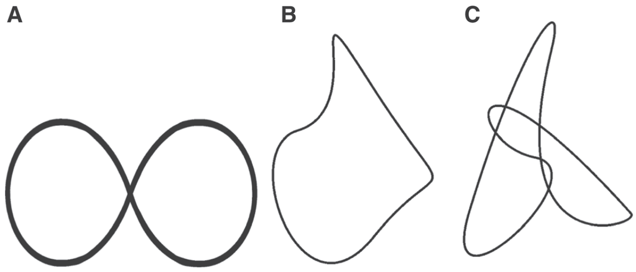

Figure 1 The movement patterns of the figure of eight and "the Fly" tests for assessing trajectory movement control. A: Figure of eight. **B**: Movement pattern 1A and 1B in the Fly test C: Movement pattern 2A and 2B in the Fly test (adopted from Kristjansson et al. (2010)). Mean cervical ROM in the performance of the figure of eight was 11° flexion/extension and 24° rotation in the horizontal plane. Mean cervical ROM in the Fly test was 14° flexion/extension and 10° rotation in the horizontal plane in movement pattern 1A, and 15° flexion/extension and 10° rotation in the horizontal plane in movement pattern 2A. Movement pattern 1B and 2B, which was the same patterns as 1A and 2A, respectively, had twice as much cervical ROM (movement ratio head to cursor 2:1).

another with a ratio 2:1 (1B and 2B), the latter implying that the head had to move twice as far to move the cursor on the screen compared to the first test. The 2:1 ratio was included to study demands of increased ROM on trajectory movement control. The tracking velocities for the Fly tests measured in head motion velocity were in the range of 2–5 °/s. The patterns were not visible to the subject and thus unpredictable. The setup was similar to the figure of eight test and subjects were instructed to follow the white cursor ("the Fly") as accurately as possible. The HC were familiarized with the test by performing one of the fly tests, and the NP performed two of the tests. Point deviation (PD), a measure of movement accuracy, was calculated as the mean absolute distance (cm) between the red cursor and the white cursor both during the FOE test and the Fly test.

Head steadiness

Isometric neck flexion (INF) was used to investigate the ability to hold the head steady under two conditions, low load and high load. For the low load test the subjects were seated in a 60 ° recumbent position with footrest and without shoulder straps. They were asked to slightly lift their head (1-2 cm) from the backrest and hold their head as steady as possible in the same position for 1 minute. For the INF high load test the subjects were positioned in supine and were asked to do craniocervical flexion while their head was positioned on the bench, then to lift their head slightly from the bench and hold their head as steady as possible in the same position for 30 s. The test was ended if the subjects touched the table with the back of their head or if the subjects chose to end the test due to fatigue or neck pain. Angular velocity of the head was calculated to assess the ability to hold the head steady during the INF test. Holding time during the high load INF test was used as a descriptive variable. Angular velocity (deg/s) was calculated as the point to point change in orientation of the forehead sensor (S1) over time, relative to the sensor placed on the spinous process of T2 (S2). Holding time in the INF tests was registered with a stopwatch.

Postural sway

Postural sway in quiet standing was assessed during 60 s for each one of four conditions. The first condition was a dual task where the FOE test with low tracking velocity was performed during quiet standing. In the second condition eyes open (EO) the subjects were instructed to focus at a point on the wall 250 cm straight in front of them. For the third condition subjects were blindfolded (EC). The fourth and last condition was performed with eyes open standing on a balance pad (EOB). Unfortunately, postural sway during the FOE in standing was not recorded in 43 subjects in HC, leaving only 48 subjects in the HC group for this analysis. The same standing position was ensured for all conditions (feet parallel with 10 cm between the medial malleoli and arms held across the chest) and the order of presentation of conditions was the same for all subjects. The instructions given were to "stand still for one minute". Sway was assessed from the antero-posterior and the mediolateral position data from the sensor (S3) placed on spinous process of L4-L5 and 95% confidence interval for sway area (cm^2) was calculated.

Statistical analysis

Outliers, those who did not perform the test correctly or were exposed to technical problems were dropped from the analyses. The number of subjects analyzed for the different variables are reported in Tables 3 and 4.

Table 3 Group comparisons of neck flexibility and proprioception

	Neck pain (n = 75)	Healthy controls (n = 91)	p
Neck flexibility			
Flexion/extension (°)[1]	110.1 (105.7-114.5)	126.2 (122.3-130.2)	<0.01
CM (°)[1]	12.3 (11.3-13.3)	16.5 (15.6-17.4)	<0.01
CM (°)[2]	12.9 (11.9-14.0)	16.0 (15.1-16.9)	<0.01
CM (°)[3]	13.7 (12.4-15.0)	15.4 (14.4-16.3)	0.03
Peak velocity (°/s)[1]	70.6 (62.5-78.7)	115.6 (108.4-122.8)	<0.01
Peak velocity (°/s)[2]	75.0 (66.8- 83.1)	112.1 (104.9-119.4)	<0.01
Rotation (°)[1]	128.2 (124.3-132.2)	140.7 (137.2-144.2)	<0.01
CM (°)[1]	19.8 (18.0-21.6)	25.1 (23.5-26.7)	<0.01
CM (°)[2]	20.6 (18.7-22.4)	24.5 (22.8-26.1)	<0.01
CM (°)[3]	21.1 (19.2-23.1))	24.0 (22.3-25.7)	0.04
Peak velocity (°/s)[1]	109.3 (98.9-119.7)	158.9 (149.6-168.3)	<0.01
Peak velocity (°/s)[2]	114.3 (103.9-124.7)	154.9 (145.7-164.2)	<0.01
Lateral flexion (°)[1]	68.1 (64.7-71.6)	72.6 (69.5-75.7)	0.06
CM (°)[1]	45.7 (40.1-51.3)	62.5 (57.5-67.5)	<0.01
CM (°)[2]	44.9 (39.4- 50.5)	63.1 (58.1-68.0)	<0.01
CM (°)[3]	52.7 (47.6-57.7)	56.9 (52.4-61.4)	0.25
Peak velocity (°/s)[1]	57.9 (52.2-63.5)	85.7 (80.6-90.7)	<0.01
Peak velocity (°/s)[2]	58.6 (53.0- 64.2)	85.1 (80.1-90.1)	<0.01
Total cervical ROM (°)[1]	306.5 (296.5-316.5)	339.5 (330.6-348.5)	<0.01
Proprioception			
JPE (°)[2]	5.6 (5.2-6.1)	5.1 (4.6-5.5)	0.11

Maximal cervical ROM, conjunct motion and peak velocity in the three primary neck movement planes.
Given values are mean (95 % CI) adjusted for 3 different models of covariates.
[1] Adjusted for age and gender (model 1).
[2] Adjusted for age, gender, and cervical ROM (model 2).
[3] Adjusted for age, gender, cervical ROM, and peak velocity (model 3).
p = p- value. ROM = range of motion. CM = conjunct motion in the two accessory movement planes. JPE = joint position error.

We used the chi square test to analyze baseline group differences for categorical variables. Multiple regression was used to investigate group differences for cervical ROM, CM, peak velocity, and JPE. Multiple robust regression with Huber's method was used for the other variables due to heteroskedasticity [27]. We adjusted for age and gender (model 1) in all analyses because age has been shown to influence several of the variables measured [28-30] and gender was not equally distributed between the groups (Table 1). In the analyses of CM we also adjusted for maximum ROM in the primary plane (model 2) and in the final model for both maximum ROM and peak velocity in the primary plane ROM test (model 3), since these covariates are shown to influence smoothness of movement in previous studies [31]. In the sole analysis of peak velocity and JPE we adjusted for maximum ROM [6]. All the variables, except ROM and CM, showed skewness of the data. Log- transformation of these variables gave acceptable normal distribution, but did not change the result of the regression analysis, thus, non-transformed data and p- values are reported for ease of interpretation. To evaluate the association between clinical parameters (NRS, NDI, duration of current neck pain episode, and TSK) and the constructs of motor control in the NP group we used correlation analysis. For the continuous variables NPRS, NDI, and TSK we used Pearson's r and for the categorical variable duration we used Spearman's rho. Since tests within each construct were highly correlated and to avoid too many results, we chose the tests with largest effect sizes in the correlation analysis. Effect size (ES) was calculated with this formula: $ES = \frac{HC_{mean} - NP_{mean}}{\sqrt{\frac{HC_{SD^2} + NP_{SD^2}}{2}}}$, where SD is the standard deviation [32]. Calculation of 95 % CI for the ES was done by first calculating the variance $\left(S_{ES}^2\right)$ for the sampling distribution of the effect size:

$S_{ES}^2 = \frac{HC_n + NP_n}{HC_n \times NP_n} + \frac{ES^2}{2(HC_n + NP_{n,}}$ where n is the group size. Then the 95 % CI was calculated using the formula

Table 4 Group comparisons of head steadiness, trajectory movement control, and postural sway

	Neck pain	Healthy controls	n=NP/HC	p[1]
Head steadiness				
INF Low load				
Angular velocity (°/s)	1.3 (1.2-1.4)	1.7 (1.6-1.8)	75/90	<0.01
INF High Load				
Angular velocity (°/s)	2.8 (2.6-2.9)	4.5 (4.3-4.7)	73/91	<0.01
Trajectory movement control				
FOE Low speed				
Point deviation (cm)	3.4 (3.1-3.7)	3.8 (3.4-4.1)	75/89	0.17
FOE High speed				
Point deviation (cm)	4.4 (4.1-4.8)	5.2 (4.8-5.6)	75/91	<0.01
FOE Standing, low speed				
Point deviation (cm)	2.9 (2.6-3.1)	3.3 (3.0-3.6)	74/91	0.02
The Fly test				
PD test 1A (cm)	2.2 (2.0-2.4)	2.5 (2.3-2.7)	75/89	0.03
PD test 1B (cm)	2.1 (2.0-2.2)	2.1 (2.0-2.3)	75/89	0.63
PD test 2A (cm)	3.1 (2.9-3.3)	3.3 (3.1-3.5)	74/88	0.33
PD test 2B (cm)	2.8 (2.7-3.0)	2.8 (2.6-2.9)	75/83	0.64
Postural sway				
Sway area EO (cm^2)	3.0 (2.4-3.5)	2.7 (2.2-3.3)	72/90	0.53
Sway area EC (cm^2)	2.5 (2.0-3.1)	2.0 (1.7-2.3)	72/87	0.12
Sway area EOB (cm^2)	11.0 (9.7-12.3)	8.1 (7.4-8.7)	73/91	<0.01
Sway area FOE (cm^2)	4.3 (3.3-5.2)	5.9 (4.2-7.5)	73/48	0.09

Given values are mean (95 % CI) adjusted for age and gender (model 1).
[1] p value adjusted for age and gender (model 1).
INF = isometric neck flexion. FOE = figure of eight. PA = point deviation. 1A = easy pattern, small ROM.
1B = easy pattern, large ROM. 2A = difficult pattern, small ROM. 2B = difficult pattern, large ROM.
EO = eyes open. EC = eyes closed. EOB = eyes open balance pad.

according to Fritz et al. [32]: 95 % $CI = ES \pm z_{0.025} s_{ES}$The significance level was defined as $p < 0.05$. All statistical analyzes were performed using STATA 13 (Stata Corp., College Station, TX, USA).

Results

The groups were similar in age and BMI, but there were a higher proportion of women in the HC group (Table 2). The NP group had a mean neck pain score of 4.6 on NRS at the day of testing and 7.4 on NRS for worst neck pain last month. A large proportion of the NP patients (74%) stated that their neck pain started more than 6 months ago (Table 2). The NP subjects showed a moderate disability measured by the NDI (mean 31.2; SD 11.6), a moderate kinesiophobia measured by the TSK (mean 24.4; SD 4.3), and a moderate pain catastrophizing measured by the PCS (mean 12.9; SD 8.5). Other characteristics of the NP group are shown in Table 2. Nine NP subjects were excluded due to NRS <3 for neck pain on the day of testing.

Neck flexibility

NP patients had significantly less maximal cervical ROM in flexion/extension and rotation compared to HC after adjusting for age and gender, while lateral flexion barely fell short of reaching significance (Table 3 and Figure 2A). Summing ROM in the three primary planes in total ROM showed a difference of 33.1° (95% CI; −46.6,-19.5; $p < 0.001$) between the two groups (Figure 2A). There was no significant gender difference in total cervical ROM or when the primary planes were analyzed separately. Peak velocity during all ROM tests was significantly lower in NP compared to HC, and remained significantly lower also after adjusted for cervical ROM in the primary plane (Table 3). CM in accessory planes during all primary planes motion was significantly smaller in the NP patients compared to HC (Table 3). The differences remained significant after adjusting for maximum ROM in the primary plane. When adjusted for peak velocity CM in flexion/extension and rotation in the NP groups were still significantly smaller compared to HC, but not for CM in lateral flexion (Table 3).

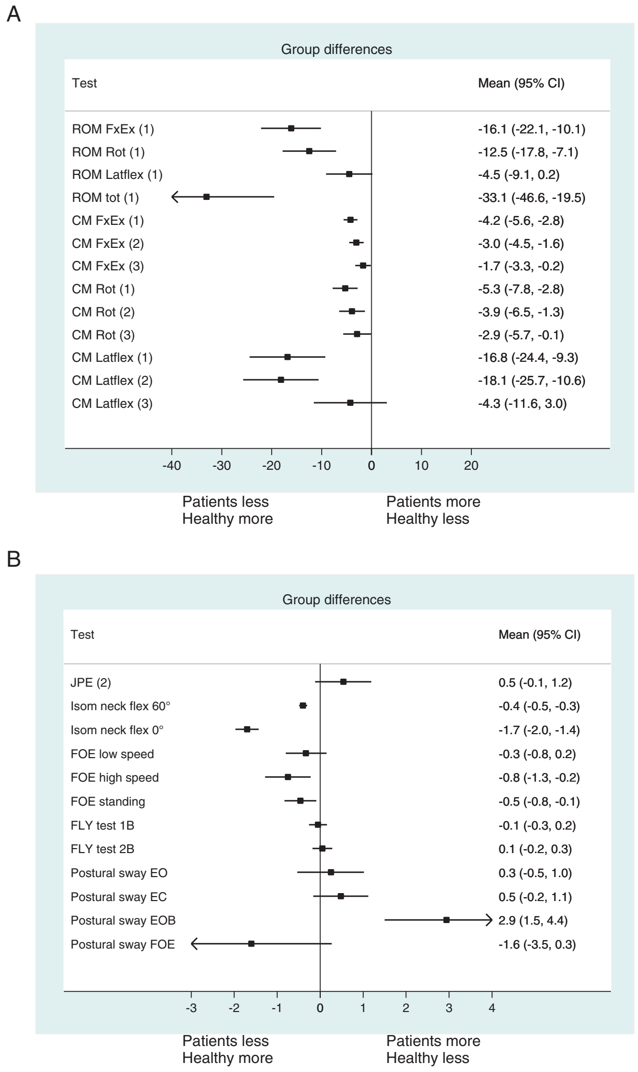

Figure 2 Forest plot of the group difference (95 % CI) between neck pain patients and healthy controls. Number in parentheses behind test variables states the analytic model applied. Analysis were adjusted for age and gender (model 1), plus cervical ROM (model 2), plus peak velocity (model 3). All variables in B are adjusted for model 1, except for JPE which is adjusted for model 2. ROM = range of motion. FxEx = flexion/extension. Latflex = lateral flexion. JPE = joint position error. FOE = figure of eight. Fly test 1B = easy pattern, large ROM. Fly test 2B = difficult pattern, large ROM. EO = eyes open. EC = eyes closed. EOB = eyes open balance pad.

Proprioception

There was no significant between group difference ($p = 0.11$) in relocation error in the JPE test (Table 3).

Head steadiness

In the low load and high load tests NP patients had markedly lower head angular velocity compared to HC. In the low load test the mean group difference was −0.4 °/s (95% CI; −0.5 to −0.3; $p < 0.001$) and in the high load test −1.7 °/s (95% CI; −2.0 to −1.4; $p < 0.001$). Largest effect sizes were found for head steadiness and neck flexibility (Table 5). All subjects in the HC group were able to hold for 60 s in the low load and 30 s in the high load test, whereas 8 subjects in NP group did not manage to

Table 5 Summary of main results

	Indicate less motion	Normal	Indicate larger motion	Effect size Mean (95 % CI)
Neck flexibility				
Flexion/extension[1]	X			**0.84 (0.52 to 1.16)***
CM[3]	X			0.37 (0.06 to 0.68)*
Peak velocity[2]	X			**1.05 (0.72 to 1.37)***
Rotation[1]	X			**0.72 (0.41 to 1.04)***
CM[3]	X			0.36 (0.05 to 0.67)*
Peak velocity[2]	X			**0.90 (0.57 to 1.22)***
Lateral flexion[1]		X		0.30 (-0.01 to 0.61)
CM[3]		X		0.19 (-0.11 to 0.50)
Peak velocity[2]	X			**1.08 (0.75 to 1.41)***
Total cervical ROM[1]	X			**0.76 (0.44 to 1.08)***
Proprioception				
JPE[2]		X		-0.26 (-0.56 to 0.05)
Head steadiness				
Low load[1]	X			**1.29 (0.95 to 1.63)***
High Load[1]	X			**1.95 (1.58 to 2.32)***
Trajectory movement control				
FOE low speed[1]		X		0.22 (-0.09 to 0.53)
FOE high sped[1]	X			0.45 (0.13 to 0.76)*
FOE standing[1]	X			0.40 (0.09 to 0.71)*
Fly test 1A[1]	X			0.36 (0.05 to 0.68)*
Fly test 1B[1]		X		0.07 (-0.23 to 0.38
Fly test 2A[1]		X		0.16 (-0.15 to 0.47)
Fly test 2B[1]		X		-0.07 (-0.39 to 0.24)
Postural sway				
Open eyes[1]		X		-0.09 (-0.40 to 0.21)
Closed eyes[1]		X		-0.26 (-0.57 to 0.06)
Balance pad[1]			X	**-0.64 (-0.95 to -0.32)***
FOE standing[1]		X		0.30 (-0.07 to 0.66)

Effect sizes for each variable with 95% CI are listed below.
Interpretation of the effect size: 0.2 = small, 0.5 = medium, >0.8 = large.
Negative or positive effect sizes indicate that the NP group has larger or smaller values, respectively, compared to HC. Statistically significant and effect sizes >0.5 are marked with * and bold numbers, respectively.

[1] Adjusted for age and gender (model 1).

[2] Adjusted for age, gender, and cervical ROM (model 2).

[3] Adjusted for age, gender, cervical ROM, and peak velocity (model 3).

* = p value <0.05.
ROM = range of motion. CM = conjunct motion in the two accessory movement planes. JPE = joint position error. INF = isometric neck flexion. FOE = figure of eight. 1A = easy pattern, small ROM. 1B = easy pattern, large ROM. 2A = difficult pattern, small ROM. 2B = difficult pattern, large ROM. EO = eyes open. EC = eyes closed. EOB = eyes open balance pad.

hold their head for 30 s in the high load test. Two of these patients had holding time <3 s in the high load test and were therefore excluded from the calculations of the kinematic variables.

Trajectory movement control

Table 4 shows that HC subjects departed more from the trajectory pattern in the FOE test than the NP subjects, indicated by the higher point deviation values. The differences were statistical significant for the high speed FOE test with a mean group difference in PD of −0.8 cm (95% CI;-1.3 to −0.2; $p < 0.01$) and the FOE test in standing (mean difference: −0.5 cm; 95% CI; −0.8 to −0.1; $p < 0.05$), (Figure 2B). HC also showed more trajectory departure (i.e. higher point deviation) in the Fly test 1A compared to the NP group (mean difference: −0.3 cm; 95 % CI; −0.6 to −0.03; $p < 0.05$). None of the other movement patterns in the Fly tests revealed any significant group differences in PD between the NP group and HC (Table 4).

Postural sway

Postural sway during quiet standing with EO and EC did not differ significantly between the groups (Figure 2B and Table 4). The NP group had a significant larger sway area for the EOB test compared to HC (mean difference: 2.9; 95% CI; 1.5 to 4.4; p > 0.01). Contrary, the NP patients had less sway area during the FOE test where subjects had to perform neck motion during the standing balance test, but this difference was not statistically significant (mean difference: −1.6; 95 % CI; −3.5 to 0.3; p = 0.09).

Associations between clinical features and constructs of motor control

Neck flexibility was the only construct that was significantly associated with clinical features, but the associations were weak. Current neck pain was significantly associated with ROM in flexion/extension (r = −0.36; p < 0.01), CM (r = −0.26; p < 0.05), and peak velocity (r = −0.34; p < 0.01) during flexion/extension (Table 5). TSK was significantly correlated with peak velocity in flexion /extension (r = 0.23; p < 0.05). NDI and duration of current neck pain episode were not significantly associated with neck flexibility (Table 6). The Fly test showed a significant correlation with NDI (r = 0.27; p < 0.05), but not for the other clinical features.

Discussion

Overall, this study points to an altered neck motor control in patients with moderate to severe neck pain with long duration. NP patients had less cervical ROM, reduced conjunct motion, lower peak velocity during cervical ROM tests, less head motion in the isometric head flexion steadiness tests, showed more "rigid" trajectory head motion patterns and more postural sway in standing on a balance pad. Except for the latter, all tests may express a general finding of stiffer and more rigid neck motor patterns in neck pain patients (Table 5).

Neck flexibility

In agreement with other studies [14,33], we found that NP subjects had clearly less neck flexibility in primary cervical planes compared to HC. Also, the finding of lower peak velocity in tests of cervical ROM among NP subjects compared to HC is in accordance with other studies of movement velocity [8,10]. CM can be perceived as a measure of freedom or smoothness of motion during tests of maximal ROM in the cervical cardinal planes. CM has previously been shown to differentiate neck pain patients from healthy controls [10,14], in agreement with this study showing significantly less CM or stiffer movement during all primary planes. A

Table 6 Correlations between clinical parameters and constructs of motor control and neck motion in neck pain patients (n = 75)

Variables	NPRS r	NDI r	Duration[1] rho	TSK r
Neck flexibility				
Flexion/extension	**-0.36****	-0.10	-0.09	-0.11
Conjunct motion	**-0.26***	0.05	-0.09	0.12
Peak velocity	**-0.34****	-0.21	-0.14	**0.231***
Proprioception				
Joint position error	0.01	0.147	0.03	0.12
Head steadiness				
INF low load	-0.1	-0.13	-0.11	-0.11
INF high load	0.05	-0.12	-0.05	-0.06
Trajectory movement control				
PD FOE fast	0.18	0.09	-0.14	-0.02
PD Fly test[2]	0.19	**0.27***	-0.21	-0.10
Postural sway				
Area EOB	0.03	-0.04	0.14	-0.07

Clinical parameters are current neck pain measured by NRS, neck disability index (NDI), duration of current neck pain episode, and kinesiophobia measured by TSK. Given values are Pearson's r for NRS, NDI and TSK and Spearman's rho for duration with corresponding p-values. Correlation coefficients with p < 0.05 are in bold.

[1] Duration of pain, five categories from short to long duration of current neck pain.

[2] Fly test with easy pattern and small neck range of motion.

* = p value < 0.05. ** = p value < 0.01.

NRS = numerical rating scale. NDI = Neck Disability Index. TSK = Tampa Scale of Kinesiophobia. INF = isometric neck flexion. PD = point deviation. FOE = figure-of-eight. EOB = eyes open balance pad.

strength of this study is that we controlled for cervical ROM and movement velocity. A recent study showed that smoothness of movement was strongly related to velocity in unconstrained head movements [31]. Less smooth movements may therefore be a result of lower velocity and not altered motor control, which implies that statistically adjusting for movement velocity is imperative when investigating smoothness of movement in unconstrained neck movements [31]. In line with this, group differences in CM in lateral flexion were no longer significant after adjusting for movement velocity. However, reduced CM in flexion/extension and rotation remained significant after adjusting for velocity, indicating that reduced CM is a robust sign of stiffer movement patterns in neck pain patients for these movement planes.

The etiology of the lower peak velocity in NP subjects compared to HC in performing unconstrained neck movements is largely unknown. Vikne et al. suggested that altered muscle activation patterns may not explain the lower peak velocity, since they found that EMG amplitude in neck muscles during unconstrained neck movements was similar between neck pain subjects and healthy controls when adjusted for ROM and movement velocity [9]. On the other hand, they found a negative correlation between fear avoidance and peak velocity measured in the sagittal plane (r value range −0.67 to −0.77), suggesting that cognitive factors might act as critical effect modifiers in the relationship between neck motor control and neck pain. Interestingly, our study confirmed that peak velocity in flexion/extension was significantly associated with kinesiophobia . However, we did not find the same association for peak velocity in rotation and lateral flexion in a secondary analysis, suggesting that movement in flexion/extension might be more related to kinesiophobia in neck pain patients. Other studies that have reported on the association between kinesiophobia and neck flexibility have included whiplash patients [34] or a combination of non-trauma and whiplash patients [35] making comparisons across studies difficult.

Head steadiness

Different tests of INF have been used in previous studies to investigate holding time [7,36,37], muscle activation patterns [38,39], head steadiness [36], and cervical muscle strength [40]. The present study used head angular velocity to investigate head steadiness, previously described in Woodhouse et al. [36]. Our result of less angular velocity in NP patients compared to HC supports the findings of Woodhouse et al., where the NP group showed a trend of less angular velocity compared to healthy controls. While Woodhouse et al. used only one sensor on the forehead (i.e. S1), we used two sensors to be able to separate head motion from upper body motion, and subjects in our study were also instructed to do craniocervical flexion in the INF test. Lower head angular velocity may indicate that NP patients stiffen their neck to avoid painful movement of the head, possibly due to increased muscle activation in superficial neck muscles to compensate for reduced activation of deep neck muscles [41], or increased co-contraction of cervical agonist–antagonist muscles to increase stability of the cervical spine [42]. Muscle activation was however not recorded in the present study.

Trajectory movement control

The FOE and the Fly test can be seen as tests of trajectory movement control, because both require continuous feedback from neck mechanoreceptors, visual and vestibular systems [43]. The Fly test has shown good reliability and discriminant validity [12]. Except for one, none of the Fly tests in this study differed significantly between the NP subjects and the HC group. Increasing the ROM demands during the Fly test did not change the results. Previous studies of trajectory movement control using the Fly test found a consistently larger deviation in trajectory movement control in neck pain subjects compared to healthy [12,43]. This was not supported by our findings. The NP subjects in the present study, compared to the non-trauma group in Kristjansson et al. [12], were similar in age and gender distribution, but had a higher score on NDI, indicating more disability. Kristjansson et al. had more men than women in the healthy control group compared to the non-trauma group and whiplash group which had more women. In the HC group we found that females had a consistently larger deviation in the Fly tests compared to men in the HC group suggesting that the group differences in Kristjansson et al. [12] may be influenced by the different gender distribution in the groups. However, Oddsdottir et al. found similar results between healthy females and men for the same Fly tests [29]. This discrepancy between the studies requires further investigation before this test can be implemented in clinical practice. The FOE test, which required a larger displacement in the horizontal plane (Figure 2), showed that NP subjects tended to depart less from the trajectory path compared to HC, a finding that was clearly significant during the fast speed FOE and the FOE in standing tests. Overall, the results from these tests of trajectory movement control indicated an altered motor control strategy by stiffening of dynamic head motion (Table 6).

Postural sway

We found no difference in postural sway in standing, when the head was kept in a static position, with eyes open and eyes closed. In a review, the majority of studies of non- traumatic neck pain patients did not find altered postural sway across different standing positions and visual conditions [44]. However, NP patients had a markedly larger sway area in the more challenging standing on a balance pad, but a trend of less postural sway when simultaneously performing a dynamic head motion test (FOE) when standing on firm surface. This indicates that stiffening motor control patterns appear only in tests that challenge the neck directly. However, this inference is based on a single postural sway test, and needs further investigation. We speculate that overall stiffening strategy of the body during the FOE test might stem from distraction caused by the dual task. A study of subjects with low back pain showed that a cognitive dual-task reduced postural sway while healthy controls increased postural sway [45]. However, Dualt et al. found that healthy also have less postural sway when performing dual task compared to single tasks [46].

Proprioception

Tests of JPE are used in studies to evaluate proprioception. Several studies are in agreement with no deficit in proprioception measured by JPE in NP compared to healthy subjects [14,47,48]. However, other have found that neck pain subjects had significantly larger repositioning error [49], or significantly larger variable error compared to healthy subjects [6]. Discrepancies between the studies in the calculation of JPE and test procedures used may partly explain the conflicting evidence. We therefore reanalyzed the data using repositioning error in the primary plane of motion [49] and the variable error, which is a measure of the variability of the repositioning [6]. The analysis revealed no significant difference between the groups, in agreement with our results for the absolute error. However, other tests of proprioception might be more relevant in NP subjects, since a main criticism of the test used in the present study is that the vestibular system may mask important deficits in afferent input from mechanoreceptors in the neck [18].

Theory of motor control

Hodges & Tucker presented a new theory of motor control adaptation to pain which concurs with the general finding of stiffer and more rigid neck motor control patterns (Table 5) in the present study [50]. The theory emphasizes increased stiffness as an important motor adaptation to acute pain to protect or avoid movement of a painful body part. However, after the acute stage protective stiffening may no longer serve a purpose. The long term consequences of increased stiffness may be decreased movement and movement variability, and consequently increased load on the spine [50]. We do not know if stiffening motor control patterns is a local or a general feature, but our results indicate that stiffening is confined to the local painful area and not a general feature, as NP patients had less stiffening (i.e. more sway) in standing balance compared to HC subjects (Table 5). Tests of neck proprioception were non- significant in this study, indicating that central rather than peripheral mechanisms are involved. However, we do not know if this reflects centrally driven neurophysiological activations or a cognitive response (fear avoidance, catastrophizing etc.), since our study showed conflicting results for the association between kinesiophobia and the constructs of motor control (Table 6).

Strength and limitations

The main strength of this study was that we included a comprehensive set of tests to evaluate different constructs of cervical motor control. This study had a larger power to detect important and relevant alterations in cervical motor control and motion compared to other studies in this field. The test setup allowed us to differentiate cervical movement from movement in the thoracic spine, which is important to avoid bias from movement of the torso during tests of cervical ROM and head steadiness. The examiners were not blinded and different examiners performed the data collection in the NP and HC groups, which could have introduced bias. However, standardized instructions were used in all tests to minimize the performance bias. NP subjects performed two and HC subjects one practice trial of the Fly test. A possible learning effect may thus have favored the NP subjects. We did however not find any significant difference between the practice trial and the session used in the data analysis, and thus, we suggest that a possible difference in learning effect between the groups are none or minimal. The HC and the NP subjects performed the same number of trials of the FOE in standing. Since neck pain episodes are frequently reported in non- clinical populations we collected the neck pain history for the HC group. 17 of 91 subjects in the HC group reported one or more previous neck pain episodes, with a median time since last episode of 40 (range 5–120) months. We did a sensitivity analysis were we excluded the 17 subjects and found that the group results for the different tests did not change. Thus, we think that previous episodes of neck pain in the HC group did not bias the conclusions in this study. Other factors like work- load, education and physical fitness may have influenced neck motor control and neck pain and but were not measured in this study.

Conclusions

NP patients had less cervical ROM, reduced conjunct motion, lower peak velocity during cervical ROM tests, less head motion in the isometric head steadiness tests, showed more “rigid” trajectory head motion patterns and more postural sway in standing on a balance pad. Overall the results clearly suggest altered motor control patterns in subjects with moderate to severe neck pain with long duration characterized by stiffening and rigidity (Table 5). The relationship between different constructs of motor control and clinical features needs further investigation and preferably in a prospective design.

Additional file

Additional file 1: Calibration and data analysis.

Abbreviations

CI: Confidence interval; CM: Conjunct motion; EC: Eyes closed; EO: Eyes open; EOB: Eyes open balance pad; ES: Effect size; FOE: Figure-of-eight; HC: Healthy controls; INF: Isometric neck flexion; JPE: Joint position error; NDI: Neck disability index; NP: Neck pain patients; NRS: Numerical rating scale; PCS: Pain Catastrophizing scale; PD: Point deviation; PSEQ: Pain self-efficacy scale; ROM: Range of motion; TSK: Tampa scale of kinesiophobia; TX: Transmitter.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

IM participated in the planning of the study design, carried out the data collection for the NP group, performed statistical analysis and writing the manuscript. OV participated in the planning of the study, performed statistical analysis and writing the manuscript. AKS and AW were involved in the planning of the study, interpretation of the data and writing the manuscript. ØS, HL and SG were involved in interpretation of the data and revision of the manuscript. HA and KA revised the manuscript and carried out the data collection for the HC group. All authors read and approved the final manuscript.

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Paper II

Title

Head steadiness in response to unpredictable perturbations in patients with non-specific neck pain

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Abstract

Background: The aim of the present study was to investigate mechanisms underlying impaired motor control in non-specific neck pain and whether observed deficits reside in voluntary control or in reflex systems.

Methods: The ability to keep the head stationary in space in response to unpredictable perturbations was tested in 71 patients with non-specific neck pain and 17 healthy controls. Subjects were exposed to pseudorandom horizontal rotations across superimposed frequencies (0.185-4.115 Hz) by means of an actuated chair in three conditions; with a visual reference, and without vision with and without a cognitive task.

Findings: Below 1 Hz, patients kept the head less stable in space compared to healthy controls. Between 1-2 Hz both groups displayed unity of movement between head and trunk.

Interpretation: Patients kept the head more stable relative to the trunk than in space compared to healthy controls which was interpreted as increased co-contraction or higher general neck muscle co-activation in patients, referred to altered voluntary control, alternatively upregulated gamma motor neuron activity.

High lights

- Patients with non-specific neck pain display reduced freedom of neck motion
- Reduced freedom of movement suggest increased muscle co-contraction
- Motor control deficits are in the frequency domain predominantly voluntarily controlled

Key words: voluntary control; reflex mechanisms; stiffness; frequency domains, gain, phase

1. Introduction

Impaired control of the head and neck in non-specific neck pain is reported in several studies showing delayed onset and reduced activity in neck muscles (Falla, 2004), deficits in direction specific force production and increased muscle co-activation (Lindstrom et al., 2011), reduced freedom of movement (Woodhouse and Vasseljen, 2008), increased general stiffness and rigidity of movement (Meisingset et al., 2015), and jerky and irregular cervical movements (Sjolander et al., 2008). Studies have in general assessed voluntary neck movements (Sjolander et al., 2008) and tasks, such as tracing an outlined figure (Woodhouse, 2010) or tracking an unpredictably moving target (Kristjansson et al., 2004). Voluntary tasks allow to a large extent individual strategies which increases variability within and between subjects, thereby limiting the probability to uncover and define specific neurophysiological impairments.

Correlations between fear of movement and neck kinematics, (Sarig Bahat et al., 2013) suggests that impaired control may reside within the voluntary dominion. Similar impairments demonstrated in whiplash-associated neck pain have been ascribed to possible deficits in reflex mechanisms (Treleaven et al., 2011). Studies are typically dedicated to describe impaired control and protocols are seldom designed to investigate specific motor control mechanisms.

Two reflex systems are proposed to contribute to motor control of the head and neck by regulating muscle stiffness. The vestibulocollic reflex (VCR) keeps the head stable in space by vestibular neurons projecting to neck motor neurons, activating neck muscles to produce compensatory head movements in the opposite direction and inhibiting muscles producing forces in the same direction relative to the perturbing force (Wilson and Schor, 1999). The cervicocollic reflex (CCR) keeps the head and neck stable relative to the trunk by means of proprioceptive input from muscle spindles (Peterson, 2004), activating muscles working with the direction of the perturbation when those are exposed to stretch. During voluntary movements, reflex activity has to be cancelled for the head to move freely (Roy and Cullen, 2001, 2004), alternatively reflex excitability may be modulated by voluntary activity serving to dampen the oscillations created by the mass-spring system of the head and neck (Peng et al., 1996), providing a basic level of muscle stiffness. Although theoretical assumptions about reflex control of the head and neck still remain to be directly demonstrated experimentally (Goldberg and Cullen, 2011), indirect methods may be applied by studying motor responses to controlled perturbations in order to tease out whether impaired control of the head and neck in non-specific neck pain may reside within the reflex or voluntary dominion.

This project used a protocol originally designed by Keshner and Peterson (1995), assessing head stability in space during exposure to horizontal plane pseudorandom rotations of different and superimposed frequencies. Below 1 Hz, fair compensation to perturbations suggests that voluntary control is predominant. Between 1-2 Hz, unity between head and trunk movements indicate that reflexes stabilizes the head relative to the trunk. Above 2 Hz resonance emerges meaning that the head moves more than the trunk (Keshner et al., 1995; Keshner and Peterson, 1995; Peng et al., 1996, 1999).

The aim of the present study was to investigate whether deficits underlying motor control impairments in non-specific neck pain reside in the reflex systems or are due to impaired voluntary control, or both. The ability to keep the head stable in space during perturbations to the body of different frequencies was explored.

2. Methods

2.1 Participants

Patients were recruited from community and hospital physiotherapy clinics (n=71). Inclusion criteria were non-specific neck pain without radiation below the elbow, pain duration >2 weeks, and pain intensity ≥ 3 on a numerical rating scale (NRS) on the day of testing. The control group consisted of staff and students (n=17) without neck and shoulder complaints. Exclusion criteria were reduced and uncorrected vision or diagnosed vestibular deficits, orthopaedic or neurological conditions (Table 1). The study was approved by the Regional Ethics Committee (2011/2522/REK) and conducted in agreement with the Helsinki declaration. Participants signed an informed consent before entering the study.

2.2 Data acquisition

Head steadiness in space was assessed while the body was exposed to pseudorandom rotations in the horizontal plane. Each subject was exposed to one trial (duration 200 s) of each of three conditions in the following order; with vision (VS), without vision (NV), and without vision with an additional mental task counting backwards from 500 in steps of seven (MA), the latter in order to divert attention from control of head position. VS aimed to investigate voluntary control with a visual reference provided by a laser pointer mounted in a rigid fixture on the head aimed toward a vertical line on a white surface 1.6 m in front of the subject. A 5 cm intersecting horizontal line guided the projected laser beam in order to keep the head stable in neutral position and the laser beam aligned in the horizontal plane. NV challenged voluntary control without visual information. The purpose of MA was to investigate the contribution of reflex control.

Sinusoidal rotations around the vertical axis were induced to the trunk by means of an actuated chair, the rotational axis coinciding approximately with the axis of the cervical spine. The participant was seated firmly strapped to the backrest and seat to minimize movement between the body and the chair (Figure 1). Only the head was allowed free movement. Cross correlations from pilot studies assured that the frequency responses of the trunk corresponded to those induced by the chair (φ_{xy} $(\tau = 0) = 0.95$). The rotation was driven by a brushed DC-motor with a 1:308 gear ratio (Maxon Motor, Sachseln, Switzerland, part no. 353295), controlled by a LabVIEW program via a NI 9505 DC Brushed Servo Drive (both of National Instruments Corporation, Austin, TX, USA). To minimize influence on the electromagnetic motion capture system the main structure of the chair was built from non-metallic materials. The DC-motor and gear were placed close to the floor and power electronics were placed 2m away from the base of the chair. Data for rotations in the horizontal plane were registered by three sensors placed on the chair, on the back of the subject at the level of the 2nd thoracic vertebrae, and on the forehead, and collected at 240 Hz by a Liberty electromagnetic motion tracking system (Polhemus, Colchester, VT, USA). The transmitter was placed ~ 20 cm above the head of the subject (Figure 1).

The construction of the sum-of-sines excitation signal was based on the original function provided by Keshner and Peterson (1995) and consisted of ten superimposed harmonic components chosen as prime numbers fitted on a fundamental base frequency of 0.005 Hz.

$$H = \{37, 49, 71, 101, 143, 211, 295, 419, 589, 823\}$$

The sinusoids of relative primes provided pseudorandom perturbations in a pattern without repetitions over the fundamental period of $T = 200$ s, preventing anticipatory preparation in the subjects and contamination between the resulting frequencies (0.185 to 4.117 Hz). Chair velocity amplitudes were decreased as frequency increased: 20^{o}/s from 0.185 to 0.355 Hz, 19^{o}/s from 0.505 to 1.055 Hz, 16^{o}/s from 1.475 to 2.095 Hz, 15^{o}/s at 2.945 Hz, and 13^{o}/s at 4.115 Hz. The maximum rotational excursion occurred at the lowest frequency and was approximately $\pm 17^{o}$. The same waveform was used for all conditions and all participants. The sum-of-sines angular velocity excitation signal, denoted by $u(t)$, may be described by the function

$u(t) = \sum_{k \in H} a_k \sin(2\pi Fkt + \phi_k\ ),$

where k represents each of the harmonics, a_k is the amplitude of the k'th harmonic (in radians/second), t is time (in seconds), and ϕ_k is the phase angle (in radians) of the k'th harmonic at $t = 0$. In the current case $\phi_k = 0 \forall k$, but the actual values used are believed to be irrelevant for the results and therefore ϕ_k is left out of the equations in the following.

This excitation induced sinusoidal rotations in the trunk and head, given approximately by the formulae

$$\theta^T(t) \approx \sum_{k \in H} A_k^T \sin(2\pi Fkt)$$

$$\theta^H(t) \approx \sum_{k \in H} A_k^H \sin(2\pi Fkt\ )$$

The superscripts here signify whether it is the trunk (T) or head (H) angle that is in question. To signify that these angles are both measured with respect to a room-fixed coordinate frame, the quantities θ^T and θ^H will be referred to as the trunk-room angle and the head-room angle, respectively. Similarly, the angle of the head with respect to the trunk will be referred to as the head-trunk angle. Note that these measured signals will include frequency content (noise) not present in the excitation signal, implying that the above formulations are not exact, hence the approximation signs.

Also note that the excitation signal is defined in terms of the angular velocity, $u(t)$, while $\theta^T(t)$ and $\theta^H(t)$ are angles. The above formulae still holds, as the angular excursion amplitude coefficients $[A_k]$ relate to the angular velocity amplitude coefficients as $A_k = -\frac{1}{2\pi Fk} a_k, \quad k \in H.$

2.3 Data analysis

Information about the subjects' motor responses to the perturbation was extracted with spectral analysis. Under the assumption of linearity, the motion of the head and trunk would be a sum-of-sines in the excitation frequencies. This assumption was validated with analyses of the spectral magnitudes for the head-room and trunk-room angles, showing satisfactory signal-to-noise ratio (SNR), albeit with quite notable noise levels for the head-room angle, particularly at the highest frequencies (Figure 2). The excitation response of a linear dynamic system may be modelled as a complex transfer function, which describes the frequency response of a system, i.e. the gain and phase shift of the output (response) signal relative to the input (excitation) signal. Such a function may be expressed as

$$G(j2\pi f) = \frac{Y(j2\pi f)}{U(j2\pi f)}, \quad \left(\frac{Response}{Excitation}\right),$$

where Y and U are polynomial functions, j is the imaginary unit and f is frequency in Hz. The transfer function relating the head-room angle (response) to the trunk-room angle (excitation) was estimated by calculating a Fourier series of the recorded time-series over the excitation frequencies. Computation of the following integrals furnished a complex signal description at the k'th harmonic:

$$\Theta_k^T = \frac{2}{T}\int_0^T \theta^T(t)e^{-j2\pi Fkt}dt\ , \qquad \Theta_k^H = \frac{2}{T}\int_0^T \theta^H(t)e^{-j2\pi Fkt}dt$$

The transfer function was subsequently evaluated at the discrete excitation frequencies by evaluating

$$G_k = \Theta_k^H/\Theta_k^T, \quad k \in H$$

Gain and phase shifts of the head-room angle relative to the trunk-room angle were recovered by taking the absolute value and argument (angle) of this complex transfer function, as follows:

$$\frac{A_k^H}{A_k^T} = |G_k|, \quad \phi_k^H - \phi_k^T = \arg G_k$$

Resulting transfer functions are presented as Bode plots with gain and phase shown for the 10 excitation frequencies. The Bode plot in an ideal way decouples the system properties of gain, phase shift and time constants/Eigen-frequencies, which allows direct comparison and statistical analyses of linear systems with different dynamics, expected in human bodies of different size and mass. Thus, our statistical analysis is also based on Bode data (i.e. decimal logarithmic gain and linear phase).

In Figure 3, the left axis shows gain on a logarithmic scale, while the right axis shows the decimal logarithm of this factor plotted on a corresponding linear scale. In the following we present both quantities; the case of unity gain, for example, will be presented as "gain=1 (log10(1)=0)", where "1" and "0" relate to the left and right axes, respectively. Statistics are based on the decimal logarithm (right axis). Theoretically, perfect compensation for the head in response to the perturbations would be represented by a gain of zero (left axis), i.e., the head is kept stationary in space and thus has no angular amplitude relative to the room at the excitation frequency in question. This is achieved by head-trunk rotations of the same amplitude as, but in the opposite direction of, that of the trunk-room angle. Gain =1 (unity, left axis) indicates that the head moves in space with the same amplitude as the trunk, and gain > 1 (left axis) indicates that the head moves more than the trunk relative to space. Perfect temporal compensation in response to perturbations would be shown as 0^o shift for phase angles; positive values denote phase lead and negative values indicate phase lag.

2.4 Statistical analysis

Kinematic rotational data generally need to be treated with special statistical methods, e.g. the Cosine statistics (Stavdahl et al., 2005), that account for the inherent cyclicity of rotations. However, for comparison of phase shifts of different transfer functions, traditional statistical methods were employed in order to avoid e.g. treating two phase angles as the same if they differ by a multiple of 2π radians. The statistics were generated with SPSS 22.0 (Statistical Package for the Social Sciences, Inc., Chicago, ш, USA). Normal distribution was confirmed with Q-Q and P-P plots. For gain and phase, separate general linear models were constructed for repeated measures with conditions as within subject factors (n=3, VS, NV, MA) with frequencies (n=10) as measures within each condition. Differences between groups (n=2: neck pain and control) were assessed with multivariate analysis across conditions with Bonferroni corrections for multiple comparisons. Sphericity was assumed according to Mauchly's test. Post hoc linear regressions were used to assess group differences for separate measures within each condition. Due to differences between the groups, age and gender were used as covariates in the analyses. Alpha-level: $p < 0.05$.

3. Results

3.1 Gain

The perturbations produced a similar general pattern across groups and conditions with increasing gains as an effect of higher frequencies, however with significant effects of group and of condition. Multivariate tests (Wilk's Lambda) showed a significant effect of group for at least one measure across conditions ($F_{10,72}$: 2.6, p=.009) and a significant effect of condition ($F_{20,304}$: 27.4, p<.001). Between 0.185-1.055 Hz, patients displayed higher gains than controls in the VS condition. At frequencies above 0.1055 Hz, no group differences were found. In the NV condition, patients displayed higher gains than controls between 0.245-0.715 Hz. In the MA condition higher gain was found in patients only at 0.505 Hz (Table 2, Figure 3).

3.2 Phase

Akin to gain, the perturbations produced a similar general pattern across groups and conditions. A phase lead ($> 0^o$) was seen for lower frequencies, while an increasing phase lag ($< 0^o$) was seen with higher frequencies. Multivariate tests (Wilk's Lambda) showed no significant effect of group across conditions ($F_{10,72}$: 1,3, p=.265), however 95% CI in the graphs indicated some localized groups differences. Post hoc tests were therefore performed for separate conditions showing significantly greater phase lead in controls in VS at 0.715 and 1.055 Hz (Table 2, Figure 3). Within subjects multivariate tests (Wilk's Lambda) showed a significant effect of condition ($F_{20,304}$: 10.2, p<.001).

4. Discussion

4.1 General motor responses

Our results lend further support to previous findings of impaired motor control of the head and neck in non-specific neck pain (Falla et al., 2004; Kristjansson et al., 2004; Meisingset et al., 2015; Sjolander et al., 2008; Woodhouse et al., 2010; Woodhouse and Vasseljen, 2008), suggesting increased stiffness of the system as a possible common denominator contributing to explain motor control difficulties. Patients showed a general pattern of keeping the head more steady relative to the trunk rather than in space when exposed to perturbations to the body by pseudorandom sinusoids of superimposed frequencies in the horizontal plane. This response was particularly evident in the frequency domain where compensation to perturbations can be controlled by voluntary activity. Compensation in this domain became however successively worse when vision was removed and when in addition attention was diverted.

4.2 Methodological considerations

Some outliers are seen in the dataset across frequencies as well as across groups, indicating that not all subjects were able to perform the task. As not being able to perform the task could potentially have been the distinction between patients and controls, those were not removed from the dataset. There were no correlations between outcome variables for gain or phase with background variables for subjects' characteristics, explaining variability or outliers in the dataset. As the task becomes increasingly difficult when moving from condition VS through NV to MA, it should be expected that the subjects' compensation would lag increasingly more behind the external perturbation as frequency increases. However, some positive phase shifts were also evident with increasing frequencies. In order to test whether these were artifacts, different conventions were tried with effect only on one single outlier. Note that there are no absolute criteria for choosing one convention over the other. In the present study the Matlab function "*P = angle(Z)"* was used which returns the phase angles, in radians, for each element of complex array *Z*. The angles lie between $\pm\pi$. Furthermore, with regard to the dynamic properties of compensatory head movements generated by voluntary, reflex, and mechanical mechanisms, total compensation, i.e., zero gain and 0^o phase angle is not attainable. The voluntary system is likely to produce a compensatory signal with phase opposite to that of the imposed rotation of the trunk with a delay of approximately 0.2 s. (Keshner and Peterson, 1995).

4.3 Responses below 1 Hz

The most apparent difference between groups was found in the condition with access to visual reference (VS) and at frequencies equal to or below 1 Hz, where head steadiness in space is maintained predominantly under voluntary control (Guitton et al., 1986; Keshner and Peterson, 1995). Therefore the present findings may be interpreted as depending on deficits in voluntary control in patients, causing increased stiffness and reduced ability to compensate for perturbations in order to keep the head steady in space. Note that voluntary control is presumed predominant and does not exclude the involvement of reflex mechanisms. It has been debated whether reflex control contributes to dampen oscillations of the mass-spring system of the head and neck (Peng et al., 1996, 1999) or if voluntary activity completely can override reflex responses (Roy and Cullen, 2001, 2004).

Both alternatives describe that head steadiness in space can be controlled voluntarily at frequencies below 1 Hz, but do not refute the possible of involvement of altered reflex control as an explanation to increased stiffness. Notably, in the MA condition when attention was directed toward a cognitive task, the movement of the head nearly followed that of the trunk in both groups with similar pattern as in the VS and NV conditions. This leaves two interpretations of the motor responses in patients: 1) neck muscle stiffness is enhanced by voluntary activation, or 2) reflex responses are enhanced increasing neck muscle stiffness. Both alternatives may potentially explain greater head steadiness relative to the trunk in patients in conditions (VS and NV) where attention was turned toward conscious control of head position. In MA, however, when attention was diverted from controlling head position, reflexes appear, at least to some extent, to stabilize the head relative to the trunk also at low frequencies (Keshner and Peterson 1995, Guitton et al., 1986). This notion supports alternative two, which suggests that reflexes are active also at lower frequency perturbations. Notably, in MA, patients displayed gain closer to one at 0.505 Hz. Further support for alternative two is the hypothesis by Johansson and Sojka (1991), suggesting a vicious circle where increased muscle tension produces metabolites activating gamma motor neurons increasing activity in muscle spindle afferents again increasing muscle stiffness (Johansson and Sojka, 1991). Pain induced increase in gamma motor-neuron activity has been corroborated in studies of experimental muscle pain showing increased amplitude of the stretch reflex but without a corresponding increase in the H-reflex amplitude (Matre et al., 1998). Thus, that study does not support the notion of a vicious circle, maybe due to the short term effect and the context of experimental pain. Nevertheless, reflex mediated increase of muscle stiffness would restrict freedom of movement for the head and neck necessary to voluntarily compensate for perturbations to the trunk when attempting to keep the head steady in space. This reasoning is corroborated by other studies on neck pain (Boudreau and Falla, 2014; Cheng et al., 2014), suggesting increased co-activation between agonist and antagonist muscles of the neck in response to unpredictable perturbations.

4.4 Responses between 1-2 Hz

In the frequency domain between 1-2 Hz, unity between head and trunk movement occurs, that is, the head moves with the trunk (Keshner and Peterson, 1995), and the VCR and CCR presumably act in a reciprocal manner, co-contraction between agonist and antagonist muscles stabilizing the head on the trunk (Roy and Cullen, 2001, 2004). Notably, unity between head and trunk motion occurred successively earlier in both groups in conditions where visual information was removed (VS) and where in addition attention was reduced (MA). This suggests an existence of underlying reflex activity at lower frequency perturbations, modulated by voluntary activity. No differences were found between groups in this frequency domain, and kinematics suggests normal reflex response in patients. However, unity between head and trunk requires just enough muscle stiffness to keep the head stable on the trunk. Muscle stiffness above the critical level to keep the head stable on the trunk does not influence unity and potentially increased voluntary or reflex induced muscle activity or co-contraction in patients cannot be proven by kinematics alone. Future studies should therefore incorporate electromyography in order to elucidate whether patients present greater muscles stiffness during unity than non-symptomatic controls.

4.5 Responses above 2Hz

Above 2Hz, amplitudes of the head exceeded the magnitude of rotations of the trunk (i.e. gain > 1, left axis, Figure 3) and studies agree on interpretations of this as an effect of mechanical resonance (Forbes et al., 2013; Goldberg and Peterson, 1986; Keshner and Peterson, 1995; Peng et al., 1996), meaning that the oscillatory response of a system is larger than the imposed perturbation. The Eigen-frequency of a system determines the threshold for mechanical resonance and depends on the systems mass and viscoelastic properties. Increased stiffness of the neck will therefore increase the threshold for when resonance emerges. With a generally increased stiffness of the system, a higher resonance frequency would be expected regardless of this being caused by voluntary control or reflex mechanisms. The present results and interpretations concerning the highest frequencies should, depending on high noise levels (Figure 2), be treated with great caution. Exposure of subjects to perturbations at even higher frequencies would in theory test if the threshold for resonance emerges later in patients compared to controls. In reality, noise levels would most likely cloud the interpretation. Future studies of responses to perturbations at higher frequencies may use modeling as an alternative to laboratory test of subjects.

5. Conclusions

Patients kept the head more stable relative to the trunk than in space, in response to perturbations across conditions and frequencies. The largest differences compared with healthy subjects were found at frequencies below 1 Hz and with a visual reference, suggesting that impaired motor control of the head and neck in patients depends on increased muscle stiffness and/or co-activation referred to altered voluntary control or alternatively upregulated gamma motor neuron activity. Reservations should be paid to that the nervous system has not been directly assessed and contribution of reflexes to voluntary control cannot be determined.

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Legends

Figure 1. An instrumented subject strapped to the actuated chair. The cube above the subject's head represents the electromagnetic transmitter. Note that the ear muffs have holes leaving the ears uncovered and hearing intact.

Figure 2. Spectral magnitudes of head movements in response to rotational perturbations in the horizontal plane, showing signal-to-noise ratio (SNR). Excitation harmonics are indicated by circles.

Figure 3. Bode diagrams of transfer functions for the three conditions with vision (VS), without vision (NV), and without vision with a cognitive task (MA), respectively. Means and 95% CI. Plotted values are not adjusted for age and gender. Solid line: heathy controls, dashed line: patients. Grey curves in the background show the individual responses. Statistics are based on decimal logarithms shown on the right axis.

Table 1 Subject characteristics. Given values are mean (SD), unless otherwise stated.

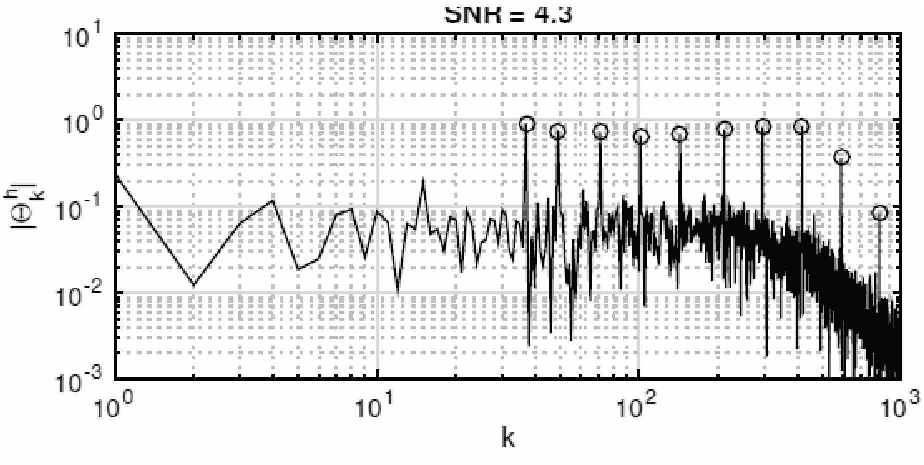
Variables	Neck pain n=71	Healthy controls n=17
Gender, female (n [%])	50 (70)	9 (53)
Age	44.0 (12.9)	31.5 (7.4)
Body Mass Index	24.2 (3.7)	23.7 (2.9)
Current neck pain intensity (NRS; 0-10)	4.7 (1.4)	-
Worst neck pain last month (NRS; 0-10)	7.3 (1.5)	-
Duration of neck pain > 3 months (n [%])	60 (90)	-
Number of pain sites (n [%])		
Only neck pain	14 (20)	
≥2 additional pain sites	34 (49)	
Neck Disability Index (NDI; 0-100)	31.7 (12.2)	-
Patient-Specific Functional Scale (PSFS;0-10)	6.5 (2.0)	
Tampa Scale of Kinesiophobia (TSK; 13-52)	24.7 (4.2)	
Pain Catastrophizing Scale (PCS; 0-52)	12.4 (7.8)	
Pain Self-Efficacy Scale (PSES; 0-60)	44.8 (10.1)	
Self-rated general health (n [%])		
Fair	30 (43)	
Good	38 (54)	
Very good	2 (3)	
Use of analgesica (n [%]	33 (48)	

NRS= numerical ratings scale

Table 2. Comparisons between patients with neck pain and healthy controls for each separate condition (with and without vision, and without vision with a cognitive task). Estimated group difference with 95% confidence intervals (CI) within each separate condition adjusted for age and gender. Positive values indicate higher gain and phase for patients compared to healthy controls. Estimates for gain correspond to decimal logarithms shown on the right axis in Figure 3, while estimates for phase angles are linear.

Frequency (Hz)	Group mean difference (95% CI)		
Gain	VS	NV	MA
0.185	**0.13 (0.02, 0 .23)***	0.11 (-0.04, .26)	0.03 (-0.12, 0.17)
0.245	**0.17 (.067, 0 .28****	**0.16 (0.03, 0.29)***	0.07 (-0.04, 0.18)
0.355	**0.21 (0.08, 0 .34)****	**0.16 (0.05, 0.27)****	0.07 (.-0.02, 0.16)
0.505	**0.18 (0.09, 0.28)*****	**0.12 (0.03, 0.21)****	**0.09 (0.02, 0.16)***
0.715	**0.17 (0.07, 0.26)****	**0.08 (0.01, 0.15)***	0.05 (-0.02, 0.13)
1.055	**0.10 (0.21, 0.18***	0.10 (-0.01, 0.21)	0.02 (-0.06, 0.11)
1.475	0.05 (-0.03, 0.12)	0.06 (-0.02, 0.14)	-0.06 (-0.19, .07)
2.095	0.04 (-0.05, 0.12)	0.05 (-0.04, 0.14)	-0.04 (-0.19, 0.10)
2.945	-0.03 (-0.13, 0.08)	-0.00 (-0.11, 0.11)	-0.08 (-0.23, 0.06)
4.115	-0.03 (-0.17, 0.10)	0.05 (-0.08, 0.17)	-0.03 (-0.19, 0.12)
Phase			
0.185	2.1 (-5.6, 9.7)	-4.6 (-24.0, 14.8)	8.1 (-3.1, 19.3)
0.245	1.6 (-8.0, 11.1)	4.8 (-13.5, 23.0)	3.8 (-9.3, 17.0)
0.355	1.3 (-8.2, 10.9)	-.503 (-21.6, 20.6)	-1.2 (13.4, 11.0)
0.505	-5.3 (-13.4, 2.8)	3.6 (-18.5, 25.8)	-7.0 (-18.5, 4.5)
0.715	**-11.2 (-19.2, -3.1)****	7.7 (-16.6, 32.1)	-10.8 (-23.2, 1.6)
1.055	**-13.5 (-23.1, -3.8)****	11.8 (-15.4, 39.0)	-12.8 (-29.9, 4.3)
1.475	-12.3 (-22.6, -1.9)*	9.7 (-20.7, 40.1)	-14.2 (-34.1, 5.6)
2.095	-5.4 (-16.0, 5.2)	11.8 (-21.6, 45.3)	-8.1 (-29.1, 12.9)
2.945	-8.8 (-22.8, 5.1)	14.1 (-19.4, 47.5)	-1.0 (-26.9, 24.9)
4.115	2.5 (-19.1, 24.1)	28.5 (-7.1, 64.1)	10.9 (-19.1, 40.8)

VS: with vision, NV: without vision, MA: without vision + cognitive task
Level of significance: *p<.050, **p<.010, ***p<0.001


SNR = 4.3
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10^0
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10^0
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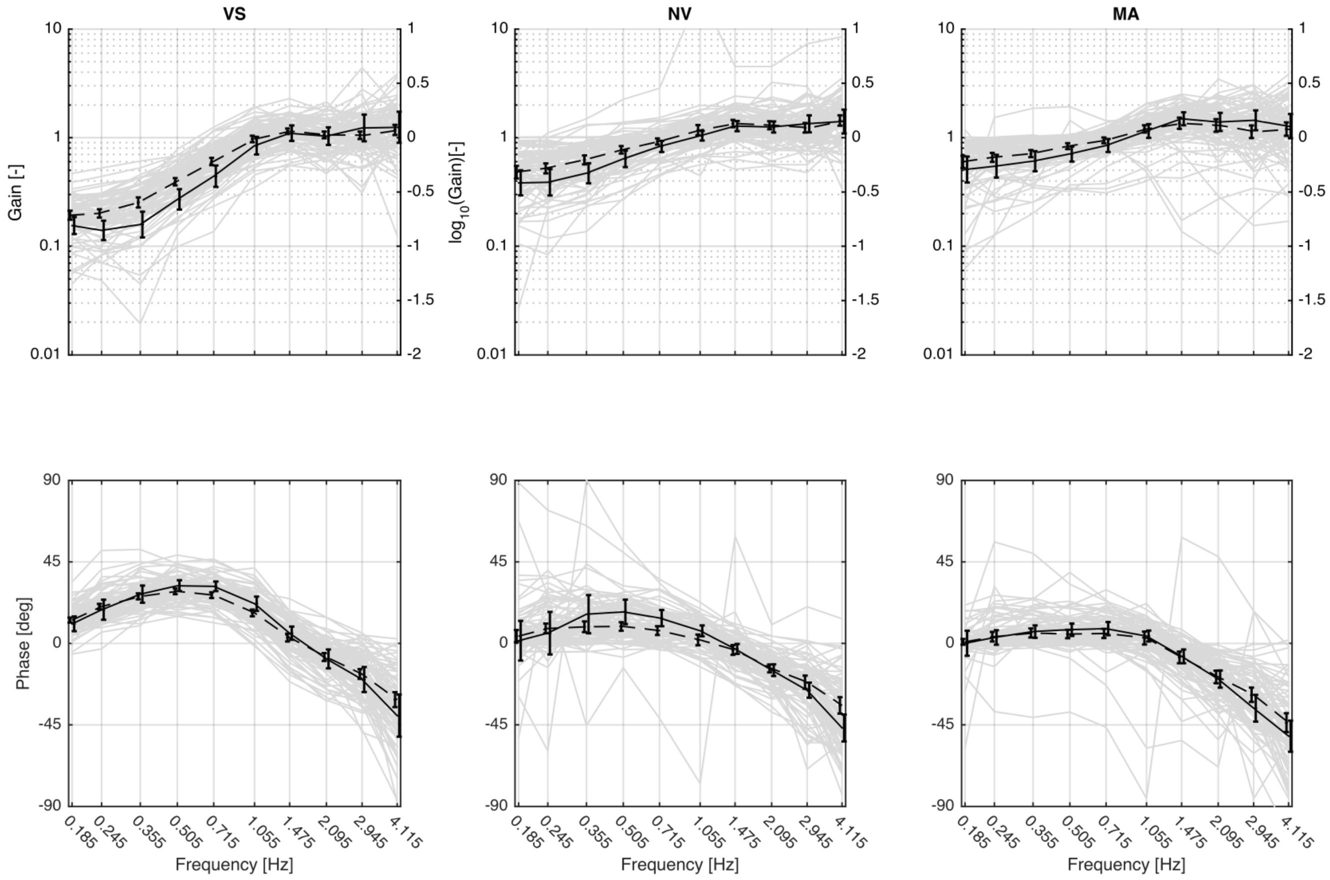
VS
NV
MA
Gain [-]
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10
1
0.1
0.01
1
0.5
0
-0.5
-1
-1.5
-2
Phase [deg]
90
45
0
-45
-90
0.185
0.245
0.355
0.505
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1.055
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Frequency [Hz]

Paper III

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Original article

Neck motion, motor control, pain and disability: A longitudinal study of associations in neck pain patients in physiotherapy treatment

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Background: Neck pain is associated with several alterations in neck motion and motor control, but most of the findings are based on cross-sectional studies.

Objective: The aim of this study was to investigate associations between changes in neck motion and motor control, and changes in neck pain and disability in physiotherapy patients during a course of treatment.

Design: Prospective cohort study.

Method: Subjects with non-specific neck pain ($n = 71$) participated in this study. Neck flexibility, joint position error (JPE), head steadiness, trajectory movement control and postural sway were recorded before commencement of physiotherapy (baseline), at 2 weeks, and at 2 months. Numerical Rating Scale and Neck Disability Index were used to measure neck pain and disability at the day of testing. To analyze within subjects effects in neck motion and motor control, neck pain, and disability over time we used fixed effects linear regression analysis.

Results: Changes in neck motion and motor control occurred primarily within 2 weeks. Reduction in neck pain was associated with increased cervical range of motion in flexion-/extension and increased postural sway when standing with eyes open. Decreased neck disability was associated with some variables for neck flexibility and trajectory movement control. Cervical range of motion in flexion-/extension was the only variable associated with changes in both neck pain and neck disability.

Conclusions: This study shows that few of the variables for neck motion and motor control were associated with changes neck pain and disability over a course of 2 months with physiotherapy treatment.

1. Introduction

Treatment offered to neck pain patients often includes a combination of different physiotherapy modalities and exercise. However, the treatment effect on non-specific neck pain and disability is similar across a wide range of reported interventions (Hurwitz et al., 2008). The effect sizes reported in interventional studies is comparable to the natural course of neck pain, suggesting that effective treatment for neck pain should be based on underlying mechanisms or modifiable factors that will induce a treatment effect larger than the natural course of neck pain (Vasseljen et al., 2013). Identification of patients who respond to a particular treatment or patients with a good or poor prognosis has become increasingly interesting in the research on neck pain and low back pain. Subgrouping of patients based on differences in underlying mechanisms, effect modifiers or prognostic factors may potentially improve the treatment efficacy in neck pain patients as shown in low back pain patients (Hill et al., 2011). It has however been reported that subgrouping of neck patients based on a clinical prediction rule to a specific treatment did not improve treatment efficacy in the short term (1–4 weeks) or long term (6 months) (Cleland et al., 2010).

An increasing number of studies have found that neck pain patients may have several alterations in motor control and neck motion compared to healthy controls (Falla and Farina, 2007; Meisingset et al., 2015; Roijezon et al., 2015). Most studies are however case–control studies and causal relationships are unclear. Changes in motor control and function may simply be a consequence of adjustments due to neck pain symptoms. Motor

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control appears often in the literature without a clear definition. In the present study, we rely on the definition by Shumway-Cook & Wollacott; “motor control is the ability to regulate or direct the mechanisms essential to movement (Shumway-Cook and Wollacott, 2001), and the term thus covers a wide range of aspects related to control of movement. There are few interventional studies on motor control in neck pain. O'Leary et al. found that changes in neck motor control are dependent on the training mode applied, but the different training modes had similar effect on neck pain and disability (O'Leary et al., 2012). Another study found similar treatment effects on postural control, a measure of motor control in neck pain patients, using three different interventions (Rudolfsson et al., 2014). The inconsistency points to a need for further longitudinal studies to investigate if changes in motor control are associated with changes in neck pain. Evidence suggests that changes in neck pain occur early in the treatment and follow up period with minimal changes in the long term (Cleland et al., 2010; Leaver et al., 2013). In contrast, the time course of changes in motor control and neck motion is unknown.

The aim of the study was therefore to investigate associations between changes in motor control and neck motion, and changes in self-reported neck pain and disability during a clinical course in physiotherapy patients.

2. Methods

We conducted a prospective cohort study among neck pain patients seeking health care in the period January 2013 to August 2014. A case–control study by Meisingset et al. using the same set of tests compared neck motor control in healthy controls and neck pain patients (Meisingset et al., 2015). The current study was a follow-up and measured clinical characteristics, neck motion, and motor control before, 2 weeks and 2 months after start of physiotherapy treatment. The study was approved by the Regional Ethics committee (ref. number 2011/2522/REC Central). All subjects gave written and informed consent and the study was conducted in accordance to the Helsinki Declaration.

2.1. Participants and treatment

Men and women (aged 18–67 years), with non-specific neck pain $\geq$3 on numerical rating scale (NRS: 0–10) at the day of testing, were recruited consecutively from 12 invited physiotherapy clinics in primary health care ($n = 60$) and from a specialized neck and back pain clinic at the university hospital ($n = 21$), totally 81 subjects. The patients were recruited to the study by a telephone interview by the first author. Exclusion criteria were markedly reduced or uncorrected vision, history of neck trauma, diagnosed with neurological or orthopaedic conditions that could affect motor control, positive Spurlings's test for neurological radiating arm pain, and pregnancy.

Patients in the private clinics received usual care physiotherapy and duration and number of treatments were at the discretion of the physiotherapists. The treatment consisted of a wide range of physiotherapy modalities (percentage of patients who received the specific modality in parentheses): individually supervised exercises (52%), massage (43%), mobilization/manipulation (45%), advice and information (27%), dry needling (23%), cognitive therapy (14%), and other modalities reported by less than 10% of the physiotherapists (exercises in group, prescribed home exercises, electrotherapy and shock wave therapy). Manual therapists treated 50% of the patients, while general physiotherapists and psychomotoric physiotherapists treated 30% and 20% of the patients, respectively.

The patients in the specialized neck and back pain clinic received a three week multimodal treatment from a group of several professions (physicians, physiotherapists, psychologists and social workers). The first and third week of the multimodal treatment consisted of four full days including patient education, physical exercise and cognitive therapy aimed at reducing fear avoidance/catastrophizing and to increase function, coping and self-management. The week in between was dedicated to individually prescribed home exercises.

2.2. Outcome measures

The primary outcome for the longitudinal analysis was current neck pain at the day of testing measured by NRS before, 2 weeks and 2 months after start of physiotherapy treatment. Secondary outcome was neck disability measured by Neck Disability Index (NDI; 0–100) at the same occasions.

2.3. Tests of motor control and neck motion

A comprehensive set of tests to evaluate motor control and neck motion, included variables sorted in 5 different constructs: 1. neck flexibility, consisting of tests of range of motion (ROM), conjunct motion (CM), defined as movement in associated planes outside primary motion plane, and peak velocity in the three cardinal planes. 2. proprioception, consisting of a test of joint position error (JPE) following cervical rotation. 3. head steadiness, consisting of isometric neck flexion laying in supine (0°) and in 60° recumbent position. 4. trajectory movement control, consisting of three tests of tracing a figure-of-eight (FOE), adapted from Woodhouse et al. and four versions of the Fly test, adapted from Kristjansson et al. (Kristjansson and Oddsdottir, 2010; Woodhouse et al., 2010). 5. postural sway, consisting of standing balance with eyes open (EO), eyes closed (EC) and eyes open standing on a balance pad (EOB). Category 1 was taken to reflect neck motion and categories 2–5 different aspects of neck motor control. Detailed description of the motor control variables and data analysis is given elsewhere (Meisingset et al., 2015).

2.4. Data collection

At baseline, all eligible patients completed a questionnaire (demographic and clinical characteristics) before the motion data was acquired (Table 1). The same assessor (the first author) performed the data collection at all occasions.

Motion data were acquired with 3 body worn sensors using the Liberty electromagnetic motion tracker system (Polhemus, Inc, Colchester, Vermont, USA) with a sampling rate of 240 Hz. Sensor 1 was placed on the subject's forehead 1 cm above arcus superciliaris, the second sensor was placed on the spinous process of Th2, and a third sensor was placed in the area of the spinous processes of L4–L5. Tight elastic bands were used to hold the sensors in position. A software tool based on Matlab (The MathWorks, Inc., Natick, MA, USA) was developed (SINTEF ICT, Applied Cybernetics and Dept. of Engineering Cybernetics, NTNU, Norway) to record and analyze the motion data. The coordinate system defined by the electromagnetic transmitter was used for calculating all variables except cervical range of motion (ROM). For this variable, a new coordinate system was calibrated for each subject to adjust the coordinate axes to the individually preferred axes of cervical motion (see Meisingset et al., 2015 for details).

The same test set up was used at 2 weeks and 2 months. The test-session, including questionnaires, lasted for approximately 1 h. Standardized instructions were used for all tests.

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Table 1
Baseline characteristics of neck pain patients. Mean (SD), unless otherwise stated.

Characteristics	Baseline value (n = 71)
Demographic variables	
Age (year)	43.4 (12.7)
Gender, M/F (n)	19/52
Body Mass Index	24.9 (4.8)
Smoker, n (%)	9 (13)
Clinical variables	
Current neck pain (0–10)	4.6 (1.4)
Worst neck pain last month (0–10)	7.3 (1.5)
Duration of neck pain, n (%)	
<3 months	6 (8)
3–6 months	15 (21)
6–12 months	9 (13)
>1 year	41 (58)
Neck Disability Index (0–100)	31.8 (12.3)
Tampa scale of kinesiophobia (13–52)	24.7 (4.2)
Pain Catastrophizing Scale (0–52)	12.7 (8.3)
Concurrent low back pain, n (%)	18 (25)
Self- rated general health, n (%)	
Poor	0
Fair	34 (48)
Good	35 (49)
Very good	2 (3)
Frequency physical activity, n (%)	
<once per week	9 (13)
1–3 days per week	51 (72)
4–7 days per week	11 (15)
Use of analgesics, n (%)	38 (54)

2.5. Statistical analysis

All statistical analyzes were performed using STATA 13 (Stata Corp., College Station, TX, USA). The significance level was defined as $p < 0.05$. Neck pain and disability, motor control, and neck motion at baseline were described using descriptive statistics, while data for 2 weeks and 2 months were given as change scores from baseline with 95% confidence intervals. Changes from baseline to 2 weeks and 2 months were analyzed on a group level using paired t-test for the normally distributed data. Variables for proprioception, head steadiness, trajectory movement control and postural sway showed non-normality. Log transformation was performed and gave acceptable normal distributed data. Log transformed data gave similar results thus non-transformed data and statistics are presented to ease interpretation of the data. When evaluating changes in neck pain and disability on an individual level it is important to consider the minimal clinically important change (MCIC) for these outcomes. We used the recommendation from IMMPACT for NRS that propose a decrease of 2 or more on NRS as the MCIC (Dworkin et al., 2008). For NDI the MCIC is considered to be 7 points (Pool et al., 2007). We performed a responder analysis based on these cutoff points for NRS and NDI, since group analysis do not indicate how many patients that experienced a clinically important change in neck pain and disability.

Fixed effect univariate regression analysis, using the command “xtreg, fe” in STATA, was used to investigate the association between the dependent variables neck pain and neck disability and motor control and neck motion as independent variables within individuals over time (Rabe- Hesketh and Skrondal, 2012). We used multiple linear regression with change score (between baseline and 2 months) for NRS and NDI as outcomes to investigate how much of the variance in changes in neck pain and neck disability that could be explained by changes in motor control and neck motion (given by r squared, R^2). Variables were selected based on the univariate association with the outcomes with a significance value of $p < 0.1$, to avoid exclusion of possible important variables in the multivariable model. We used effect size, hedges g, to compare the size of changes in the different constructs of motor control (Fritz et al., 2012). The effect sizes were interpreted as low (0.2–0.5), medium (0.5–0.8) or large (>0.8) as described by Cohen (Cohen, 1988). An a priori sample size calculation was not performed in this study, as this study is a follow up of a case–control study (Meisingset et al., 2015). Post hoc sample size calculation is not recommended and we therefore rely on the confidence intervals, and not p-values, when interpreting the results in this study (Walters, 2009).

3. Results

3.1. Patient characteristics and treatment

Only subjects with baseline and at least one follow up test (n = 71, flowchart, Fig. 1) were analyzed since the main objective of the study was to investigate associations between changes. Mean neck pain intensity at baseline was 4.6 (SD 1.4) and for approximately 60% of the subjects the duration of their neck pain was more than 1 one year. The subjects' demographic and clinical characteristics at baseline are presented in Table 1.

The reported median number of physiotherapy treatments at two weeks and two months for patients treated in primary health care was 2.5 (range: 1–8) and 6 (range: 3–20), respectively. Patients in the multimodal treatment had a total of 13 h with physical exercise and approximately 14 h with patient education and reflection in groups. The physical exercise consisted of general exercise in addition to specific neck strengthening exercises, as described elsewhere (Andersen et al., 2008).

3.2. Changes in neck pain and disability

Mean and standard deviation at baseline and change scores at 2 weeks and 2 months for NRS and NDI are shown in Table 2. The proportion of subjects with clinically significant changes on the primary outcomes NRS and NDI were 35% and 40% at 2 weeks, respectively, and 63% and 68% at 2 months, respectively. At 2 months the effect sizes for changes in neck pain and disability were 0.8 for both outcomes.

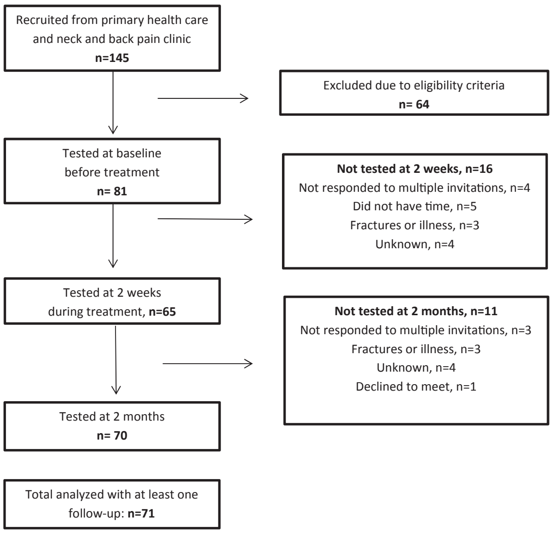

Fig. 1. Flow chart of the subjects.

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Table 2
Neck pain, neck disability, motor control and neck motion at baseline with change scores from baseline to post tests at 2 weeks and 2 months. Given data are mean (SD) at baseline and change scores with 95% CI at 2 weeks and 2 months.

Variables	Baseline (n = 71)	Change baseline-2 weeks[a] n = 65	Change baseline-2 months[a] n = 70
Current neck pain (NRS; 0–10)	4.6 (1.4)	−0.9 (−1.3 to −0.5)**	−1.5 (−2.0 to −1.0)**
Neck Disability Index (NDI; 0–100)	31.8 (12.3)	−6.1 (−8.3 to −4.0)**	−10.6 (−13.5 to −7.7)**
Neck flexibility			
Flexion-/extension (°)	110.0 (21.6)	1.5 (−1.8 to 4.9)	4.2 (1.3 to 7.1)**
Conjunct motion (°)	12.3 (4.9)	0.2 (−1.4 to 1.8)	0.1 (−1.2 to 1.4)
Peak velocity (°/s)	70.5 (24.5)	7.5 (3.1 to 11.8)**	10.5 (5.1 to 16.0)**
Rotation (°)	127.4 (20.6)	5.1 (2.5 to 7.8)**	7.4 (5.1 to 9.8)**
Conjunct motion (°)	21.6 (7.3)	−0.4 (−2.2 to 1.4)	−0.9 (−2.4 to 0.7)
Peak velocity (°/s)	107.9 (36.2)	9.6 (1.9 to 17.3)*	15.2 (8.4 to 22.1)**
Lateral flexion (°)	67.9 (16.8)	2.8 (1.2 to 4.4)**	3.2 (1.6 to 4.9)**
Conjunct motion (°)	45.5 (20.9)	−2.4 (−5.5 to 0.7)	0.7 (−2.7 to 4.1)
Peak velocity (°/s)	58.3 (18.5)	4.7 (1.7 to 7.7)**	6.6 (3.5 to 9.7)**
Proprioception			
Joint Position Error (°)	5.1 (1.9)	−0.1 (−0.5 to 0.3)	−0.2 (−0.6 to 0.3)
Trajectory movement control			
PA FOE high speed (cm)	4.5 (1.7)	−0.7 (−1.0 to −0.3)**	−0.9 (−1.2 to −0.6)**
PA FOE low speed (cm)	3.5 (1.2)	−0.7 (−1.0 to −0.5)**	−0.8 (−1.0 to −0.6)**
PA standing FOE (cm)	3.0 (1.0)	−0.1 (−0.4 to 0.2)	−0.3 (−0.5 to −0.1)**
PA Fly test 1A (cm)	2.4 (0.9)	−0.3 (−0.4 to −0.1)**	−0.4 (−0.5 to −0.3)**
PA Fly test 1B (cm)	2.2 (0.6)	−0.2 (−0.4 to −0.1)**	−0.2 (−0.4 to −0.1)**
PA Fly test 2A (cm)	3.1 (0.9)	−0.4 (−0.5 to −0.2)**	−0.4 (−0.6 to −0.3)**
PA Fly test 2B (cm)	3.0 (0.7)	−0.3 (−0.5 to −0.1)**	−0.4 (−0.5 to −0.2)**
Head steadiness			
INF low load (°/s)	1.32 (0.24)	−0.03 (−0.08 to 0.03)	0.09 (0.03 to 0.16)**
INF high load (°/s)	2.68 (0.81)	0.05 (−0.06 to 0.17)	0.03 (−0.06 to 0.13)
Postural sway			
Sway area EO (cm^2)	3.1 (3.0)	−0.7 (−1.3 to −0.1)*	−0.8 (−1.5 to −0.21)*
Sway area EC (cm^2)	2.6 (2.6)	0.0 (−0.6 to 0.5)	−0.02 (−0.4 to 0.4)
Sway area EOB (cm^2)	10.9 (5.9)	−1.5 (−2.6 to −0.4)**	−1.4 (−2.5 to −0.2)*
Sway area FOE (cm^2)	4.4 (4.2)	−0.9 (−1.8 to −0.1)	−1.2 (−2.0 to −0.4)*

FOE = figure of eight. PA = point accuracy. 1A = easy pattern, small ROM. 1B = easy pattern, large ROM. 2A = medium pattern, small ROM. 2B = medium pattern, large ROM. INF = isometric neck flexion. EO = eyes open. EC = eyes closed. EOB = eyes open standing on balance pad.

$^{*}p < 0.05$. $^{**}p < 0.01$.

[a] Change scores are obtained by subtracting baseline scores from the scores at the different follow up tests. A positive value indicates increased values at the follow up test.

3.3. Changes in neck motion and motor control

Changes in neck motion and motor control from baseline to 2 weeks and 2 months are shown in Table 2, while effect sizes for changes between baseline and 2 months and between 2 weeks and 2 months are shown in Fig. 2. Changes occurred mainly between baseline and two weeks in all constructs of motor control and neck motion. At two months, no change was found for proprioception, conjunct motion, high load INF, and sway area with eyes closed. The largest effect sizes at two months after start of treatment were found for neck flexibility and trajectory movement control.

3.4. Associations between neck pain, disability, and motor control

Table 3 shows the associations between changes in motor control and neck motion and changes in neck pain and neck disability independent of time. Associations with neck pain were found only for ROM in flexion-/extension (β = −0.04; 95%: −0.07 to −0.01) and sway area with eyes open (β = −0.16; 95% CI: −0.31 to −0.01). The results indicate that individuals had larger ROM in flexion/extension and more postural sway when they had lower levels of pain.

Neck Disability Index showed a significant association only with variables within the constructs neck flexibility and trajectory movement control. Decreased neck disability within a subject was associated with larger ROM in flexion/extension (β = −0.18; 95% CI: −0.32 to −0.04) and increased peak velocity in lateral flexion (β = −0.16; 95% CI: −0.30 to −0.02). For trajectory movement control 3 of 6 variables showed a significant association with neck disability, indicating that subjects departed less from the trajectories in two of the FOE test and one of the Fly tests at times when they reported less neck disability.

At two months the explained variance in neck pain and neck disability for the variables that were statistically significant in the univariate analysis were 25% ($R^2 = 0.25$) and 19% ($R^2 = 0.19$), respectively.

4. Discussion

Neck pain patients in physiotherapy treatment showed several, but small changes in neck motion and motor control from baseline to 2 months. Increased neck flexibility, less departure from trajectory patterns, less static head steadiness and altered postural control were not or only to a small extent reflected in neck pain and disability improvement. Cervical sagittal ROM (flexion-/extension) was the only variable associated with changes in both neck pain and neck disability.

At 2 months approximately 2/3 of the subjects had a clinically significant reduction in neck pain and disability. The effect sizes for changes in neck pain (ES = 0.8) and disability (ES = 0.8) at 2 months are large compared to two systematic reviews that found low or medium effect sizes (Leaver et al., 2010; Bertozzi et al., 2013). These reviews included only randomized controlled trials (RCT) and caution must be shown when comparing with observational studies like ours where therapists may use different treatments and also individually adapt the treatment to each patient. However, studies of subjects with low back pain suggest that the course of pain may be unrelated to study designs (Artus et al., 2014). The absolute change in pain at two months in our study was modest and only marginally larger than the natural course of neck pain observed in a general population study, which reported an absolute change of 1 point on NRS at two months after the start of a neck pain episode (Vasseljen et al., 2013).

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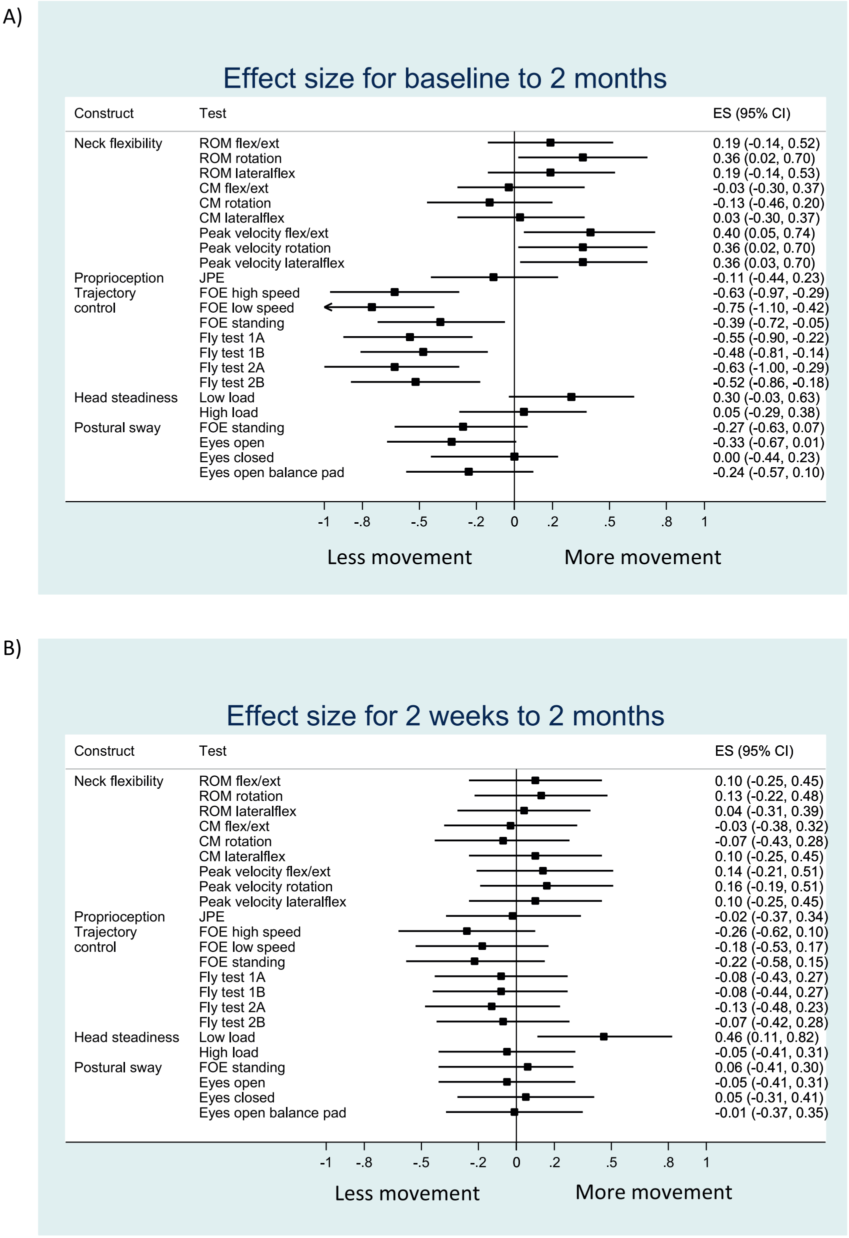

Fig. 2. Effect sizes for changes in motor control and neck motion at 2 months after baseline (A) and between 2 weeks and 2 months (B). Positive effect sizes on the right side of the vertical line indicate increased values for at follow-up test, while negative values indicate decreased values. Interpretation of the effect size: High = <−0.8 or >0.8. Medium = −0.5 and 0.5. Low = <−0.2 or >0.2. Confidence intervals not overlapping 0 indicate statistically significant effect sizes ($p < 0.05$). ROM = range of motion. CM = conjunct motion. JPE = joint position error. PD = point deviation. FOE = figure-of-eight. 1A = easy pattern, small ROM. 1B = easy pattern, large ROM. 2A = medium pattern, small ROM. 2B = medium pattern, large ROM.

The treatment in the present study was not necessarily aimed at improving motor control and neck motion, which may explain the minor improvements in most variables, and still far from values observed in healthy controls (Meisingset et al., 2015). Changes in motor control and neck motion were however independent of the type of physiotherapists who treated the patients, and whether they came from primary health care or the specialized neck and back pain clinic, indicating that different treatment approaches had little influence on neck motor control and motion. Most of the physiotherapists combined different

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Table 3
Prospective univariate associations between neck pain (NRS; 0–10), neck disability (NDI; 0–100) and variables for motor control and neck motion within individuals. Interpretation of the β coefficient for the univariate model is as follows: One point increase in the variable for motor control is associated with an increase in neck pain or neck disability at the value of the β coefficient. Variables with statistically significant associations with neck pain are in bold.

Variable	Neck pain (NRS; 0–10)		Neck disability (NDI; 0–100)	
	β	95% CI	β	95% CI
Neck flexibility				
Flexion-/extension ROM	−0.04	**−0.07, −0.02**	**−0.18**	**−0.32, −0.04**
Conjunct motion	−0.01	−0.07, 0.05	0.13	−0.17, 0.42
Peak velocity	−0.01	−0.02, 0.01	−0.05	−0.14, 0.04
Rotation ROM	−0.02	−0.06, 0.01	−0.11	−0.28, 0.07
Conjunct motion	−0.06	−0.11, 0.00	0.01	−0.28, 0.31
Peak velocity	−0.01	−0.02, 0.00	−0.04	−0.11, 0.02
Lateral flexion ROM	−0.04	−0.10, 0.02	−0.02	−0.30, 0.27
Conjunct motion	−0.02	−0.05, 0.00	−0.12	−0.25, 0.01
Peak velocity	−0.03	−0.05, 0.00	**−0.16**	**−0.30, −0.02**
Proprioception				
Joint position error	−0.09	−0.30, 0.13	−0.3	−1.4, 0.8
Trajectory movement control				
PD FOE low speed	0.11	−0.28,0.51	1.6	−0.3, 3.6
PD FOE high speed	−0.12	−0.40, 0.17	**1.7**	**0.3, 3.1**
PD Fly test 1A	−0.33	−0.97, 0.30	−0.5	−3.7, 2.7
PD Fly test 1B	−0.19	−0.83, 0.46	2.0	−1.3, 5.2
PD Fly test 2A	0.21	−0.34, 0.75	0.2	−2.6, 2.9
PD Fly test 2B	0.18	−0.41, 0.78	**3.8**	**0.9, 6.8**
PD standing FOE	−0.06	−0.44, 0.32	**2.3**	**0.5, 4.2**
Head steadiness				
INF low load	0.41	−0.81, 1.63	0.5	−5.7, 6.7
INF high load	0.22	−0.59, 1.04	−1.9	−6.0, 2.1
Postural sway				
Area standing FOE	−0.10	−0.20, 0.01	−0.5	−1.0, 0.1
Area EO	−0.16	**−0.31, −0.01**	−0.6	−1.4, 0.1
Area EC	−0.03	−0.16, 0.22	0.1	−0.9, 1.0
Area EOB	−0.02	−0.10, 0.06	−0.2	−0.6, 0.2

ROM = range of motion. PD = point deviation. FOE = figure-of-eight. 1A = easy pattern, small ROM. 1B = easy pattern, large ROM. 2A = medium pattern, small ROM. 2B = medium pattern, large ROM. INF = isometric neck flexion. EO = eyes open. EC = eyes closed. EOB = eyes open standing on balance pad.

treatment modalities, and therefore, it is difficult to analyze the effect of a specific treatment on changes in motor control and neck motion. Some evidence indicates that changes in motor control is dependent on motor control specific training (O'Leary et al., 2012). However, Rudolfsson et al. found no difference between three different interventions (neck coordination training, strength training, and massage) in improving postural control and the effect sizes for changes in postural control were low (ES < 0.3) (Rudolfsson et al., 2014).

The patients were characterized by mostly chronic neck pain (92% > 3 months) and few experienced complete pain relief. It is conceivable that larger changes in motor control could have been observed if patients had gained better pain relief. Complete absence of pain is however unlikely within several months after an incident pain episode, but for most people this has little implications for everyday life (Vasseljen et al., 2013). Another explanation for the marginal changes in motor control may be that these patients experienced more or less ongoing pain or were in a state of continuous strain due to multiple stressful intrinsic and extrinsic factors, known as allostatic load (McEwen, 1998; Holte et al., 2003). Alternatively, motor control and neck motion may be stronger associated with other factors than pain, such as fear of movement or catastrophizing (Sarig Bahat et al., 2013).

The time course of changes in neck motion and motor control indicated that most of the changes occurred early in the treatment, except for ROM in flexion/extension that increased more from 2 weeks to 2 months than during the first 2 weeks after start of treatment. Interestingly, cervical ROM in flexion/extension was the only variable that was associated with both reduced neck pain and neck disability, indicating that increased cervical ROM in flexion-/extension might be important in the treatment of neck pain patients. A review study by Howell et al. concluded that there is a lack of information regarding the association between cervical ROM and neck disability and neck pain (Howell, 2011). The studies in the review had a cross-sectional design, in contrast to the longitudinal design in the present study and thus our study adds information regarding neck pain and disability and association with potential modifiable treatment variables. However, a large proportion of the motion and motor control variables (18 of 23) were not associated with changes in neck pain or neck disability. Of the trajectory tests, only one of the Fly tests and two of FOE tests were associated with changes in neck disability, which underlines the uncertainty of the longitudinal association between trajectory movement control and neck disability. This finding is in accordance with Oddsdottir et al. who found no association between improved trajectory movement control and neck disability in whiplash patients during a 12 months follow-up (Oddsdottir and Kristjansson, 2012). They did however find an association with neck disability in patients who did not improve their performance in the Fly test.

5. Strength and limitations

A main strength of this study is the repeated measures design with two follow up tests using a comprehensive set of objectively measured tests for investigating different constructs of cervical motor control and neck motion. Longitudinal associations between neck motor control and neck pain has to our knowledge not been investigated before with such a comprehensive set of motor control tests in clinical populations.

We used fixed effect linear regression analysis that makes the results more generalizable to clinical settings, where individual changes are more relevant than mean group statistics. Furthermore, the outcome estimates are less biased due to confounding, since time-invariant factors (e.g., age, gender, and socioeconomic status) are stable within subjects and thus implicitly controlled for. The study had a relatively large sample compared to other studies in this field and we are confident that the sample size was large enough to discover clinically relevant associations between neck motor control and neck pain and disability. Multiple testing of changes in different variables increases the probability of type 1 error, although the emphasis in our study was on associations. Changes observed in this study, statistically speaking, should be viewed as hypothesis generating rather than tests of predetermined hypotheses.

6. Conclusions

Constructs of motor control and neck motion showed small changes from start of the intervention to posttest at 2 months, with changes mainly occurring between baseline and 2 weeks. Few of the variables for motor control and neck motion were associated with neck pain and disability indicating that factors other than motor control may explain a larger proportion of the changes in neck pain and disability within individuals. Physiotherapists have traditionally measured cervical ROM in neck pain patients, and results from the present study suggest that ROM in flexion-/extension seems to be a valid and possible important modifiable factor for clinicians.

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Paper IV

Predictors for global perceived effect after physiotherapy treatment in patients with neck pain: An observational study

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OBJECTIVE: We investigated the prognostic importance of a number of sensorimotor and psychological factors for global perceived effect (GPE) after physiotherapy treatment in neck pain patients. In addition to baseline values, change scores were used as independent variables to tease out treatment modifiable factors. DESIGN: Clinical prognostic cohort study. SETTING: Primary and secondary health care physiotherapy clinics. PARTICIPANTS: Patients (n=70) with chronic non-specific neck pain. INTERVENTION: Usual care physiotherapy treatment. METHODS: A 3-dimensional motion tracking system was used to measure a range of neck motion and sensorimotor variables, in addition to collecting self-reported outcomes covering personal, somatic, and psychological factors at baseline before treatment and at 2 months. Logistic regression was used to analyze associations between the prognostic variables and the primary outcome GPE at 2 months. RESULTS: At baseline, neck motion and motor control, pain duration, and patient-specific function were the strongest predictors for improvement at 2 months, with no effect of psychological factors. Among the change variables, reduced pain intensity (OR: 1.86; 95% CI: 1.31, 2.62), increased patient-specific function (OR: 1.46; 95% CI: 1.11, 1.92), reduced disability (OR: 1.12; 95% CI: 1.05, 1.20), reduced kinesiophobia (OR: 1.21; 95% CI: 1.07, 1.37) and catastrophizing (OR: 1.09; 95% CI: 1.09, 1.18), and increased self-efficacy (OR:1.12; 95% CI: 1.03, 1.21) were significantly associated with GPE. Reduced pain intensity and kinesiophobia were the two variables most strongly associated with improvement. CONCLUSIONS: The prognostic value of different variables depends on whether they are applied as baseline factors or as change scores.

Introduction

Investigation of predictors and possible modifiable factors related to neck pain treatment is important in order to develop effective interventions and to reduce the episodic and recurrent nature of neck pain (1). Evidence suggests that self- reported measures such as neck pain intensity, disability, and psychological factors are stronger predictors than clinical signs (2). Inconsistent results are however found for psychological factors (e.g. kinesiophobia, catastrophizing, coping) in predicting outcome in neck pain (3). Pain may also affect neck motion and motor control directly or indirectly, with little knowledge of how this may predict treatment outcome. Altered neck motion and motor control are frequently reported in neck pain relative to healthy controls (4-7). Impaired motor control is suggested to contribute to long-term disability, and modification of these impairments may thus be important for a positive treatment outcome (8). The relative importance of pain, function, psychological factors, neck motion and motor control for overall effect of common neck pain interventions is not determined. Within a biopsychosocial framework information of which factors are most important for positive patient reported outcome is insufficient.

Global perceived effect (GPE) scales are recommended as an overall outcome measure in pain studies, as it may cover additional aspects to pain relief and physical function that is important to the individual (9, 10). Measuring improvement by simple questions like GPE is relevant both for clinicians and researchers, and also represents an open and straight forward way for the patient to assess the treatment effect. It may be argued that the overall mark of treatment success should relate to whether the patient perceives the treatment worthwhile and effective.

The present study aimed to investigate the relative contribution of neck motion and motor control, somatic and psychological factors as prognostic factors for improvement after treatment. The secondary aim was to investigate whether changes in these factors were associated with improvement.

Methods

Design

We conducted an observational cohort study in patients with non- specific neck pain (NP, n=81) receiving usual care treatment in primary health care (n=61) or at a secondary care specialized neck and back pain clinic (n=20). Personal, somatic, and psychological factors in addition to tests of neck motion and motor control were measured at baseline before start of treatment and at 2 months follow-up. Flow of the subjects is shown in Figure 1. Results of tests of neck motion and motor control and association with pain and disability are presented in detail in a recently published study (11). All participants gave their written informed consent.

Participants and treatment

NP patients were included consecutively from physiotherapy clinics in primary health care and the specialized neck and back pain clinic from January 2013 to August 2014. The inclusion criteria were: men and women between 18-67 years old with non-specific neck pain, neck pain duration of more than 2 weeks, and neck pain intensity ≥ 3 on the day of testing measured by the Numerical Rating Scale (NRS; 0-10). Exclusion criteria were markedly reduced or uncorrected poor vision, history of neck trauma, diagnosed with neurological or orthopaedic conditions that could affect neck motor control, positive Spurlings`s test for neurological radiating arm pain, and pregnancy. Subject characteristics at baseline are shown in Table I.

Patients in the primary health care received usual care physiotherapy and the duration and number of treatments was at the discretion of the physiotherapists. The treatment, as reported by the physiotherapists, consisted of a wide range of physiotherapy modalities (percentage of patients who received the specific modality in parentheses): individually supervised exercises (52%), mobilization/manipulation (45%), massage (43%), advice and information (27%), dry needling (23%), cognitive therapy (14%), and other therapies reported by less than 10% of the physiotherapists were exercise in group, prescribed home exercises, electrotherapy and shock wave therapy. Certified manual therapists treated 50% of the patients, while general physiotherapists and psychomotor specialized physiotherapists treated 30% and 20% of the patients, respectively.

The patients in the secondary care specialized neck and back pain clinic received a three week multimodal treatment from a group of several professions (physicians, physiotherapists, psychologists and social workers). The first and third week of the multimodal treatment consisted of four full days of patient education, physical exercise and cognitive therapy aimed at reducing fear avoidance/catastrophizing and to increase function, coping and self-management. The week in between was dedicated to individually prescribed home exercises.

Outcome measure and variables

Outcome measure

The primary outcome was patients' global perceived effect of change, measured with the Global Perceived Effect Scale (GPE; 1-7). At 2months the subjects were asked: “Since the start of the treatment, my overall status is: 1= very much improved, 2= much improved, 3= minimally improved, 4= No change, 5= minimally worse, 6= much worse, 7= very much worse (12).

Baseline prognostic factors and change scores

At baseline, all participants completed a questionnaire which included potential prognostic factors such as personal factors, neck pain characteristics, psychological factors, and level of physical activity (see Table 3 for a complete list of prognostic factors). These variables were also collected at 2 months.

Personal factors and pain characteristics

When used as a predictor, age was dichotomized with age ≥ 45 as cut-off, in accordance with previous prognostic studies (13, 14). Other personal factors were gender and body mass index (BMI; continuous). Neck pain intensity was measured with Numeric Rating Scale (NRS; 0-10) and categorized as moderate (NRS=3-5) and severe (NRS≥ 6). Duration of current neck pain episode was dichotomized using 6 months as cut- off (< 6months as reference). Number of additional pain sites was dichotomized into multiple pain sites (≥ 2 additionally pain sites) with < 2 sites as reference category. Recurrence of neck pain was dichotomized with > 3 neck pain episodes per year versus ≤ 3 episodes per year as reference category. Neck disability was measured by Neck Disability Index (NDI;0-100, lower scores, less disability) (15). Function was measured using the Patient- Specific Functional Scale (PSFS; 0-10, where the original PSFS was reversed (16), with 0 indicating no problem with the activity and 10 indicating inability to perform the activity due to neck pain.

Psychological factors

Kinesiophobia was measured using the Tampa Scale of Kinesiophobia with 13 items (TSK; 13-52) (17). Pain Catastrophizing Scale (PCS; 0-52) was used to assess pain catastrophizing (18). Lower score in TSK and PCS means lower fear avoidance and catastrophizing thoughts, respectively. Self- efficacy was measured using the Pain Self- Efficacy Scale (PSES; 0-60) where higher number indicates more self-efficacy (19).

Physical variables

A physical activity index (PAI; 0-15) was calculated based on three questions quantifying intensity of activity, duration, and number of sessions during one week, where higher numbers indicate more physical activity (20). Different constructs of neck motion and motor control (neck flexibility, proprioception, head steadiness, trajectory movement control, and postural sway) were objectively measured at baseline and follow-up at 2 months. Motion data for the neck motion and motor control variables were acquired in a laboratory setting with body worn sensors using the Liberty electromagnetic motion tracker system (Polhemus, Inc, Colchester, Vermont, USA), with a sampling rate of 240 Hz. One sensor was placed on the subject's forehead 1 cm above arcus superciliaris, the second sensor was placed on the spinous process of Th2, and a third sensor was placed in the area of the spinous processes of L4-L5. Detailed description of the neck motor control and motion variables and association with neck pain, disability, and kinesiophobia is given elsewhere (4, 11).

Statistical analysis

Global perceived effect at 2 months was the primary outcome, dichotomized as "improved" (GPE score 1 and 2) and "not-improved" (GPE score 3-7) (21). We used univariable logistic regression analysis to estimate odds ratios with 95% confidence interval (CI) for the baseline prognostic variables in relation to the primary outcome GPE. Baseline prognostic variables with $p<0.1$ in the univariable analysis were entered in a multivariable model. Only significant variables after stepwise backward selection ($p \leq 0.05$) were retained in the final multivariable model. For the secondary aim, we calculated change scores from baseline to 2 months, where positive change scores represent "improvement". In order to avoid multiple testing we reduced the number of neck motion and motor control variables in the analysis of change scores by including only those that significantly contributed in the final multivariable model for the baseline predictors. Change scores with $p<0.1$ in the univariable analysis were then entered in a multivariable model. Only significant variables after stepwise backward selection

($p \leq 0.05$) were retained in the final multivariable model. Age and gender were included as covariates in the multivariable analyses. The multivariable models were checked for multicollinearity. R^2 was used to assess the explained variance for the multivariable models. All statistical analyses were performed using STATA 13 (Stata Corp., College Station, TX, USA). The significance level was defined as $p< 0.05$.

Results

Seventy patients completed the follow-up at 2 months (Figure 1). The patients lost to follow up from baseline (n=11) were similar in age, gender distribution, severity of neck pain, disability, and psychological features as patients included in the analyses. Subject characteristics at baseline before start of treatment are shown in Table I. Most of the subjects (92 %) had chronic symptoms, defined as duration of current neck pain episode longer than 3 months.

Global perceived effect

Fifty percent of the patients were classified as improved 2 months after start of treatment. Patients in the “improved” category reported lower level of neck pain intensity (mean decrease: 2.1 points on NRS; 95% CI: 1.2-3.0), reduced level of disability (mean decrease: 11.4 points on NDI; 95% CI 6.3-16.5) and increased functioning (mean decrease: 1.6 points on PSFS; 95% CI: 0.5-2.6) compared to patients classified as “not improved” (Table II).

Table III presents the associations between baseline prognostic factors and improvement at 2 months measured by the GPE. In the univariable analyses, baseline prognostic factors that were significantly associated with improvement at 2 months were lower neck pain intensity (NRS ≤ 6), higher functioning measured by the PSFS, larger ROM in rotation and lateral flexion, higher peak velocity in flexion/extension and lateral flexion in tests of ROM, and less deviation in two out of seven tests of trajectory movement control. Variables for proprioception, head steadiness, and postural sway were not associated with improvement at 2 months. Four variables were retained in the multivariable model: pain duration, PSFS, ROM in rotation and one test for trajectory movement control. The explained variance for GPE in the multivariable model was 28%.

Table IV shows the univariable analyses of change scores. Reduced kinesiophobia (OR: 1.21; 95% CI: 1.07 to 1.37), reduced catastrophizing (OR: 1.09; 95% CI: 1.01 to 1.18), increased self- efficacy (OR: 1.12; 95% CI: 1.03 to 1.21), decreased neck pain intensity (OR: 1.86; 95% CI: 1.31 to 2.62), less disability (OR: 1.12; 95% CI: 1.05 to 1.20), and increased function (OR: 1.46; 95% CI: 1.11 to 1.92) all gave increased odds for improvement at 2 months. In the multivariable analysis for change scores, reduced pain intensity and less kinesiophobia were the only variables retained in the model explaining 28% of the variation in GPE.

Discussion

The strongest baseline predictors for improvement at 2 months were pain duration less than 6 months, moderate function, larger ROM in neck rotation, and better trajectory movement control. During the treatment, reduced pain intensity and kinesiophobia were the strongest predictors for global perceived effect. Interestingly, improvement in psychological variables during treatment and not their baseline values were associated with global perceived effect.

Strength and limitations

The vast and conceptually different constructs and prognostic factors explored in this study contributes to a more comprehensive understanding of the relative importance of different predictors for favorable treatment outcome in patients with chronic neck pain. Besides baseline factors, investigating changes in prognostic factors over the course of treatment enabled us to study whether treatment modifiable factors were related to a positive treatment outcome. The observational study design can however only point to associations between the changes and GPE, and gives no specific evidence of causal relationships.

Some estimates had wide confidence intervals (Table III), indicating risks of type 2 errors. This applies particularly to some of the baseline prognostic factors (e.g. age, gender, pain duration, multiple pain sites and NDI). There is also a possibility that some of the significant results were random due to multiple testing. We therefore emphasized the results from the multivariable analyses. We also acknowledge that potentially important predictors for a positive treatment outcome, for instance patient`s expectations to treatment (22), the therapist-patient relationship (23), and level of physical fitness were not included in this study.

Baseline prognostic factors

Larger ROM in rotation and better performance in trajectory movement tests at baseline gave higher odds of improvement independently of neck pain severity, pain duration, and self-rated function. Recent reviews on prognostic factors conclude that there has been limited or no evidence for ROM as predictors for treatment outcome in non-specific neck pain (2, 24). This study however supports the routinely measure of cervical ROM as a part of the physiotherapists`clinical examination as relevant (25). This is the first study to show that better fine neck motor control, i.e. trajectory movement control, is a significant baseline predictor for improvement in patients with non-specific neck pain. However, the clinical role of trajectory movement control needs to be further elaborated, as 5 out of 7 tests were not significantly associated with improvement. As for proprioception, head steadiness, and postural sway we found no significant association with improvement at 2 months. In a previous cohort study, we found that these constructs neither were associated with pain or disability (11).

Our results showed a worse prognosis for those with pain intensity score of 6 or higher. This is in line with findings showing that neck pain subjects with severe neck pain have an unfavorable natural course (26) as well as alterations in motor control (27) compared to patients with milder symptoms. Recent systematic reviews also conclude that severe neck pain is associated with lower odds of improvement after treatment (2, 24). The multivariable analyses suggested that pain duration is an important predictor for improvement, which is supported in other studies (24). Other variables representing the chronicity and multimorbidity in neck pain complaints, such as recurrences and number of pain sites, were not significantly associated with improvement, although wide confidence intervals make these results uncertain. Two instruments were used to measure function/disability. In contrast to baseline NDI, baseline self- reported function measured by PSFS predicted improvement at two months. The main difference between the two instruments is that patients define their main problems in the PSFS, while NDI consists of 10 predetermined items related to pain and function. The correlation between the PSFS and NDI in the present study was low (r=0.45), indicating that the two measures captured different aspects of impairments. The PSFS is recommended for clinicians, as PSFS better reflects individual functional status and change over time (28), which is supported by the present study.

Change from baseline to two months

The percentage of patients experiencing improvement at 2 months (i.e. GPE 1-2; very much improved or much improved) were marginally lower than reported in other studies, which might be explained by differences in inclusion criteria, study design, or outcome measures (3, 29), or by the proportion of acute/sub-acute versus chronic neck pain patients (3, 30). However, the percentage of patients reporting improvement or recovery from neck pain in previous studies varies considerably, from 24 % to 95 % (31-33), likely due to a large number of different outcome measures used to define improvement or recovery.

In contrast to baseline, reduced kinesiophobia and catastrophizing, and improved pain self-efficacy during the treatment period were all significantly associated with perceived effect. This raises the question whether physiotherapy treatment, although mainly focused on somatic health, is mediated through effects on psychological factors such as kinesiophobia, catastrophizing and pain self- efficacy. Only kinesiophobia was retained in the multivariable model together with neck pain intensity, indicating a possible explanatory overlap of the psychological factors. This is corroborated by a large study of low back pain patients which found that self-efficacy, catastrophizing, and kinesiophobia could be markers of the same underlying psychological construct, namely pain related distress (34). Studies of low back pain suggest that high self- efficacy may be a more important mediator than fear avoidance in the relation to pain and disability (35, 36).

Unlike baseline values, changes in ROM in rotation and trajectory movement control were not associated with improvement. However, patients experiencing improvement had larger ROM in rotation at baseline compared to patients not improving, but they had similar improvement in ROM from baseline to 2 months, which explain the lack of effect for the change scores in this study. Currently, no clear evidence exist for the mediating role of factors such as neck motion and motor control in the treatment of neck pain (37).

Clinical implication

Physiotherapists routinely measure sensorimotor and motion domains in patients with neck pain which seems justified by the baseline prognostic value of the variables in our study. Patients with high pain intensity (i.e. NRS≥ 6) had lower odds for improvement after treatment, indicating that these patients should receive closer attention by the clinicians. Improvement after physiotherapy treatment seem to be mediated by changes in psychological factors, pain, disability, and function, rather than changes in neck motion and motor control.

A recent study reported that one third of physiotherapists do not look into psychological factors when consulted by neck pain patients (25). This study underlines the relevance of mapping and addressing psychological factors, in addition to traditional sensorimotor and motion domains at the beginning and throughout a clinical course.

Ethical Approval: The study was approved by the Regional Ethics committee

Conflict of Interest: None

Figure 1 **Flow chart of the subjects**

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Table I **Subject characteristics at baseline.** Given values are mean (SD), unless otherwise stated.

Characteristics	Baseline (n=70)
Age	43.2 (12.6)
Females, n (%)	52 (74)
Body mass index	24.9 (4.9)
Current neck pain (NRS;0-10)	4.6 (1.4)
Neck Disability (NDI; 0-100)	31.7 (12.3)
Function (PSFS; 0-10)	6.5 (2.2)
Psychological factors	
Kinesiophobia (TSK; 13-52)	24.8 (4.2)
Catastrophizing (PCS;0-52)	12.9 (8.2)
Self-efficacy (PSES; 0-60)	44.6 (9.7)
Pain characteristics	
Use of analgesics, n (%)	37 (53)
Pain duration, n (%)	
< 3 months	6 (8)
3-6 months	15 (21)
> 6 months	49 (71)
Multiple pain sites, n (%)	
≥ 2 additionally pain sites	36 (51)
Neck pain recurrence, n (%)	
First episode	12 (17)
1-3 episodes/year	21 (30)
>3 episodes/year	37 (53)
Physical activity index (0-15)[1]	3.0 (2.3)
ROM rotation in horizontal plane (^{0})	127.5 (20.7)
Fly test 2A (cm)	3.2 (0.8)

NRS= numerical rating scale (0= no pain, 10= worst possible pain). NDI= neck disability inde. PSFS= patient-specific functional scale (0= no problem performing activity, 10= inability to perform activity due to neck pain). TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale.ROM= neck range of motion

[1] Kurtze et al. (2008). Higher score indicate more physical activity.

Table II **Descriptive statistics for follow- up at 2 months according to global perceived effect after treatment.** The subjects are divided into two groups according to whether they reported improvement or not at 2 months. Improvement was defined as a score of 1 (= very much improved) or 2 (=much improved) on the global perceived effect scale. Not improved was defined as scores from 3-7 (= slightly improved to very much worse). Values are shown in mean (SD).

	Global perceived effect	
	Not-improved n= 35	Improved n=35
Patient self-reported outcomes		
Pain intensity (NRS;0-10)	4.5 (1.9)	1.9 (1.6)
Neck Disability Index (NDI;0-100)	28.8 (13.3)	13.3 (7.8)
Patient Specific Functional Scale (PSFS; 0-10)	5.4 (2.1)	2.4 (1.8)
Psychological factors		
Kinesiophobia (TSK:13-52)	23.9 (5.1)	21.2 (4.7)
Catastrophizing (PCS: 0-52)	8.9 (7.5)	7.5 (5.6)
Self-efficacy (PSES;0-60)	47.5 (10.6)	52.4 (8.6)
Physical activity index (0-15)	3.0 (2.3)	3.8 (2.9)
Neck motor control and motion		
Rotation ROM (°)	127.1 (20.6)	142.8 (18.3)
Fly test 2A (cm)	3.0 (0.8)	2.5 (0.6)

Patient-Specific Functional Scale: 0= no problem at performing activity. 10= Inability to perform activity due to neck pain. NRS= numerical rating scale (0-10). Neck disability index (0= no disability, 100= 100 % disability). TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale. ROM= neck range of motion. Physical activity index; higher score indicate more physical activity

Table III Univariable and multivariable analysis of baseline predictors for Global Perceived Effect (GPE) at 2 months after start of treatment. Statistical significant associations ($p<0.05$) are in bold.

	GPE 35 of 70 improved OR (95% CI)	P- value	Multivariable model GPE[2] OR (95% CI)	P-value
Patient self-reported outcomes				
Old age (≥45 years vs < 45 years)	0.44 (0.17; 1.16)	0.09		
Gender (female vs male)	0.74 (0.25; 2.18)	> 0.3		
Body mass index (per unit)	0.96 (0.87; 1.07)	> 0.3		
Pain duration (≥6 months versus < 6 months)	0.38 (0.13; 1.09)	0.07	**0.18 (0.04; 0.76)**	0.02
Multiple pain sites (≥2 additional sites vs < 2 sites)	0.63 (0.25; 1.62)	> 0.3		
Recurrence (>3 episodes/year vs ≤3 episodes/year)	0.56 (0.22; 1.45)	0.23		
Pain intensity: Moderate (NRS= 3-5)	ref			
Severe (NRS≥6)	**0.22 (0.07; 0.71)**	0.01		
Neck Disability Index, low (NDI<30)	0.98 (0.94; 1.01)	0.21		
Patient Specific Functional Scale, moderate (PSFS<7)	**0.72 (0.57; 0.93)**	0.01	**0.69 (0.50; 0.95)**	0.03
Psychological factors[1]				
Kinesiophobia (TSK:13-52)	1.06 (0.95; 1.19)	> 0.3		
Catastrophizing (PCS: 0-52)	1.03 (0.97; 1.09)	> 0.3		
Self-efficacy (PSES;0-60)	1.00 (0.95; 1.05)	> 0.3		
Physical activity index[1]	1.06 (0.86; 1.31)	> 0.3		
Neck motor control and motion				
Neck flexibility				
Flexion-/extension ROM	1.02 (1.00; 1.04)	0.09		
Peak velocity	**1.02 (1.00; 1.05)**	0.04		
Rotation ROM	**1.05 (1.01; 1.08)**	0.004	**1.04 (1.00; 1.08)**	0.03
Peak velocity	1.01 (1.00; 1.03)	0.13		
Lateral flexion ROM	**1.04 (1.00; 1.07)**	0.03		
Peak velocity	**1.04 (1.01; 1.08)**	0.01		
Trajectory movement control[3]				
figure-of-eight low speed	0.81 (0.55; 1.20)	0.29		
figure-of-eight high speed	0.77 (0.56; 1.05)	0.09		
Fly test 1A	0.62 (0.32; 1.17)	0.14		
Fly test 1B	**0.30 (0.12; 0.80)**	0.02		
Fly test 2A*	**0.44 (0.23; 0.85)**	0.01	**0.39 (0.16; 0.94)**	0.04
Fly test 2B*	0.97 (0.49; 1.91)	> 0.3		
figure-of eight low speed in standing	0.58 (0.32; 1.05)	0.07		
Postural sway				
Sway area standing figure-of-eight	0.92 (0.81; 1.04)	0.19		
Sway area eyes open	0.93 (0.79; 1.10)	> 0.3		
Sway area eyes closed	0.97 (0.81; 1.16)	> 0.3		
Sway area eyes open on balance pad	1.03 (0.95; 1.12)	> 0.3		

[1] OR estimates are based on unit increases in the independent variable.

[2] Variables with $p<0.1$ from the univariable analyses were included in the multivariable model. Age and gender were included as covariates.

[3] Outcome variables for tests of trajectory movement control was the deviation in the tracking tasks.

OR=odds ratio. Patient-Specific Functional Scale: 0= no problem at performing activity. 10= Inability to perform activity due to neck pain. NRS= numerical rating scale (0-10). Neck disability index (0= no disability, 100= 100 % disability). TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale. ROM= range of motion. 1A= easy pattern,small range of motion. 1B=easy pattern,large range of motion. 2A= medium pattern, small range of motion. 2B= medium pattern, large range of motion

Table IV **Univariable and multivariable analysis of Global Perceived Effect (GPE) and association with change scores from baseline to 2 months.** Statistical significant associations ($p<0.05$) are in bold.

	GPE 35 of 70 improved OR (95% CI)	P-value	Multivariable model GPE[2] OR (95% CI)	P-value
Patient self- reported outcomes				
Pain intensity (NRS;0-10)	**1.86 (1.31;2.62))**	< 0.001	**1.88 (1.27; 2.78)**	0.002
Neck Disability Index (NDI;0-100)	**1.12 (1.05; 1.20)**	0.001		
Patient Specific Functional Scale (PSFS; 0-10)	**1.46 (1.11; 1.92)**	0.007		
Psychological factors				
Kinesiophobia (TSK:13-52)	**1.21 (1.07; 1.37)**	0.003	**1.21 (1.05; 1.39)**	0.01
Catastrophizing (PCS: 0-52)	**1.09 (1.01; 1.18)**	0.04		
Self-efficacy (PSES;0-60)	**1.12 (1.03; 1.21)**	0.009		
Physical activity. Index	1.05 (0.85; 1.30)	> 0.3		
Neck motor control and motion				
ROM cervical rotation	1.00 (0.96; 1.05)	> 0.3		
Fly test 2A	0.87 (0.44; 1.72)	> 0.3		

[1] Odds ratio estimates are based on unit increases in the independent variable.

[2] Age and gender were included as covariates

OR= odds ratio. PSFS: 0= no problem at performing activity. 10= Inability to perform activity due to neck pain. NRS= numerical rating scale (0-10). NDI: 0= no disability, 100= 100 % disability. TSK= Tampa scale of kinesiophobia. PCS= pain catastrophizing scale. PSES= pain self-efficacy scale. ROM= range of motion. 2A= medium pattern, small range of motion

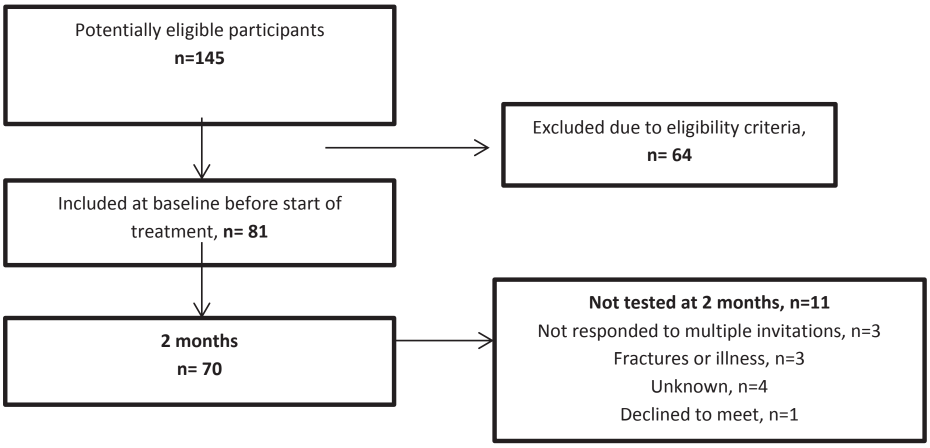

Figure 1 Flow chart of the subjects