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Sensorimotor control in idiopathic neck pain

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Sensorimotor control in individuals with idiopathic neck pain and healthy individuals:
A systematic review and meta-analysis

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Sensorimotor control in individuals with idiopathic neck pain and healthy individuals:
A systematic review and meta-analysis

Objective: To (1) identify reported tests used to assess sensorimotor control in individuals with idiopathic neck pain and (2) investigate whether these test can quantify differences between individuals with idiopathic neck pain and healthy individuals.

Data sources: Databases AMED, CINAHL, Cochrane Central Register of Controlled Trials, EMBASE, MEDLINE, PEDro, SCOPUS and SportDiscus.

Study selection: Studies reporting sensorimotor outcomes in individuals with idiopathic neck pain or healthy individuals were identified. 1677 records were screened independently by two researchers for eligibility: 43 studies were included in the review with 30 of these studies included in the meta-analysis.

Data extraction: Methodological quality was determined using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Data were extracted using a standardised extraction table.

Data synthesis: Sensorimotor control was most commonly assessed by joint position error and postural sway. Pooled means for joint position error following cervical rotation in individuals with neck pain (range 2.2-9.8°) differed significantly ($p=0.04$) compared to healthy individuals (range 1.66-5.1°). Postural sway, eyes open, ranged from 4.85-10.5cm² (neck pain) and 3.5-6.6cm² (healthy) ($p=0.16$), and for eyes closed, 2.51-16.6cm² (neck pain) and 2.74-10.9cm² (healthy) ($p=0.30$). Individual studies, but not meta-analysis, demonstrated differences between neck

pain and healthy groups for postural sway. Other test conditions and other tests were not sufficiently investigated to enable pooling of data.

Conclusion: The findings from this review suggest sensorimotor control testing may be clinically useful in individuals with idiopathic neck pain. However, results should be interpreted with caution because clinical differences were small and therefore further cross-sectional research with larger samples is needed to determine the magnitude of the relationship between sensorimotor control and pain and assess any potential clinical significance.

Key words: cervical spine; idiopathic neck pain; sensorimotor control; systematic review

List of abbreviations

IQR interquartile range

JPE joint position error

Around 70% of the population will experience neck pain at least once in their lives.¹ Neck pain is also related to high health care costs² and is ranked fourth highest in terms of disability,³ which further emphasizes the need for effective interventions for neck pain. Traditional rehabilitation programs as advocated by both national and international physiotherapy guidelines⁴ seem to be unsuccessful in treating many neck pain problems.⁵ Though short-term effects have been demonstrated, joint mobilisation, massage, traction, and exercise therapy focussed on overall muscle strength do not show sustained effects on patient symptoms in the long-term.⁶

Sensorimotor control is becoming an increasingly reported outcome in neck pain research.⁷ In addition to the term sensorimotor control, other common terms used to describe the components of sensory input and motor output for adequate motor control include proprioception, kinesthesia and somatosensory control. Terminology in the field of sensorimotor control can be confusing as different terms are used interchangeably to address the same system.⁸ In the present review, sensorimotor control testing is used as an umbrella term to describe tests that encompass all the afferent and efferent information streams, as well as the central integration components contributing to joint stability.⁸

Most commonly, individuals suffering from whiplash associated disorders have been studied in investigations of sensorimotor control. Although traumatic cases form an important subgroup in individuals with neck pain, individuals with idiopathic neck pain (which occurs spontaneously) present more frequently in the clinic.⁹ Important differences in individuals with traumatic neck pain, including vestibular deficits and greater balance disturbances¹⁰, limited head steadiness¹¹, structural cervical muscle changes¹², and widespread sensory hypersensitivity¹³ limit

the generalisability of findings from this population to people with idiopathic neck pain. As neck disorders due to trauma appear to involve other balance systems and a more complex presentation, traumatic neck pain and idiopathic neck pain may be regarded clinically as different conditions.¹³

Diverse methods for assessing the sensorimotor system have been reported.¹⁴⁻¹⁷ In a recent review by Michiels et al.,¹⁸ some recommendations for assessment were made based upon examination of a limited number of tests, however these recommendations are limited by lack of a systematic search of the literature and by a lack of qualitative appraisal or meta-analysis. Although in some of the available tests different subsystems might be involved, for example the oculomotor and vestibular systems,^{16,19,20} all methods measure sensorimotor control of the neck. There is currently no evidence to support any one method to measure deficits in the cervical sensorimotor system.²¹⁻²³ Armstrong et al.²⁴ suggest that effective interventions for idiopathic neck pain cannot be established before it is clear how sensorimotor differences between neck pain and healthy control groups can be identified. Therefore, the first important step is to achieve consensus on the best method to assess sensorimotor control in the neck.²⁴

The present systematic review and meta-analysis focussed on the assessment of sensorimotor control in individuals with idiopathic neck pain. The research questions explored are: (1) What tests are used to assess cervical sensorimotor control in individuals with idiopathic neck pain? and (2) Can sensorimotor control tests identify and quantify differences between individuals with idiopathic neck pain and healthy individuals? The findings will inform understanding of the assessment of sensorimotor control in individuals with idiopathic neck pain,

and will be important for future research investigating assessment and interventions for cervical sensorimotor control deficits.

ACCEPTED MANUSCRIPT

METHOD

Identification and selection of studies

A systematic review was conducted searching the electronic databases AMED, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, MEDLINE, PEDro, SCOPUS and SportDiscus up to July 2015. A search strategy, agreed upon by all authors, with terms for sensorimotor control and neck pain was developed. Keywords for the sensorimotor system, included proprioception, sensorimotor control, somatosensory control, vestibular system, postural balance, and sensory feedback. Terms for neck and neck pain were consistent with search strategies recently used by the Cochrane Back Review Group.²⁵ Appendix 1 provides the search strategy used for the database MEDLINE.

To be included, studies needed to report an outcome measure of the sensorimotor system in a population of individuals with idiopathic (also reported as insidious onset) neck pain or healthy individuals. Idiopathic neck pain is defined as neck pain and perceived in either the upper or lower cervical spine with the absence of trauma at the onset of pain development.²⁶ Specific neck pathologies and degenerative or inflammatory diseases were not included. Studies describing participants with only headache or only radiating pain to the arm (i.e., without neck pain per se) were not included. Studies must have specifically excluded individuals with traumatic neck pain to be included in the review. Studies were restricted to those investigating adults (18 years of age or older) as the development of the central nervous system in younger participants may be incomplete compared to adults.²⁷

Titles and abstracts initially, and full-texts secondly, were screened by two reviewers. When the reviewers did not independently agree on the inclusion of a

study, this was resolved by consensus or involvement of a third reviewer. The level of agreement between reviewers was assessed using Cohen's Kappa.

Assessment of characteristics of studies

The methodological quality and risk of bias of included studies were determined using the U.S. National Institute of Health's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.²⁸ Quality assessment was undertaken independently by two reviewers. Disagreements were resolved by consensus or involvement of a third reviewer. Studies were not excluded for high risk of bias.

Data analysis

Outcome measurement data were extracted by the first author using an extraction table agreed upon by all authors. For intervention studies, only the (cross-sectional) baseline data were extracted. For studies that reported data for two or more groups (e.g., participants were measured at baseline and then randomized into intervention groups), baseline data were combined as outlined by The Cochrane Handbook.²⁹ For studies reporting outcomes as medians and interquartile ranges (IQRs), outcomes were converted to means and standard deviations for statistical purposes using the calculations recommended by Wan et al.³⁰ For the joint position error (JPE) test, findings are reported as error in degrees or centimetres. For comparison purposes, outcomes reported in centimetres were converted to degrees using standard trigonometric functions (inverse tangent of opposite-adjacent ratio).

Statistical analyses were performed using Stata 13 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP.). Mean

outcomes reported for different sensorimotor control tests were weighted and pooled. Sample size was used as a weighting factor. Other factors commonly used in the pooling of data for systematic reviews of intervention and diagnostic test accuracy studies were not considered relevant for this review.²⁹ For pooled groups, medians and IQRs are presented. To compare individuals with idiopathic neck pain and healthy individuals, the nonparametric Wilcoxon rank-sum test was used to investigate differences between pooled means.

This review was conducted according to the PRISMA guidelines.³¹ The protocol for this systematic review was prospectively registered on PROSPERO, registration number CRD42015024115.

RESULTS

Flow of studies through the review

After removing duplicates, the electronic database search resulted in 1673 studies (Figure 1). Four additional titles were identified through hand-searching reference lists of included studies. From 1677 records, six were excluded because these were meeting or conference abstracts only, and 54 further studies were not in English or Dutch and therefore excluded. The resulting 1617 titles and abstracts were screened by two reviewers, and 123 were considered as potentially eligible. Reasons for exclusion of the 1494 studies following title and abstract screening were primarily due to failure to meet the inclusion criteria. More specifically, these records either reported outcomes in a different population, did not report the results of sensorimotor control testing or did not involve living human participants. Two reviewers evaluated the full text, and 43 studies were finally included. Studies were included if they either reported a comparison of sensorimotor outcomes between individuals with idiopathic neck pain and healthy individuals, or if they reported outcomes for one of these groups. Both observational studies and intervention studies were included. Studies were excluded if they (1) reported outcomes for a different participant sample than the one described above, (2) did not test sensorimotor control, (3) did not involve living human adults (e.g., model-based, animal and cadaveric studies), or if (4) neck pain was the result of specific pathology. The agreement for the title/abstract and full-text screenings was 0.96 (for chance corrected Kappa $k_w = 0.73$, substantial³²) and 0.85 ($k_w = 0.64$, substantial) respectively. All disagreements were resolved by consensus. Thirty studies reported data suitable for meta-analysis.

Characteristics of studies

Evaluation of the methodological quality and risk of bias of included studies is presented in Table 1. The overall methodological quality for cross-sectional studies ranged from poor to good, and for intervention studies from moderate to very good. The inter-rater agreement for the quality assessment was 0.87 ($k_w = 0.75$, substantial). A common finding that increased the risk of bias was the lack of (reporting for) blinding (34/43 studies, 79%). High risk for measurement error occurred when error assessment was performed manually (mainly in JPE testing), this is not using computerized outcome registration.³

In order to pool data from different studies for JPE and postural sway outcomes, some calculations were performed. For JPE, five studies^{34,36,43,44,52} reported position error in centimetres. To compare data from these studies with other data reported in degrees, centimetres were converted to degrees. In postural sway testing, two studies^{45,46} reported a sway area in mm^2 , and these data were converted to cm^2 to compare these findings with that of other studies.

Sensorimotor outcomes in individuals with neck pain and healthy individuals

In the 43 included studies (Table 2), six different tests were used to assess sensorimotor control in individuals with idiopathic neck pain and healthy individuals. The most commonly used tests were the assessment of JPE and postural sway. Table 3 provides an overview and descriptions of included tests. In the following paragraphs, descriptions of individuals with neck pain refer to individuals with idiopathic neck pain.

For JPE testing, sample sizes of included studies ranged from 7 to 91 individuals. Results were reported and analysed for separate movement directions.

Means for JPE to the neutral head position following rotation ranged from 2.2° - 9.8° (median 3.14° , IQR 2.79° - 3.33°) in individuals with neck pain, and 1.66° - 5.1° (median 2.67° , IQR 2.1° - 3.5°) in healthy individuals. Following flexion-extension movements, means for JPE ranged from 3.2° - 3.5° in individuals with neck pain, and 1.72° - 4.4° in healthy individuals. For JPE following lateral flexion, one study⁵² reported a mean of 2.75° in individuals with neck pain and three studies reported means ranging from 2.1° - 3.2° in healthy individuals. JPE to a pre-set target position was assessed in seven studies. Six studies used a target of 30° left and right rotation, and one study⁶⁴ used a target which was 65% of the range of motion to either side. Only one of these studies⁴⁷ investigated the error from the target in individuals with neck pain and found a mean error of 6.67° following movements in the transverse plane. All seven studies presented mean JPEs from the target for healthy individuals, ranging from 2.2° - 5.46° . Three studies reported JPEs from the target following flexion-extension and lateral flexion for healthy individuals, ranging from 2.9° - 3.5° and 1.8° - 3.6° respectively (Table 4).

Data from 22 studies were pooled for JPE to the neutral position following rotation. This was the only JPE condition with sufficient reported outcomes for meta-analysis. A significant difference ($p=0.04$) existed in JPE between individuals with idiopathic neck pain and healthy individuals (Figure 2).

In postural sway testing, sample sizes of included studies ranged from 9 to 107 individuals. Mean sway areas for eyes open (four studies) ranged from 4.85cm^2 - 10.5cm^2 (median 7.68 , IQR 4.85 - 10.5) for individuals with neck pain and 3.5cm^2 - 6.6cm^2 (median 4.36cm^2 , IQR 3.76cm^2 - 5.65cm^2) for healthy individuals, and for eyes closed (six studies) this ranged from 2.51cm^2 - 16.6cm^2 (median 8.84cm^2 , IQR 2.51cm^2 - 16.6cm^2) (neck pain) and 2.74cm^2 - 10.9cm^2 (median 6.53cm^2 , IQR 4.19cm^2 -

6.99cm²) (healthy). Only one study⁵⁷ reported anteroposterior and mediolateral sway distances (0.45cm and 0.20cm respectively) in individuals with neck pain (eyes open). In three studies investigating healthy individuals, anteroposterior distance ranged from 0.28cm-2.33cm (eyes open) and from 0.44cm-2.30cm (eyes closed). The mediolateral distance ranged from 0.14cm-0.15cm with eyes open and from 0.15cm-3.0cm with eyes closed (Table 5).

Data were pooled for postural sway during both the eyes open and eyes closed conditions. Meta-analyses did not show significant differences (Figure 3) between individuals with idiopathic neck pain and healthy individuals (eyes open: $p=0.16$, eyes closed: $p=0.30$).

The subjective visual vertical was assessed in one study⁶⁹ investigating individuals with idiopathic neck pain. This study compared individuals with neck pain (mean error 2.43°) and healthy individuals (mean error 1.92°) and reported a significant difference between these two groups. Four other studies on healthy individuals reported means for subjective visual vertical ranging from 0.3°-0.55°.

Smooth pursuit neck torsion was assessed in four studies. One study⁶⁶ assessed smooth pursuit neck torsion in individuals with idiopathic neck pain and reported a gain (ratio of eye movement to target movement) difference between the neutral position and a rotated position of 0.06. Three studies reported the smooth pursuit neck torsion difference between the neutral position and a rotated position in healthy individuals, ranging from 0.01-0.02.

The Fly® test was investigated in three studies. While one study⁴⁸ reported outcomes for healthy individuals only, another¹⁶ found significant differences between individuals with neck pain and healthy individuals using three fly patterns. A

third study by Meisingset et al.⁴⁹ found only one out of four patterns to be significantly different between neck pain and healthy groups.

Two studies investigated head steadiness in both individuals with neck pain and healthy individuals.^{11,49} Meisingset et al.⁴⁹ found significant differences in head steadiness between individuals with idiopathic neck pain and healthy individuals. In contrast, Woodhouse et al.¹¹ did not show significant differences between idiopathic neck pain and healthy groups.

DISCUSSION

Findings

This systematic review examined whether sensorimotor control tests can identify and quantify differences between individuals with idiopathic neck pain and healthy individuals. In this first ever quantitative review of this topic, meta-analysis for JPE showed a significant difference between idiopathic neck pain and healthy groups. Consequently, this test may clinically be useful in the examination of individuals with idiopathic neck pain. Meta-analyses for postural sway testing did not show significant differences between individuals with idiopathic neck pain and healthy individuals. However, some individual studies showed differences between these groups. Although the other tests were not reported in a sufficient number of studies to conduct meta-analyses, individual studies for subjective visual vertical, smooth pursuit neck torsion, The Fly® test and head steadiness showed significant differences between individuals with idiopathic neck pain and healthy individuals. Further research would be needed prior to confidently recommending these tests for clinical use.

Included studies had a low to high risk of bias. Most commonly, a lack of blinding of assessors was found, which increased the susceptibility to bias when measurements were taken. The assessment of sensorimotor control, especially when performed manually, can be influenced by knowledge of the condition of a participant.⁷⁵ Furthermore, even though tests were described similarly across studies, procedures, and consequently variances of tests, may have differed considerably resulting in statistical heterogeneity.

This review also found that the use of terminology in the area of sensorimotor control is inconsistent. As defined, sensorimotor control addresses sensory input and

motor output, as well as the coupling between these two.⁷⁶ Consequently, a sensorimotor test should preferably address all these aspects. Because different subsystems may be addressed in sensorimotor control testing (i.e. proprioception, kinesthesia, visuomotor control, vestibular control), differentiating which subsystem is actually being tested is difficult as they would all theoretically simultaneously affect the test outcomes. Including all subsystems is not problematic if the aim is to test sensorimotor control in general, but when aiming to differentiate the contributions of different subsystems, isolating the subsystem(s) of interest would be necessary.

Sensorimotor tests

Most studies investigated sensorimotor control using JPE as the outcome measure. In JPE testing, questions can be raised regarding its validity and its usefulness in the assessment of specific subsystems. Since the neutral neck position is such a commonly adopted position, a memorized position of the head⁴⁷ might be recalled during the test. Recalling a memorized head position may not only involve a sensory component because memory may be relied on more than proprioception. Therefore, the validity of the test in terms of evaluating sensorimotor control may be limited. In studies which use a pre-set target in the transverse plane, recalling a head position from previous experience is less likely as it is a less commonly adopted position for the neck. An advantage of JPE testing is the exclusion of the visuomotor system by blindfolding participants. Blindfolding allows for more specific investigation of the proprioceptive and vestibular subsystems without the interference of the visuomotor system.

Although similar test procedures were used for postural sway testing, the wide range in outcomes (especially in idiopathic neck pain participants, see Figure 3) may

be due to variances between studies regarding exact test procedures, equipment, participant characteristics and measurement errors. These factors are better controlled within single studies but may vary across different studies and measurement settings. Differences in test procedures may therefore have affected the outcomes of meta-analyses in postural sway conditions, limiting comparability of findings between studies. In postural sway testing, the motor output in a quiet stance task is not specifically controlled by the cervical spine; there is no cervical movement through range in response to the sensory input. However, considering the high density of proprioceptive receptors and afferent pathways for the vestibular system in the neck,⁷⁷ postural sway testing is suggested as an appropriate outcome for cervical sensorimotor control.⁸

In subjective visual vertical testing, a tilted line (not aligned with the vertical) is presented on a computer screen, disk or virtual reality device. As the participant is asked to reposition the line by aligning it with the true vertical using an arm task (e.g. moving a computer mouse), the motor output component (and its relevance for the neck) is questionable. Therefore it might be argued that this test does not adequately evaluate cervical sensorimotor control. A variation on the subjective visual vertical test, involving cervical motor output, has been introduced by Geisinger et al.⁷⁸ In the head tilt response test, a line is presented on a virtual reality device. The line is tilted and the participant has to reposition the line along the vertical, not by using an arm task, but by laterally flexing the cervical spine. This better represents a motor output component specific for the neck in cervical sensorimotor control. Similar to subjective visual vertical testing, the outcome measure in the head tilt response test is the error from the real vertical as measured in degrees. This study was excluded from the current review as it did not report outcomes in individuals with idiopathic neck pain. It

is recommended that future research investigates this potentially valid sensorimotor test in idiopathic neck pain.

The validity of the smooth pursuit neck torsion test for sensorimotor control may also be questionable in terms of cervical motor output. This is because it does not include a cervical motor output component but is mainly focused on sensory input (and the response of the eyes following this input). However, since smooth pursuit neck torsion assesses cervical proprioceptive reflexes⁹ (as measured through eye movements) and is believed to isolate the vestibular system (because the trunk, and not the head, is rotated),⁶⁷ the smooth pursuit neck torsion test is considered valuable for sensorimotor testing.^{9,66}

The Fly® appears to be a test that includes both sensory and motor components. The (visual) input in this test is a moving target on a computer screen, and the motor output is the movement of the neck. Furthermore, because the target is constantly moving in an unknown pattern, memorizing a certain head position is not an issue in this test. On the other hand, the random pattern does not allow for differentiation between different cervical movement directions (as JPE testing does). The study by Meisingset et al.⁴⁹ is one of the studies reporting outcomes of The Fly® test and demonstrated findings different to those reported in other studies using this test.^{16,48} Instead of using the original software,⁴⁸ a customised program using similar movement patterns was developed by Meisingset et al.⁴⁹ Although this program might appear similar, error calculations were possibly not consistent with the original test. Hence, their results must be compared and interpreted carefully due to potential software differences.

Although it is assumed that head steadiness is related to proprioceptive ability, sensory input is limited. Head steadiness while attempting to hold the head up

off the treatment table surface in the supine position may also reflect muscle endurance. Hence, it may be argued that head steadiness testing is more a muscle performance test than a sensorimotor control test.

Recently, new sensorimotor tests have been reported by Chen and Treleaven³⁷ ('JPE torsion' and 'Enbloc' tests). The JPE torsion test is a trunk torsion test (the head is kept still and the trunk is rotated relative to the head, similar to smooth pursuit neck torsion testing) in which the repositioning error of the trunk is measured. As the influence of the vestibular system is avoided in the JPE torsion test (because the trunk rather than the head is moved), it is a potentially useful test for differentiating sensorimotor subsystems. In the Enbloc test, the repositioning error of the head and trunk as a block is measured. These tests were investigated in individuals with traumatic neck pain. No literature reporting on these tests in individuals with idiopathic neck pain is available and hence these tests were excluded from the present review. Further investigations of these new tests may help inform our understanding of the various subsystems contributing to sensorimotor control being evaluated in each test.

Study limitations

Meta-analysis was not possible for most sensorimotor tests due to the insufficient amount of literature, despite many studies meeting the criteria for inclusion in the review. Meta-analysis of JPE demonstrated statistically significant differences in JPE between idiopathic neck pain and control groups, however, the clinical relevance of the actual difference in median errors (0.47°) is questionable. Meta-analyses of postural sway did not show significant differences between the two groups. The small number of studies in these meta-analyses, and consequently the

relatively large variance, is likely to contribute to this finding. Furthermore, small sample sizes in some of the pooled studies limit the overall generalizability of individual studies and therefore their results. In addition, as the homogeneity of the samples of pooled studies is unknown, the findings of meta-analysis must be interpreted carefully. Finally, it should be acknowledged that a limitation of reporting the assessment of cervical sensorimotor control in general is the unknown validity of testing due to the absence of a gold standard.

A strength of the present review is the method of study inclusion. Initial searches revealed the literature on sensorimotor tests was limited, but combining data from different study designs allowed for a larger pool of data. This improves the power of reported outcomes and reduces the chance for a type II error.

Recommendations

The findings of the present review support the use of sensorimotor tests to identify differences between individuals with idiopathic neck pain and healthy individuals. Further research is needed to determine the clinical meaning of statistically significant differences in sensorimotor control tests. Future research should therefore not only focus on comparing sensorimotor test outcomes, but also critically assess the clinimetric characteristics of these tests. Newly proposed tests such as the head tilt response test, JPE torsion test, Enbloc test and cervical torsion test should be investigated to determine their value for cervical sensorimotor testing in individuals with idiopathic neck pain.

CONCLUSIONS

The present systematic review investigated the use of tests for sensorimotor control in individuals with idiopathic neck pain compared to healthy individuals. Six tests were identified in the literature that reported data in individuals with idiopathic neck pain, with varying results. Meta-analysis found a significant difference between idiopathic neck pain and healthy groups in JPE testing, and this test may clinically be useful in assessing sensorimotor control. Heterogeneity amongst studies likely contributed to non-significant findings for meta-analyses for postural sway testing. Tests for postural sway, smooth pursuit neck torsion, subjective visual vertical, head steadiness and The Fly® test demonstrated differences in individuals with idiopathic neck pain compared to healthy individuals within single studies, though there were not enough reported data for meta-analyses for these tests. Future research should further inform the clinical meaning of differences and differentiating capabilities of these tests.

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List of figure legends

- Figure 1 Flow of studies through the review.
- Figure 2 Significant difference ($p=0.04$) between medians (and IQRs) of pooled data for joint position error (JPE) to the neutral head position (NHP) in individuals with idiopathic neck pain and healthy individuals.
- Figure 3 No significant differences between medians (and IQRs) for postural sway (eyes open: $p=0.16$, eyes closed: $p=0.30$) in individuals with idiopathic neck pain and healthy individuals.

Appendix 1. Example of search strategy used for the database MEDLINE

Database: MEDLINE. Results: 733

Subject headings and keywords included terms for the sensorimotor system, the neck and neck pain, consistent with search strategies recently used by the Cochrane Back Review Group. The search strategy was customized for searches in other databases, and limited to humans where possible.

#	Searches	Results
1	Neck/	23122
2	Neck.tw.	137020
3	exp Cervical Vertebrae/	30939
4	cervical vertebrae.tw.	1736
5	cervical.tw.	154685
6	cervico*.tw.	10490
7	Neck Muscles/	4896
8	Cervical Plexus.tw.	389
9	Atlanto-Axial Joint/	2398
10	Atlanto-Occipital Joint/	1413
11	Spinal Nerve Roots/	9357
12	Cervical Atlas/	2062
13	(odontoid or cervical or occip* or atlant*).tw.	200863
14	exp Cervical Plexus/	7007
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	355913
16	Neck Pain/	4658
17	cervical pain.tw.	637
18	exp Neck Injuries/	6640
19	neckache.mp. or neck ache.tw. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	33
20	cervicodynia.tw.	9
21	cervicalgia.tw.	64
22	((injur* or pain* or ach* or sore or stiff* or discomfort) adj3 neck).tw.	10177
23	15 and (pain/ or (wounds.mp. and injuries/) or Radiculopathy/ or (Sprains.mp. and Strains/)) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	7081
24	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23	22629
25	15 or 24	358526
26	exp Proprioception/	22928
27	proprioception.tw.	2548
28	exp Somatosensory Disorders/	16666
29	somatosensory disorders.tw.	15
30	sensorimotor.mp.	15800
31	sensory motor.mp.	3966

32	exp Vestibule, Labyrinth/	14927
33	Postural Balance/	15286
34	postural balance.tw.	384
35	Feedback, Sensory/	1308
36	sensory feedback.tw.	1210
37	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	74067
38	25 and 37	3905
39	Randomized Controlled Trial/	386986
40	Controlled Clinical Trial/	88814
41	random*.tw.	673685
42	trial.tw.	349305
43	Observational Study/	8813
44	exp Cohort Studies/	1407638
45	Cross-Sectional Studies/	187828
46	Non randomized controlled trial*.tw.	360
47	Case-Control Studies/	192898
48	Intervention Studies/	7380
49	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	2500958
50	38 and 49	752
51	limit 50 to humans	733

Table 1. Methodological quality and risk of bias assessment of included studies.

Study	1) Research question or objective clearly stated	2) Study population clearly specified and defined	3) Participation rate of eligible persons $\geq 50\%$	4) Subjects selected from same or similar population	5) Sample size justification	6) Exposure(s) of interest measured prior to outcome(s)	7) Timeframe sufficient	8) Different levels of exposures as related to the outcome are examined	9) Exposure measures clearly defined, valid, and reliable	10) Exposure(s) assessed more than once over time	11) Outcome measures clearly defined, valid, and reliable	12) Outcome assessors blinded to the exposure status	13) Follow-up after baseline $\leq 20\%$	14) Adjusted for potential confounding variables	Total (0 to 14)
Al Saif & Al Senany, 2015 ³⁴	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗	✓	✓	n/a	✗	9
Anastasopoulos et al., 1997 ³⁵	✓	✗	✗	✓	✗	✗	✓	✓	✓	✗	✗	✗	n/a	✗	5
Beinert et al., 2015 ³⁶	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	n/a	✓	11
Chen & Treleaven, 2013 ³⁷	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✗	n/a	✓	10
Cramer et al., 2013 ³⁸	✓	✓	✗	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	12
Docherty et al., 2012 ³⁹	✓	✓	✗	✓	✗	✓	✗	✓	✓	✗	✗	✗	n/a	✗	6
Elsig et al., 2014 ⁴⁰	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	n/a	✗	10
Endo et al., 2008 ⁴¹	✓	✓	✓	✓	✗	✗	✓	✗	✗	✗	✓	✗	n/a	✗	6
Grod et al., 2002 ⁴²	✓	✓	✗	✓	✗	✗	✗	✗	✗	✗	✗	✗	n/a	✗	3
Heikkila & Astrom, 1996 ⁴³	✓	✗	✗	✓	✗	✗	✓	✓	✗	✓	✓	✗	✓	✗	7
Heikkila & Wenngren, 1998 ⁴⁴	✓	✓	✗	✓	✗	✗	✓	✓	✗	✗	✓	✗	✓	✗	7
Jørgensen et al., 2011 ⁴⁵	✓	✓	✗	✓	✗	✗	✓	✗	✓	✗	✓	✓	✓	✓	9
Juul-Kristensen et al., 2013 ⁴⁶	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	n/a	✗	10
Kristjansson et al., 2003 ⁴⁷	✓	✓	✓	✓	✗	✓	✓	✗	✓	✗	✓	✓	n/a	✗	9
Kristjansson et al., 2004 ⁴⁸	✓	✓	✗	✓	✗	✓	✓	✗	✗	✗	✓	✓	✓	✗	8
Kristjansson & Oddsdottir, 2010 ¹⁶	✓	✗	✗	✓	✗	✓	✓	✓	✓	✗	✓	✓	✓	✗	9
Malmstrom et al., 2009 ²²	✓	✓	✗	✓	✗	✗	✓	✗	✗	✗	✓	✗	n/a	✓	6
Meisinget et al., 2015 ⁴⁹	✓	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✗	n/a	✓	9

Michaelson et al., 2003 ⁵⁰	✓	✓	✗	✓	✓	✗	✓	✗	✗	✗	✗	✓	n/a	✗	6
Nagai et al., 2014 ⁵¹	✓	✓	✗	✓	✗	✗	✓	✗	✓	✗	✓	✗	n/a	✗	6
Palmgren et al., 2006 ⁵²	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✗	✓	✗	8
Panichaporn et al., 2013 ⁵³	✓	✓	✗	✓	✗	✗	✓	✗	✗	✗	✓	✗	n/a	✗	5
Pereira et al., 2008 ⁵⁴	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✗	n/a	✗	7
Pinsault et al., 2008 ⁵⁵	✓	✓	✗	✓	✗	✗	✗	✗	✗	✗	✗	✗	n/a	✗	3
Quek et al., 2014 ⁵⁶	✓	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✗	n/a	✓	9
Quek et al., 2013 ⁵⁷	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✗	n/a	✓	8
Reddy & Gangavelli, 2011 ⁵⁸	✓	✓	✗	✓	✗	✓	✓	✗	✗	✗	✗	✗	n/a	✗	5
Reddy et al., 2012 ⁵⁹	✓	✓	✗	✓	✗	✓	✓	✗	✗	✗	✓	✗	✓	✗	7
Röijezon et al., 2008 ⁶⁰	✓	✓	✗	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✗	10
Rubin et al., 1995 ⁶¹	✓	✓	✗	✓	✗	✗	✗	✗	✗	✗	✗	✗	✓	✗	4
Rudolfsson et al., 2014 ⁶²	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	12
Sjolander et al., 2008 ⁶³	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✗	✓	n/a	✓	8
Teng et al., 2007 ⁶⁴	✓	✗	✗	✗	✗	✗	✓	✗	✗	✗	✗	✗	n/a	✗	2
Tjell & Rosenhall, 1998 ⁶⁵	✓	✓	✗	✓	✗	✗	✓	✗	✗	✗	✓	✓	n/a	✗	6
Treleaven et al., 2011 ⁶⁶	✓	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✓	n/a	✓	10
Treleaven et al., 2005 ⁶⁷	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✓	n/a	✓	9
Treleaven et al., 2003 ⁶⁸	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✗	n/a	✗	7
Treleaven & Takasaki, 2015 ⁶⁹	✓	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✗	n/a	✗	8
Van den Oord et al., 2010 ⁷⁰	✓	✓	✓	✓	✗	✗	✓	✗	✓	✗	✓	✓	n/a	✓	9
Woodhouse et al., 2010 ¹¹	✓	✓	✗	✓	✗	✗	✓	✓	✓	✗	✓	✗	n/a	✗	7
Woodhouse & Vasseljen, 2008 ⁷¹	✓	✓	✗	✓	✗	✗	✓	✗	✗	✗	✓	✗	n/a	✓	6
Yoshikawa et al., 2008 ⁷²	✓	✓	✗	✗	✗	✗	✗	✓	✗	✗	✗	✗	n/a	✗	3
Yu et al., 2011 ⁷³	✓	✓	✗	✓	✗	✓	✓	✓	✓	✗	✓	✗	n/a	✗	8

Risk of bias for included studies, assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.²⁸

n/a = not applicable.

Table 2. Summary of included studies.

Sample				Results	
Publication	Design	Neck pain	Healthy	Neck pain	Healthy
JPE					
Al Saif & Al Senany 2015 ³⁴	RCT	-	30 (15 F) 25.6±2.1 yr		4.75° [†]
Beinert et al., 2015 ³⁶	Case-control	-	10 (? F) 21.8±3.5 yr		4.6°(2.0)
Chen & Treleaven, 2013 ³⁷	Cross-sectional	-	26 (15 F) 31.0±11.9 yr		2.57°(0.8)
Cramer et al., 2013 ³⁸	RCT	51 (42 F) 47.8±10.4 yr	-	9.8°(3.1)*	
Elsig et al., 2014 ⁴⁰	Case-control	30 (25 F) 36.9±13.62 yr	30 (25 F) 37.2±13.5 yr	3.25°(0.96)	2.67°(.055)
Heikkila & Astrom, 1996 ⁴³	Cross-sectional	-	34 (21 F) 35 (range 26-53 yr)		1.74°(1.2)
Heikkila & Wenngren, 1998 ⁴⁴	Cross-sectional	-	39 (24 F) 35 (range 26-53 yr)		1.77°(1.2)
Kristjansson et al, 2003 ⁴⁷	Case-control	20 (9 F) 30.0±9.1 yr	21 (11 F) 26.9±6.4 yr	3.33°(1.42)	2.48°(1.12)
Malmström et al., 2009 ²²	Cross-sectional	-	15 (7 F) 45 yr (range 29-74)		1.7°(1.2)
Meisingset et al., 2015 ⁴⁹	Cross-sectional	75 (55 F) 43.1±12.9 yr	91 (48 F) 40.8±3.8 yr	5.6 (5.2-6.1) [§]	5.1 (4.6-5.5) [§]
Nagai et al., 2014 ⁵¹	Cross-sectional	-	27 (0 F) 34.3±6.1 yr		Target 30: 3.1 (1.6) Target 60: 2.2 (1.3)
Palmgren et al., 2006 ⁵²	RCT	41 (27 F) 31.9±8.5 yr	-	2.79° [†]	

Pereira et al., 2008 ⁵⁴	Repeated measures case-control	-	30 (22 F) 25.6±5.1 yr		tran 3.0°(1.9) sag 3.2°(2.7)
Pinsault et al., 2008 ⁵⁵	Group comparison study	7 (4 F) 56±9 yr	7 (3 F) 64±12 yr	2.1°(0.4)	2.2°(0.9)
Reddy & Gangavelli, 2011 ⁵⁸	Cross- sectional	-	25 (? F) ? (range 18-30 yr)		tran 3.5°(4.3) sag 3.4 (2.0)
Reddy et al., 2012 ⁵⁹	Pretest posttest study	-	25 (? F) ? (range 18-30 yr)		tran 3.6 sag 3.4
Röijezon et al., 2008 ⁶⁰	Clinical trial	14 (10 F) 35±10 yr	-	2.54°(0.73)	
Sjolander et al., 2008 ⁶³	Controlled comparative group study	9 (9 F) 40±9 yr	16 (13 F) 41±9 yr	2.8 (1.2)	2.1 (0.7)
Teng et al., 2007 ⁶⁴	Cross- sectional	-	20 (9 F) 21.9±3.9 yr		sag 2.9 (2.2) tran 2.7 (2.1) Cor 1.8 (1.4) 2.25°(0.2)
Treleaven et al., 2003 ⁶⁸	Cross- sectional	-	44 (29 F) 34.1±1.8 yr		
Treleaven et al., 2011 ⁶⁶	Cross- sectional	36 (25 F) 37.1±12 yr	-	tran 3.1 (0.7) sag 3.5 (0.7)	
Van den Oord et al., 2010 ⁷⁰	Cross- sectional		83 (0 F) ?		2.8 (1.4)
Woodhouse & Vasseljen, 2008 ⁷¹	Case-control	57 (38 F) 38.19±10.8 yr	57 (28 F) 38.2±10.9 yr	3.17 (1.1)	2.86 (1.2)

Postural sway

Beinert et al., 2015 ³⁶	Case-control	-	10 (? F) 21.8±3.5 yr		Sway 38.0 (4.6) cm
Endo et al., 2008 ⁴¹	Cross-sectional	-	20 (4 F) 37.9±9.3 yr		EO 3.50 (1.47) EC 4.19 (2.52)
Jørgensen et al., 2011 ⁴⁵	Cross-sectional	85 (85 F) 45±8.2 yr	107 (107 F) 45±8.6 yr	EO 485 (236) EC 884 (587)	EO 470 (286) EC 699 (386)
Juul-Kristensen et al., 2013 ⁴⁶	Cross-sectional	-	10 (10 F) 35.90±12.45 yr		EO 401.50 (327.49) EC 653.50 (285.96)
Michaelson et al., 2003 ⁵⁰	Comparative group study	9 (9 F) 40±9 yr	16 (13 F) 41±9 yr	EO 10.5 (7.3) EC 16.6 (11.7)	EO 6.6 (4.7) EC 10.9 (6.5)
Panichaporn et al., 2013 ⁵³	Cross-sectional	-	14 (11 F) 44.4±5.96 yr		EO ML 0.14 (0.08) AP 0.28 (0.10)
Quek et al., 2014 ⁵⁶	Cross-sectional		20 (20 F) 71.40±5.1 yr		EO 2.33 (0.9) EC 2.30 (1.1)
Quek et al., 2013 ⁵⁷	Cross-sectional	54 (30 F) 66.0±4.9 yr	-	AP 0.45** ML 0.20**	
Rubin et al., 1995 ⁶¹	Cross-sectional	-	52 (27 F) 36.43±16.36 yr		ML EO 0.15 EC 0.15 AP EO 0.40 EC 0.44
Rudolfsson et al., 2014 ⁶²	RCT	101 51.2±8.9 yr	-	2.51 (0.66)*	
Treleaven et al., 2011 ⁶⁶	Cross-sectional	36 (25 F) 37.1±12 yr	-	EO 14.2 (50) EC 39.1 (104)	
Yoshikawa et al, 2008 ⁷²	Prospective clinical study	-	29 (8 F) 59.8 (range 28-75 yr)		EC 2.74 (2.0)
Yu et al., 2011 ⁷³	Cross-sectional	-	20 (? F) 30.25 yr (SEM 2.1)		EC AP 14.25 (2) ML 29.75 (2.7)

SVV					
Anastasopoulos et al., 1997 ³⁵	Case-control	-	29 (? F) 45.5±18.3 yr		0.3°(0.8)
Docherty et al., 2012 ³⁹	Cross-sectional	-	50 (40 F) 47.9±8.7 yr		-0.37°(0.75)
Grod & Diakow, 2002 ⁴²	Cohort study	-	17 (7 F) 38.6 (range 12-66 yr)		0.55°(0.62)
Panichaporn et al., 2013 ⁵³	Cross-sectional	-	14 (11 F) 44.4±5.96 yr		0.80 (0.45)
Treleaven & Takasaki, 2015 ⁶⁹	Cross-sectional	36 (20 F) 32.7±13.8 yr	48 (35 F) 29.4±10.8 yr	2.43°(0.98)	1.92°(0.96)
SPNT					
Pereira et al., 2008 ⁵⁴	Repeated measures case-control	-	30 (22 F) 25.6±5.1 yr		0.02 (0.03)
Tjell and Rosenhall, 1998 ⁶⁵	Double-blind clinical study	-	30 (15 F) 47 (range 29-59 yr)		0.02 (0.02)
Treleaven et al., 2005 ⁶⁷	Prospective observational study	-	50 (30 F) 29.9 (range 19-45 yr)		0.01 (0.01)
Treleaven et al., 2011 ⁶⁶	Cross-sectional	36 (25 F) 37.1±12 yr	-	0.05 (0.01)	
The Fly® test					
Kristjansson et al., 2004 ⁴⁸	Case-control		20 (20 F) 29.3±8.6 yr		A: 4.07 (0.96) B: 3.79 (0.93) C: 4.24 (1.10)

Kristjansson & Oddsdottir, 2010 ¹⁶	Case-control	18 (11 F) 38.0±8.3 yr	18 (8 F) 32.2±10.9 yr	A: 2.06 (0.52) B: 2.70 (0.88) C: 3.42 (1.30)	A: 1.78 (0.33) B: 2.17 (0.44) C: 2.64 (0.52)
Meisingset et al., 2015 ⁴⁹	Cross-sectional	75 (55 F) 43.1±12.9 yr	91 (48 F) 40.8±3.8 yr	1A 2.2 (2.0-2.4) 1B 2.1 (2.0-2.2) 2A 3.1 (2.9-3.3) 2B 2.8 (2.7-3.0)	1A 2.5 (2.3-2.7) 1B 2.1 (2.0-2.3) 2A 3.3 (3.1-3.5) 2B 2.8 (2.6-2.9)
Head steadiness					
Woodhouse et al., 2010 ¹¹	Cross-sectional	57 (38 F) 45 (range 32-54 yr)	57 (28 F) 37 (range 28.5-47 yr)	Low: 1.08 (0.30) [†] High: 2.08 (0.73) [†]	Low: 1.15 (0.30) [†] High: 2.33 (0.76) [†]
Meisingset et al., 2015 ⁴⁹	Cross-sectional	75 (55 F) 43.1±12.9 yr	91 (48 F) 40.8±3.8 yr	Low 1.3 (1.2-1.4) High 2.8 (2.6-2.9)	Low 1.7 (1.6-1.8) High 4.5 (4.3-4.7)
<p>For the sample, total participants (female participants) are reported, as well as mean age ± SD (or range, if SD was not reported). Unreported data about the sample was recorded as a question mark. Reported results are errors from the mean for JPE and SVV, sway area or distance for postural sway, error in distance over time for the Fly Test(R), gain (ratio between eye movement and target movement) for SPNT and head velocity for head steadiness. For four studies^{38,52,57,62} baseline data were combined.</p> <p>yr = year, JPE = joint position error (NHP = neutral head position, tran = transverse plane, sag = sagittal plan, cor = coronal plane), SVV = subjective visual vertical, SPNT = smooth pursuit neck torsion, CLMT = continuous linear movement test, AP = anteroposterior displacement, ML = mediolateral displacement.</p> <p>* Baseline data were combined</p> <p>† Calculated from median and IQR</p> <p>‡ No SD reported</p> <p>§ Mean and 95% CI reported</p> <p> Error in degrees calculated from error in centimetres</p>					

Table 3. Methods to assess sensorimotor control.

Test	Number of studies	Number of participants		What it measures	Outcome measure (unit)	Test execution
		Neck pain	Healthy			
Joint position error	22	340	630	Ability to reposition the head to given position	Error from NHP or target (° or cm)	Repositioning test in which the cervical spine is actively moved (by the participant) in the transverse, sagittal or coronal plane (i.e., rotation, flexion-extension, lateral flexion), and is then repositioned to the neutral head position (NHP) or a pre-set target position. After each trial, the examiner repositions the head to the NHP. The error is measured using a laser pointer or electromagnetic motion tracking system (e.g. Fastrak).
Postural sway	13	285	298	Amount of movement during quiet stance	Sway area (cm ²) or distance from center of pressure	Recorded during stance on a force platform in both eyes open and eyes closed conditions.
Subjective visual vertical	5	36	158	Ability to reposition a (computer-)screen presented line aligning the true vertical	Error from true vertical (°)	A tilted line is presented on a computer screen, disk or virtual reality device. Participants have to reposition the line aligning to the true vertical by using the computer mouse or control knob.
Smooth pursuit neck torsion	4	36	110	Eye movements while torso is rotated relative to the head	Smooth pursuit neck torsion (ratio between eye and target movement in neutral and torsion positions)	Participants focus their eyes on a moving target and keep the head still, in a neutral position and a position in which the torso is rotated relative to the head (torsion). The velocity of eye movements while following the target is recorded. The gain (ratio between eye movement and target movement) is calculated. The outcome measure (smooth pursuit neck torsion) is the difference between the gain in neutral and the average gain in torsion (right and left).
The Fly ®	3	93	129	Ability to follow a computer-presented target moving in certain patterns	Error from target (cm or mm)	Participants have to follow a target (the 'Fly') on a computer screen by moving their head/neck. The accuracy is measured using a Fastrak system. For different difficulty levels (i.e. different fly patterns) the accuracy of the performance is reported.
Head steadiness	2	132	148	Ability to keep the head still over a period of time	Angular velocity (°/sec)	Head steadiness is assessed by investigating the ability to hold the head still in a given position over a certain time and is expressed in angular velocity, measured by an electromagnetic motion tracking system.

Tests used to assess sensorimotor control.

NHP = Neutral head position.

Table 4. Ranges for reported means of JPE and the number of included studies.

Direction	JPE to NHP		Healthy	n	JPE to target*			
	Neck pain	n			Neck pain	n	Healthy	n
Rotation	2.2°-9.8°	10	1.66°-5.1°	19	6.67°	1	2.2°-5.46°	7
Flexion-Extension	3.2°-3.5°	2	1.72°-4.4°	8	-	-	2.9°-3.5°	3
Lateral flexion	2.75°	1	2.1°-3.2°	3	-	-	1.8°-3.6°	3

Ranges for reported means of JPE.

JPE = joint position error, NHP = neutral head position, n = number of included studies.

* 5 studies used a 30° target, 1 study used a target t which was 65% of maximum range of motion

Table 5. Ranges for reported means of postural sway and the number of included studies.

Condition	Sway area (cm ²)				Sway distance (cm)			
	Neck pain	n	Healthy	n	Neck pain	n	Healthy	n
Eyes open	4.85-10.5	2	3.5-6.6	4	AP 0.45 ML 0.20	1	AP 0.28-2.33 ML 0.14-0.15	3
Eyes closed	2.51-16.6	3	2.74-10.9	5	-	-	AP 0.44-2.30 ML 0.15-3.0	3

Ranges for reported means of postural sway.

AP = anteroposterior, ML = mediolateral, n = number of included studies.