Sensorimotor control and cervical range of motion in women with chronic neck pain
Kinematic assessments and effects of neck coordination exercise

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To my family
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Abstract

Introduction: Neck pain is a common problem in society and is more prevalent among women. The consequences of neck pain for the individual often include activity and participation limitations, thus affecting many dimensions of life. There is still a lack of understanding of the underlying mechanisms of the disorder and likewise of efficient rehabilitation for people with neck pain. However, coordination exercises have shown promising short-term effects. To carry this line of research forward, there is a need to improve methods for objective characterization of impairments and to investigate novel methods of rehabilitation.

Aims: To characterize impairments of active cervical range of motion of the upper and lower cervical levels in women with chronic neck pain with a novel method (Study I and II) and identify the influence of head posture and movement strategies (Study II). Further, to investigate the effects of a novel method for neck coordination exercise on sensorimotor function and neck pain (study III) and the consistencies of motor variability metrics in a goal directed arm movement task to aid the design of future clinical research (Study IV).

Methods: All studies were laboratory based with kinematic assessments of neck movements (Study I-III), balance (Study III) and goal directed arm movements (Study III, IV). The studies had designs that were: cross-sectional (I and II), randomized controlled trial (III) or test-retest reliability study (IV). Participants in Study I (n=135) and II (n=160) were women with chronic non-specific neck pain and healthy controls. In Study III, women with chronic non-specific neck pain (n=108) were randomized into three different individually supervised 11 week interventions. Study IV included healthy women (n=14).

Results: It was found that cervical range of motion impairments in women with non-specific neck pain were direction- and level-specific; impairments were greater in extension in the upper and flexion in the lower levels of the cervical spine. The magnitude of impairments in range of motion was associated to self-ratings of functioning and health. Possible group differences in natural head posture were rejected as a cause for the direction specific effects. Neither could the effects be explained by a strategy to minimize torque in the cervical spine during movement execution. The neck coordination training was not superior to strength training (best-available) and massage treatment (sham) in improving sensorimotor functions or pain according to short-term and 6 months follow ups. The results from the study
of the goal directed movement task showed that between and within-subject sizes of most motor variability metrics were too large to make the test suitable for application in clinical research.

**Conclusions:** Women with chronic non-specific neck pain have direction- and level-specific impairments in cervical sagittal range of motion. The underlying causes of these specific impairments remains unresolved, but the direction specific impairments are not related to natural head posture. The clinical validity of the method of characterization of cervical range of motion was supported and it can be useful in future clinical research. The novel method of neck coordination exercise showed no advantages on sensorimotor functions or pain compared with best-available treatment in women with chronic non-specific neck pain.
Abbreviations

1RM  one repetition maximum
ANCOVA  Analysis of covariance
ANOVA  Analysis of variance
BMI  Body mass index
CCF  Cranio-cervical flexion
CI  Confidence interval
CoM  Centre of mass
CON  Control group
COP  Center of pressure
COP-A  Center of pressure area
CRP  Average continuous relative phase
CV  Coefficient of variation
DASH  Disabilities of the arm, shoulder and hand
FHP  Forward head posture
HCM  Head center of mass
HCM_ext  Head center of mass horizontal migration in global extension
HCM_flex  Head center of mass horizontal migration in global flexion
HCM_global  Total range of head center of mass horizontal migration in extension and extension
HCM_prot  Head center of mass horizontal migration during protraction
HE  Head extension
LC  Lower cervical level
LC_ext  Lower cervical extension in global extension
LC_flex  Lower cervical flexion in global flexion
LC_NHP  Lower cervical angle in the natural head position
MANOVA  Multivariate analysis of variance
NCE  Neck coordination exercise
NDI  Neck disability index
NP  Women with non-specific neck pain
NRS  Numeric rating scale
O-PLS  Orthogonal partial least squares regression
PPT  Pressure pain thresholds
Ra-A  Rambling area
RCT  Randomized controlled clinical trial
ROM  Range of motion
RPE  Borg rating of perceived exertion
RQ  Research questions
SD  Standard deviation
SF-36 MCS  Short Form Health Survey mental component summary
SF-36 PCS  Short Form Health Survey physical component summary
SF-36  Short Form Health Survey
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ST</td>
<td>Strength training</td>
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<tr>
<td>TAU</td>
<td>Treatment-as-usual</td>
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<td>Tr-A</td>
<td>Trembling area</td>
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<td>TSK</td>
<td>TAMPA Scale of Kinesiophobia</td>
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<td>UC</td>
<td>Upper cervical level</td>
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<tr>
<td>UC_ext</td>
<td>Upper cervical extension in global extension</td>
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<tr>
<td>UC_flex</td>
<td>Upper cervical flexion in global flexion</td>
</tr>
<tr>
<td>UC_NHP</td>
<td>Upper cervical angle in the natural head position</td>
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<tr>
<td>VE</td>
<td>Variability in end point precision</td>
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Svensk sammanfattning

Avhandlingsstıtle: Sensomotorisk funktion och rörelseomfång i nacken hos kvinnor med långvarig nacksmärta: Utvärdering med rörelseanalys och effekter av nackkoordinationsträning


Syftet med avhandlingen kan sammanfattas i tre delar: Att detaljerat mäta nedsättningar i Nackens rörelseomfång hos kvinnor med långvarig Nacksmärta; att utvärdera effekten av en ny metod för Nackkoordinationsträning på rörelsefunktion och smärta hos kvinnor med långvarig Nacksmärta; samt att utvärdera ett nytt test för att mäta precision och koordination vid målriktade armrörelser och ämnat för framtida klinisk forskning.

Resultaten visade att kvinnor med långvarig Nacksmärta hade specifika nedsättningar i Nackens rörelseomfång; i övre Nackregionen var Bakåtbojning mer begränsad medan i nedre Nackregionen var Framåtbojning mer begränsad. Vi kunde utesluta att resultaten berodde på skillnader i huvudets normala hållning. Graden av rörelsebegränsning i Nacken uppgisade samband med personernas självskattade funktion, Symtom och hälsa. Nackkoordinationsträningen var inte bättre än styrketräning eller massage för att förbättra rörelsefunktion eller för att minska smärta. Det nya testet för armrörelser var inte lämpat för kliniska studier av rörelseprecision.

Slutsatserna från avhandlingsarbetet är att kvinnor med långvarig Nacksmärta hade begränsningar i Nackens rörelseomfång vid framåt- och bakåtbojning av huvudet som är specifika vad gäller nivå i halsryggen och riktning. Att graden av röelsebegränsning uppgisade samband med självskattad funktion, symtom och hälsa styrker testets kliniska validitet. Ytterligare forskning behövs för att förstå orsakerna bakom de specifika nedsättningarna. Nackkoordinationsträningen som utvärderades kan inte rekommenderas för kvinnor med långvarig Nacksmärta eftersom korttidsuppföljning och 6-månadersuppföljning visade att träningsformen inte var bättre än styrketräning eller massage, vare sig när det gällde att förbättra sensomotorisk funktion eller att minska smärta.
Original Papers

This thesis has resulted in the following enclosed papers:


II. Rudolfsson, T., Svedmark, Å., Björklund, M., Srinivasan, D., Djupsjöbacka, M. Direction specific impairments in cervical range of motion in women with chronic neck pain: Influence of head posture and gravitationally induced torque [Manuscript]


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Introduction

Epidemiology of neck pain
Neck pain is a common problem in the industrialized society. The yearly incidence of self-reported neck pain has been estimated to 21% (Hogg-Johnson et al., 2008) and the recurrence of symptoms are common (Haldeman et al., 2008). In the general population, the one-year prevalence ranged from 30 to 50% in different studies (Hogg-Johnson et al., 2008) and the prevalence in the working population is similar in magnitude; 27 to 48% (Côté et al., 2008). Geographic differences have been reported where for example, Scandinavian countries have shown higher prevalence compared with other European countries (Fejer et al., 2006). Neck pain has been shown to be more frequent among women than men (Hogg-Johnson et al., 2008, Fejer et al., 2006). The ratio between women and men in one-year prevalence ranged from 1.1 to 3.4 between studies (Fejer et al., 2006) and the Swedish Work Environment Authority reported that the most common disorder among women is pain in the upper back or neck, where the one-week prevalence were 45% compared to 26% for men (2014). There is a great amount of uncertainty in the estimates of prevalence’s of neck pain that partly originates from different definitions of neck pain between studies (Fejer et al., 2006), sampling within the study populations (Hoy et al., 2010) and other factors. But in spite of this, research clearly show that neck pain is a common problem in the general as well as the working population and especially among women.

Neck pain disorders
Neck pain disorders is an umbrella term for problems in the neck-shoulder region. There are many different ways of categorizing these conditions but the most commonly used is the International Classification of Diseases and Related Health Problems (ICD). It is primarily designed for specific diagnoses of known origin. For neck pain there are only a few specific diagnoses, such as cervical radiculopathy (radiating pain caused by nerve root compression) and disc disorders. Diagnose codes are also based on the location of symptoms, such as cervicalgia and cervicobrachialgia. A large proportion of people with neck disorders are diagnosed with symptom based codes. In lack of a detailed origin or known mechanism behind the pain, these conditions are often referred to as non-specific neck pain.

When the neck disorders are persistent, they are commonly referred to as chronic in the literature. There are no definitive criteria for this classification, but duration of symptoms greater than three or six months is commonly used (SBU, 2006). An intermediate label between acute and
chronic is sub-acute disorders, commonly used for 4-12 weeks of pain duration (SBU, 2006).

**Biopsychosocial model**
The biopsychosocial model is a general perspective of illness that was first introduced in the late seventies by Engel (1977). This perspective acknowledges the biological, cultural, social and psychological components in health and illness and criticized the biomedical model, dominant at the time, for the reductionist approach of assigning biological criteria as the ultimate definition of disease. The biopsychosocial model has since been adopted for research on musculoskeletal pain (for an early example, see 1987). The adoption of the biopsychosocial model has broadened the view of neck disorders and contributed to change of perspectives on prevention and rehabilitation strategies.

**Risk factors for neck pain**
The research on risk factors for neck disorders has been extensively reviewed. Risk factors for the onset of neck pain have been identified both within individual and environmental factors. Within physical exposure at the workplace, risk factors are poor workstation design, work posture, sedentary work postures, repetitive work and precision demanding work (Côté et al., 2008). Other factors related to working life are low social support at work and job insecurity (Côté et al., 2008), as well as both high and low job demands (Macfarlane et al., 2009). Individual risk factors are poor psychological health and smoking (Hogg-Johnson et al., 2008). Female gender has also been associated with higher incidence of neck pain (Hogg-Johnson et al., 2008).

To summarize, repetitive work and aspects of working posture of the arms, shoulders and head seems to be important for the development of neck pain (Côté et al., 2008).

**Characteristics associated with neck pain**
Common impairments in body functions associated with neck pain are headache, reduced joint mobility, joint instability, and increased muscle tension as well as structural impairments of the cervical spine, muscles and nerves (John D. Childs, 2008). Neck pain is also often accompanied by activity limitations, where the one-year prevalence of pain interfering with daily activities was between 11-14% in workers (Côté et al., 2008). From qualitative research on experiences of health-care workers living with musculoskeletal pain, an active process of striving for balance was revealed. This process involved acceptance and handling; that is making strategies to minimize the effect of their illness. To continue to work was a priority; hence, during intensive episodes of pain, balancing could partly be achieved.
by restricting participation in social life (Wiitavaara, 2007). Thus, living with chronic pain may have a substantial impact on the individual. Neck pain is also a problem at the society level, with costs in health-care, medication and absenteeism from work. As an example, the cost of neck pain in the Netherlands was estimated to be US $686 million in 1996 (Borghouts et al., 1999).

Reducing the prevalence of neck pain

For the future, how do we reduce the prevalence of neck pain and the associated problems for the affected individual and society? As touched upon earlier, the current state of knowledge has identified many risk factors for the development of neck disorders. Within the environmental factors, many seem feasible to reduce by preventive interventions. The results from such trials are mixed, but systematic reviews concluded that modifying workstations and worker posture were not effective (Côté et al., 2008, Driessen et al., 2010). Evidence of preventive effectiveness of resistance training has also been reviewed with negative findings (Sihawong et al., 2011). However, a recent study investigated the effect of neck strength endurance training and stretching in office worker. The participants (n = 567) were required to be symptom free and exhibit reduced cervical flexion ROM and neck strength endurance at baseline. The intervention group showed significantly lower incidence of neck pain (12.1%) compared to controls (26.7%) in the one year follow up. It is clear that more effective prevention of neck pain is necessary and efficient rehabilitation is important.

One recent approach to rehabilitation has emerged from the adoption of the biopsychosocial model (Engel, 1977). To accomplish this, a combined effort of several health care professions is usually required and this approach is commonly referred to as multimodal rehabilitation. In a systematic review, multimodal rehabilitation of chronic low back or neck/shoulder pain has shown moderate evidence on improved return to work capacity compared to less intensive interventions but no effects on pain intensity (SBU, 2010). The composition of the interventions differed among the studies but key modalities seem to be psychological interventions in conjunction with exercise or manual therapy (SBU, 2010).

Interventions with one single modality are more common. Manual, exercise and low-level laser interventions have shown to be more effective than sham-treatment or treatment as usual (Hurwitz et al., 2008). A Cochrane review found moderate evidence that strengthening and stretching program that focused on the neck and shoulders had effect on pain (Kay et al., 2005). Ylinen and co-workers focused their review on exercises and concluded that specific training for the neck and shoulders showed effect on neck disorders (Ylinen, 2007). There is a great diversity in the exercises leading up to the positive findings in these reviews. Besides dynamic and
isometric resistance training at low to high intensity, these reviews extend to include slow-paced movement of the eyes and head for coordinative training. A common conclusion is that the interventions should be individually supervised to have effect (SBU, 2006). However, the effect is not a full recovery. As an example, the effect of supervised exercise on pain relief was estimated to only 20-30% (SBU, 2006). In conclusion, the best evidence for effect of single treatment interventions on pain and disability seems to incorporate supervised strength training.

In summation, great efforts have been taken to reduce the prevalence of neck pain. However, the results of preventive and rehabilitation interventions are not sufficient; hence, the need for efficient rehabilitation will continue to be extensive.

**Core problem addressed in this thesis**

This thesis has its starting point in the lack of efficient rehabilitation and the possible causes for this problem are multiple. Some general aspects of this issue were highlighted in an editorial by McCarthy and Cairns, who suggested that we need refined methods and approaches to rehabilitation research (McCarthy and Cairns, 2005). This process encompasses the biopsychosocial perspective on rehabilitation. The starting point is the heterogeneity in the neck pain population where we would need improved measures to characterize the patients as to provide a more specific diagnostic profile (Figure 1). The second step would be to link this profile to a suitable intervention. Finally, they identified a weak link between interventions and the outcomes used in studies.

![Figure 1 A model of management for pain syndromes. Reprinted from McCarthy and Cairns (2005) with permission.](image)
Within the research on non-specific neck pain, there is clearly motivation to improvements in the first step involving the characterization of patients. The International Classification of Functioning, Disability and Health (ICF), is a generic classification system for health and health-related domains. For the management of low back patients, an ICF-core set including 78 categories have been developed based on large clinical samples. This core-set is a subsample of the categories in the ICF-classification, reflecting the most relevant characteristics to assess for clinicians and other health professionals when dealing with patients with low back pain. However, for characterization of people with neck pain there are no specific guidelines available. A development of an equivalent core set for the management of neck pain should be highly prioritized.

In creating a diagnostic profile with the level of detail necessary to design the rehabilitation, we are also closing in on a great conundrum. We for example still don’t know the pathophysiological mechanism of non-specific musculoskeletal pain. Although several models have been proposed (for a review, see Visser and van Dieen, 2006), the mechanism remains unclear. This uncertainty is problematic for diagnoses and course of the treatment, and is most likely a major contributing factor to the lack of efficient rehabilitation.

However, several models predict that components of motor control are of importance. One such component is impaired proprioception (e.g., Johansson et al., 2003), that is, the sense to determine the configuration and movement of the body segments without vision or tactile feedback. Thus, proprioceptive impairment can affect eye-hand coordination postural control. Another component is muscle coordination, where pain has been associated with a reorganization of muscle coordination to reduce the load on the affected muscle (Falla, 2008). Thus, developing clinical tests for assessment of sensorimotor impairments could be one approach to gain a more detailed characterization.

The second step in the model by McCarthy and Cairns (2005) is to link the profile to a suitable intervention. This step is carried out daily in the clinical practice by means of established experience, but has not received much attention in the scientific literature. To achieve this, current evidence of effective interventions must be incorporated in a decision model. However, there are still uncertainties in the evidence of effectiveness of several single-component interventions for neck pain and investigating the long-term effect is often neglected. Thus, there is a continued need of stronger evidence on methods of rehabilitation with well-chosen control interventions.

For the third step of selecting valid outcomes - The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) has provided valuable guidelines. IMMPACT has recommended that rehabilitation interventions should be evaluated in 6 different conceptual
domains (Turk et al., 2003). These consist of: (1) pain, (2) physical functioning, (3) emotional functioning, (4) participant ratings of improvement and satisfaction with treatment, (5) symptoms and adverse events and (6) participant disposition. This has been complemented with recommendations of specific outcome measures (Dworkin et al., 2005). A convergence of outcome measures between studies should be highly prioritized since it is a requirement for future meta-analyses. It is a challenge to obtain precise estimates of all these dimensions and for practical reasons; the chosen outcomes are often matched to test the underlying hypothesis of why the selected intervention would be effective. Thus other outcomes than the primary outcome is probably underpowered for statistical analysis, and can only contribute to the knowledge when incorporated in a meta-analysis of similar interventions.

**Delimitations of the thesis**

Based on this general overview, the scope of this thesis was mainly delimited to objective characterization of impairments in physical functioning and sensorimotor functions in women with non-specific neck pain. The scope was also delimited to provide evidence on the effectiveness of single-component sensorimotor interventions in women with non-specific neck pain.

The multimodal approach to rehabilitation is generally recommended for people with chronic pain who displays complex symptoms spanning over several outcome domains (SBU, 2010). However, the expected contribution of each component is often unknown and conclusions of cost-effectiveness is not possible due to insufficient evidence (SBU, 2010). Hence, the need of determining the effects of novel single-component exercises of rehabilitation in the neck pain population was identified. Turning to McCarthy and Cairns (2005) and the second step of matching interventions to the diagnostic profile, the evidence and guidelines in this field are sparse. However, an underlying assumption of a profile suitable for sensorimotor exercise is that the neck pain is likely to be accompanied by an activity limitation. Hence, a delimitation of the population to those for whom symptoms extend to include activity limitation can be appropriate for evaluation of single-component exercises.

**Impairments in motor functions**

Deviations of motor functions from the general population can be interpreted as impairment or functional adaption based on divergent theoretical viewpoints (Latash and Anson, 1996). A requirement for a well-functioning system to change is that constraints or opportunities on some level are introduced. Consequently, adaption occurs because there is a favorable option.
Regardless terminology, the empirical deviations in this section is reported to be associated with a neck pain condition, but the causal relationship is not known. Throughout this thesis, the term impairment is used to describe any deviation of motor functions from the general population.

**Cervical range of motion**

A common finding in people with neck pain is reduced active sagittal cervical range of motion (ROM) (Hagen et al., 1997, Jordan et al., 1997, De Loose et al., 2009, Woodhouse and Vasseljen, 2008, Chiu and Lo, 2002, Vogt et al., 2007). Jordan and co-workers (Jordan et al., 1997) only studied ROM in extension but included an unusually large sample (n = 199, age = 20 - 60). They concluded that ROM in women with neck pain was reduced compared to controls in all ages between 20 - 60 years but the corresponding results for men were only significant in ages between 20-40 years. This gender difference may be attributed to insufficient power because there were fewer men in each group after the age stratification. However, reduced ROM have also been reported in male machine forest operators (Hagen et al., 1997) and fighter pilots (De Loose et al., 2009) so impairments seem to be present in both genders. There are also negative findings, for example people with mild and transient symptoms compared to CON showed no difference in flexion/extension ROM (Lee et al., 2004). The clinical relevance of measuring ROM is also partly supported by that impairments in cervical ROM have been associated to self-rated pain during activities (Hagen et al., 1997). In addition, interventions including cervical ROM exercises have also been recommended for neck pain (Gross et al., 2009, Kay et al., 2005).

Common measurement techniques are to use goniometers or kinematic methods to measure the angle between the head and the trunk (Williams et al., 2010), which assumes the biomechanical model of the cervical spine as a single joint. This two–segment model is commonly used in clinical research.

There are level dependent differences in functional anatomy of the cervical spine (for a review, see Bogduk and Mercer, 2000). It is acknowledged that the source of pain can stem from different cervical levels and it has been suggested that the magnitude of sensorimotor impairments is more prominent when pain is located in the upper cervical region compared to lower regions (Treleaven et al., 2011). Hence, for the purpose of characterization of impairments, an objective measure of cervical ROM that separates the contribution of the upper and lower levels would be beneficial.

One such method has been described in the field of kinematic research (Hsu et al., 2007). In this method, the thorax, cervical spine and head forms a three-segment model that allows for decomposing sagittal trunk-head ROM into flexion/extension at the upper and lower cervical levels.
Implementing this methodology in a test of cervical ROM can be useful to characterize level specific impairments in people with neck pain.

If we reconnect to the first step of McCarthy and Cairns and the creation of a diagnostic profile (2005); one approach to determine if the impairments are clinically important for the characterization could be to study the associations between impairments and self-rated function and activity limitations.

**Habitual head posture**

Head posture assessment is common part of a clinical examination and in research on neck pain (for a review, see Silva et al., 2010). Aspects related to head posture was also suggested to be risk factors for neck pain (Côté et al., 2008). The most common attribute is a slightly protracted head, termed forward head posture. To maintain an upright head posture with the head slightly protracted the upper cervical spine must be extended. Such posture could result from impairments in the deep cervical flexors (Falla et al., 2004a), as evidence from functional anatomy has shown that greater lordosis of the cervical spine is associated with a smaller cross-sectional area of the deep cervical flexor longus colli (Mayoux-Benhamou et al., 1994).

There is a great diversity in the methodology and conditions investigated in studies assessing head posture in people with neck pain. The results are also conflicting regarding head posture and the association to neck pain (Silva et al., 2010). Given that head posture has gained a lot of attention in the field of ergonomics and is routinely assessed in workplace interventions, further insights is needed to clarify the association to neck pain.

**Goal directed arm movements**

Huysmans and co-workers (2010) let people with neck pain and healthy controls perform a two-dimensional target-matching task. Participants were standing with the chin resting on a digitizer tablet. The three targets were visible on top of the tablet, and the task was to point to the target from beneath the table. The precision was estimated by the variable error. They found reduced precision in the neck pain group compared to controls. Sandlund and co-workers (2008) investigated precision in a three-dimensional task and found reduced precision in the depth and vertical axis but not in the horizontal. The samples were similar in age with a mean age around 40 and with respect to pain ratings and disability. The total sample size was 49 (Huysmans et al., 2010) and 46 (Sandlund et al., 2008) with a larger proportion of the female gender in both studies. These studies indicate that the precision of goal directed arm movements may be impaired in people with neck pain.

One tentative explanation can be impaired proprioception in people with neck pain. Studies of arm movement to visible targets in healthy controls
have shown that both vision and proprioception plays important role on precision of the task (van Beers et al., 2002) and that these different sensory modalities are integrated to achieve higher precision than separately available (van Beers et al., 1996). Prior to reaching to a target, in the state of motor planning, visual information about the task position in a head-centered coordinate system is fused with the position of the hand in a body-centered system (Buneo et al., 2002). Hence, it is evident that proprioceptive information is important for precise arm movements.

A limitation of the assessment of precision in motor planning in the work by Sandlund and co-workers (2008) might be the utilization of a single target. The field of motor learning gives some insights to this issue. Research has shown that random practice promotes retention of motor learning better than blocked practice (Shea and Morgan, 1979). One tentative explanation to these findings has been presented as the forgetting-hypothesis (Lee and Weeks, 1987). This hypothesis is tightly coupled to the process of motor planning, and predicts that it is the process of repeated retrieval and creation of the solution of the motor problem that enhances learning, not a repetition of the solution. Along this line of reasoning, attempts to measure the quality of motor planning, such as the precision in a goal-directed arm-movement would greatly benefit from random target allocation.

Other inspiration and suggestions for further development is found within the ecological theory of motor control. A central concept is the perceived possibilities for action, termed affordances, and that movement arise as an interaction between the person and the affordances. Much can be learnt by adopting this perspective. For any study of human movement, creating an ecologically valid task setting with recognized affordances may offer the possibility to study motor control in natural movement.

Altogether, a further development of a measurement model for goal-directed arm movements may be necessary for characterizing sensorimotor impairments in people with neck pain. However, all human movement has great natural variability. The consistency of this motor variability is important for the planning of the study and the interpretation of the result. Hence, a natural first step could be to investigate the consistencies of relevant metrics in a healthy population prior to clinical adoption of the test.

Postural sway
Several studies have reported impaired postural control in people with neck pain (for a review, see Ruhe et al., 2011). Postural sway is usually studied by measuring centre of pressure migration with a force plate and people with neck pain have been shown to be more sensitive to proprioceptive perturbations (Koskimies et al., 1997), and showed increased sway energy compared to controls in narrow stance but not in comfortable stance (Field et al., 2008). There are also findings in in parameters that are more closely
related to the postural control system such as stiffness and damping (Karlberg et al., 1995), but a large proportion of the sample in this study showed signs of more severe conditions, such as cervical root compression.

The dynamics of postural sway is considered to consist of a slow and fast component (Zatsiorsky and Duarte, 1999, Kiemel et al., 2006). The size of the slow component has been attributed to errors in estimation position of centre of mass (CoM) (Kiemel et al., 2006), and the fast component is considered to represent forces controlling CoM.

A common model for assessing postural control is measuring body sway with a force plate in quiet bi-pedal standing (Field et al., 2008, Koskimies et al., 1997, Karlberg et al., 1995), and for a better understanding of the impairments of postural sway in people with neck pain it can be useful to quantify the measurement in components related to the postural control system (Kiemel et al., 2006, Zatsiorsky and Duarte, 1999, Karlberg et al., 1995).

**Cervical muscle coordination**

Much of the research devoted to impairments of the deep cervical flexors in neck pain has been carried out with the cranio-cervical flexion (C-CFT) test (Jull et al., 1999). With the help of a trained instructor, the purpose is to teach the participant to perform a small upper cervical flexion movement while the superficial flexors are to be held as relaxed as possible. Falla and co-workers inserted electrodes via the nose to measure electromyography of the deep cervical flexors during this test and found reduced activation in people with neck pain compared to controls (Falla et al., 2004c). In contrast, this group has shown increased activation of the superficial flexors in this test (Jull et al., 2004, Falla et al., 2004c). This together suggests an altered coordination between the deep and superficial flexors in people with neck pain.

There is also evidence that supports an increased co-activation of superficial cervical agonists and antagonists. This was investigated in isometric contraction of flexion/extension in people with chronic tension-type headache with electromyographic recordings of the sternocleidomastoid and splenius capitis (Fernandez-de-las-Penas et al., 2008).

The deep cervical flexors also has a postural function (Mayoux-Benhamou et al., 1994). With that in mind, a study of rapid voluntary arm movements were performed and reported delayed onset of the deep cervical flexors in neck pain compared to controls (Falla et al., 2004b). This suggests that activation of deep segmental muscles are not pre-planned, i.e., feed-forward controlled, to support the cervical spine from postural perturbations in neck pain as opposite to controls.

The strength of the evidence in studies of altered muscle coordination is modest at best because of small sample sizes and difficulties in establishing
clinically relevant differences. However, direct measurements of muscle activity indicates altered activation between deep and superficial cervical flexors, increased co-activation of superficial flexor/extensors and impaired feed-forward control of the deep cervical flexors. However, there is limited research on the effect of impaired muscle coordination on activity limitations or other sensorimotor functions.

The current evidence of impairments of muscle coordination suggests that coordinative training of the cervical spine can be an effective intervention of neck pain. These impairments might also lead to altered movement strategies of the head.

**Fast cervical rotations**
The study of fast cervical rotations in people with neck pain has found indications of impaired movement smoothness characteristics (Sjölander et al., 2008, Grip et al., 2008),

In this task, the resulting output of the sensorimotor system is evaluated purely with respect to the kinematic characteristics of the head. It is difficult to decompose this information and draw conclusions on what mechanisms are contributing to the impairments. Possible contributing factors to impairments in fast cervical rotations could stem from muscle coordination impairments but it may also be related to a fear of injury.

**Cervical muscle strength**
There is relatively strong evidence that people with neck pain have reduced isometric strength in the neck muscles compared to controls (for a review, see O'Leary et al., 2009). The magnitude of self-rated disability and pain has though not been found correlated with maximum strength (Jordan et al., 1997, Ylinen et al., 2004). However, Ylinen and co-workers (Ylinen et al., 2004) found a significant association between increased pain during the test and reduced strength and suggested that pain might be a confounder in measurement of maximum neck strength.

**Sensorimotor rehabilitation interventions**
Revel and co-workers compared the short-term effect of an eight-week proprioceptive rehabilitation program with treatment as usual (Revel et al., 1994). This program included slow-paced movement involving head relocation exercises, eye-head coordination in slow-pursuits and neck movement to maintain the gaze to a fixed target during perturbations of the trunk. They found increased head repositioning accuracy, range of motion of cervical axial rotations as well as decreased pain compared to treatment as usual. Jull and colleagues (Jull et al., 2007) evaluated the short-term effect of a six-week cranio-cervical flexion (C-CF) exercise compared with the proprioceptive exercise protocol of Revel and coworkers (Revel et al., 1994).
Improvements from baseline within groups, i.e., uncontrolled effects, were reported for head repositioning accuracy, NDI and pain. However, there was no difference in improvements between groups. The C-CF exercise was further evaluated in comparison to a neck flexor strengthening exercise (Jull et al., 2009). The C-CF exercise group showed improved coordination between the deep and superficial neck flexors in the C-CF test after the six weeks intervention. Significant uncontrolled effects were reported in both groups for pain intensity and NDI, but no difference in improvements between groups. This study also investigated the latency of activation of cervical musculature in a rapid arm movement task, but found no difference between groups.

The frequency of exercise was twice a week in all studies and the length of the programs were similar. Both proprioceptive exercise and specific coordinative training of the deep cervical flexors seems to improve head repositioning accuracy (Revel et al., 1994, Jull et al., 2007) and reduce pain (Revel et al., 1994, Jull et al., 2007, Jull et al., 2009). In addition, specific coordinative training of the deep cervical flexors seems to improve coordinative patterns between the cervical flexors (Jull et al., 2009). Most effects were only significant in uncontrolled comparisons; hence, the superiority of either intervention cannot be determined. Additionally, the follow-ups took place one week after the intervention period, thus the long-term effect is unknown.

Röijezon and co-workers investigated the clinical applicability of a new method of neck coordination exercise (Röijezon et al., 2008). In contrast to previous sensorimotor interventions that included closed skills tasks that are predictable to the participant, this method utilized an unpredictable open skills task and visual feedback during performance were required. In motor learning theory, such design should increase learning and transfer to other functions (Guadagnoli and Lee, 2004). In this uncontrolled trial, participants were positive to the method and showed improvements in sensorimotor functions, general health and disability. However, since the study was uncontrolled with only 14 participants the strength of the evidence was low. Nevertheless, these indications of improvements were seen after only a four-week intervention period, so this raises an interest for further evaluation.

In total, the evidence of exercises directly targeting sensorimotor function is promising but the long term effects are unknown. The method by Röijezon and co-workers (Röijezon et al., 2008) showed indications of transfer to other sensorimotor functions in an uncontrolled evaluation. This motivates the need for determining the short- and long-term effect of this exercise compared to best available treatment.
Aims of the thesis

This thesis aim to contribute to the field of musculoskeletal rehabilitation by increasing the knowledge about sensorimotor impairments in women with non-specific neck pain, improve methods for objective characterization of impairments and to study the effects of interventions on sensorimotor function in women with non-specific neck pain. More specifically, this thesis set out to answer the following research questions:

1. Are there specific impairments of active cervical ROM in flexion/extension with respect to upper and lower levels of the cervical spine in women with non-specific neck pain compared with controls?
2. To what extent are cervical ROM impairments of the upper and lower cervical levels associated with pain, self-rated function and activity limitations in women with non-specific neck pain?
3. Can different movement strategies explain possible impairments in active cervical ROM in women with non-specific neck pain?
4. Are head postures in sitting different in women with non-specific neck pain compared to healthy controls?
5. To what extent does neck coordination training improve sensorimotor function and pain in women with non-specific neck pain compared to best available treatment?
6. What are the consistencies of motor precision metrics in goal directed arm movements in healthy controls?

For research question 5, the following pre-registered hypotheses were tested (ISRCTN trial registration number, ISRCTN92199001):

- The primary hypothesis was that neck coordination exercise had better short- and long-term effects in the form of decreased postural sway and improved end-point precision in goal-directed arm-movements compared with strength training or massage.

- The secondary hypothesis was that neck coordination exercise had a better long-term effect than massage on cervical range of motion, fast cervical rotations and neck pain.
Methods

Study designs
For research questions (RQ) 1-4, a cross-sectional design was deemed appropriate as the causality of impairments was not addressed. RQ 5 was best answered with a randomized controlled trial and RQ 6 required a test-retest reliability design.

RQ 1-5 required a sample from the population of women with non-specific neck pain experiencing activity limitations (NP) and RQ 1-4 and 6 required healthy controls (CON). An overview of design, study samples and laboratory tests is presented in Table 1, along with the partitioning of research questions into separate studies.

Table 1 Overview of design, study samples and laboratory tests

<table>
<thead>
<tr>
<th>Study</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research questions</td>
<td>1, 2</td>
<td>1, 3-4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Design</td>
<td>Cross-sectional</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RCT</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Test-retest</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Sample recruitment</td>
<td>A</td>
<td>B</td>
<td>A</td>
<td>C</td>
</tr>
<tr>
<td>Study populations</td>
<td>CON</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>NP</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>Head movements</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Postural sway</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Goal directed arm movements</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

RCT: Randomized controlled trial; CON; controls; NP: non-specific neck pain

Participants

Definition of sample A
The first study sample included CON and NP and was used for cross-sectional comparisons for RQ 1 and 2 and to evaluate effects of exercise for women with neck pain (RQ5) (ISRCTN trial registration number, ISRCTN92199001).

Inclusion criteria for all participants were women of age range 25-65 and the ability to speak Swedish. Participants with chronic non-specific neck pain, lasting more than three months, must have indicated the neck as the most painful area on pain drawings (Margolis et al., 1986) and reported limitations in activities involving the neck, shoulders and arms. The criteria
of these limitations were >9 points normalised points (0-100) of the first 19 questions from the Disability Arm Shoulder Hand (DASH) questionnaire (Atroshi et al., 2000). Exclusion criteria were trauma related onset of neck pain or diagnoses of fibromyalgia or severe conditions such as cancer and stroke or surgery to the back, neck or shoulder. Participants were also excluded if they had performed strenuous exercise more than three times per week during the last six months. If participants had experienced dizziness or reported pain below the shoulders, this was considered as signs of vestibular disorders or cervical radiculopathy and was furthered investigated in a clinical examination were positive findings led to exclusion.

**Definition of sample B**

The second sample was used for cross-sectional comparisons for RQ 3 and 4. The criteria for inclusion/exclusion followed that from sample A but with the following modifications. The history of pain was minimum six weeks. The inclusion criteria measured by the DASH-questionnaire was replaced by a rating of more than “no disability” but less than “complete disability” on the Neck Disability Index (NDI) (Vernon and Mior, 1991). Participants must have reported impaired capacity on the quality or quantity to work during the last month (Martimo et al., 2009). An additional exclusion criterion was concurrent low back pain.

**Definition of sample C**

The third sample was used for test-retest reliability analyses for RQ 6. The criteria for inclusion were healthy right-handed women with experience of pipetting; they were nurses or university students in nursing and health education programs. The age range was 20-45. Exclusion criteria were any pain or injury to the arm or shoulder.

**Laboratory tests**

All tests except postural sway were performed seated in a rigid wooden chair with back support, and belts crossed over the chest attached to the sides to minimize trunk movement. In all tests except postural sway, kinematics was assessed with an electromagnetic tracker system (FASTRAK, Polhemus Inc., Colchester, VT, USA), consisting of a transmitter and a set of receivers, that measures the three-dimensional position and orientation. The receivers were placed on the participants and the transmitter was rigidly attached to the front of the chair. All instructions to the participants were pre-recorded.

**Head movements: Cervical range of motion test**

To answer RQ 1-4, we applied a simple method for separating upper and lower cervical levels in sagittal flexion/extension (e.g., Hsu et al., 2007). In this method the thorax, cervical spine and head form a three-segment model
that allows measurement of flexion and extension at the upper and lower cervical levels.

**Setup and testing procedure**

The three-segment model included the thorax, cervical spine and the head and two receivers were used for the measurement. The kinematics of the head was measured by a receiver located on the forehead attached to a rigid head band. The relationship between the head receiver and the centre of the Co-C1 joint was determined by landmarks collected bilaterally of the mastoid processes. A second receiver was attached to the dorsal spinal process of Th2. The sampling frequency was 60 Hz. This protocol were used for sample A to answer RQ 1,2 and 5.

Participants were instructed to close their eyes and sit in a normal upright position, this defined the starting position. Three repetitions of maximum flexion/extension were carried out at slow pace with randomized starting direction.

**Definition of the three-segment model**

The three segment model was constructed by coupling the thorax, cervical spine and head segment (Figure 2). The inferior end of the thorax segment was defined to start in a virtual point 20 cm below the Th2 receiver and end in the centre of the receiver. This receiver also defined the inferior end of the virtual cervical spine segment that ended in the Co-C1 joint by the estimation of the forehead receiver. Lastly, the head segment was defined from the Co-C1 joint to the forehead receiver.

The angle between the thorax and cervical segment denoted the angle of lower cervical (LC) levels and the angle between the cervical segment and the head segment was denoted the angle of the upper cervical (UC) level. The participants starting position defined zero flexion/extension.
Figure 2. Illustration of the three-segment model (white lines) for measuring upper and lower angles for flexion and extension superimposed on a photograph of one of the supervisors (MB) in the normal upright starting position. The arrows indicate the location of the two receivers. The axes illustrate the orientation of the laboratory coordinate system. Reprinted from Rudolfsson et al. (2012) with permission.

**Changes in the protocol for sample B**

Based on conclusions from interpretation of results from sample A in study I, modifications of the protocol for data collection were performed for sample B and study II. Landmarks of the cantus of the eyes relative the head receiver were collected in order to anatomically anchor the distal part of head segment. The inferior end of the thorax segment was anchored to the midpoint between Th8 and processus xiphoideus in relation to the thorax receiver. Landmarks of the external auditory meatus was collected to allow for estimation of the location of the centre of mass (CoM) of the head. The sampling frequency was 40 Hz.

In addition to the test of maximum flexion/extension, a test of maximum protraction/retraction with three repetitions at slow pace was carried out. The instructions of the test were to push the head forward/backward as far as possible. The retraction task was only used to avoid drift in starting posture. The instructions prior testing were also elaborated. The starting posture was obtained by a self-balancing procedure in which the participants performed flexion/extension movements with decreasing amplitude until a natural posture was obtained (Solow and Tallgren, 1971). This natural head posture was used to define zero flexion extension of all angles. The UC angle in this posture were denoted UC_NHP and the LC angle were denoted LC_NHP.
Outcome measures
The maximum values of ROM in flexion and extension for the UC and LC was calculated relative the starting posture as outcomes for the test of cervical flexion/extension ROM. Flexion was defined as positive direction for both angles. In addition, the angle between the thorax segment and the cervical segment at the starting position was used to describe the starting posture.

Additional outcome measures were calculated for Sample B. The position of centre of mass of the head relative the receiver on the thorax (Th2) was calculated for the test of cervical flexion/extension and protraction. The estimation of the participants head CoM were based on data from seven women (see table 16 in Yoganandan et al., 2009). If the auditory meatus and eyes are horizontally aligned, the CoM of the head corresponds to a position 2.91 cm superior to the auditory meatus. To estimate the gravitationally induced torque acting on the cervical spine during the ROM tests, the horizontal lever arm, i.e., the anterior-posterior projection of the distance between the Th2-receiver and the CoM of the head was calculated during the ROM tests for each direction separately. The lengths of this lever arm at maximum ROM from the global cervical flexion/extension test was summarised (HCM_global) and used together with the head CoM migration from maximal protraction (HCM_prot) as outcome variables.

To estimate head posture in convention with the literature, a measures describing a protracted head, often called forward head posture (FHP), and a measure describing head extension (HE) as the orientation of the ear-eye line relative the horizontal was used (Silva et al., 2010). These were defined so that greater values describe a greater protraction and head extension.

Postural sway
Measurements of postural sway were assessed with six degrees of freedom force platform (AMTI model OR6-5, Advanced Mechanical Technology, Inc., Watertown, MA, USA). The sampling frequency was 200 Hz.

During the test, the participants stood barefoot with a stance width of 18 mm, eyes closed, and arms crossed over the chest. The instructions were to stand as naturally as possible, without tension or intentional body sway. A short practise trial was carried out before the test and the test duration was then 190 s.

The centre of pressure (COP) migration was decomposed into the slow rambling and fast trembling components by the method of Zatsiorsky and Duarte (1999). In short, separately for the anterior-posterior and medio-lateral directions, the COP position when the horizontal force were equal to zero were identified. These positions were interpolated with a cubic spline to form the rambling trajectory. The trembling trajectory was calculated as the difference between the COP trajectory and the rambling trajectory. The
magnitude of the COP, rambling and trembling trajectory was calculated as the 95% confidence ellipse area respectively. These were used as outcomes and denoted COP area (COP-A), rambling area (Ra-A) and trembling area (Tr-A) for RQ5.

**Head movements: Fast cervical rotations**
Receivers were placed on the head and Th2 as described in the test of cervical range of motion. Instructions were to turn the head as fast as possible to the right/left. Three repetitions in each direction was carried out with start in neutral face forward position. Eyes were closed during the test. The sampling rate was 60 Hz.

The orientation of the head receiver and Th2 receiver were software aligned to the laboratory coordinate system when the participants sat in their starting position. Thus, head rotations were calculated relative the Th2 receiver around the vertical axis. The initial aim was to analyze the jerkiness of the movement. However, results available after the planning of RQ5 indicated that this measure has poor sensitivity and reliability (Röijezon et al., 2010), thus the peak velocity of fast cervical rotations that has substantially better sensitivity and reliability (Röijezon et al., 2010) was used instead for RQ5.

**Precision of goal directed arm movements**

**Single target task**
The set-up was identical to Sandlund et al. (2008) and used to answer RQ 5. A wooden pointer mounted on a plastic plate was attached to the palm of the right hand. The pointer was in line with the third digit and extended 20 cm. This was done to eliminate influence of fine motor control of the hand by keeping fingers extended and restricting possible contribution of movements distal to the wrist. A receiver rigidly attached to the plate estimated the tip of the pointer during the test and the sampling rate was 30Hz. The target was 1 cm in diameter, consisted of soft foam rubber extending from a stick parallel to the frontal plane, and was mounted on a tripod. The target was placed at eye-height in front of the participant at the distance of the wrist of the extended left arm, and then 20 cm to the left of the participants’ left acromion.

The instructions were to place the pointer tip at the target as fast and accurately as possible, without corrections and to hold the pointer still for a few seconds.

Movement termination was defined as the time when velocity of the pointer tip dropped below 10% of maximum velocity plus additional 0.5 s (Sandlund et al., 2008). The end-point precision was estimated as the variable error (VE) by means of the volume of a confidence ellipsoid spanned
by three axes representing the variable error in the three dimensions of the 15 trials (Adamovich et al., 2001).

**Multiple targets task**
A model for goal directed arm movements to multiple targets was used for answering RQ6. For this model, a repetitive precision work task consisting of pipetting liquids was selected. To minimize contribution of movement below the wrist, the grip of the pipette was secured from changing during the session by Velcro tape around the hand. The table height was adjusted so that the lower arms would be horizontal when arms were relaxing on the table. The starting position was a big pickup-tube and the target was one of eight small tubes, as indicated by light emitting diodes mounted below the tubes (see Figure 3).

![Figure 3. Workstation set-up](image)

One test session consisted of transferring liquid from the start tube twenty times to each target tube. In total, 160 cycles were performed with randomized target allocation paced by a metronome to a cycle time of 2.8 s per cycle. For familiarization with the task, all test sessions were preceded by 100 pipetting cycles. The participants carried out three sessions distributed over a three week period with identical conditions.

In this setup, two FASTRAK systems were synchronized to allow for 8 receivers. One receiver was attached to the pipette to estimate the position of the end of the kinematic chain during the task. Following receivers were located at the dorsal surface of the forearm close to the wrist, close to the distal end of the upper arm and on the right shoulder on top of the acromion. One receiver was attached to the table. Anatomical landmarks were collected bilaterally for all joints in the kinematic chain. Thumb forces were recorded using a thin-film finger-tip force sensor (A201, Tekscan Inc, USA).
Only the part of the pipetting movement where liquid were transferred to the target, denoted the transfer phase, was used for further analyses. This phase started at the time the pipette tip was in the pickup-tube and its velocity was at minimum, and ended when the disposal of liquid in the target tube was done, defined by when the force on the pipette’s push button was maximum.

The kinematic variables calculated are described in Table 2 and Table 3. The measure of motor variability was the cycle-to-cycle standard deviation of the variables, with the exception for the position if the pipette tip (A6-A7 in Table 2), for which the variability was calculated according to the method described in the single-target test.

### Table 2. Pipette-tip kinematic variables describing motor performance in each cycle

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Peak velocity magnitude (cm/s)</td>
</tr>
<tr>
<td>A2</td>
<td>Percent time-to-peak velocity (%)</td>
</tr>
<tr>
<td>A3</td>
<td>Average velocity magnitude (cm/s)</td>
</tr>
<tr>
<td>A4</td>
<td>Distance-to-target at peak velocity (%)</td>
</tr>
<tr>
<td>A5</td>
<td>Distance-to-target near end of movement (%)</td>
</tr>
<tr>
<td>A6</td>
<td>Three-dimensional (3D) trajectory position at peak velocity (cm, cm, cm)</td>
</tr>
<tr>
<td>A7</td>
<td>3D trajectory position near end of movement (cm, cm, cm)</td>
</tr>
</tbody>
</table>

### Table 3. Kinematic variables describing shoulder-elbow coordination

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>Time-lag of peak velocities (%)</td>
</tr>
<tr>
<td>C2</td>
<td>Cross correlation of joint angle time-series</td>
</tr>
</tbody>
</table>
| C3       | Average continuous relative phase (CRP,°) | Average of CRP across cycle, where CRP at each time instant is(Hamill et al., 2000):

\[
CRP = \phi_{\text{shoulder}} - \phi_{\text{elbow}}
\]

\(\phi\): phase angle as computed in B8 |
| C4       | Time-normalized CRP(°) | CRP recordings are time-normalized to give 11 samples |
**Self-rated characteristics**

Participants with neck pain filled out questionnaires about their health, functioning and symptoms one week prior the testing. The DASH questionnaire was used to measure physical functioning of the upper extremities (Atroshi et al., 2000), and disability related to the neck problems was measured with Neck Disability Index (Vernon and Mior, 1991). Pain was assessed with a 0-10 Numerical Rating Scale (NRS) (Dworkin et al., 2005). Specific for Sample A was that for assessing fear of movement or re-injury, the Tampa Scale of Kinesiophobia (TSK) (Kori et al., 1990) was used and additional single-item questions that were considered to be of importance were also included. The characteristics were used to answer RQ2, hence specified in detail in Table 4.

All participants in Sample A and B also completed a questionnaire of their general health; the Short-Form Health Survey (SF-36) (Ware and Sherbourne, 1992).

<table>
<thead>
<tr>
<th>Total scores/index scores</th>
<th>From NDI</th>
<th>From DASH</th>
<th>Additional questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSK 1-19</td>
<td>Headache</td>
<td>Arm, shoulder or hand pain</td>
<td>Symptom duration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm, shoulder or hand pain during activity</td>
<td>Physically active at leisure time during the last year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tingling (pins and needles) in your arm, shoulder or hand</td>
<td>Can you, due to neck problems:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weakness in your arm, shoulder or hand</td>
<td>Bend the head forward</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Turn the head to the sides</td>
</tr>
<tr>
<td></td>
<td>Car driving</td>
<td></td>
<td>Severity of neck condition</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Do you experience:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neck tension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neck weakness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Jaw disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neck pain during activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neck pain during rest</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pain right now (NRS)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pressure pain thresholds</td>
</tr>
</tbody>
</table>


**Interventions**

Three interventions were used to answer RQ 5. All sessions were individually supervised and carried out two times a week for 11 weeks in total.
Neck coordination exercise
The device for neck coordination exercise and the training method is described in detail by Röijezon and co-workers (2008). The general idea behind the method was to provide neck coordination training by an unpredictable open skills task. The task involved controlling the movement of metal ball on a plate on the head with visual feedback of the ball movements via mirrors (Figure 4). The plate had 5 exchangeable surfaces with different rolling resistance, to provide levels of progression for task difficulty. The device was fastened on the head with straps around the chin and head. The exercise was performed in sitting, and all trials started with the instructions to roll the ball into one of four starting positions, indicated by light emitting diodes. Then the task was to roll the metal ball (weight 220 g) from the starting position to the centre of the plate and hold it still for 3 s. The trial was cancelled if not completed within 45 s. An exercise session was 3 blocks with 6 trials each. The difficulty of the task was increased by changing to a faster surface upon completion of 5 out of 6 trials in a block. The basic programme was carried out for at least 8 sessions (Röijezon et al., 2008) and the progression programme consisted of 12 levels of increasing dose, task variability and difficulty. Two experienced physiotherapist led the exercise intervention after had completed 8 h of education in the programme.

Figure 4. Illustration of the device for the neck coordination exercise. The figure is a reprint from Röijezon et al (2008) under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0).
Strength-training

The strength training program consisted of exercises targeting the neck and shoulder regions. The combination of isometric exercises for the neck and dynamic exercises for the arm/shoulders together in a high-intensity regimen was inspired by the program of Ylinen and co-workers (2006). The frequency of training and the contraction velocities for the dynamic exercises were set to follow established principles for healthy adults (Kraemer et al., 2002). The equipment used was dumbbells, a training bench with adjustable back support, a cable pulley and a head harness. Each session consisted of 3 isometric and 3 dynamic strength exercises.

The isometric exercises targeted the neck muscles. The head harness was connected to the cable pulley for adjustable resistance and the contractions were held for 3 s. Two exercises were performed seated on the bench, and while maintaining the neck stable in relation to the trunk, participants were instructed to tilt slightly forward or to the sides (left/right). The third exercise was performed in supine position, and consisted of small rotations of the head to the left or right. The dynamic exercises targeted the muscles of the shoulder and arms with demands on postural stability of the head and neck. These were, standing chest press, seated shoulder press with dumbbells, and seated row with a straight back.

The rate of progression was determined alternating via a percentage of the participant’s one repetition maximum (1RM) or a rating on the Borg rating of perceived exertion (RPE) scale (Borg, 1970). The 1RM was determined by submaximal testing for the dynamical exercises (Taylor and Bandy, 2005) and with maximal test for the isometric neck flexors (Ylinen et al., 1999). The first three sessions was aimed at learning the exercises correctly and corresponded to an RPE of 11-13 (“fairly light” – “somewhat hard”). The dose was 1 set of 15 repetitions for the isometric exercises and 2 sets of 15 repetitions for the dynamic exercises. The fourth session was devoted to determinations of 1RM. Session 5-11 started with a load of 60% of 1RM (RPE≈13) and with 1×12 repetitions of the isometric exercises and 2×12 for the dynamic. When a participant’s RPE reached < 12, the load was increased at the next session. At the eleventh session or when 80% of the 1RM determined at the fourth session was reached, the last 1RM was determined. After this, the load was set to 75% of 1RM (RPE > 16); repetitions were reduced to 1×8 for the isometric and 2×8 for the dynamic exercises. Increase of load for the remaining sessions was performed when the RPE reached < 14. Two experienced physiotherapist led the exercise intervention after that they had completed 8 h of education in the programme.
Massage
Massage treatment was selected as the sham intervention because it is commonly accepted as pleasant and creditable while there is no strong evidence of effectiveness (Ezzo et al., 2007). Two certified massage therapists performed classical massage to upper body including the back, neck and shoulders. Care was taken not to massage the affected body regions too forcefully.

Primary and secondary outcomes of RQ5
The primary outcomes were chosen from the test of postural sway and goal directed arm-movements and were COP-A, Ra-A, Tr-A and VE. The first four secondary outcomes were chosen from the tests of head movements and were UC-ROM, LC-ROM, axial ROM, and the peak speed of fast cervical rotations and the fifth was pain assessed with NRS.

Statistical analyses
Group differences were tested with t-tests, analysis of variance (ANOVA) or analysis of co-variance (ANCOVA). If residuals of the model could not be assumed to be normal distributed the data was transformed by an appropriate function.

The primary and secondary hypotheses of RQ5 was analysed with a repeated measures multivariate ANOVA (MANOVA) separately. Univariate changes from baseline of group difference between the a priori contrasts including confidence intervals were also calculated.

Associations between self-rated characteristics and ROM-variables (RQ2) were carried out with Orthogonal Partial Least Square regression (O-PLS) (e.g., Eriksson et al., 2006). Models were created for the ROM of the upper and lower cervical levels separately, denoted response variables. The same set of self-rated characteristics, denoted predictors, was used for both models. Explained variance (R²) and cross-validated explained variance (Q² are outcomes. Individual predictor coefficients with confidence interval not overlapping zero was considered significant.

Consistency of motor variability
A nested random effects model was applied to partition the data (eqn. 1), were \( \mu \) is the grand group mean, \( \alpha_{sub} \) is the subject effect, \( \beta_{day(sub)} \) is the effect of days within subject and \( \epsilon_{test(day,sub)} \) is the residual effect of repeated tests within day and subject. The empirical value of cycle-to-cycle variability of each metric \( p \) is denoted \( p_{sub,day,test} \) for each subject, day of testing and test. The eight targets are treated as individual tests.

\[
p_{sub,day,test} = \mu + \alpha_{sub} + \beta_{day(sub)} + \epsilon_{test(day,sub)} \quad (eqn.1)
\]
Eqn. 1 was solved using ANOVA in MATLAB to estimate the between-subjects, between-days within-subject, and within-day within-subject variance components ($S_{BS}^2$, $S_{BD}^2$, and $S_{WD}^2$), corresponding to the variances of $\alpha_{sub}$, $\beta_{day(sub)}$ and $\epsilon_{test(day,sub)}$ along with their 95% confidence intervals. These variances represent the consistencies of the metric.

To obtain sample sizes for sufficient power in future studies, standard statistical procedures were used (i.e., Kraemer and Thieman, 1987). The gross relative variability between subjects was estimated with the coefficient of variation (CV) for each metric in accordance with:

$$CV = \sqrt{\frac{S_{BS}^2 + S_{BD}^2/n_d + S_{WD}^2/n_d \times n_t}{|mean|}}$$  \hspace{1cm} (eqn. 2)

where $n_d$ corresponds to the number of days of repeated measurements and $n_t$ to the number of tests performed within a day.

The necessary sample size in each group ($n_s$), to determine a statistically significant different in a comparison between independent samples, was calculated according to (Mathiassen et al., 2002):

$$n_s = 2 \frac{CV^2}{\Delta^2} \left( t_{2n_s-2,1-\beta} + t_{2n_s-2,1-\alpha/2} \right)^2$$  \hspace{1cm} (eqn. 3)

where $\Delta$ is the effect as a fraction of the mean.

The equivalent equation for repeated measures design (within groups) also included the individual correlation ($\rho$) between the two conditions (Mathiassen et al., 2003):

$$n_s = 2(1-\rho) \frac{CV^2}{\Delta^2} \left( t_{n_s-1,1-\beta} + t_{n_s-1,1-\alpha/2} \right)^2$$  \hspace{1cm} (eqn. 4)

**Sample size determination**

The size of sample A used for cross-sectional analysis of RQ1-2 was determined by the requirements of the RCT (RQ5) and no additional power calculations were performed. For the RCT, sample size was estimated from the test of postural sway and the variable CoP-A. The least clinical relevant change was determined to 1 cm$^2$ based on cross-sectional comparisons between healthy controls and people with neck pain (unpublished data), and on data from Röijezon and co-workers (2008). The standard deviation of the test-retest difference of CoP-A for people with neck pain were 1.07 cm$^2$ (unpublished data). The required number of participants per group to detect
a significant difference (α = 0.05) in CoP-A (β = 0.05) for a repeated measures ANOVA where n=30.

Sample B used for cross-sectional analyses of RQ3 was collected as a part of an ongoing RCT not further investigated in this thesis (Current Controlled Trials registration ISRCTN49348025). Thus, the sample size was determined with respect to the primary outcomes of the ongoing RCT (Björklund et al., 2012). However, to verify that the sample size was adequate for the present RQ and the test of cervical ROM, additional power calculations were performed. Data was used from an unpublished test-retest reliability sample of 13 healthy women measured twice with one week interval. Estimations of minimum size of group difference to detect at a power of 80% (β = 0.2) and significance level α = 0.05 were calculated to detect a 20% difference for the ROM-measures. The effect size was based on differences between controls and women with neck pain from the range of motion analysis of RQ1. For the postural measures, the effect size was determined to 5°. For an unpaired t-test (eqn. 3), the required number of participants per group was 7, 43, 16 and 21 for the outcome variables HCM_global, HCM_prot, FHP and HE respectively.

Sample C was used to estimate consistencies in motor variability for future power calculations, and was thus not preceded by a sample size determination.

**Ethical considerations**

All laboratory tests consisted of active movements performed by the participants. The tests were not considered harmful and have been used previously without any documented adverse effects. Prior to entering the study, all participants were informed about the study and the possibility to withdraw at any time without giving reasons. All participants gave their written consent. The data from the kinematic assessment and answers from questionnaires were stored securely together with a subject number only.

All studies were approved by the regional ethics review board in Uppsala (Study I and III; Dnr: 2007/206, Study II; Dnr: 2011/081 and Study IV; Dnr: 2012/344).
Results

Participants

Sample A was used both for cross-sectional comparisons between healthy controls and women with neck pain (RQ1-2) and to evaluate the effects of exercise for women with neck pain (RQ5). Descriptive data of participants in the cross-sectional comparisons are presented in Table 5.

Table 5 Descriptive data for the neck pain and control groups (mean ± SD, for Duration median and range). The NDI and TSK scores are normalized to the range of 0 to 100.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CON (n = 33)</th>
<th>NP (n = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47±10</td>
<td>51±9*</td>
</tr>
<tr>
<td>BMI</td>
<td>24.9±4.1</td>
<td>26.7±4.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.0±14.2</td>
<td>73.4±13.7</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167±7</td>
<td>166±6</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>56±4</td>
<td>41±7**</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>51.8</td>
<td>47±7*</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4.4±1.4</td>
<td>4.0±0.9**</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>N/A</td>
<td>120 (6-456)</td>
</tr>
<tr>
<td>NRS pain</td>
<td>N/A</td>
<td>3.5±2.0</td>
</tr>
<tr>
<td>NDI</td>
<td>N/A</td>
<td>28±11</td>
</tr>
<tr>
<td>TSK</td>
<td>N/A</td>
<td>27±13</td>
</tr>
</tbody>
</table>

CON: Control group; NP: Neck pain group; BMI: Body mass index; SF-36 PCS: Short Form 36 physical component summary; SF-36 MCS: Short Form 36 mental component summary; Physical activity: How physically active at leisure time have you been in the last year? (1-6); NRS pain: Numerical rating scale of pain (0-10); NDI: Neck Disability Index; TSK: TAMPA Scale of Kinesiophobia; N/A: not applicable. * p<0.05, ** p<0.01, t-test (Mann-Whitney for Physical activity) NP-CON. Reprinted from Rudolfsson et al. (2012) with permission.

The recruitment of participants with neck pain in sample A is illustrated in Figure 5, along with the numbers of participants analysed at short-term and 6-months follow up (RQ5).
Figure 5. Flow diagram of recruitment process, group allocation and participation in the three interventions. All participants who completed a follow up were included in the corresponding analysis. NCE: Neck Coordination Exercise; ST: Strength Training; TAU: Treatment as usual.

*Reported elsewhere. **Two subjects excluded due to incorrect inclusion and missing pre test data. ***One subject could not attend short-term evaluation due to illness but attended the six month evaluation. ****Two subjects excluded due to trauma not related to interventions. *****One subject is missing postural sway measures, thus n=27 for primary outcome measures. Reprinted from Rudolfsson et al. (2014) with permission.

The randomization in study III allocated 36 participants in each of the three groups and demographics and clinical characteristics of those who completed the baseline measurement are presented in Table 6.
Table 6 Baseline demographic and clinical characteristics of the participants in the three intervention groups. The NDI and DASH scores are normalised to the range of 0-100.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>NCE (n=35)</th>
<th>ST (n=35)</th>
<th>Massage (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50.7 (8.6)</td>
<td>51.6 (9.0)</td>
<td>51.2 (9.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.1 (13.1)</td>
<td>74.1 (14.0)</td>
<td>73.5 (14.8)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.0 (5.1)</td>
<td>164.7 (5.0)</td>
<td>165.1 (8.5)</td>
</tr>
<tr>
<td>Pain duration(a) (months)</td>
<td>120 (72, 204)</td>
<td>123 (60, 234)</td>
<td>84 (27, 180)</td>
</tr>
<tr>
<td>Pain (NRS)(b)</td>
<td>5 (4, 6)</td>
<td>6 (4, 6)</td>
<td>6 (4, 7)</td>
</tr>
<tr>
<td>DASH 1-19(a)</td>
<td>21.1 (14.5, 34.2)</td>
<td>25 (15.8, 31.6)</td>
<td>26.3 (15.8, 42.1)</td>
</tr>
<tr>
<td>NDI</td>
<td>26.0 (10.3)</td>
<td>28.6 (10.1)</td>
<td>30.8 (11.1)</td>
</tr>
<tr>
<td>SF-36 PCS(a)</td>
<td>43.1 (39.0, 46.2)</td>
<td>39.0 (36.3, 45.9)</td>
<td>39.0 (35.7, 47.3)</td>
</tr>
<tr>
<td>SF-36 MCS(a)</td>
<td>49.4 (38.8, 55.3)</td>
<td>52.3 (42.6, 56.1)</td>
<td>46.5 (33.0, 54.5)</td>
</tr>
</tbody>
</table>

NRS: Numerical Rating Scale, DASH: Disability Arm Shoulder Hand questionnaire. NDI: Neck Disability Index. Treatment expectations: SF-36 PCS and MCS: Short Form health survey Physical Component Summary and Mental Component Summary. \(a\):Median and 25\textsuperscript{th}-75\textsuperscript{th} percentiles. Reprinted from Rudolfsson et al. (2014) with permission.

Sample B consisted of 140 NP and 40 CON and the descriptive statistics is presented in Table 7.

Table 7. Descriptive statistics for the control and neck pain groups (mean and SD, for Duration median and inter quartile range). The NDI is normalised to the range of 0 to 100

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CON (n=40)</th>
<th>NP (n=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 (12)</td>
<td>47 (12)</td>
</tr>
<tr>
<td>BMI</td>
<td>23.3 (2.8)</td>
<td>24.7 (4.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.4 (11.8)</td>
<td>65.9 (8.8)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.2 (5.6)</td>
<td>165.8 (5.6)</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>55.9 (3.6)</td>
<td>41.7 (6.8)</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>54.2 (7)</td>
<td>49.8 (8.5)</td>
</tr>
<tr>
<td>Physical activity (1-6)</td>
<td>5.0 (0.8)</td>
<td>4.3 (1.0)</td>
</tr>
<tr>
<td>Duration (months)</td>
<td>N/A</td>
<td>60 (24-124)</td>
</tr>
<tr>
<td>NRS pain</td>
<td>N/A</td>
<td>4.62 (1.8)</td>
</tr>
<tr>
<td>NDI</td>
<td>N/A</td>
<td>23.2 (8.8)</td>
</tr>
</tbody>
</table>

CON: Control group; NP: Neck pain group; BMI: Body mass index; SF-36 PCS: Short Form 36 physical component summary; SF-36 MCS: Short Form 36 mental component summary; Physical activity: How physically active at leisure time have you been in the last year? (1-6); NRS pain: Numerical rating scale of pain (0-10); NDI: Neck Disability Index; N/A: Not applicable

Sample C consisted of 14 women at the average age of 25 (SD 4.6) years, height 168.4 cm (SD 7.8) and weight 62.1 kg (SD 6.8).
Cervical range of motion (RQ1-3)

Descriptive data for cervical ROM of sample A are presented in Table 8 and Figure 6. To allow for comparisons of ROM-values between sample A and B, sample B is also included in Table 8. Note that the procedure for data collection was slightly modified between the samples (see Methods).

Table 8 Descriptive data (mean, SD) for flexion/extension ROM in the upper and lower cervical levels and axial ROM separately for the control and neck pain group,

<table>
<thead>
<tr>
<th>ROM-variable</th>
<th>Sample A</th>
<th>Sample B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CON (n = 33)</td>
<td>NP (n = 102)</td>
</tr>
<tr>
<td>UC flexion</td>
<td>33.9(6.0)</td>
<td>32.6(6.1)</td>
</tr>
<tr>
<td>UC extension</td>
<td>50.9(8.2)</td>
<td>40.4(9.2)</td>
</tr>
<tr>
<td>UC total range</td>
<td>84.7(8.0)</td>
<td>73.0(11.2)</td>
</tr>
<tr>
<td>LC flexion</td>
<td>21.1(4.5)</td>
<td>16.0(5.4)</td>
</tr>
<tr>
<td>LC extension</td>
<td>5.4(4.2)</td>
<td>3.0(2.8)</td>
</tr>
<tr>
<td>LC total range</td>
<td>26.5(6.7)</td>
<td>19.0(6.5)</td>
</tr>
<tr>
<td>Axial rotation total range</td>
<td>136.2(15.0)</td>
<td>115.2(17.0)</td>
</tr>
</tbody>
</table>

CON: control group; NP: neck pain group; UC: Upper cervical level; LC: lower cervical level; N/A: Not applicable.

Figure 6 Histogram of sagittal ROM in extension (A, C) and flexion (B, D) separate for the upper (A, B) and lower (C, D) cervical levels for neck pain (n = 102) and control subjects (n = 33). The control subjects are mirrored downwards below the x-axis to allow for visual group comparisons. Reprinted from Rudolfsson et al. (2012) with permission.
**Comparisons between upper and lower cervical levels**

For RQ1, sample A was analysed with an ANCOVA for ROM in flexion/extension and found a significant main effect of group (F (1, 132) = 41.44, p < 0.01) and significant interactions for cervical level × group (F (1, 132) = 5.43, p = 0.02) and direction × group (F (1, 132) = 4.98, p = 0.03). In addition, the covariate FHP as well as all other main effects and interactions were also significant.

The significant level × group interaction was further investigated. Readouts from Table 8 shows that total ROM for the upper levels were numerically more reduced (mean 11.7°) than for the lower levels (mean 7.5°) for NP compared to controls. However, these differences might just reflect that the magnitude of ROM was greater in the upper levels (>70°) compared to the lower (<30°) in both groups. To determine if the contribution between the upper and the lower levels to the total ROM differed between CON and NP, the UC/LC ratio was calculated. The ratio was positively skewed, thus log-transformed prior to analysis. An ANCOVA with covariate FHP had a significant main effect of group (F (1, 132) = 4.49, p = 0.036) and FHP (F (1, 132) = 16.58, p =< 0.001) and the UC/LC ratio was greater for the NP group. The greater ratio implies that in a relative comparisons, the NP group had more pronounced ROM impairments at the lower cervical levels.

**Direction specific comparisons**

Two separate ANCOVAs of 2 (group: CON - NP) × 2 (direction: flexion - extension) factorial designs with within-subjects on the second factor and FHP as covariate were conducted for the upper and lower cervical levels separately. In both models, the main effect of group (UC: p < 0.01, LC: p < 0.01) and group × direction (UC: p < 0.01, LC: p = 0.02) were significant. The directions specificity were however different at the two levels; the NP group showed greater reduction in extension for the upper cervical and in flexion for the lower cervical levels compared to controls. This effect is clearly visible in Figure 6.

**Reproducibility of results**

Sample B was first analysed in the same manner as sample A. The separate ANCOVAs of ROM in global flexion-extension showed significant interaction for direction × group for both the upper (p = 0.01) and lower (p < 0.01) cervical levels as well as significant main effects of group. The group difference in UC/LC ratio was also significant (p = 0.02). Hence, the results from Sample A regarding direction- and level-specific impairments in ROM were reproducible in Sample B.
Influence of head posture on range of motion
The third research question was to explore movement strategies behind possible impairments in active cervical ROM in people with neck pain compared to healthy controls. However, the conclusions drawn from Sample A (results for RQ1) led to the replacement of the exploratory approach to specific research questions. Concerning the direction specific impairments, we could not rule out that the starting posture was different between groups in Sample A. As described in the method, the protocol was changed to anatomically anchor the segments of the model for Sample B and a new procedure of obtaining starting position was introduced. This was done to answer the following research question:

3. A Can reduced extension in the upper and flexion in the lower cervical levels in people with neck pain compared to healthy controls be explained by starting posture?

Sample B was analysed to determine if posture, estimated from the three-segment model (UC_NHP and LC_NHP), influenced the direction specific impairments of ROM (UC extension, LC flexion) in NP compared to CON. Descriptive data for these variables for sample B is presented in Table 9

Table 9. Descriptive statistics for all kinematic variables separately for the control and neck pain groups. All variables have unit degrees except for the HCM variables that have unit cm

<table>
<thead>
<tr>
<th>Variable</th>
<th>CON</th>
<th>NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC flex</td>
<td>36.3 (7.8)</td>
<td>33.7 (7.0)</td>
</tr>
<tr>
<td>UC ext</td>
<td>-53.3 (9.9)</td>
<td>-46.0 (10.6)</td>
</tr>
<tr>
<td>LC flex</td>
<td>16.3 (5.3)</td>
<td>11.8 (6.0)</td>
</tr>
<tr>
<td>LC ext</td>
<td>-2.6 (5.9)</td>
<td>-1.8 (4.7)</td>
</tr>
<tr>
<td>HCM Flex</td>
<td>9.7 (1.5)</td>
<td>8.2 (1.9)</td>
</tr>
<tr>
<td>HCM Ext</td>
<td>-10.2 (2.5)</td>
<td>-7.9 (2.7)</td>
</tr>
<tr>
<td>HCM Global</td>
<td>19.9 (3.2)</td>
<td>16.2 (3.8)</td>
</tr>
<tr>
<td>HCM Prot</td>
<td>5.2 (2.0)</td>
<td>4.3 (1.5)</td>
</tr>
<tr>
<td>UC_NHP</td>
<td>9.5 (12.2)</td>
<td>10.6 (9.8)</td>
</tr>
<tr>
<td>LC_NHP</td>
<td>68.4 (7.4)</td>
<td>70.1 (7.5)</td>
</tr>
<tr>
<td>FHP</td>
<td>46.3 (6.4)</td>
<td>45.8 (5.8)</td>
</tr>
<tr>
<td>HE</td>
<td>34.2 (8.6)</td>
<td>33.6 (7.4)</td>
</tr>
</tbody>
</table>

CON: control group; NP: neck pain group; UC_flex: Upper cervical flexion in global flexion; UC_ext: Upper cervical extension in global extension; LC_flex: Lower cervical flexion in global flexion; LC_ext: Lower cervical extension in global extension; HCM_flex: Head center of mass horizontal migration in global flexion; HCM_ext: Head center of mass horizontal migration in global extension; HCM_global: Total range of head center of mass horizontal migration in global extension and extension; HCM_prot: Head center of mass horizontal migration during protraction; UC_NHP: upper cervical angle in the natural head position; LC_NHP: lower cervical angle in the natural head position; FHP: Forward head posture, the degree of head protraction in the natural sitting position; HE: Head extension, orientation of the head relative the horizontal plane in the natural sitting position;
We hypothesised that that reduced extension in the upper- and reduced flexion in the lower cervical levels in people with neck pain can be explained by initial head posture.

Therefore, the parameter estimates of group differences in degrees along with 95% confidence intervals were calculated for both ANOVA and ANCOVA models. For UC extension, these were for the ANOVA -7.3 [-11.0; -3.5] and for the ANCOVA -7.9 [-10.8; -5.1]. The corresponding analysis of LC flexion was for the ANOVA 4.4 [2.3; 6.5] and for the ANCOVA 3.9 [1.9; 5.8]. These group differences was not considered substantially reduced in the ANCOVA models, which in turn lends support to that the direction specific ROM impairments can't be explained by starting posture.

**Gravitationally induced torque**

From the findings of reduced contribution to ROM from the lower levels in NP compared to CON from Sample A, we proposed that this could reflect a strategy to minimize the torque exerted on the cervical spine during the ROM task. By retaining the head CoM closer to the thorax, the lever arm between the thorax and the gravitational forces acting on the head will be minimized. This led to the following research question:

3.B Are people with neck pain performing cervical ROM limited by torque avoidance behaviour compared to controls?

General predictions of such behaviour would be that for tasks that produce less torque on the cervical spine, the magnitude of impairment would decrease compared to a high torque task.

Head translation in protraction and retraction was introduced as an alternate test of assessing cervical sagittal ROM in Sample B (see Methods). This was done because the postural aspects are very different from global flexion/extension. This test requires that the head is kept in horizontal alignment throughout the movement and therefore, the HCM migration is dependent on simultaneous extension in the upper and flexion in the lower cervical spine (anti-phase pattern). The task was deemed suitable for two reasons. First, head translation was shown to produce a greater intervertebral ROM in the Co-C1 and C1-C2 levels compared to global flexion/extension (Ordway et al., 1999). Second, the HCM migration during this task would be less than in global flexion/extension because of the anti-phase movement in the cervical spine.

These two tasks formed an experimental condition and we hypothesized that people with neck pain performing maximal cervical flexion/extension are limited by torque avoidance behavior so that the difference in head CoM migration between neck pain and controls will be greater in maximal global flexion/extension than in maximal protraction. Kinematics for the tests are
shown in Figure 7 for one representative NP participant and descriptive data of head CoM migration for the two groups are presented in Table 9.

Due to the different magnitude in HCM migration between the two tests (see Table 9), the HCM of global flexion/extension and protraction was normalised by scalar multiplication so the mean value for the CON group was equal to one for both outcomes..

A repeated measures ANOVA of the two test conditions showed a significant main effect of group (F(1, 158) = 21.57, p = <0.001) and a non-significant interaction for group × test (F(1, 158) = 0.501, p = 0.48). The non-significant interaction supports that the groups have equal behaviour in response to the two different tasks.

**Figure 7.** Upper (UC), lower (LC) and thorax segment (Thx) angles from the 3-segment model (upper panel), and head center of mass migration (HCM, lower panel) for one trial of global cervical flexion (left column), global cervical extension (middle column) and head protraction (right column) for a representative subject in the neck pain sample

**Associations to health, functioning and symptoms (RQ2)**

The NP group from sample A was analysed to determine the association between self-rated characteristics and ROM-variables. The O-PLS model for the total range of UC ROM had an explained variance (R²Y) of 16% and the cross-validated explained variance (Q²) of 8%. The corresponding result for LC was 19% and 9% and for ROM in axial rotation 20% and 13%. The regression coefficients are presented in Table 10.
Table 10. The O-PLS regression coefficients of the significant predictors of ROM and Spearman’s rank-order correlation coefficient (ρ).

<table>
<thead>
<tr>
<th>Category</th>
<th>Predictor</th>
<th>UC ROM Coef</th>
<th>UC ROM ρ</th>
<th>LC ROM Coef</th>
<th>LC ROM ρ</th>
<th>Axial ROM Coef</th>
<th>Axial ROM ρ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head movement impairments</td>
<td>Bend the head forward</td>
<td>-0.079</td>
<td>-0.33</td>
<td>-0.101</td>
<td>-0.33</td>
<td>-0.058</td>
<td>-0.27</td>
</tr>
<tr>
<td></td>
<td>Bend the head backward</td>
<td>-0.060</td>
<td>-0.31</td>
<td>NS</td>
<td>NS</td>
<td>-0.069</td>
<td>-0.34</td>
</tr>
<tr>
<td></td>
<td>Turn the head to the sides</td>
<td>-0.063</td>
<td>-0.30</td>
<td>-0.044</td>
<td>NS</td>
<td>-0.080</td>
<td>-0.38</td>
</tr>
<tr>
<td>Activity limitations</td>
<td>DASH 1-19</td>
<td>-0.066</td>
<td>-0.26</td>
<td>-0.085</td>
<td>-0.28</td>
<td>-0.056</td>
<td>-0.27</td>
</tr>
<tr>
<td></td>
<td>Car driving</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.045</td>
<td>NS</td>
</tr>
<tr>
<td>Pain and symptom related</td>
<td>Pain right now</td>
<td>-0.039</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.03</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Neck pain during activity</td>
<td>-0.051</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.058</td>
<td>-0.28</td>
</tr>
<tr>
<td></td>
<td>Arm, shoulder or hand pain during</td>
<td>-0.047</td>
<td>NS</td>
<td>-0.047</td>
<td>NS</td>
<td>-0.052</td>
<td>-0.20</td>
</tr>
<tr>
<td></td>
<td>activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arm, shoulder or hand pain</td>
<td>-0.035</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Neck pain during rest</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.058</td>
<td>-0.25</td>
</tr>
<tr>
<td></td>
<td>PPT subocciput</td>
<td>NS</td>
<td>NS</td>
<td>0.062</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Neck stiffness</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.055</td>
<td>-0.27</td>
</tr>
<tr>
<td></td>
<td>Neck condition</td>
<td>-0.045</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.062</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Neck tension</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>-0.030</td>
<td>NS</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Physical activity during leisure</td>
<td>0.056</td>
<td>0.24</td>
<td>NS</td>
<td>0.20</td>
<td>0.029</td>
<td>NS</td>
</tr>
</tbody>
</table>

O-PLS: Orthogonal Partial Least Squares regression; UC: Upper cervical level; LC: Lower cervical level; Coef: O-PLS regression coefficients; ρ: Spearman’s rank-order correlation coefficient; DASH: disabilities of the arm, shoulder and hand; PPT: Pressure pain thresholds. Note. Reprinted with permission from Rudolfsson et al. (2012)
Head posture in sitting (RQ4)
Descriptive statistics of FHP and HE obtained in sample B are presented in Table 9 and independent t-tests were conducted to compare FHP and HE between groups. There was no significant difference between groups, neither for FHP (t(158)=-0.44, p =0.66), nor HE ( t(158)=-0.43, p =0.67).

Effects of neck coordination exercise (RQ5)
The total number of training sessions offered were 22 and 29 participants completed the intervention in the NCE group (Figure 5).

The repeated measures MANOVA was significant for the short-term evaluation of all primary outcomes (time × group: F(8, 160) = 2.18, p = 0.03). The only significant univariate analysis was for the outcome end-point precision (VE). This was not present in the predefined contrasts (Table 11), but additional analysis revealed that VE was significantly improved for the ST group compared to the Massage group with the effect −0.11 [−0.20, −0.02]. The analysis of the 6-month effect showed no difference between interventions (time × group: F(8, 156) = 1.03, p = 0.42).
Table 11 Descriptive statistics of primary outcome measures for all participants at baseline, short-term and at six months and effects of exercise as change from baseline compared between groups

<table>
<thead>
<tr>
<th>Outcomes&lt;sup&gt;a&lt;/sup&gt;</th>
<th>NCE Mean (SD)</th>
<th>ST Mean (SD)</th>
<th>Massage Mean (SD)</th>
<th>NCE vs. ST&lt;sup&gt;b&lt;/sup&gt; [95% CI]</th>
<th>NCE vs. Massage Effects&lt;sup&gt;b&lt;/sup&gt; [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoP-A (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2.50 (0.60)</td>
<td>2.48 (0.71)</td>
<td>2.56 (0.69)</td>
<td>-0.02 [-0.25, 0.21]</td>
<td>-0.06 [-0.36, 0.24]</td>
</tr>
<tr>
<td>Short-term</td>
<td>2.42 (0.51)</td>
<td>2.36 (0.59)</td>
<td>2.47 (0.75)</td>
<td>-0.04 [-0.23, 0.15]</td>
<td>-0.09 [-0.33, 0.16]</td>
</tr>
<tr>
<td>Six months</td>
<td>2.43 (0.52)</td>
<td>2.40 (0.69)</td>
<td>2.50 (0.75)</td>
<td>-0.04 [-0.23, 0.15]</td>
<td>-0.09 [-0.33, 0.16]</td>
</tr>
<tr>
<td>Ra-A (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>2.07 (0.58)</td>
<td>2.05 (0.65)</td>
<td>2.15 (0.65)</td>
<td>-0.02 [-0.31, 0.27]</td>
<td>-0.02 [-0.31, 0.27]</td>
</tr>
<tr>
<td>Short-term</td>
<td>2.03 (0.48)</td>
<td>1.95 (0.51)</td>
<td>2.07 (0.66)</td>
<td>0.00 [-0.24, 0.25]</td>
<td>0.00 [-0.24, 0.25]</td>
</tr>
<tr>
<td>Six months</td>
<td>2.04 (0.50)</td>
<td>2.01 (0.63)</td>
<td>2.12 (0.69)</td>
<td>-0.04 [-0.24, 0.16]</td>
<td>-0.07 [-0.31, 0.16]</td>
</tr>
<tr>
<td>Tr-A (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.96 (0.32)</td>
<td>0.99 (0.32)</td>
<td>0.97 (0.33)</td>
<td>0.00 [-0.09, 0.09]</td>
<td>-0.01 [-0.14, 0.12]</td>
</tr>
<tr>
<td>Short-term</td>
<td>0.91 (0.25)</td>
<td>0.93 (0.32)</td>
<td>0.93 (0.35)</td>
<td>0.00 [-0.09, 0.09]</td>
<td>-0.01 [-0.13, 0.10]</td>
</tr>
<tr>
<td>Six months</td>
<td>0.90 (0.27)</td>
<td>0.92 (0.34)</td>
<td>0.93 (0.33)</td>
<td>0.01 [-0.09, 0.11]</td>
<td>0.01 [-0.13, 0.10]</td>
</tr>
<tr>
<td>VE (cm&lt;sup&gt;3/4&lt;/sup&gt;)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>0.60 (0.15)</td>
<td>0.64 (0.18)</td>
<td>0.58 (0.18)</td>
<td>0.08 [-0.01, 0.17]</td>
<td>-0.03 [-0.10, 0.04]</td>
</tr>
<tr>
<td>Short-term</td>
<td>0.61 (0.15)</td>
<td>0.58 (0.17)</td>
<td>0.60 (0.16)</td>
<td>0.07 [-0.02, 0.17]</td>
<td>-0.03 [-0.11, 0.05]</td>
</tr>
<tr>
<td>Six months</td>
<td>0.63 (0.17)</td>
<td>0.60 (0.20)</td>
<td>0.61 (0.14)</td>
<td>0.07 [-0.02, 0.17]</td>
<td>-0.03 [-0.11, 0.05]</td>
</tr>
</tbody>
</table>

<sup>a</sup>Transformed data are presented as outcomes. CoP-A, Ra-A and Tr-A by the square root and VE by the fourth root. <sup>b</sup>Negative values of effects favour the neck coordination exercise. The effect is calculated on only the participants who completed the follow ups, respectively (see fig. 2). CoP-A: centre of pressure area, Ra-A: rambling area, Tr-A: trembling area, VE: variability in end point precision, SD: standard deviation, CI: Confidence interval, NCE: Neck coordination exercise, ST: Strength training. Reprinted from Rudolfsson et al. (2014) with permission.
The repeated measures MANOVA of secondary outcomes on sensorimotor function for NCE compared to Massage was not significant (time × group: $F(4, 53) = 1.12, p = 0.36$). The effect on neck pain was also non-significant (time × group: $F(1, 55) = 1.7, p = 0.20$).

Table 12. Descriptive statistics of secondary outcome measures for all participants in the neck coordination exercise (NCE) and massage groups and effects of exercise as change from baseline compared between groups

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>NCE</th>
<th>Massage</th>
<th>NCE vs. Massage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Effects$^a$ [95% CI]</td>
</tr>
<tr>
<td>UC-ROM (degrees)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>71.8 (13.1)</td>
<td>72.5 (9.6)</td>
<td>-0.5 [-3.7; 2.6]</td>
</tr>
<tr>
<td>Six months</td>
<td>70.1 (13.4)</td>
<td>71.9 (7.6)</td>
<td></td>
</tr>
<tr>
<td>LC-ROM (degrees)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>20.4 (6.8)</td>
<td>16.9 (5.4)</td>
<td>-2.0 [-4.0; 0.1]</td>
</tr>
<tr>
<td>Six months</td>
<td>22.4 (7.1)</td>
<td>21.5 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Peak Speed (degrees/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>227.8 (78.8)</td>
<td>213.6 (87.9)</td>
<td>1.2 [-26.3; 28.7]</td>
</tr>
<tr>
<td>Six months</td>
<td>234.4 (96.0)</td>
<td>222.3 (84.8)</td>
<td></td>
</tr>
<tr>
<td>Axial ROM (degrees)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>118.0 (16.5)</td>
<td>112.3 (15.9)</td>
<td>-2.6 [-7.6; 2.5]</td>
</tr>
<tr>
<td>Six months</td>
<td>118.5 (16.5)</td>
<td>116.5 (17.8)</td>
<td></td>
</tr>
<tr>
<td>Pain (NRS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.8 (1.5)</td>
<td>5.8 (1.7)</td>
<td>-0.7 [-1.8; 0.4]</td>
</tr>
<tr>
<td>Six months</td>
<td>3.8 (1.7)</td>
<td>4.0 (2.1)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$Positive values of effects favour the neck coordination exercise. The effect is calculated on only the participants who completed the six month follow up (see fig. 2). UC-ROM: Upper cervical range of motion (ROM), LC-ROM: Lower cervical ROM, Peak Speed: peak speed of fast cervical axial rotation, Axial ROM: ROM of slow paced maximum cervical axial rotations, NRS: Numerical Rating Scale (Dworkin et al., 2005). Note. Reprinted with permission from Rudolfsson et al. (2014).

Goal directed arm movements (RQ6)
To answer RQ6, the variance components of the motor variability metrics were calculated. Table 13 presents these results along with group means of kinematic variables and the cycle-to-cycle standard deviations. These components describe how variability is partitioned between-subjects, between-days within-subjects, and within-day within subjects.
Table 13. Means, motor variability metrics (cycle-to-cycle SDs) and variance components of kinematic motor variability metrics

<table>
<thead>
<tr>
<th>Kinematic Variable</th>
<th>Mean of variable</th>
<th>Mean of Cycle-to-cycle SD</th>
<th>Between-subjects variance of cycle-to-cycle SD $S_{bs}^2$ (95% CI)</th>
<th>Between-day variance of cycle-to-cycle SD $S_{bd}^2$ (95% CI)</th>
<th>Within-subject variance of cycle-to-cycle SD $S_{wd}^2$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cycle-time (seconds)</td>
<td>1.7</td>
<td>0.2</td>
<td>0.0004 (0.0 - 0.002)</td>
<td>0.001 (0.0 - 0.003)</td>
</tr>
<tr>
<td>PIPETTE-TIP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>Peak Velocity (cm/s)</td>
<td>96.7</td>
<td>15.3</td>
<td>6.3 (0 - 25.6)</td>
<td>10.0 (5.2 - 20.8)</td>
</tr>
<tr>
<td>A2</td>
<td>Average Velocity (cm/s)</td>
<td>39.8</td>
<td>7.3</td>
<td>1.7 (0.4 - 5.5)</td>
<td>0.7 (0.2 - 1.6)</td>
</tr>
<tr>
<td>A3</td>
<td>Time-to-peak velocity (%)</td>
<td>44.1</td>
<td>9.7</td>
<td>3.5 (1 - 10.9)</td>
<td>1.5 (0.7 - 3.1)</td>
</tr>
<tr>
<td>A4</td>
<td>Distance-to-target at peak velocity (%)</td>
<td>56.8</td>
<td>11.2</td>
<td>16.6 (5.7 - 49.5)</td>
<td>5.1 (2.7 - 10.6)</td>
</tr>
<tr>
<td>A5</td>
<td>Distance-to-target near end of movement (%) *</td>
<td>4.3</td>
<td>4.2</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>A6</td>
<td>Trajectory variability at peak velocity (cm³)</td>
<td>NA</td>
<td>13.1</td>
<td>114.2 (22.9 - 383.8)</td>
<td>65.8 (36.5 - 134.1)</td>
</tr>
<tr>
<td>A7</td>
<td>Trajectory variability near end of movement (cm³)</td>
<td>NA</td>
<td>1.3</td>
<td>1.2 (0.0 - 4.8)</td>
<td>1.5 (0.9 - 3.1)</td>
</tr>
<tr>
<td>SHOULDER-ELBOW COORDINATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>Time lag of peak velocities (%)</td>
<td>25.6</td>
<td>9.6</td>
<td>1.4 (0 - 6.5)</td>
<td>3.2 (1.7 - 6.7)</td>
</tr>
<tr>
<td>C2</td>
<td>Cross-correlation</td>
<td>0.9</td>
<td>0.04</td>
<td>0.0002 (0 - 0.0008)</td>
<td>0.0003</td>
</tr>
<tr>
<td>C3</td>
<td>CRP (°)</td>
<td>-2.3</td>
<td>4.1</td>
<td>0.3 (0.0 - 1.2)</td>
<td>0.4 (0.2 - 0.8)</td>
</tr>
<tr>
<td>C4</td>
<td>Time-normalized CRP (°)</td>
<td>xx</td>
<td>2.9</td>
<td>0.2 (0.0 - 1.1)</td>
<td>0.7 (0.4 - 1.4)</td>
</tr>
</tbody>
</table>

# Variance components not computed because of violated assumptions in random effects model (refer to methods section for details); NA: Not applicable; * Negative variance component reported as zero; xx: mean values are not reported because time-normalized variables have mean ‘curves’ which cannot be summarized by one number.
The variance components are important for study design since they can be used to determine the number of subjects necessary to detect a group difference of a specified size. To exemplify with a cross-sectional observational design, the CV was calculated using eqn. 2 for the example of one day of testing ($n_d = 1$) and one test ($n_t = 1$) by using the mean of cycle-to-cycle SD and the three variance components, all from Table 13. The resulting number of required subjects to detect a difference in an independent t-test with 20% difference and power of 80% is illustrated in Table 14. The results revealed a large uncertainty in the estimates of the variance components. Hence, to illustrate that, the corresponding number of subjects were calculated for the upper 95%CI bound of the variance components (Table 14).

Table 14. CV, number of participants required for detecting a delta 0.2 of the mean

<table>
<thead>
<tr>
<th>Kinematic Variable</th>
<th>CV</th>
<th>95%CI upper bound</th>
<th>N subjects</th>
<th>95%CI upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle-time (seconds)</td>
<td>0.35</td>
<td>0.50</td>
<td>55</td>
<td>101</td>
</tr>
<tr>
<td>PIPETTE-TIP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1 Peak Velocity (cm/s)</td>
<td>0.35</td>
<td>0.51</td>
<td>50</td>
<td>105</td>
</tr>
<tr>
<td>A2 Average Velocity (cm/s)</td>
<td>0.30</td>
<td>0.43</td>
<td>37</td>
<td>75</td>
</tr>
<tr>
<td>A3 Time-to-peak velocity (%)</td>
<td>0.28</td>
<td>0.42</td>
<td>33</td>
<td>72</td>
</tr>
<tr>
<td>A4 Distance-to-target at peak velocity (%)</td>
<td>0.47</td>
<td>0.73</td>
<td>90</td>
<td>214</td>
</tr>
<tr>
<td>A5 Distance-to-target near end of movement (%)</td>
<td>1.16</td>
<td>1.83</td>
<td>526</td>
<td>1322</td>
</tr>
<tr>
<td>A6 Trajectory variability at peak velocity (cm³)</td>
<td>1.5</td>
<td>2.35</td>
<td>884</td>
<td>2161</td>
</tr>
<tr>
<td>A7 Trajectory variability near end of movement (cm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHOULDER-ELBOW COORDINATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1 Time lag of peak velocities (%)</td>
<td>0.31</td>
<td>0.44</td>
<td>39</td>
<td>79</td>
</tr>
<tr>
<td>C2 Cross-correlation</td>
<td>0.75</td>
<td>1.07</td>
<td>222</td>
<td>443</td>
</tr>
<tr>
<td>C3 CRP (°)</td>
<td>0.28</td>
<td>0.40</td>
<td>32</td>
<td>65</td>
</tr>
<tr>
<td>C4 Time-normalized CRP (°)</td>
<td>0.39</td>
<td>0.60</td>
<td>62</td>
<td>141</td>
</tr>
</tbody>
</table>

# Variance components not computed because of violated assumptions in random effects
CV: Coefficient of variation; CI: Confidence interval; CRP: Continuous relative phase.
Discussion
The general aim of this thesis was to improve methods for objective characterization of impairments and to study the effects of interventions on sensorimotor function in women with chronic neck pain.

Main findings
The main results from applying a model for separating upper and lower cervical contribution in ROM-assessment was that impairments where direction- and level-specific in NP compared to CON; reduced extension in the upper and flexion in the lower levels of the cervical spine. In addition, the lower levels contributed to a lesser extent to total sagittal ROM in NP compared to CON. Two Additional investigation did not support that these findings could be explained by differences in head posture or a kinematic strategy of retaining the CoM of the head close to the thorax in order to minimize gravitationally induced torque in the cervical spine. The magnitude of ROM impairments in the upper and lower levels was associated with self-ratings of function and health in NP.

A specific device for neck coordination exercise showed no superiority in improving sensorimotor functions or decreasing pain in people with neck pain compared to strength training or massage.

The results from the study of the goal directed movement task showed that between and within-subject sizes of most motor variability metrics were too large to make the test suitable in clinical research.

Cervical range of motion
The main novel contribution to assessment of active sagittal cervical ROM was the implementation of a three-segment model that separated the contribution of the upper and lower cervical levels of the spine. We analyzed the ratio between ROM in the upper and lower levels and the result supported that lower levels contributed to a lesser extent to total sagittal ROM in NP compared to CON. In addition, we found reduced extension in the upper and reduced flexion in the lower levels in NP compared to CON. Together, these findings support that a three-segment model gives additional information for characterizing cervical ROM impairments in NP compared to more traditional single-joint models for ROM assessment.

These results were replicated in a second sample. The reproducibility of the results supports that the direction- and level-specific findings can be generalizable to the population of women with non-specific neck pain.

The direction-specific differences between groups in sample A could have been a result of the participants’ self-selected posture, since we used that posture to define zero flexion/extension. The results of reduced flexion in the lower levels and extension in the upper levels correspond well to a predicted
result if the NP were sitting with a more protracted head posture than the CON participants when zero flexion/extension was defined. For this sample a measure of a protracted head, FHP showed trend of group difference ($p=0.055$). The FHP was included as a covariate in the analysis of direction specific impairments but did not explain the direction specific differences. However, we could not control for posture in the upper cervical level since the head segment of the 3-segment model was not anchored in a standardized way. Thus, the assessment of postural aspects was a clear limitation in the measurement protocol.

To determine if aspects of posture could explain the direction-specific findings, the protocol was modified for the second sample to anatomically anchor the entire three-segment model and to use a standardized procedure of self-balancing the head into a natural head posture (Solow and Tallgren, 1971). We hypothesized that reduced extension in the upper- and reduced flexion in the lower cervical levels in people with neck pain can be explained by initial head posture. Independent t-tests of UC_NHP and LC_NHP showed no difference between groups. In addition, the group difference of the posture adjusted model (ANCOVA) was on par with the unadjusted (ANOVA) for both the upper and lower cervical levels. These results do not support our hypothesis.

The lesser contribution of the lower levels to total sagittal ROM may reflect a strategy to retain the head CoM close to the thorax to minimize the gravitationally induced torque acting on the cervical spine. This strategy is in line with theoretical reasoning behind recommendations of training control of the cervical spine in gradually increasing cervical ROM (Jull et al., 2008). To investigate this possibility, we hypothesized that the group difference in head CoM migration would be greater in a high torque task compared to a low torque task. This was tested in global flexion/extension (high torque) contrasted to protraction (low torque) in the second sample. The results did not support the hypothesis.

For both groups, the magnitude of the head CoM migration in protraction was much lower than in global flexion/extension (about 50%). This supports that the gravitationally induced torque was lower in the protraction task compared to global flexion/extension, so a clear contrast was achieved. The protraction task requires keeping the head in horizontal alignment during the movement. Thus, demands on muscle coordination can be challenging since protraction requires flexion in the lower levels and simultaneous extension in the upper levels of the cervical spine. This probably requires coordination between deep and superficial muscles and between the lower and upper levels for deep cervical muscles. There might also be demands of direction specificity to avoid co-contraction of antagonists. These coordinative aspects are not required in the global flexion/extension task. Muscle impairment in people with neck pain have been reported both for
deep and superficial cervical muscles. It has been shown that people with neck pain have reduced strength in the deep cervical flexors (Falla et al., 2004a, O’Leary et al., 2007) and more recent findings suggest similar structural and functional changes to the deep cervical extensors (Schomacher and Falla, 2013). In the superficial muscles, there are reports on increased co-contraction of antagonist musculature during isometric flexion/extension (Fernandez-de-las-Penas et al., 2008). These findings have been corroborated by Lindstrom and co-workers (2011) who tested direction-specificity of neck muscles with isometric circular contractions and found reduced precision in force production. Hence, the added complexity of inter-segmental coordination intrinsic to the protraction task might be a factor for the group difference in this task and the lack of significant interaction between test and group.

Considering the demands on coordination in protraction, the negative finding for the test of the hypothesis and that the protraction test separates groups as well as global flexion/extension, it is possible that different mechanism determine the performance in the two test. A post-hoc analysis of associations between HCM migration in the two tests revealed very low correlations; r=0.24 for NP and r=0.25 for CON. Thus, the explained variance was only 6%. This renders it likely that the two tests reflect different underlying mechanism.

Three-segment model limitations and validity
The magnitude of sagittal ROM for CON in sample A were 84.7° for the upper cervical levels and 26.5° for the lower levels. By summation, this results in a total ROM of 111.2°. These values of sagittal ROM are in correspondence with a radiographic measurement of sagittal ROM for the levels Co-C7 of 106.5° (Ordway et al., 1997). The common definition of the upper cervical spine from functional anatomy is from C0 to C2 (e.g., Swartz et al., 2005). It should thus be stated clearly that the term upper cervical levels used in this thesis is not equivalent to the common definition of upper cervical spine (e.g., Swartz et al., 2005). To get an approximate estimate of the inter-vertebral contribution of ROM to our two cervical levels we used an MRI image of the cervical spine from the litterature (Yuh et al., 1994 ,fig. 2-68). The intersection halfway between Th2 and Co-C1 were at the C6 vertebral level and hence, the upper cervical levels likely contain contribution from flexion/extension from a wider range than the common definition of Co to C2 (e.g., Swartz et al., 2005). However, for our model, no definite range can be defined. The contribution of inter-vertebra rotations to the angles of our 3-segment model are related to the distance from the segment junctions of the model, so that rotations close to a junction is fully mapped to that corresponding angle, and the contribution decreases in
proportion to the distance of the intervertebral joint to the segment model junction.

A limitation with the model is that it uses the rigid body assumption for the thorax in the anchoring of the inferior end of the thorax segment. Since landmarks are collected relative to the Th2 receiver, thoracic flexion/extension between the instance landmarks are collected and natural head posture is recorded can introduce errors in the position estimate of the inferior end of the thorax segment. Such error will decrease the precision of the LC neutral posture. The magnitude of such error was not investigated but should receive attention in future testing of the method.

The three-segment model is most likely not suitable for assessing cervical angles for more complex movement such as protraction. From Figure 7 it is evident that the magnitude of UC extension is substantially smaller in protraction than in global extension. This was a general finding in our data. Given that results from radiology studies show that greater magnitudes of extension in upper cervical levels can be achieved in protraction compared to global extension (Ordway et al., 1999) the angles obtained from the 3-segment model in protraction are likely not valid. The reason for this most likely that the cervical spine is modelled by one segment, and if rotations of opposite direction (flexion and extension) occur simultaneously within this segment, they will partly cancel out in the model angles.

**Associations between ROM impairments and self-ratings**

The results showed that ROM-variables were associated to self-rated head movement impairments, symptoms, activity limitation and physical activity in the NP group (Table 10). The cross-validated explained variance was modest (8 - 13%). The modest explanatory power of the predictors should be interpreted in light of the natural variability in ROM in healthy controls, evident from the histograms in Figure 6. For the NP sample it seems likely the variability in ROM is a sum of such natural variability and variability resulting from the neck pain condition. Hence, if it would be possible to remove the natural variance, the explained ROM variance would likely be higher. Among the significant predictor variables 4 categories can be identifies; ratings of head movement impairments, activity limitations, symptoms and physical activity. Head movement impairments appeared to have slightly stronger associations to reduced ROM compared to the other predictor categories (Table 10). The finding of significant predictors in the symptoms category are coherent with previous findings of correlation between pain intensity during activities and reduced ROM in flexion, extension and axial rotations (Hagen et al., 1997).
Head posture
We aimed to determine if head posture in sitting is different in women with non-specific neck pain compared to controls. The results showed no difference between groups in FHP and HE. The strength of the results is supported by the fact that sample size was about twice the size deemed sufficient to detect a $5^\circ$ difference between groups from the preceding power calculation. The context of the assessment was in a laboratory environment; the participants were sitting in a chair with back-support, eyes closed and had performed a procedure of self-balancing to obtain their natural head posture (Solow and Tallgren, 1971). As both context and tasks are important determinants of motor behavior (Schmidt and Wrisberg, 2008), these results should not be generalized to other context and tasks like computer work in working life.

Effects of neck coordination exercise
A device for neck coordination exercise was selected as the main intervention of interest and the effects of exercise were contrasted to those of strength training and massage.

The participants in the NCE group showed equally good adherence to training as the comparing interventions. One participant had increased headache and neck pain throughout the intervention period and 10 participants showed transient symptoms on a few occasions. Adverse events were not investigated in the contrasting interventions but it is likely that transient symptoms were present in the strength-training group also, considering the relatively high intensity of the program. Overall, we concluded that the NCE was feasible with no serious adverse effect.

The short-term and 6 months follow up showed that the NCE was not superior to strength training (best-available) and massage treatment in improving sensorimotor functions or pain. It must be noted that the NCE group learned the training task and showed improvement in neck coordination by advancing in the progression program, but these effects should be called skill acquisition.

Clinical implications of the RCT
The NCE is a very specific device for neck coordination exercise. It is assumed that controlling the metal ball requires fine coordinative movement of the upper cervical spine. These movements are small in amplitude and with low force requirements. There are many appealing aspects, such as that it is an unpredictable open skills task and is dependent on processing of visual feedback. However, the results of the RCT should not be generalized to other forms of neck coordination training.

The RCT evaluated transfer of exercise to sensorimotor functions and strength training was included as best-evidence for its effect on pain and
disability. A rather surprising indirect observation was the lack of effect from best-available on sensorimotor impairments. The strength-training though showed effect on precision in goal directed arm movement. However, that effect could also be attributed to the principles of tasks specificity training considering that the intervention included seated shoulder presses with dumbbells and chest presses. The general lack of effect of best-evidence raises again a more general concern about the efficiency of rehabilitation for people with neck pain.

Time has passed since the start of the RCT in this thesis but there are no major changes to recommendations for rehabilitation. Falla and co-workers (2013) investigated the effect of an 8-week exercise program for the neck flexor and extensor muscles. The program consisted of 6 weeks of isolated cranio-cervical flexion strengthening and additional 2 weeks of exercise of the global muscles addressed via supine head lifts for flexors 4-pt kneeling head lifts for extensors. The short-term follow up showed increased direction specificity of neck muscle activity of the cervical muscles reduced pain and in the short-term follow up. This is in line with previous findings of retraining of cervical function (Jull et al., 2007, Jull et al., 2009). The study by Falla and co-workers (2013) strengthens the evidence on short-term effects of specific coordinative training of the deep cervical flexors on muscle coordination and pain relief. The evidence of long-term effect is still lacking.

In the present RCT, strength-training was chosen as best-available single treatment (Kay et al., 2005). These recommendation remains, as there are no major changes in evidence of most effective treatment in a more recent review (Kay et al., 2012). Massage was used as sham-treatment (Ezzo et al., 2007) in this thesis, and a more recent update on the effectiveness of massage continues to hold no recommendation for practice (Patel et al., 2012).

**Goal directed arm movements**

A new test of goal directed arm movement was developed in the form of a pipetting task including multiple randomized targets to motivate and stimulate new motor solutions. We estimated the sizes of between- and within- subject variability along with their 95% confidence intervals for commonly used metrics. These fundamental properties are needed to design studies with sufficient power for clinical investigations. The result section (Table 14) exemplified the number of participants needed to obtain a power of 80% at a detectable difference of Δ=0.2 in a cross-sectional study. However, depending on the size of the variance components, fewer participants can be required by changing design to a repeated measures assessment (eqn. 2).

The end point variability of the pipette tip was of primary interest in this task because of the reduced precision in goal directed arm movement
reported in people with neck pain (Huysmans et al., 2010, Sandlund et al., 2008). A tentative explanation for reduced precision is that people with neck pain might have impaired proprioception, which is an important factor in motor planning (Buneo et al., 2002, van Beers et al., 2002).

The results of the pipetting test shows that the number of participants required to detect a relevant difference are beyond what is reasonable in a clinical trial. This raise some considerations around the task design. For example, the task consisted of pipetting liquid to randomly assigned tubes, indicated by light emitting diodes. Prior to actually executing the task, it is suggested that there are three information-processing stages (Schmidt and Wrisberg, 2008). These are labeled perception, decision and action stages (Schmidt and Wrisberg, 2008). Thus, prior to motor planning, the target has to be identified and decisions of how to respond must be taken. The target tubes in this pipetting task were relatively small and closely arranged in a matrix (Figure 3). One tentative explanation to the lack of discriminative power could be that the affordances of the task were not clear. Due to the close arrangement of target tubes it is possible that the participants’ decision was to first transfer the pipette to a location above the matrix of tubes and then rely largely on visual feedback when approaching the target, thus minimizing the priority of optimizing motor planning of the task.

Methodological considerations
The samples of women with non-specific neck pain in this thesis are relatively well described by rigorous inclusion/exclusion criteria for the studies and by the reported questionnaire data. Participants have undergone a screening by a physiotherapist to verify that these criteria are fulfilled. They were recruited by advertising, thus, they should be considered as convenience samples. Hence, there is a slight risk of bias in the recruitment that might lower the generalizability from the samples to the population of women with chronic non-specific neck pain who experienced activity limitations due to neck pain. For this population however, true random sampling is almost unattainable.

Study I was not preceded by a power calculation. However, the results from that study were reproduced in Study II, which strengthens the reliability of the finding. Study II included a power calculation of the individual tests to reassure that we could detect the impairments in cervical ROM required to go further and test the hypotheses of possible explanations to the findings. Study III included a power calculation on one of the outcomes only, thus it may have been underpowered for the other outcomes. Study IV was not preceded by a power calculation but aimed at providing estimates for future power calculations. Since the confidence intervals for many of the estimates were large, the results contains some uncertainty. A larger group would have improved the precision of the estimates.
**Future research**

One of the starting points of this thesis was the need of improved measures to characterize the patients to provide a more specific diagnostic profile (McCarthy and Cairns, 2005). Relating to the results of this thesis, further research on characterization on the specific ROM impairments should focus on gaining knowledge of the mechanisms behind the impairments since that would substantially increase the clinical validity of the test. Such research could investigate the role of coordination between the upper and lower levels of the cervical spine in search for clues behind the direction- and level-specific impairments. Another possibility is to further evaluate the possible torque avoidance behaviour in other tasks with different torque requirements.

Another possibility that could be investigated is that long term pain conditions might lead to a more cautious behaviour and contribute to the persistence of problems. This possibility could be investigated in longitudinal cohort studies.

Research on how to individually assign different component of rehabilitation interventions is needed (McCarthy and Cairns, 2005). The research of the effectiveness of proprioceptive or coordinative interventions should investigate the use of cut-offs for different levels of sensorimotor impairments prior to such training modalities.
Conclusions

- Women with non-specific neck pain have direction- and level-specific impairments in active sagittal cervical ROM; with greater impairments in extension in the upper cervical levels and flexion in the lower levels of the cervical spine.

- The clinical relevance of using a 3-segment model that separates the upper and lower cervical levels for characterisation of cervical ROM impairments for women with non-specific neck pain is supported by a several findings; the level-dependent differences, the magnitude of group difference and the associations between the magnitude of ROM impairments and self-rated health, functioning and symptoms.

- The results suggest that there is no association between a protracted head posture and chronic non-specific neck pain in women when posture is assessed in sitting without performing any explicit task. Assessment in other contexts such as during prolonged computer work should receive focus in future research on the role of head posture in neck pain.

- The novel method for neck coordination exercise is not superior to strength training or massage in improving sensorimotor functions and pain and therefore cannot be recommended for women with chronic non-specific neck pain.

- The consistencies of motor variability metrics in the new work task for studying motor performance in goal directed arm movements were of magnitudes not suitable for the study of precision of arm-movements in clinical research. However, variability of shoulder-elbow coordination and movement velocities can be studied with sample sizes of 40-60 per group in cross-sectional designs.
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