THE EFFECT OF NECK PAIN ON PERFORMANCE IN TESTS OF PROPRIOCEPTION, CERVICO-CEPHALIC KINESTHESIA AND OCULAR MOTOR FUNCTION

by

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ABSTRACT

The aim of this work is to understand the relationships between neck pain, cervical proprioception and ocular motor performance Two systematic literature reviews used the GRADE approach. First, moderate quality evidence was identified for greater cervical joint positioning errors (JPE) in the transverse plane among participants with whiplash, but mostly low-to-very low quality evidence was found for participants with non-traumatic neck pain, and for other cervical and ocular tests. Limited and low quality evidence indicated little or no correlation between performance across the tests, which questions their construct validity for cervical proprioception.
Next, test-retest studies established adequate intra-examiner reliability of ocular tracking in a smooth-pursuit (SPNT) test, in a novel, non-predictable ocular tracking test designed to overcome limitations in the SPNT test and of the cervical JPE and cervico-cephalic kinesthesia tests.

A cross-sectional study then evaluated the effect of mechanical neck pain on smooth pursuit in the non-predictable ocular tracking test and found impaired performance in a neck pain group, compared with healthy control participants. The construct validity of this test and of existing tests was evaluated by examining convergence of correlation in their performance. In healthy participants, convergence between transverse plane cervical JPE, cervico-cephalic kinesthesia and ocular tracking tests, indicated common neurological processes. In the neck pain group there was convergence between the cervico-cephalic kinesthesia and ocular tracking tests. However performance may not be attributed to altered cervical proprioception across all of the tests.

A theoretical model suggested that impaired cervical proprioception or cognitive functions underlie deficits in the neck pain group, while compensatory adaptations in vestibular gain or efference copy underlie the absence of impairment in the cervical JPE test.

Dedicated to Ben and Millie, in recognition of your support during the many lost hours that weren’t spent together

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LIST OF CONTENTS

List of contents continued

List of contents continued

List of contents continued

List of contents continued

List of contents continued

List of contents continued

List of contents continued

List of contents continued

List of contents continued

LIST OF TABLES

List of tables continued

List of tables continued

LIST OF FIGURES

List of figures continued

LIST OF ABBREVIATIONS

AE	Absolute error
ANOVA	Analysis of variance
BQ	Bournemouth Questionnaire
C1 (2,3…)	Cervical vertebra 1 (2,3…)
CE	Constant error
CHA	Cervicogenic headache
CNFDS	Copenhagen Neck Functional Disability Scale
CNS	Central nervous system
COR	Cervico-ocular reflex
CROM instrument	Cervical range of motion instrument
cv	Coefficient of variation
EMG	Electromyography
EOG	Electro-oculography
FABQ	Fear Avoidance Beliefs Questionnaire
FEF	Frontal eye field
fMRI	Functional magnetic resonance imaging
GRADE	Grades of Recommendation, Assessment, Development and Evaluation
HEB Wales	Health Evidence Bulletin Wales
HRA	Head repositioning accuracy
hSP	Horizontal smooth pursuit
ICC	Intra-class correlation coefficient
JPE	Joint position error
N/A	Not applicable
k	Cohen’s kappa coefficient
NDI	Neck Disability Index
NRS	Numeric Rating Scale
p	p (probability) value
PET	Positron emission tomography
PRISMA	The Preferred Reporting Items for Systematic Reviews and Meta-analyses
r	Pearson's r
R^2	Coefficient of determination
RMSE	Root mean square error
ROM	Range of motion
rs	Spearman's rho b
RTA	Road traffic accident

SCI	Spinal cord injury
SD	Standard deviation
SEF	Supplementary eye field
SEM	Standard error of measurement
SF-36	Short form of the US Medical Outcomes Survey Questionnaire
SP	Smooth pursuit
hSP	Horizontal plane smooth pursuit
vSP	Vertical plane smooth pursuit
cSP	Combined horizontal and vertical plane smooth pursuit
SPECT	Single positron mission computerised tomography
SPNT	Smooth pursuit neck torsion
STROBE guidelines	Strengthening the Reporting of Observational Studies in Epidemiology Guidelines
Ƭ	Kendall's tau
T1 (2,3..)	Thoracic vertabra 1 (2,3…)
TSK (-II)	Tampa Kinesophobia Scale (-version II)
VE	Variable error
VOR	Vestibulo-ocular reflex
vSP	Vertical smooth pursuit
WAD (I,II,III)	Whiplash associated disorder (grade I,II,II)

INTRODUCTION

Neurophysiological studies indicate that activation of cervical spine proprioceptors has perceptual and sensorimotor effects that include changes in the perceived head and trunk mid-line, perceived head position, perceived motion of visual objects and effects on eye movements. Existing studies used proposed measures of cervical proprioception that include the cervical joint position error (JPE), cervico-cephalic kinesthesia and smooth pursuit neck torsion (SPNT) tests. Impaired performance in the tests is reported in mechanical neck pain, although not all studies found deficits. There are however possible limitations in the validity of the tests, since neither is able to isolate the role of cervical proprioception from other neurophysiological processes. This thesis examines sensorimotor control of voluntary head and ocular movements in order to increase understanding of the nature of functional impairments in mechanical neck pain. It also evaluates the validity of tests of cervical proprioception and examines the neurophysiological processes that determine performance ability in those tests.

1.1 MECHANICAL NECK PAIN

Cervical spinal pain is usually defined as pain in the posterior or lateral neck between the superior nuchal line and the first thoracic spinous process[2]. Neck pain that is classified as mechanical has no identifiable pathoanatomic cause[3;4]. Mechanical neck pain is a common disorder, incurring substantive direct and indirect costs[5;6]. The reported prevalence varies widely with geographical area, age and gender[7]. A review by Childs et al (2008) reported that most studies found higher prevalence among women than men, with lifetime prevalence ranging from 14%-71%[3]. The disability level among people with neck pain also varies, with most experiencing low

levels, but approximately 5% being sufficiently disabled to lose time from work each year[5].

1.2 EFFECTS OF NECK PAIN ON PHYSICAL FUNCTION

Performing every day activities depends upon strength, endurance, flexibility, proprioception and coordination[8]. It is proposed that these functions may be impaired in mechanical neck pain and that their restoration should be an aim of rehabilitative approaches[8]. Many studies have attempted to make objective measurements to establish and quantify altered physical function in neck pain, with alterations in motor functions (cervical motion and muscle activity)[9-14] being widely reported. This raises the question of whether such motor changes might reflect efferent reponses to altered sensory input signalling cervical joint position (proprioception) in neck pain. Revel et al (1991) reported reduced ability to reposition the head to neutral position in participants with neck pain, and were the first to propose impaired cervical proprioception as a mechanism for the deficit observed[15]. Since then many studies have attempted to evaluate whether proprioception of the cervical spine is impaired in neck pain and how this may in turn affect motor control[16] (i.e. sensorimotor control).

1.3 CERVICAL SPINE PROPRIOCEPTION

The term proprioception ('proprio-ception') was first used by Sherrington (1907) to describe deep receptors activated by the organism's own action[17] and describes the ability to sense position and movement of one's own limbs and body[18].
Proprioception can be divided into two submodalities: the sense of stationary position and the sense of movement (kinesthesia)[18].

Afferent information from muscle spindles in the cervical region is believed to be the most important sensory cue for head-trunk proprioception[19]. High densities of muscle spindles are demonstrated in human neck muscles, including rectus capitis posterior major, rectus capitis posterior minor, obliquus capitis inferior, and the obliquus capitis superior, located deep in the suboccipital region. These muscles function in fine rotatory movements of the head and help maintain stability of the cervical spine[20-22]. A differential distribution of spindles between different cervical muscles has been shown[23]. It is suggested that higher densities reported in slow-twitch muscle fibres might indicate a role in postural activities[20]. More recent studies investigated intrafusal fiber type, general morphology, and myosin heavy chain composition of muscle spindles in human deep cervical muscles, reporting features expected to confer relatively higher dynamic sensitivity, that might reflect adaptation of the fusimotor system to the particular task of controlling head posture and movements[24]. Properties of contractility and recruitment of the distinct spindle types in different cervical muscles remain to be characterised, but their anatomical and morphological complexity supports the likelihood of a primary role for muscle spindles in head-trunk proprioception.

Other potential sources of proprioceptive cue in the cervical spine region include mechanoreceptors identified in cervical facet joints[25] and intervertebral discs[26]. In other joints skin strain is known to provide a proprioceptive cue[27], however there have been no studies of characteristics of articular or cutaneous mechanoreceptors around the neck and similarly, no investigation of the role of Golgi tendon organs.

1.4 THE FUNCTION OF PROPRIOCEPTION IN SENSORIMOTOR CONTROL

Evidence of the role that neck proprioception plays in motor control comes from experimental studies where receptors in the neck are either stimulated or have their activation blocked. De Jong et al (1977) reported that anaesthetic injections into the neck induced ataxia, nystagmus and disequilibrium[28]. A number of studies have evaluated the effects of stimulating receptors by vibrating neck muscles, reporting changes in postural stabilisation in standing and/or stepping on the spot[29-31] or in walking[31;32], changes in perception of the head and trunk mid-line[33-35], perceived head position[36;37], perceived whole-body rotation[38], alterations in gaze direction[39;40], illusions of visual target displacement[37] and lateralisation of sound[41]. Other studies have used pyschophysical tasks to separate visual, vestibular and neck propriceptive stimulation, reporting effects of proprioception on perception of self-motion or motion of the head[38;42;43], position or illusory movement of stationary visual objects[44-46] and effects on eye movements[43;47;48]. Together these findings provide strong evidence that cervical proprioception contributes to control of posture and balance, perception of position and motion of the head and trunk, perception of the location and motion of visual objects and of sound and to movements of the eyes. Together these functions represent a wide field of research in sensorimotor control that includes reflex movements and more complex voluntary movements.

1.5 EVALUATION OF PROPRIOCEPTIVE FUNCTION IN CONTROL OF VOLUNTARY OCULAR AND HEAD MOVEMENT

To evaluate whether proprioception is impaired in individuals with mechanical neck pain, reliable[49] and valid[50] tests of ocular and head sensorimotor control are needed. Several tests have been proposed as measures of cervical spine proprioception and have been used to evaluate deficits in voluntary ocular and head sensorimotor

control in mechanical neck pain. Each however possesses limitations that are discussed below (1.5.1-1.5.3).

1.5.1 Cervical joint position error tests

The most widely used is the cervical joint position error (JPE), or head repositioining test. First described by Revel et al (1991), the ability to relocate neutral head position following an active neck movement is proposed to provide a measure of cervical JPE, in turn indicating neck proprioception[15]. Impaired test performance has been reported in whiplash associated disorder (WAD)[51-55], where bony or soft tissue injuries are sustained as a result of acceleration-deceleration forces to the neck[56], and in non-traumatic neck pain patients[52;57], although not all studies found deficits[58;59]. However, this test may give an incomplete or invalid measure of proprioceptive contribution to head movement control[55;60] for several reasons, discussed below.

<u>Limitations of cervical joint position error tests</u>

Firstly, since only error in repositioning to a static head position is evaluated in cervical JPE tests they are unable to indicate how proprioception relates to ongoing control during repositioning motion. Furthermore, there are uncertainties about the validity[61;62] (1.5.7) of the cervical JPE test, i.e. whether measured performance does actually represent proprioception[62]. Factors other than cervical proprioception that may be measured by cervical JPE tests are described below.

A possible role for motor efference copy

Secondly, it is widely accepted that sensorimotor control utilises copies of efferent signals for movement execution (providing a signal of the expected outcome of the movement) that is compared with sensory reafferent information (feeback on the sensory consequences of the movement)[63]. When an active head motion is performed prior to repositioning in the cervical JPE test, motor efference copy might provide a cue regarding the head movement that need only be reversed to return the head to its start position (without the need to utilise cervical proprioceptive information, or a perceived straight ahead representation).

A possible role for vestibular processes

A further challenge to the validity of the cervical JPE test as a measure of cervical proprioception exists whereby active head movements stimulate the semicircular canals generating signals encoding the time course of head velocity that could influence performance in the test. The vestibular nuclei integrate this vestibular head motion in space information (a reafference signal regarding the outcome of the motor command) with cervical proprioceptive inputs, enabling computation of body in space motion. Motor efference copy is also received by the vestibular nuclei, enabling intended versus actual movement to be calculated, which may involve reciprocal connections with the fastigial nucleus of the cerebellum[64]. Vestibular, proprioceptive and motor efference copy signals[63] are projected to higher multisensory cortical levels enabling spatial orienting processes. fMRI has indicated convergence of vestibular afferent signals (following caloric stimulation of the semicircular canals) with cervical proprioceptive inputs (following cervical muscle vibration) in a number of cortical areas. These include the somatosensory regions of the perisylvian cortex (insula and retroinsular cortex), tempero-parietal junction and in somatosensory area

SII)[65]. Thus integration of vestibular and cervical proprioception signals occurs from the lowest level of the vestibular nuclei, through to cortical areas. Evidence that vestibular activity interacts with cervical proprioception in spatial orientation functions, including perception of the straight ahead position in the body's mid-sagittal plane(as required in the cervical JPE test), comes from observations that experimental stimulation of inputs, both via neck muscle vibration and caloric stimulation respectively, distorts ego-centred spatial perception[65-67]. Further evidence comes from the observation that both cervical muscle vibration and vestibular stimulation can modulate deficits in spatial orientation, including distortion of the subjective straight ahead position in the transverse plane that occurs in patients with unilateral spatial neglect[67].

The role of sensorimotor transformation and efferent processes

Finally, performance of the cervical JPE test necessitates effective transformation of sensory signals (cervical propriceptive and/or vestibular) into motor output in order to accurately relocate the perceived straight-ahead position. As described above, cortical areas that receive cervical proprioceptive inputs and that might subserve transformation into head motor output have been identified. However evidence of their specific functions in relation to head movement without a visual target is lacking. Accurate head repositioning also requires effective efferent output, muscular function and biomechanical articular processes to generate the required head movement. Altered cervical kinematics (velocity, smoothness, axis of motion)[10;68-70], muscle morphology[71-73] and muscle activity[74;75] are reported in neck pain. Thus altered motor processes might contribute to determining cervical JPE test performance.There are however conflicting reports whereby other studies found no alterations of kinematics[69] or muscle activity[69;76]. Lack of consistent methods and differences in

participants (differences in aetiology and/or chronicity of neck pain) between studies may account for the disparate findings.

It is clear that a number of different neurophysiological processes, in addition to cervical proprioception, must contribute to performance in the cervical JPE test. Thus it is possible that impaired performance reported[51;52;52-55;57;] might not be due to altered cervical proprioception.

1.5.2 Cervico-cephalic kinesthesia test

An important function of the proprioceptive system in sensorimotor control is to enable moment-to-moment correction of movements, with complex non-learned movements being particularly challenging[77-79]. The cervico-cephalic kinesthesia test (originally named 'The Fly' by Kristjansson et al (2004), describing the insect-like appearance of the visual target motion on the display screen) was devised to overcome limitations of the cervical JPE test (1.5.1)[60]. This included enabling ongoing control during non-learned movements to be evaluated (thus reducing the potential contribution of motor efference copy) and reducing the likelihood of vestibular activation during performance of the test[60]. Whiplash[60] and non-trauma neck pain[80] patients are reported to make greater errors compared with healthy controls when required to move their head to track a slow, unpredictably moving visual target.

<u>Limitations of the cervico-cephalic kinesthesia test</u>

While some limitations of the cervical JPE test are overcome, the roles of sensorimotor transformation of proprioceptive signals and of efferent motor control

processes are still involved. In addition, the role of visual and visuomotor processes cannot be isolated from the role of proprioception in performance of the test.

The role of visual processes, visuomotor transformation and ocular motor processes

The cervico-cephalic kinesthesia test requires a form of gaze movement, whereby combined ocular and head movements[81] are made towards a visual target. Visual sensory and ocular motor processes are discussed below (1.5.3). In relation to head movements, sensory information (both visual and cervical proprioceptive signals) must be transformed into motor commands for execution of the movement by cervical muscles[82]. In humans, fMRI indicated that a number of brain cortical and subcortical areas were active during gaze movement as well as during eye only and head only movement towards a visual target, suggesting common processes in movements towards visual targets both with the head restrained and unrestrained[83]. Cortical areas corresponded to the frontal eye field (FEF), supplementary eye field (SEF), intraparietal sulcus, precuneus and middle temporal area (MT) in non-human primates and subcortical areas were the basal ganglia, thalamus and superior colliculus. The processes carried out in these areas may include visuomotor transformation[84;85] for ocular and/or head movements[76]. In humans, fMRI indicated that cervical muscle vibration (proprioceptive stimulus) also activated several of the areas described above, including FEF and the intraparietal sulcus. This supports a role in polysensory (both visual and proprioceptive signals) transformation, perhaps into trunk or space centred coordinates[83].

1.5.3 Smooth pursuit neck torsion test

Other studies evaluating the effect of neck pain on sensorimotor control have used tests of ocular motor function. Deficits following whiplash injury are consistently

reported in reflex[86-89] eye movements. Other studies reported deficits in voluntary eye movements[90-92] using a particular proposed test of cervical proprioception, the Smooth Pursuit Neck Torsion (SPNT) test, devised by Tjell et al (1998)[90]. Ability to match the velocity of eye movement to that of a moving visual target (smooth pursuit gain) is measured as participants track a target following a horizontal trajectory, described as 'sinusoidal'[55;90;91] (i.e. oscillating leftwards and rightwards at a fixed frequency). However, in previous studies [55;90;91] only periods of the cycle where target velocity was constant were analysed (deceleration and acceleration periods during target direction reversal, resulting from the motor driving the laser visual target, were excluded), thus the analysed component of ocular tracking was comparable to that evaluated with a triangular, rather than a sinusoidal target trajectory. Smooth Pursuit (SP) gain is measured both with the head and trunk facing forward and with the trunk rotated beneath the head introducing neck torsion[55;90;91].

In all instances within this thesis, the gain is calculated by comparison of momentary target velocity and movement velocity (i.e. movement velocity divided by target velocity) throughout the valid portions of each trial, and then averaged. For consistency with existing literature and simplicity of description, however, this thesis uses the terms target and movement velocity without consideration of direction. Thus a target with constant speed is descibed as constant velocity, despite it moving left or rightwards.

Smooth pursuit ocular movements in humans have been extensively studied using a variety of psychometric task paradigms[93;94]. Different processes are believed to underlie initiation and maintenance of smooth pursuit ocular tracking[93;94]. The SPNT test evaluates maintenance of smooth pursuit ocular tracking of a predictable visual

target with the head restrained. Accurate pursuit eye movements depend upon accurate calculation of target velocity in space[95]. This is computed from retinal signals, efference copy of motor output signalling eye velocity and signals of the velocity of head rotation. Head rotation velocity in turn and perception of target motion in space is signalled by the interaction of vesibular with cervical proprioceptive cues[96]. Vestibular signals alone cannot distinguish whether the head or whole body is moving and cervical proprioceptive signals thus provide important information about head rotation relative to the trunk, contributing to pursuit movements[95]. With the head restrained in the SPNT test there is no vestibular stimulation, thus trunk rotation beneath the static head reproduces a paradigm designed to isolate the 'neck signal'[94;96;97] in studies of interactions between cervical proprioception, vestibular signals and retinal signals (i.e. the contribution of cervical proprioception to pursuit performance). Differences in both the SP gain and also the difference in SP gain between neck neutral and neck torsion positions are reported following whiplash injury and have been attributed to impaired cervical proprioception[60;90;91;98;99]. However, not all studies reported deficits[100;101].

Limitations in the SPNT test

Smooth pursuit ocular tracking depends upon a complex interaction between different neural signals. Retinal error information signalling visual target direction and velocity of motion across the retina is a key determinant of smooth pursuit velocity control[102], however visual target position also has some influence[103-105]. These retinal signals interact with extra-retinal signals including ocular motor signals (efference copy of motor output signalling eye velocity)[102], vestibular information (signalling head in space displacement) and cervical proprioceptive information[94] (signalling head-re-trunk displacement).

The role of cervical proprioception in head-restrained smooth pursuit ocular tracking

The role of cervical proprioceptors in smooth pursuit tracking of visual targets is not clearly understood. In humans fMRI studies demonstrated frontal eye fields (FEF) activation by neck muscle vibration[106] and furthermore in monkeys *passive* trunk-under-head rotation generates inputs to pursuit neurons in the (FEF)[95]. FEF output signals eye velocity (with the head restrained) and gaze velocity (combined eye and head motion) in trunk-centred coordinates, that projects via the cerebellum to brainstem ocular motor output nuclei[95]. However, a group of brainstem neurons (Eye-head neurons) in the medial vestibular nuclei that are believed to be the primary input to extraocular motoneurons during smooth pursuit showed negligible response to cervical proprioceptor stimulation during *active* trunk-under-head rotation in rhesus monkeys[107]. While it is not known whether active, compared with passive trunk-under-head rotation might have different effects on activity in brain areas comprising the smooth pursuit system, in rhesus monkeys the context in which neck rotation occurs has been shown to strongly modulate FEF activity during *head-on-trunk rotations*[107]. Following from this, it might be reasoned that active trunk-under-head rotation (the neck torsion conditions) in the SPNT test might not influence ocular motor output and ocular movement. However, there are some differences between primate species[95] and it is not know whether cervical proprioceptor signals are represented in eye-head neuron outputs in humans. Thus it is unclear from existing literature whether cervical proprioception has any influence by way of cortical activity on smooth pursuit when the head is restrained, either with or without active head-under-trunk rotation.

The unclear role of the cervico-ocular reflex

Previous theories for reported deficits in neck pain in the SPNT ocular tracking test in WAD have proposed that altered proprioceptor activation associated with neck pain influences the cervico-ocular reflex causing reductions in SP velocity gain[108;109]. It is established that cervical proprioception when the neck is rotated initiates the cervico-ocular reflex[110] that shifts eye position to maintain fixation of a visual target[87], in conjunction with the vestibulo-ocular and other ocular stabilisation reflexes[87].The cervico-ocular reflex pathway involves a loop through the cerebellum and pontine nuclei (including the vestibular nuclei) to the ocular motor output nuclei for cranial nerves III, IV and VI[111;112]. In normal human participants the gain of the cervico-ocular reflex is low, thus it makes only a small contribution to shifts in ocular position[113]. However in humans with labyrinthine deficits the gain of the cervico-ocular reflex is raised, putatively an adaptation to compensate for reduced gain identified for the vestibulo-ocular reflex[114-116]. The gain of the cervico-ocular reflex is also increased in patients with WAD, although no reciprocal decrease in vestibulo-ocular reflex gain appears to occur[86;87], which might support theories that it is changes in the cervico-ocular reflex that result in greater SPNT differences reported in WAD[108;109]. There are however several arguments against the likelihood that altered cervico-ocular reflex gain accounts for the impaired smooth pursuit tracking previously reported:

Firstly, it has been demonstrated in squirrel monkeys that the Cervico-ocular reflex is suppressed during visual fixation of earth stationary targets during passive neck rotation. It is unclear whether previous studies using the SPNT test had a stationary target for fixation[90-92] prior to the onset of target motion.

Secondly, for ocular motion in smooth pursuit to be enabled, it is suggested that the vestibulo-ocular reflex must be cancelled[94;117]. This has been documented when a visual target moves in phase with head motion (where a reflex counter rotation of the eyes would prevent foveation of the target) with indications that the cerebellar flocculus may provide the mechanism[117]. An analogous situation where operation of the cervico-ocular reflex would generate an undesirable effect on smooth pursuit tracking is where the visual target remains aligned with respect to the head as the trunk is rotated under the head (as in this thesis). Whether or not the cervico-ocular reflex is in fact cancelled during smooth pursuit in this situation has not been reported, however if it were, depending on the cancellation mechanism, it is possible that the SPNT test might not involve the cervico-ocular reflex.

Thirdly, the cervico-ocular reflex is reported to be modified (ocular responses reduced) by contact with a rigid, immobile earth-centred point of reference[118]. In previous studies of the SPNT test participant's heads were manually stabilised and although it is not clear whether this would provide such a cue, it is possible that experimental methods could reduce or remove a contribution of the cervico-ocular reflex to task performance. Similarly, the possible effect on the cervico-ocular reflex of trunk-under-head rotation having been generated actively rather than passively (potentially enabling motor efference copy to influence responses) is unknown.

It is unclear what the contribution of cervical proprioception is to performance of the SPNT test. Both the validity of the test as a measure of cervical proprioception and also the effect of mechanical neck pain on cervical proprioception are thus uncertain.

The role of cognitive processes in smooth pursuit

The smooth pursuit system has considerable capacity to learn visual target direction, timing and velocity information that may be stored in short term memory enabling regular periodic stimuli (as in the SPNT test) to be tracked with zero phase lag, or even with the eye moving ahead of the target[119]. Even for complex target trajectories, phase lag between the eye and the target is less than that expected if ocular tracking was based on the need to continuously correct direction and velocity relying on visual feedback, suggesting that predictive processes contribute[93;120;121].

Maintenance of smooth pursuit utilises prediction of future motion of the ocular target, enabling periodic stimuli to be tracked with zero lag between target and ocular motion (timing of response) as well as enabling ocular movements to be correctly scaled and directed[93]. It is proposed that previously experienced motion information is stored (i.e. a form of visual working memory) and used to predict future movement. With the predictable target used in the SPNT test (triangular waveform trajectory), stored target information could be released when required to generate the appropriate ocular motion[93]. It is possible that the use of prediction to enable ocular tracking might reduce the dependence of the SPNT test on moment-to-moment cervical proprioception. If this were the case, deficits reported in WAD may be due to impaired prediction, rather than impaired cervical proprioception.

Attention selectively enhances visual processing in a region of the visual field[122]. Evidence that attention plays a part in maintenance of smooth pursuit is derived from observations that when secondary tasks are embedded within the pursuit target smooth pursuit performance improves[93], while distracting tasks reduce smooth pursuit gain[123].

A further cognitive process involved in smooth pursuit is the detection of errors signalled by mismatches between predicted and actual (based on retinal feedback) information about target velocity, which also depends upon working memory[93].Thus it is possible that deficits in smooth pursuit reported in the SPNT test in WAD could be due to inaccuracy in stored motion velocity information, or to deficits in the detection of velocity mismatches and their subsequent correction. In the absence of ability to utilise prediction, ocular tracking of a non-predictable target would be visually-driven, placing greater load on visual working memory and/or velocity mismatch detection and correction. There is some evidence that cognitive processes, including working memory, attention and immediate recall, may be impaired in mechanical neck pain[124]. The reason for such impairment is unclear, but it is proposed that emotional aspects of pain may be the cause[125-127] (discussed in detail in 6.3.6). If these cognitive processes were impaired, deficits reported in the SPNT test in WAD could reflect these, rather than impaired cervical proprioception.

While the cervico-cephalic kinesthesia test was devised to overcome limitations of the cervical JPE test, including reducing the predictability of the visual target, no such developments have occurred to reduce limitations of the existing SPNT test. This thesis thus includes the design of a novel test of ocularmotor function to reduce the potential contribution of predictive processes to ocular tracking.

Responses to more irregular ocular target trajectories place additional challenges on predictive processes underlying smooth pursuit. It has however been demonstrated that even tracking of more complex trajectories in 2-dimensions (generated by summating sinusoidal waveforms of different frequencies) involves prediction in

monkeys[121], the flocculus and parafloccular regions of the cerebellum being implicated in predictive control. It is thus possible that the visual target trajectories previously used in the cervico-cephalic kinesthesia test, although placing greater challenge on predictive processes for head and/or gaze movement, may still potentially be predicted. In order to investigate whether smooth pursuit is impaired in neck pain when predictive control is excluded or minimised, a non-predictable visual target trajectory must be used for both the cervico-cephalic kinesthesia test and the novel test of non-predictable ocular tracking.

Additional tests that have been used to evaluate cervical spine proprioception in mechanical neck pain, but were not included in the research, as they either did not measure voluntary movement control or had other limitations, are provided in Table 1.1.

Table 1.1 Tests of cervical proprioception in mechanical neck pain that were not included in the research

CERVICAL PROPRIOCEPTION TEST	REASON FOR EXCLUSION
Cervico-ocular reflex (COR) measurement	Dosn't evaluate voluntary motor control. Isolates the effect of cervical proprioception on simple reflex eye movements.There is evidence of alterations in gain of the COR in individuals with neck pain[128-130]. However reciprocal changes in the gain of the vestibular-ocular reflex (VOR)[129-131] suggest that this may not have much impact on functional ability
Subjective visual vertical perception	Dosn't evaluate motor control. Little literature to consider[132;133]
Upper limb proprioception	Voluntary movement of the arm. Evaluated in a number of studies, but the role of peripheral joint proprioception can not be isolated from cervical spine proprioception[134-137]
Posturography (standing balance)	Largely reflex motor control. A sizeable amount of literature for impairment in neck pain[138-142], but the effect of proprioception can not be isolated from the many other factors that contribute to standing balance

1.5.4 Unclear quality of evidence for impaired performance of the cervical JPE, cervico-cephalic kinesthesia and SPNT tests in mechanical neck pain

While impairments in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests are reported in mechanical neck pain, there are also conflicting reports of no impairment (1.5.1-1.5.3). There have however been no critical reviews appraising the quality of individual studies and of existing evidence. This thesis thus takes a systematic approach to reviewing the evidence for impaired cervical poprioception in mechanical neck pain, as measured by the cervical JPE, cervico-cephalic kinesthesia and SPNT tests.

1.6 RELIABILITY OF OUTCOME MEASURES

Physical function measures should demonstrate acceptable test-retest reliability[143]. There has been little examination of this for the tests described above. Methodologies for the cervical JPE test have varied widely in terms of the number of trials used, the parameters of JPE used and the repositioning procedure. A few studies have evaluated its reliability[15;52;143-145], with variable results reported. For the cervico-cephalic kinesthesia test 'acceptable' reliability (ICC = .60-.86) has been demonstrated[60], however some sources recommend that only 'substantial' reliability (ICC = .81-1.0) should be considered adequate[49]. Thus, although they have been widely used, there is no clear concensus on the optimal test protocols to generate reliable measures in the cervical JPE and cervico-cephalic kinesthesia tests. No studies have reported reliability of the SPNT test. This thesis will thus establish reliable methods for measurement using the tests.

1.7 VALIDITY OF CERVICAL PROPRIOCEPTION TESTS

In the cervical JPE, cervico-cephalic kinesthesia and SPNT tests the underlying construct of proprioception cannot be entirely isolated from other factors such as vestibular function, visual feedback, motor learning or prediction (1.5.1–1.5.3). It is therefore unclear whether performance in these tests, each requiring different motor tasks, are equally dependent on proprioception. This questions their measurement validity as tests of cervical proprioception i.e. whether they are in fact measures of what they purport to measure[50]. There are different forms of validity – face validity refers to the apparent validity of the data collection process[50], rather than the actual concept that is measured. Apparent limitations (1.5.1-1.5.4) in the likelihood that the cervical JPE, cervico-cephalic kinesthesia and SPNT test processes measure cervical proprioception thus undermine their face validity.

Content validity refers to the scope of an outcome measure to capture the overall dimension of the concept being measured[50]. By their nature the cervical JPE, cervico-cephalic kinesthesia and SPNT tests each measure sensorimotor control within a specific movement context (ability to relocate static neutral head position, to move the head to follow a visual target and to make smooth pursuit ocular movements to track a visual target in a static position with or without neck torsion, respectively). Thus individually they are unlikely to have full content validity for cervical proprioception. This would be an issue if a single test was used to obtain an overall measure of cervical proprioception, but not if a narrower component of cervical proprioception is the focus of clinical evaluation.

Criterion-related validity refers to the ability of a measurement to either agree with a pre-existing measure whose validity is established (concurrent validity), to

demonstrate predictive ability (e.g. for patient outcome) or to demonstrate diagnostic sensitivity and specificity[62]. Demonstrating concurrent validity is problematic since there are no measures of voluntary eye or head movement control with established validity for cervical proprioception. Limited evidence exists for the predictive and diagnostic abilities of the cervical JPE[53] and SPNT[90;92;146] tests. However, conflicting findings are also reported[54;146-148;]. Consideration of characteristics for which predictive or diagnostic relationships are reported for cervical JPE or SPNT test performance (cervical dizziness[90], WAD[92], and pain intensity[53;146-148]), indicates that these characteristics do not have clear association with cervical proprioception. No studies have evaluated predictive or diagnostic properties of the cervico-cephalic kinesthesia test. Thus evidence for criterion-related validity is very limited.

The final component of validity is construct validity whereby measurements derived from different tests that are proposed to measure the same, or related constructs, should thus demonstrate correlations that support the theoretical relationship[149]. Construct validity would be supported by either convergence (where expected positive associations are identified), or divergence (where expected inverse, or near zero correlations are identified)[50]. If the cervical JPE, cervico-cephalic kinesthesia and SPNT tests are all measures of a single underlying construct (e.g. cervical proprioception), then correlation would be anticipated between performance in each test. The only study to evaluate this reported only low levels of correlation between the cervical JPE and the SPNT tests[55], questioning their construct validity.The cervico-cephalic kinesthesia test has not been included in any comparison between tests, so although it appears to overcome limitations of the JPE test, its construct validity is untested.

There are serious limitations in the extent to which all forms of the validity of the cervical JPE, cevicocephalic kinesthesia and SPNT tests have been established. Construct validity is the most appropriate form to investigate, where a clear positive convergence of correlation between the cervical JPE, cervico-cephalic kinesthesia and SPNT tests would be expected and can be evaluated. There is no specific method for testing face validity of measures and this thesis is not concerned with the content validity of measures of proprioception, since quantification of cervical proprioception per se is not an aim. Evaluation of criterion vailidity is not appropriate since there are no clear criterion measures of cervical proprioception against which to evaluate measurements obtained in the tests.

1.8 CONCLUSION

The effect of mechanical neck pain on cervical proprioception has been widely studied among various populations. The widely used sensorimotor tests that are proposed as measures of cervical proprioception in voluntary ocular and head movement control are the cervical JPE, cervico-cephalic kinesthesia and SPNT tests. While deficits in their performance have frequently been found in neck pain, conflicting findings have also been reported. Variability in study methods and the absence of any systematically approached review including critical appraisal of the evidence make it impossible to draw conclusions on whether and/or how sensorimotor control in eye and head movement tasks is impaired in mechanical neck pain. There are limitations in the established reliability of the cervical JPE, cervico-cephalic kinesthesia and SPNT tests. There is uncertainty of the neurophysiological processes that are measured by the tests that thus challenge their face validity as measures of cervical proprioception and they do not have established construct validity. Thus where sensorimotor deficits are reported it is

unclear whether these reflect cervical proprioception deficits. A more complex ocular tracking test using a non-predictable target may overcome the limitation conferred by the predictable nature of the SPNT test, contributing to greater understanding of functional impairments in neck pain (i.e.whether ocular tracking of non-predictable visual targets is impaired).

Establishing the level of evidence for the effect of mechanical neck pain on sensorimotor control of voluntary head and ocular movements, as well evaluation of the effect of mechanical neck pain on performance of a novel test of complex ocular motor function, will contribute to greater understanding of functional impairments that may occur in neck pain conditions. Evaluation of the level of evidence for the convergence of correlations across the cervical JPE, cervico-cephalic kinesthesia and SPNT tests and measurement of correlation between these existing tests and and a novel test of non-predictable ocular tracking, that may be determined by different underlying neurophysiological processes, will contribute to greater understanding of the constructs underlying test performance. Improved understanding of the functional deficits occurring in neck pain may contribute to development of physical rehabilitation approaches targeted towards improving performance of the specific tasks where deficits are identified as well as to valid and reliable outcome measurement methods.

1.9 RESEARCH AIMS AND OBJECTIVES

The research is exploratory in nature and has several specific aims that are stated below, along with objectives related to each aim.

1.9.1 Research Aim 1

- Establish the level of existing evidence for impaired performance of the predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE test in neck pain and for correlation between performance across tests

Objectives

- Conduct a literature review that takes a systematic approach to appraisal of the evidence for impaired sensorimotor control in mechanical neck pain, as measured by the cervical JPE, cervico-cephalic kinesthesia and predictable ocular tracking tests.

- Conduct a literature review that takes a systematic approach to appraisal of the evidence for convergence in correlation between performance in the predictable ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests.

1.9.2 Research Aim 2

- Design a novel test of ocular motor function that overcomes limitations of the predictable ocular tracking test (i.e. the existing SPNT test).

Objective

- Design a test of smooth pursuit ocular tracking of a visual target that follows a complex non-predictable trajectory, in 2-dimensions.

1.9.3 Research Aim 3

– Establish reliability of outcome measures

Objectives

- Conduct methodological studies to evaluate the test-retest reliability of non-predictable and predictable ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests
- Identify protocols and parameters with acceptable reliability that will determine outcome measures to be used for subsequent studies

1.9.4 Research Aim 4

– Establish whether ocular tracking of a complex ocular target following a non-predictable trajectory is impaired in mechanical neck pain

Objective

- Conduct a cross-sectional study to compare performance in the non-predictable target ocular tracking test between a group of partcicipants with mechanical neck pain and a control group of healthy participants

1.9.5 Research Aim 5

– Evaluate the construct validity of the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests as measures of cervical proprioception

Objectives

- Conduct a cross-sectional study to evaluate the construct validity of performance in the non-predictable and predictable ocular tracking, cervical JPE and cevicocephalic kinesthesia tests as measures of a common

sensorimotor process in both participants with neck pain and a healthy control group by

i. Comparing between group differences in performance concurrently measured across the tests

ii. Identifying and comparing associations between performance across the tests with age, gender and symptom-related characteristics

iii. Establishing whether there is convergence in correlations between performance in the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE test

2 LITERATURE REVIEW

2.1 INTRODUCTION

Many studies have evaluated cervical spine proprioceptive function during movement in participants with mechanical neck pain[16]. Functional outcome measures of cervical proprioception include head repositioning tests of cervical JPE (1.5.1)[9;15;52-54;58;59;145;150], the cervico-cephalic kinesthesia test (1.5.2)[60;80] and the SPNT test of (1.5.3)[55;90-92]. To date, there has not been a rigorous review appraising the quality of evidence for proprioceptive impairment in neck pain, or for the construct validity of the cervical JPE, SPNT and cervico-cephalic kinesthesia tests, evaluated by convergence in correlation between performance in the tests (1.7). The first aim of the research (1.9.1) is thus to take a systematic approach to identifying relevant studies, evaluating the quality of individual studies and summarising the level of evidence across studies using the cervical JPE, cervico-cephalic kinesthesia, and SPNT and tests, firstly for proprioceptive impairment in participants with mechanical neck pain, compared with healthy controls (Review 1), and secondly for correlation between performance across the tests (Review 2).

2.2 SYSTEMATIC APPROACHES TO REVIEWING OBSERVATIONAL STUDIES

2.2.1 Background

Appraisal of evidence entails both assessment of quality of individual studies and also judgements on the overall strength of evidence for each outcome of interest[151;152]. Preliminary searches suggested that most studies in both Review 1 and Review 2 would be observational studies, of cross-sectional design. Literature regarding quality assessment of observational studies, including those of cross-sectional design, was reviewed in order to determine the most suitable appraisal tool.

2.2.2 Review of the literature on appraisal of evidence from observational studies

Assessment of individual observational studies

There are many articles evaluating available tools for assessment of quality of individual studies. In the health-related literature most are in the context of conducting systematic reviews of studies of clinical effectiveness (i.e. intervention). Among these, few mention how non-randomised studies should be assessed for quality[152-154]. Epidemiological studies make more use of observational designs[154] and the Guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (2005) specified a set of criteria to be considered in assessing risk of bias during quality appraisal in observational studies. These guidelines do not however comprise a tool for conducting assessments[155].

The Cochrane handbook[152] states that methods for appraising randomised trials may not be applicable to non-randomised study designs. It suggests that some items in the Cochrane 'risk of bias' tool might be applied to non-randomised studies, with the addition of extra items according to study design[152]. There are however no reports evaluating this approach.

Two reviews identified over 200 tools for assessing non-randomised studies[153;154], of which nineteen are suitable for cross-sectional studies[154]. Eleven of these were based on scales, providing a quantitative score for each study. The use of tools based on scales in systematic reviews is criticised[152] due to difficulties with assigning weights (i.e.contribution to the total quality score) to individual items within the tool[156]. Also, inconsistencies between tools in their criteria for assigning high or low scores

for the same item questions their validity[157]. Disregarding these, of the checklist-based tools, only three addressed all of the criteria deemed important for assessment of risk of bias derived from the STROBE guidelines[155]. These are the Fowkes tool[158], The HEB Wales tool[159] and the DuRantCS tool[160]. However, measurement properties, including the reliability and validity[161] have not been reported for any of these tools.

A review of systems for grading both the quality of evidence and strength of recommendations for the purpose of clinical guideline development, carried out by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) working group, identifed shortcomings in existing approaches[162]. This led to the development of a new system – the GRADE approach, that addressed these weaknesses[151]. One element of GRADE addresses assessment of the quality of individual studies, recommending a simple scheme of assessment against 5 criteria for study limitations that introduce risk of bias for RCTs and against 4 criteria for observational studies[1]. For the latter, criteria were derived from tools identified in earlier reviews[153,154]. The GRADE study limitation criteria for observational studies, provided in Table 2.1, are checklist-based, encompass the same domains as the Fowkes, HEB Wales and DuRant tools but with fewer sub-points, and address recommendations made in the STROBE guidelines. Advantages of the GRADE approach to appraisal of individual observational studies are that studies of different designs may be appraised consistently, explicit instructions are given on how to systematically assign study quality judgements, and the simple criteria are devised to place emphasis on the transparent reporting of reasons for quality judgements made.

Table 2.1 The GRADE criteria for assessment of limitations in observational studies

LIMITATION NO.	EXPLANATION OF STUDY LIMITATION
1	Failure to develop and apply appropriate eligibility criteria (inclusion of control population) • Under- or overmatching in case-control studies • Selection of exposed and unexposed in cohort studies from different populations
2	Flawed measurement of both exposure and outcome • Differences in measurement of exposure (e.g. recall bias in case-control studies) • Differential surveillance for outcome in exposed and unexposed in cohort studies
3	Failure to adequately control confounding • Failure of accurate measurement of all known prognostic factors • Failure to match for prognostic factors and/or lack of adjustment in statistical analysis
4	Incomplete follow-up

Reproduced from Guyatt et al (2011)[1]

Summarising and grading quality of evidence across studies

Another aspect of assessing quality of evidence is the issue of how to summarise the quality assessment across studies to obtain an assessment of the overall quality (grade) of a body of evidence, and how (if the purpose is clinical guideline development) to translate the resulting evidence assessment into strength of clinical recommendations.

GRADE was devised with systematic reviews of clinical intervention and diagnostic studies for the purpose of clinical guideline development in mind. It is not recommended that the whole approach would be applied if the focus is studies on prognosis or aetiology[151]. Table 2.2 lists steps in the GRADE approach and indicates those that may be applied to this review. Despite a few modifications (indicated in Table 2.2), and the fact that the entire GRADE approach would not be applied, these

steps are consistent with other methodological recommendations for conducting systematic reviews[152]. It was decided to follow the relevant steps of GRADE for this review, since in addition to providing clear criteria for assessment of individual studies of both randomised and observational design , GRADE also provides a clear framework for identification and appraisal of evidence, specifies explicit criteria for grading quality of evidence and provides a systematic and transparent approach to the literature review[151]. The methodology described below therefore addresses each of the relevant steps in the GRADE approach that are identified in table 2.2.

Table 2.2 The GRADE approach

STEP IN THE GRADE APPROACH	NOTES
Establish the guideline panel	N/A
Define the scope of the guidelines	**In this case scope of the review**
Prioritise the problems	**To be addressed by review**
Ask precise clinical questions	**To be answered by review**
Decide on the relative importance of outcomes	**N/A (of relevance to clinical recommendations in guidelines)**
Identify the existing evidence for every clinical question	**i.e. the search strategy**
Develop evidence profiles	**According to criteria in table 2.1**
Grade the quality of existing evidence for each outcome separately	**i.e. for each cervical proprioception measure within one test**
Determine the overall quality of available evidence across outcomes	**i.e. across all included cervical proprioception measures within one test**
Decide on the balance between desirable and undesirable consequences	N/A
Decide on the strength of recommendation	N/A
Formulate the recommendation reflecting its strength	N/A
Write the guideline	N/A

Overview of steps followed during the development of an evidence-based clinical practice guideline. Steps relevant to this review are indicated in bold type. Notes are included on relevance to this review, where appropriate. N/A indicates applicable to clinical guidelines, not to the current review. Reproduced from Brozek et al (2009)[151]

The adaptation and use of GRADE to conduct a systematically approached review of evidence derived from observational studies has not been previously evaluated, therefore a descriptive reflection will be provided.

2.3 METHODOLOGY FOR SYSTEMATIC APPROACH TO THE LITERATURE REVIEW

2.3.1 Review scope & objectives

An approach to a systematic review should establish clearly defined broad and/or narrow questions or objectives that determine relevant concepts to include in the search strategy[152]. The broad for aim of the review (1.9.1, 2.1) had 2 objectives (1.9.1) firstly to evaluate whether and/or how mechanical neck pain is associated with altered cervical spine proprioceptive function and secondly to assess the construct validity of tests of cervical proprioception by evaluating correlation between their performance. Since criteria for addressing these 2 objectives were different, it was decided to conduct 2 narrower component reviews[152].

2.3.2 Identification of cervical proprioception tests to prioritise

A number of tests are proposed as measures of cervical spine proprioception. A preliminary review of the literature indicated that those that evaluated voluntary ocular or head motor control (1.5) utilised either joint position error measurement in head repositioning tests[15;52-55;57;150;163-165], the cervico-cephalic kinesthesia[60;166], or the SPNT test of ocular motor function[55;90;91]. The objectives of the literature review were thus focused on these tests.

2.3.3 Identification of neck pain conditions to prioritise

Consideration was also given to the neck pain conditions to be assessed. A cross-sectional study by Revel et al (1991) was the first to describe a test for evaluating cervical poprioception, the cervical JPE test, and to report impairment in participants with neck pain[15] . The study compared a group with chronic neck pain of unspecified aetiology to healthy controls, reporting greater head repositioning absolute error in the neck pain group following both rotation and flexion/extension movements. There is a likelihood of heterogeneity of neck pain type in the study and, with the exception of 2 studies among a specific population comprised of military helicopter pilots and crew[167;168], subsequent studies have evaluated effects in specific sub-classifications of neck pain. Most early studies included participants with Whiplash Associated Disorder (WAD)[51;53;54;60;90;91;165;169]. There is some rationale to anticipate possible differences between WAD and neck pain of non-traumatic aetiology, based on the potential for trauma to vestibular receptors[170;171], the CNS[170] , cervical proprioceptors[54;172], or generalised sensory hypersensitivity[173] reported following whiplash. More recent studies have however evaluated effects on proprioception in non-traumatic onset neck pain[57;135;163;164]. Due to the possible confounding effects of considering all types of neck pain together, it was decided to review neck pain in WAD and neck pain of non-traumatic aetiology separately, for each outcome measure. For the review of correlation between the proprioception tests no such distinction between neck pain types was needed, since analysis in studies would be between tests, rather than between participants. Furthermore, correlation is more readily detected when there is greater variability in measurements across participants[174], which might be expected with a heterogeneous group.

2.3.3 Development of clinical questions to be answered by the reviews

Systematic approaches to reviews of clinical literature should address precise clinical questions[151]. While clinical management questions usually have 4 components – patient population, intervention, comparison and outcomes[151;152], in this instance the questions are not concerned with management and so do not include specification of any interventions. The precise questions to be answered by the reviews thus included the patient population and outcomes components that were derived from the broad aims of the review and following prioritisation of the problems are specified in Table 2.3

Table 2.3 Clinical questions to be answered by the review

REVIEW 1 OBJECTIVE - evaluate whether and/or how mechanical neck pain alters cervical spine proprioceptive function
Clinical questions: 1. In individuals with mechanical neck pain in WAD, is cervical JPE impaired? 2. In individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired? 3. In individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired? 4. In individuals with mechanical neck pain of non-traumatic aetiology, is performance in the cervico-cephalic kinesthesia test impaired? 5. In individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired? 6. In individuals with mechanical neck pain of non-traumatic aetiology, is ocular motor function in the SPNT test impaired?
REVIEW 2 OBJECTIVE - assess the construct validity of tests of cervical proprioception by evaluating correlation between their performance
Clinical question: 1. Is there correlation between performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests?

2.3.4 Identification of existing evidence

Inclusion and exclusion criteria

Tables 2.4 and 2.5 provide detailed inclusion and exclusion criteria for reviews 1 and 2.

Studies of participants with mechanical neck pain[3;4] with no identifiable pathoanatomic cause were included. This classification usually requires that symptoms are provoked by movement but often excludes patients with neurological deficits, cervicogenic headaches or systemic inflammatory conditions, although these criteria have been inconsistently applied in clinical studies[4]. For the purpose of this review, criteria for mechanical neck pain were kept broad to keep the findings as generalisable as possible.

Literature search strategy

The literature search strategy was developed based on identification of relevant concepts and possible terms for these[152]. Two key concepts were identified as mechanical neck pain and proprioception. Studies that addressed these were the target for both reviews, as illustrated in fig 2.1.

Table 2.4 Eligibility criteria for inclusion and exclusion of studies in Review 1

CRITERIA FOR STUDY INCLUSION	CRITERIA FOR STUDY EXCLUSION

Participants
• Had self-reported mechanical neck pain [3], with or without radiculopathy or cervicogenic headaches[a]
• Aetiology of neck pain was either /or
  ○ following a whiplash injury (an RTA or trauma with similar mechanism)[53]
  ○ of non-traumatic aetiology (or described as 'idiopathic')[53;59]
• Included a control group of healthy individuals who were asymptomatic for neck pain[d]
	Participants
	• Had known congenital anatomical anomalies or serious underlying pathology[b]
	• Had sustained head trauma alongside neck injury[c]
	• Neck pain group contained both participants with WAD and neck pain of non-traumatic aetiology, or the classification was unspecified[d]

Study design • Systematic reviews • Controlled studies	Study design • Reviews (with no quality assessment of studies)[e]
Outcome measures • Included either cervical JPE &/or cervico-cephalic kinesthesia &/or SPNT test[f]	Outcome measures • Did not include at least one eligible outcome measure

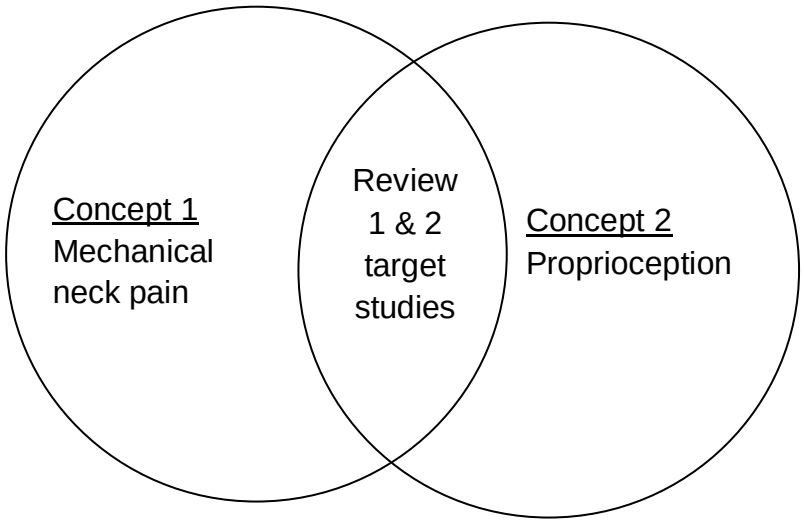
[a] broad criteria to improve generalisability
[b] excluded according to the definition of mechanical neck pain[3]
[c] risk ofinjury to the CNS or otoliths could influence performance in the tests[175]
[d] would not enable the individual questions within the review to be answered
[e] would not contribute to the aims of the review. Bibliographies scrutinised for additional eligible references
[f] identified as priorities for the review. Enable individual questions to be answered

Table 2.5 Eligibility criteria for inclusion and exclusion of studies in Review 2

CRITERIA FOR STUDY INCLUSION	CRITERIA FOR STUDY EXCLUSION
Participants • Had self-reported mechanical neck pain[3], with or without radiculopathy or cervicogenic headaches[a] And/or • Were healthy individuals who were asymptomatic for neck pain neck pain	Participants • Had known congenital cervical anatomical anomalies or serious underlying pathology[b] • Had sustained head trauma[c]
Study design • Systematic reviews • Controlled or uncontrolled studies • Analysis included tests of association between eligible outcome measures	Study design • Reviews with no quality assessment of studies[e]
Outcome measures • Included at least two of either cervical JPE test &/or cervico-cephalic kinesthesia test &/or the SPNT test[f]	

[a] broad criteria to improve generalisability
[b] excluded according to the definition of mechanical neck pain[3]
[c] risk ofinjury to the CNS or otoliths could influence performance in the tests[175]
[d] would not enable the review question to be answered
[e] would not contribute to the aims of the review. Bibliographies scrutinised for additional eligible references
[f] identified as priorities for the review. Enable the review question to be answered

Fig 2.1 Illustration of how key concepts combine to form the target studies for the reviews



A preliminary literature search identified possible terms for these concepts[152]. Relevant papers were searched for related terms (in titles, abstracts or key words) until saturation of terms was reached (no further new terms arose). A broad term list was then condensed into categories (provided in Table 2.6) and developed into sets of search terms for the 'mechanical neck pain' and 'proprioception' concepts, forming the basis of the search strategy. The search included both controlled vocabulary (MeSH) terms, text words, synonyms, alternative spellings and related terms. Searches were limited to studies in humans and to English language articles. The same search strategy (provided in Appendix 1) was used for both reviews, since the same concepts were relevant.

Table 2.6 Search strategy development

MECHANICAL NECK PAIN CONCEPT	PROPRIOCEPTION CONCEPT

Anatomical
• Neck
• Cervical
• Cervical spine
Neck symptoms
• Pain
• Cervicalgia
• Cervicobrachial pain
• Cervicobrachialgia
• Dizziness
Diagnostic/aetiologic terms
• Cervical strain
• Whiplash
• Whiplash-associated disorders
• WAD
• Cervical
  ○ Spinal cord injuries
  ○ SCI
  ○ Degenerative changes
  ○ Osteoarthritis
• Cervicogenic headaches
• CHA
• Chronic non-traumatic neck pain
• Chronic neck pain
• Non-traumatic neck pain
• Cervicobrachial pain syndrome
• Cervical radiculopathy
• Flexion-extension injury
	Definitions of proprioception
	• Kinesthesis
	• Kinesthesia/kinesthesia
	• Kinesthesiologic sensibility
	• Proprioception
	• Proprioceptive
	• Proprioceptor
	• Position sense
	
	Measurement of proprioception
	• Head position sense
	• Cervico-cephalic relocation
	• Neck repositioning test
	• Neck position sense measurement
	• 3-Space Fastrak
	• Electromagnetic tracking
	• Polhemus
	• Error
	• Head repositioning error
	• Joint position error
	• Repositioning error
	• JPE
	• Joint position sense
	• Head repositioning accuracy
	• HRA
	• Ocular motor function
	• Electronystagmography
	• Optotrak
	• Smooth pursuit
	• Smooth pursuit gain
	• Smooth pursuit neck torsion test
	• Eye movement

Identified terms within each concept are condensed into categories

Identification of studies

Studies were identified using methods recommended in the Cochrane handbook for systematic reviews of interventions (2011)[152]. Searches of the bibliographic databases MEDLINE and EMBASE were conducted in 2005 and updated on 17th February and 18th April 2012, respectively. Electronic search strategies for MEDLINE and EMBASE are provided in Appendix 1. A priori journal searches were conducted for terms related to proprioception and neck pain in titles and/or keywords of Manual Therapy, Clinical Chiropractic, Archives of Physical Medicine and Rehabilitation, Spine and the Journal of Rehabilitation Medicine. Post hoc searches were conducted using the related articles features in MEDLINE and in SciVerse ScienceDirect. Post hoc searches of all journals containing relevant studies were carried out using related articles or subject search features. Reference lists were hand checked in all relevant retrieved articles. Grey literature (unpublished findings) was sought using general internet searches based on key authors and research institutions in the field[152].

Study selection

References were collated in a Reference Manager database (Reference Manager 10). Duplicated references were eliminated. One reviewer (GS) screened titles and abstracts of identified articles for likely eligibility. A limitation of the reviews was that, for pragmatic reasons, references were not double-screened. Full text of potentially relevant articles was then obtained, where possible, for further eligibility screening and data extraction.

Data extraction and management

Data from eligible studies were imported into tables, forming the evidence catalogues for both reviews. Data included study design and focus, study participants, outcomes measured, methodological details and results[152;176].

2.3.5 Data analysis

Evidence profiles

Summaries of the assessment of risk of bias in individual studies and assessment of quality of evidence across studies were presented in tabulated format (evidence profiles) for both reviews.

Assessment of risk of bias in individual studies

Individual studies were assessed for risk of bias according to the GRADE criteria (Table 2.1), or other limitations[151]. This was recorded in a risk of bias summary table for each review question[151].

Assessment of quality of evidence across studies

A feature of GRADE is its explicit criteria for determining quality of evidence across a number of studies[151]. The GRADE approach specifies that evidence from observational studies is initially rated as low quality evidence, but upgraded if additional criteria are met. The primary criteria are very large effect sizes (judged by risk ratios), biases likely to decrease the true intervention effect, or the presence of a dose-response gradient[1;151]. These are however relevant to intervention studies and would be unlikely to apply to included studies here. Firstly, calculation of risk ratios is not possible where the outcome (e.g. proprioception impairment) within the patient group cannot be defined as present or not[177]. In addition, there was no intervention,

therefore neither the effect of biases on an intervention effect, nor dose-response gradients could be calculated.Therefore no study could obtain greater than a ‘low quality’ rating, although providing the best way to examine association between neck pain and proprioceptive function.

Restricting the level of evidence to two categories (low or very low quality), would limit differentiation between quality in studies. Brozek et al (2009) advise that additional design features of extremely rigorous well-conducted observational studies may warrant consideration for rating up quality of evidence, provided this is preceeded by exclusion of other serious limitations[178]. It was decided a priori that individual studies and evidence summarised across studies could be upgraded to moderate risk of bias and moderate quality, respectively, if they were well-performed so as to minimise potential sources of bias, and had particular design features that further minimised risk of bias.This decision was supported by the principle of transparency as a feature of the GRADE approach, whereby it is acknowledged that judgements on upgrading or downgrading quality of evidence may not be clear cut[178], but the emphasis is on documenting clearly reasons for such decisions[151]. The a priori specified criteria for determining quality of evidence in observational studies, derived from the GRADE approach[1;151] are provided in Table 2.7.

Table 2.7 Criteria determining the quality of evidence in observational studies

GRADE CRITERION
• Evidence was initially graded as 'low' quality based on observational study design[1;151]

• Evidence was downgraded to 'very low' if[151]
  ○ The best available evidence overall for each outcome possessed ***limitations*** in study design or execution (including factors that increase risk of bias)
  ○ There was ***inconsistency*** of results between studies (where no plausible explanation, such is differences in populations studied, could be identified)
  ○ There was ***indirectness*** of evidence (differences in populations studied or outcome measurements used)
  ○ There was ***imprecision*** of results (studies included relatively few participants so estimates of the effect would be expected to have wide confidence intervals)
  ○ There was ***publication bias*** (e.g. failure for studies to have been reported)

• Evidence was upgraded to 'moderate' if the best available evidence was from studies that
  ○ Adequately met all risk of bias criteria and had no other limitations
  ○ Were extremely rigorous, with additional design features minimising risk of bias (e.g. analyses controlling for prognostic imbalance)
 	
and if among comparable studies there was not (as detailed above) substantial[151]
  ○ ***Inconsistency*** of results
  ○ ***Indirectness*** of evidence measurements
  ○ ***Imprecision*** of results
  ○ ***Publication bias***

• In rating quality of evidence across studies of varying quality the focus was on higher quality studies[1]
• Rating down only occurred where there was substantial risk of bias or other serious study limitations across most of the body of evidence[151]

For each review question, risk of bias and quality for individual studies was considered alongside other up- or downgrading factors across studies in a quality assessment table[1]. Quality assessment was conducted separately for individual outcomes, as specified by GRADE[151], for example in the cervical JPE test repositioning errors in different planes of motion were considered separately. A text summary of evidence was generated that considered all outcomes from the relevant quality assessment table.

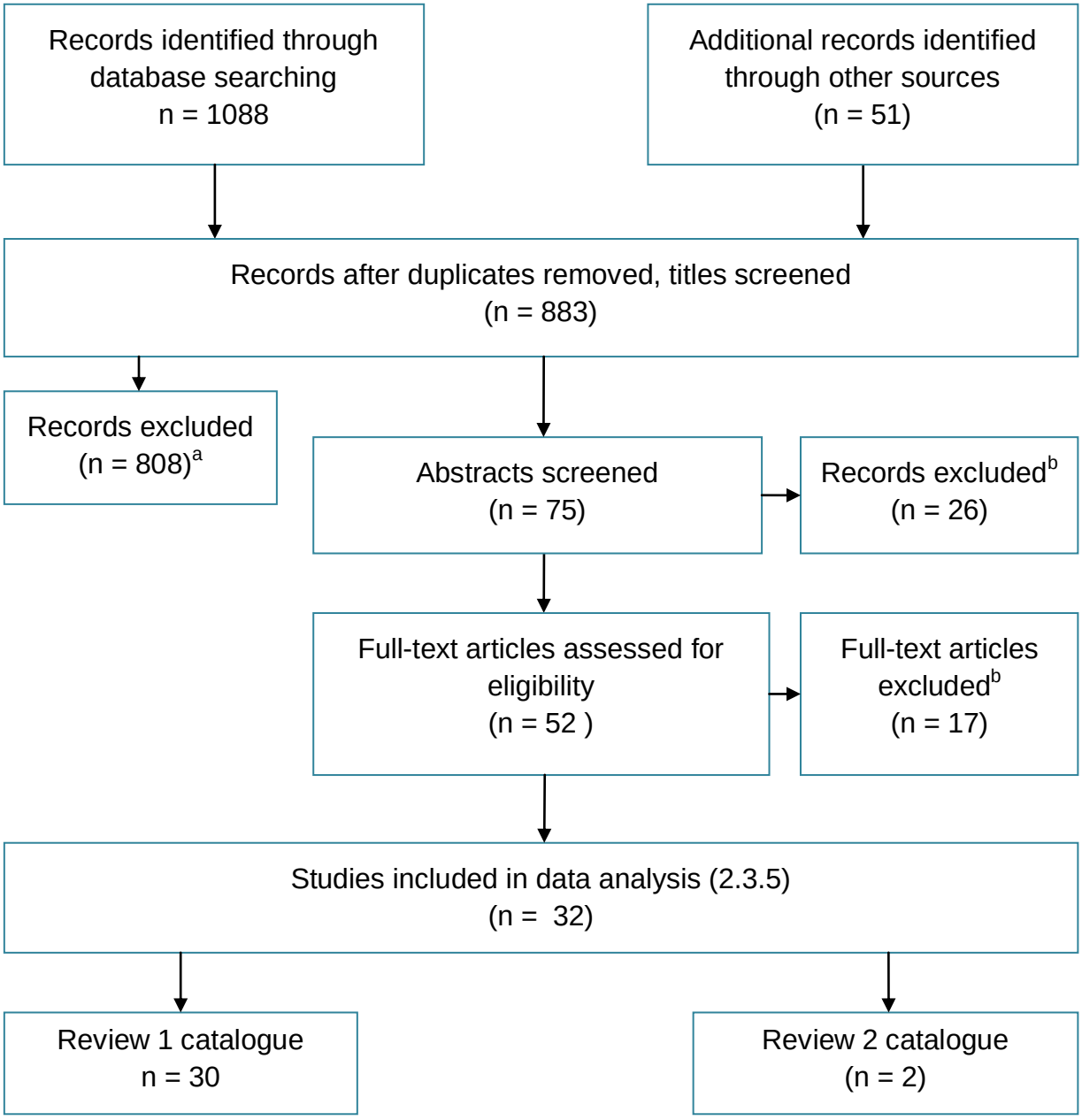
2.4 RESULTS

2.4.1 Identification of existing evidence

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement includes specification of data relating to the search results that should be reported[176]. A flow chart of the search results is provided in Figure 2.2. Initial database searches of MEDLINE and EMBASE identified 740 and 348 records respectively. Journal searches yielded 35 potentially relevant articles in Manual Therapy (15), Clinical Chiropractic (4), Archives of Physical Medicine and Rehabilitation (9), Spine (6) and the Journal of Rehabilitation Medicine (1). 16 additional records were identified by reference searching. Following duplicate removal 883 unique records were retained. Inspection of these did not indicate any apparent means of modifying database searches to exclude studies that were not relevant. Titles were therefore manually screened for possible relevance, followed by further screening of abstracts (n = 75) for eligibility (according to criteria in Tables 2.4 and 2.5). Of 52 full-text articles that were further assessed for eligibility, 14 did not meet the inclusion and exclusion criteria. Reasons for exclusion following screening of abstracts or assessment of full texts are detailed in Appendix 2. The final evidence

catalogues contained 30 records for review 1 and 2 records for review 2. Extracted data from each record in the catalogues is provided in Appendix 3.

Figure 2.2 PRISMA Flow chart of search results showing sources of records and exclusions at each stage of the review[176]



[a]Title indicated that that record was not relevant to review 1 or review 2
[b]Abstract or full text indicated ineligible participants (n = 25), study design (n = 3) and/or outcome measures (n = 16) (according to criteria in Tables 2.4 and 2.5). Excluded records are provided in Appendix 2

2.4.2 Review 1 evidence catalogues and appraisal

The catalogue for Review 1 is provided in Appendix 3 and tabulated results of appraisal of risk of bias in individual studies are presented in Appendix 4. Results of the appraisal of evidence, for each question within Review 1, are detailed in sections 2.4.3 – 2.4.8. Within each review question, the findings and limitations of individual studies are provided for each outcome separately[151]. This is followed by a summary of the quality of evidence across the outcomes within each review question.

2.4.3 Evidence appraisal - in individuals with mechanical neck pain in WAD, is cervical JPE impaired?

The majority of studies in Review 1 investigated participants with whiplash associated disorder (WAD) to evaluate cervical proprioception[51-55;58;60;68;98;140;145;147;148;150;165;179-185;186]compared with healthy controls. Appendix 4 provides results of appraisal of risk of bias and limitations in individual studies.Table 2.7 provides assessment of quality of evidence across studies that is further explained below. Each outcome is considered individually[1]

Table 2.8 Quality assessment of evidence across studies: in individuals with mechanical neck pain in WAD, is cervical JPE impaired?

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: IMPAIRED HEAD-TO-NEUTRAL JPE WITH MOVEMENT IN THE SAGITTAL PLANE						
11	Cross-sectional[51;53;54;58;98;181;183;184;187] prospective cohort[165], case-series[150]	3 studies that had no serious limitations and with features[a] that minimised risk of bias[53;165;184]. Remainder had no serious[b] limitations [54;58;98;181;187] or serious[b,c] limitations[51;150;183]. Some had limitations in reliability[d]	Some[f]	Some[g,i]	Some[h]	Low quality evidence – findings of studies with particular methodological features minimising risk of prognostic imbalance[53;165;184] were inconsistent, 2 reported deficits following extension [53;184] although a further 1 did not[165]. Indirectness in participants and in JPE variables may account for the inconsistency.Therefore overall quality of evidence was not downgraded for inconsistency. Of remaining studies with no serious[54;58;98;181;187] or serious limitations[51;150;183], most did report deficits in extension and/or flexion[54;181;183;188;51;150;187], although there was some inconsistency [58;98].
OUTCOME: IMPAIRED HEAD-TO-NEUTRAL JPE WITH MOVEMENT IN THE TRANSVERSE PLANE						
13	cross-sectional[10;51-54;58;98;182-184;187] prospective cohort[165], case-series[150]	3 studies with no serious limitations and with features[a] that minimised risk of bias[53;165;184]. Remainder had no serious[b] limitations[10;52;54;58;98;187] or serious[c,d] limitations[51;150;182;183]	Some[f]	Some[g]	Some[h]	≈Moderate quality evidence - findings of studies with particular methodological features mimimising risk of prognostic imbalance[53;165;184] consistently reported deficits for right[53;165;184] and/or left[184] rotation. Evidence was upgraded[178] due to particular design features that reduced study limitations[i]. Findings deficits were also largely consistent among studies with no serious [10;52;54;58;98;187] or serious limitations[51;150;182;183], with only one reporting no deficit[58].

Table 2.8 continued

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE SAGITTAL PLANE (FLEXION/EXTENSION)						
2	Cross-sectional[58;68]	Both studies had no serious[b] limitations	Some[f]	Some[g]	Some[h]	≈Very low quality evidence - 2 studies with no serious limitations[58;68] consistently report no effect of WAD on head-to-target repositioning following extension. For head-to-target repositioining folowing flexion, there were inconsistent findings for impairment in WAD. Inconsistency, indirectness in populations studied and imprecision resulted in rating down of evidence quality
OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE TRANSVERSE PLANE (ROTATION)						
6	Cross-sectional[52;58;68;140;145;181]	4 studies with no serious[b] limitations[52;58;68;181]. Others had serious limitations or very serious limitations[140;145]	Some[f]	Some[g,i]	Some[h]	≈Very low quality evidence - Most studies with no serious limitations report no deficit[52;58;68], there is however some inconsistency[181]. A further 2 studies with serious[42] or very serious limitations[140;145] did report deficits. Inconsistency among studies of sufficient quality, indirectness and imprecision resulted in rating down of evidence quality
OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE FRONTAL PLANE (LATERAL FLEXION)						
3	Cross-sectional[140;145;181]	1 study with no serious[b] limitations[181]. Others had serious[145] or very serious[c] limitations[140]	Some[f]	Some[g,i]	Some[h]	≈Very low quality evidence–a single study with no serious limitations reports JPE deficits following combined lateral flexion with rotation in WAD I&II, but not in WAD III[181]. 2 further studies with serious[145] or very serious limitations[140;145] also report deficits in lateral flexion. Paucity of studies of sufficient quality, indirectness and imprecision resulted in rating down of evidence quality

[a] Analysis methods controlled for prognostic imbalance, reducing limitations in observational study design[53;165;184]
[b] Unclear if there is prognostic imbalance[51;52;58;68;140;145;150;182;183;187], unclear eligibility criteria[51;145;150;183;187] or unclear risk of examiner bias[51;140;145;150:10;183]
[c] Unclear if follow-up was adequate or if there were dropouts, however longitudinal analysis not relevent to review question[150]
[d] Poor reliability of outcome measurement protocol for repositioning following extension
[f] Different findings
[g] Different populations studied
[h] Small sub-groups of participants[51;58;140;145], but some studies had adequate sample size
[i] Differences in outcome measurement method
≈ indicates quality of evidence judgements that were considered to be borderline. Results for publication bias are not presented, but were judged unlikely for all outcomes and did not influence evidence quality grades

Outcome: impaired head-to-neutral repositioning in the sagittal plane

Three studies had no serious limitations and additionally, used analysis methods to minimise the risk of prognostic imbalance[53;165;184]. There was some evidence among these for JPE deficits in repositioning of the head-to-neutral following a movement in the sagittal plane, in both acute[53] and chronic[184] WAD. Findings were however inconsistent and there was indirectness (different patient groups and measures of error)[165]. Sterling et al (2004) found that among participants with acute symptoms (< 1 month post-trauma) only a sub-group (n = 12) with severe symptoms (NDI = 69.5) had extension JPE deficits with greater AE absolute error (AE) compared to groups with mild or moderate symptoms and a healthy control group ($p<.01$)[53]. Hill et al also (2009) reported JPE deficits for repositioning following extension, in chronic WAD (greater than 3 months duration)[184] whereby constant error (CE) was greater for both in WAD with dizziness and in WAD without dizziness, when compared to healthy controls. A directional bias was reported whereby WAD groups tended to overshoot the target[184]. No significant difference in AE, root mean square error (RMSE) or variable error (VE) for repositioning following extension was found between groups. In contrast to these two reports of JPE deficits in WAD, Sterling et al (2003) reported conflicting findings, with no extension JPE deficit found in an acute onset (< 1 month post-collision) WAD group[165]. However, while JPE measurements were taken at baseline (less than 1 month post-collision) this prospective study by Sterling et al (2003) grouped patients according to their symptom level at 3 months post-collision[165], which may have been different from what their baseline NDI score would have been, making direct comparison with their 2004 study[53] difficult. A further limitation that might contribute to the inconsistency of findings in these studies is that all used a protocol of 3 trial repeats, which has been reported as having poor reliability for ($ICC_{?\ model} = .29$) for measurement of head-to-neutral repositioning

following extension[144]. None of these studies evaluated repositioning to neutral following flexion movements[53;165;184].

A further 8 studies had no serious[54;58;98;181;183;187] or serious[51;150;83] limitations, but did not posess additional design features to further reduce the risk of bias. Most reported deficits in repositioning in the sagittal plane following extension[54;181;183;187] or flexion[51;150;181]. However this finding was not consistent, with some reporting no deficits following extension[58;98] or flexion[58]. There was indirectness in the populations studied with sagittal plane deficits reported in recent WAD[183], chronic WAD III[181], chronic WAD II or III[51;54] and chronic WAD of unspecified grade[187]. Studies that found no deficits included participants with mild-moderate disability[58], WAD I or II[58;181], or chronic WAD of unspecified grade with a high variance in disability[98]. It is possible that severity of symptoms or disability level might determine whether or not there is a JPE deficit in WAD for repositioning in the sagittal plane. In support of this, Sterling et al (2004) found a deficit following extension when comparing participants with severe acute symptoms to healthy controls, but not when comparing sub-groups with mild or moderate symptoms (participants with acute WAD grade II or III were grouped according to symptom severity, measured by the Neck Disability Index (NDI)). This differed from findings for repositioning following rotation, where both the moderate and the severe symptom groups were impaired[53]. Feipel et al (2006) also reported a deficit for chronic WAD III, but not for WAD I or II, compared with healthy controls[181].

Outcome: impaired head-to-neutral repositioning in the transverse plane

For repositioning following rotation, three studies with no serious limitations and that used analysis methods to minimise that risk of prognostic imbalance in individuals

with acute[53;165] or chronic[184] WAD consistently reported JPE deficits, following either right rotation[53;165;184] or left rotation[184]. Sterling et al (2004) controlled for potential gender imbalance between patients and asymptomatic controls[53]. They reported increased JPE following right, but not left head rotation in sub-groups with both moderate (NDI = 39.5) and severe (NDI = 69.5) symptoms when classified within 1 month post-collision, compared with both a mild symptom and an asymptomatic group[53].

A prospective study by Sterling et al (2003) also reported impaired JPE following right (but not left rotation or extension) repositioning that was present at baseline and remained to 3 months in sub-groups categorised as having moderate and severe symptoms (based on NDI scores at 3 months)[165]. No change over time in JPE was identified between measurements at <1, 2 and 3 months post-collision. Together, these studies indicate an association between early symptom severity and early JPE (right rotation and extension)[53] and also association between early JPE (right rotation) and having moderate or severe symptoms at 3 months[165].

A further study with minimised risk of bias by Hill et al (2009) evaluated a range of measures of error in 50 chronic WAD participants with dizziness, 50 without dizziness and a group of 50 healthy controls[184]. They reported greater JPE for repositioning in WAD with dizziness compared to healthy controls following right rotation (AE and RMSE) and left rotation (AE, RMSE and CE). In WAD without dizziness only CE following right rotation was greater compared with the control group. Comparing the WAD groups with and without dizziness to each other indicated greater AE and RMSE associated with dizziness following both directions of rotation.

Of the remaining studies with no serious[10;52;54;58;98;182;183] or serious[51;150;88] limitations, largely consistent results of greater JPE among WAD participants were reported for right rotation[54;150;182;183;187], left rotation[54;98;182;183] and the mean of left and right rotation[52]. JPE deficits in the transverse plane were reported among participants with recent WAD[183], chronic WAD[52;98;150;182;187] or chronic WAD II or III with dizziness[54]. There was some inconsistency however, with other studies reporting no rotation JPE deficits in mild-moderate WAD[58], chronic WAD I or II[10], WAD II or III without dizziness[54] or chronic WAD of 1-2 years duration[51]. Two of these studies included groups with relatively low grades of WAD[10;58] and are in accordance with the finding by Sterling et al (2004) that subgroups within WAD II or III identified by cluster analysis as having moderate or severe disability had greater right rotation JPE than a subgroup with only mild disability[53]. As for repositioning following movement in the sagittal plane, it is possible that JPE deficits may be associated with higher pain and/or disability levels.

Another possibility is that participants with WAD who also experienced symptoms of dizziness of suspected cervical origin have greater JPE deficits than participants with WAD with no dizziness. Treleaven et al (2003) compared these two groups, finding a significantly greater JPE following right rotation in the group with dizziness[54]. The study did not have serious limitations, however a potentially confounding imbalance in pain index scores was evident that was not controlled for in the analysis. Only one other study, with serious limitations, has compared JPE between WAD with dizziness and WAD without dizziness. Heikkila et al (1998) also reported significantly greater right rotation JPE in WAD with dizziness compared with WAD without dizziness participants[51]. Measurements of JPE in the study were however made 1-2 years post-collision, with the group classifications being based on the initial acute

presentation shortly after the injury. Some participants no longer had any symptoms at the time that JPE was measured and thus the association between JPE and current symptoms of dizziness can not be ascertained[51].

Outcome: impaired head-to-target repositioning in the sagittal plane

Only 2 studies, both with no serious limitations, have evaluated head-to-target repositioning in WAD compared to healthy controls following flexion or extension movements[58;68]. These reported no difference between groups for repositioning following extension in chronic WAD. Findings were however inconsistent for repositioning following flexion. Armstrong et al (2005) found no JPE deficit in a group of mild or moderate disability WADII participants[58]. In contrast, Grip et al (2007) did report JPE deficits following flexion, but only in CE (not AE or VE)[68].

Outcome: impaired head-to-target repositioning in the transverse plane

For repositioning to a pre-determined, remembered mid-range target following a rotation movement, results are inconsistent. Most studies with no serious limitations reported no JPE deficit in WAD[52;58;68]. A study by Kristjansson et al (2003) included a group with chronic WAD (3-24 months) and a healthy control group[52]. They minimised most sources of bias except that imbalance in pain and disability between the WAD group and a non-tauma neck pain group was not controlled for. This would not however affect the comparison between WAD patients and healthy controls which thus provides the best evidence indicating no effect of WAD on head-to-target repositioning following rotation. In contrast, Feipel et al (2006)[181] also addressed most sources of bias and reported increased JPE deficits among a WAD I & II subgroup, but no deficit among a group with a higher level WAD III injury. The relatively small size of the WAD I & II subgroup (n = 8) however makes this finding

uncertain[181]. Increased JPE was also reported in participants with WAD by Loudon et al (1997)[42] and Madeleine et al (2004)[140] for repositioning to targets at both 30 degrees and 50 degrees from the midline position. These were however both studies with serious[42] or very serious limitations[140], and the latter although describing a tendency to greater errors in WAD, presented no descriptive or statistical results[140].

Outcome: impaired head-to-target repositioning in the frontal plane

A single study with no serious limitations[181] and 2 with serious[140;145] have reported JPE deficits following lateral flexion[140;145] and combined rotation with lateral flexion movements[181]. Feipel et al (2006) reported greater JPE following combined rotation and lateral flexion movement in a group of WAD I or II patients, but no such deficit in a group with WAD III[181]. The study addressed most potential sources of bias. Loudon et al (1997) also reported greater JPE in chronic WAD following lateral flexion as the primary plane but had a number of potential sources of bias[145]. The only other study to report a 'tendency' to greater errors in chronic WAD did not present any statistical or descriptive results[140]

Evidence summary - in individuals with mechanical neck pain in WAD, is cervical JPE impaired?

For head-to-neutral repositioning tests there is overall moderate quality evidence for impaired cervical JPE when participants with WAD are compared to healthy controls when repositioning follows movement in the transverse plane. Evidence for impairment when repositioning follows sagittal plane movement is of low quality.There is no evidence available regarding head-to-neutral repositioning in the frontal plane in WAD.

For head-to-target repositioning tests there is very low quality evidence for impaired cervical JPE when participants with WAD are compared to healthy controls in their ability to relocate remembered targets following movement in either the sagittal, transverse or frontal planes

2.4.4 Evidence appraisal - in individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired?

A number of studies have evaluated whether greater errors in cervical JPE are associated with neck pain of non-traumatic origin compared with healthy controls[10;52;59;68;163;164;182;189-191]. Appendix 4 provides results of appraisal of risk of bias and limitations in individual studies.Table 2.9 provides assessment of quality of evidence across studies that is further explained below. Each outcome is considered individually[1].

Outcome: impaired head-to-neutral repositioning in the sagittal plane

For head repositioning to a neutral location following an active movement in the sagittal plane, two studies with no serious[164] or serious limitations[191] and with small sample sizes reported greater errors for head repositioning following flexion, but not extension movements in chronic non-trauma neck pain compared with healthy controls[164;191]. There was also potential prognostic imbalance due to either gender imbalance between groups[164] or the possibility that individuals suffering with dizziness or vertigo may have been included in the neck pain group (these symptoms were not specified as exclusion criteria in this group but were excluded from the control group)[191]. A further study by Cheng et al (2010) did report greater

Table 2.9 Quality assessment of evidence across studies: in individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired?

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	EVIDENCE SUMMARY
OUTCOME: IMPAIRED HEAD-TO-NEUTRAL JPE FOLLOWING MOVEMENT IN THE SAGITTAL PLANE (FLEXION/EXTENSION)						
4	Cross-sectional[59;164;189;191]	3 studies with no serious [a,b] limitations[59;164;189] and 1 study with serious limitations[191]	Some[c]	Some[d,e]	Some	Low quality evidence for JPE following flexion findings of impairment were consistent in 2 studies with no serious limitations [189;51] and a third that had serious limitations[191]. A single inconsistent finding, from a study with no serious limitations was from a different (currently asymptomatic) population[59]. For JPE following extension, a single study with no serious limitations but utilising an outcome measurement method with poor reliability and unclear validity reports a deficit[189].There is inconsistency, whereby other studies with no serious limitations or serious limitations report no deficit in symptomatic non-trauma neck pain[164;191] or in currently asymptomatic individuals with a history of neck pain[59]
OUTCOME: IMPAIRED HEAD-TO-NEUTRAL JPE FOLLOWING MOVEMENT IN THE TRANSVERSE PLANE (LEFT/RIGHT ROTATION)						
7	Cross-sectional[10;52;59;164;182;190;191]	5 studies with no serious[a,b] limitations[10;52;59;164;64] and 2 with serious[a] limitations[55;58]	Yes[c]	some[d]	Some[f]	≈Very low quality evidence for impaired JPE following left and right rotation in non-trauma neck pain evidence quality was downgraded due to marked inconsistency in findings among the best available studies. In studies with no serious limitations, 2 reported deficits[52;182] while 3 found no deficit[10;59;164]. A further 2 studies with serious limitations reported conflicting findings[55;58].There was indirectness in populations sampled and some imprecision whereby some studies had very small sample sizes[164;182;190;191]
OUTCOME: IMPAIRED HEAD-TO-NEUTRAL JPE FOLLOWING MOVEMENT IN THE FRONTAL PLANE (LATERAL FLEXION)						
2	Cross-sectional[59;164]	2 studies with no serious[a] limitations[59;164]	No	Yes[d]	Yes[f]	Low quality evidence – *no effect* in non-trauma neck pain on JPE following lateral flexion. There are consistent findings of *no effect* from the only 2 studies evaluating this outcome which both had no serious limitations[59;164]. There was indirectness in the populations sampled and the only study with currently symptomatic participants had small sample sizes[164]

Table 2.9 continued

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
	OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE SAGITTAL PLANE (FLEXION/EXTENSION)					
2	Cross-sectional[59;68]	Both studies with no serious[a] limitations[59;68]	No	some[d]	No[g]	Low quality evidence - *no effect* for head-to-target repositioning with flexion or extension. There are consistent findings of *no effect* in 2 studies with no serious limitations[59;68], although there was some indirectness in populations sampled whereby 1 study used currently asymptomatic participants with a history of neck pain[59].
	OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE TRANSVERSE PLANE (ROTATION)					
3	Cross-sectional[52;59;68]	3 studies with no serious[a] limitations[52;59;68]	No	Some[d]	No[g]	Low quality evidence – *no effect* of non-trauma neck pain on head-to-target repositioning with rotation. There are consistent findings of *no effect* in 3 studies with no serious limitations[52;59;68] although there was some indirectness in populations sampled whereby 1 study used currently asymptomatic participants with a history of neck pain[59].
	OUTCOME: IMPAIRED HEAD-TO-TARGET JPE WITH MOVEMENT IN THE FRONTAL PLANE (LATERAL FLEXION)					
1	Cross-sectional[59]	1 study with no serious[a] limitations[59]	N/A[h]	Some[d]	No[g]	≈Low quality evidence – *no effect* of non-trauma neck pain on head-to-target repositioning following lateral flexion was reported in a single study with no serious limitations[59], this was however in participants with a history of mild neck pain, but who were currently asymptomatic. Altough only 1 study existed, evidence quality was not downgraded since this had adequate sample size

[a]Unclear if there is prognostic imbalance[52;59;68;163;164;182;190;191], unclear eligibility criteria[190] or unclear risk of examiner bias[10;191]
[b]Poor reliability for repositioning following extension[189] and/or unclear validity[182;189] of outcome measurement protocol
[c]Different findings
[d]Different populations studied
[e]Differences in outcome measurement method[189]
[f]Small groups of participants in most studies[164;182;189-191], but some studies had adequate sample size[10;52;59;163;192]
[g]Studies had adequate sample size[52;59;68;163]
[h]Could not be evaluated due to only a single study being available
≈ indicates quality of evidence judgements that were considered to be borderline. Results for publication bias are not presented, but were judged unlikely for all outcomes and did not influence evidence quality grades

errors for repositioning following both extension and flexion in young adults with chronic neck pain[189]. The study, however, cannot be compared directly to the others since it used a different method for evaluation of cervical JPE in repositioning to neutral, whereby the subject performed the test with their eyes open. There is further inconsistency, with Teng et al (2007) reporting no deficit in either JPE following flexion or extension, although this was among a different population of young and middle aged adults with a history of mild chronic neck pain, who were currently asymptomatic[59].

As well as differences in test method, the inconsistency in findings for an effect of non-trauma neck pain on cervical JPE in repositioning to neutral following extension might relate to indirectness in populations sampled, with some studies specifying current chronic neck pain of over three months duration[164;191] while others included a younger adult sample[189], or currently asymptomatic individuals with a history of mild, chronic neck pain[59]. In addition, two studies utilised a protocol of only three trial repeats of repositioning following each direction of motion[59;189] which was shown to have poor reliability ($ICC_{?model}$= .29) for measurement of head-to-neutral repositioning following extension[144]. Others utilised ten trial repeats, using the manual method of JPE measurement described by Revel et al (1991)[15]. No studies have reported evaluation of the reliability of this method for repositioning in the sagittal plane using ICCs, making comparison between the protocols difficult. This highlights the importance of establishing protocols that produce reliable estimates for outcome measures used in studies.

Outcome: impaired head-to-neutral repositioning in the transverse plane

A number of studies have evaluated this outcome, however findings were inconsistent[10;52;59;164;182;190;191]. Kristjansson et al (2003) reported greater JPE in a study with no serious limitations and moderate sample size that considered and minimised most sources of bias in a chronic (> 3 months) non-trauma group, compared with asymptomatic controls.There was however potential prognostic imbalance in age distribution between groups[52]. Two further studies also reported similar deficits in chronic non-trauma neck pain compared with asymptomatic controls. Pinsault et al (2008) reported greater AE and VE following left and right rotation[190] , while Sjolander et al (2008) reported significantly greater VE (but not CE) following right rotation, but not left rotation[182]. Both of these studies however had small sample sizes. In contrast, four studies with chronic non-trauma neck pain participants[10;59;164;191] did not find any greater JPE for repositioning following rotation compared with asymptomatic controls. These all had either small sample sizes[164;191], used a currently asymptomatic neck pain group[59] or had the possibility of experimenter bias, associated with using a manual method of JPE measurement without blinding of the examiner[10;191].

Outcome: impaired head-to-neutral repositioning in the frontal plane

Two studies, with no serious limitations, evaluated head-to-neutral repositioning following lateral flexion movements[59;164]. Both reported that cervical JPE was not impaired. Of these, only Palmgren et al (2009) used participants with current neck pain symptoms[164], but this was a pilot study with small sample size. It is thus unclear whether deficits might be apparent in a larger study.

Outcome: impaired head-to-target repositioning in the sagittal plane

For repositioning to a remembered target in the sagittal plane with either flexion or extension, two studies with no serious limitations by Grip et al (2007) and Teng et al (2007), reported consistent findings of no significant difference between healthy controls and either participants with non-specific neck pain[68], or young and middle-aged adults with a history of mild chronic neck pain who were currently asymptomatic[59]. Both studies had moderate sample size but had some potential confounding associated with gender imbalance between groups[59] or lack of specification of whether participants with vestibular disorders were excluded[68].

Outcome: impaired head-to-target repositioning in the transverse plane

Three studies, with no serious limitations, by Grip et al (2007), Teng et al (2007) and Kristjansson et al (2003) found no deficit in JPE for repositioning to a remembered target with rotation in non-trauma neck pain[59;68;52]. As well as JPE, Grip et al (2007) also evaluated axis of motion during repositioning tasks and did find significant, pain-related differences in flexion and left rotation, compared to healthy controls. This indicates that different kinematic patterns utilised during the tasks did not result in JPE differences.

Outcome: impaired head-to-target repositioning in the frontal plane

Only a single study, with no serious limitations, by Teng et al (2007) evaluated repositioning to a remembered target in lateral flexion. The study found no deficit in currently asymptomatic participants with a history of mild neck pain, compared with individuals with no neck pain history.

Evidence summary - in individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired?

Studies comparing participants with non-traumatic neck pain with healthy controls are generally of lower quality and with less consistent findings than for participants with WAD. For head-to-neutral repositioning in the sagittal plane there was overall low quality evidence for greater errors following flexion among chronic non-trauma neck pain participants, compared to healthy controls. However there was only very low quality evidence for greater errors following extension. There is some evidence, which is overall of very low quality, for deficits in repositioning in the transverse plane. No evidence was found that indicated impairment with head-to-neutral repositioning in the frontal plane. Rather, studies that existed provided low quality evidence of no impairment. For head-to-target repositioning no evidence was found that indicated deficits for any plane of movement when participants with non-traumatic neck pain were compared to healthy controls. Rather, studies that existed provided low quality evidence of no impairment.

2.4.5 Evidence appraisal - in individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired?

Two studies evaluated the effect of WAD on performance in a complex test of head movement control, the cervico-cephalic kinesthesia test that is proposed as a measure of proprioception. Appendix 4 provides results of appraisal of risk of bias and limitations in individual studies. Table 2.10 provides assessment of quality of evidence across studies that is further explained below.

Outcome: impaired mean error between visual target and head position

Two studies with no serious limitations reported consistent findings of greater error when tracking a visual target by moving the head in participants with WAD, compared with asymptomatic controls[60;80]. There was some inconsistency in the groups studied, whereby Kristjansson et al (2004) used only female participants[60] but the later study by the same group in 2010 used both male and female participants[80]. Both had moderate but adequate sample sizes of n = 18-20 per group. Neither study was upgraded since prognostic balance between groups was unclear. Age distributions were not described in the earlier study[60] while in the later study there was an apparent imbalance in the gender distribution between the WAD and control group that was not controlled for in the analysis.

Evidence summary - in individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired?

There is some low quality evidence for deficits in WAD, compared with healthy controls in performance in cervico-cephalic kinesthesia test.

2.4.6 Evidence appraisal - in individuals with mechanical neck pain of non-traumatic aetiology, is performance in the cervico-cephalic kinesthesia test impaired?

A single study evaluated the effect of non-traumatic neck pain on performance in the cervico-cephalic kinesthesia test, compared with healthy controls[80]. Appendix 4 provides results of appraisal of risk of bias and limitations in individual studies. Table 2.11 provides assessment of quality of evidence across studies that is further explained below.

Table 2.10 Quality assessment of evidence across studies: in individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired?

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: IMPAIRED MEAN ERROR BETWEEN VISUAL TARGET AND HEAD POSITION						
2	Cross-sectional[60]	Both studies had no serious [a] limitations[60;80]	No	Some[b]	No[c]	Low quality evidence – consistent findings for an effect of WAD on increasing error from 2 studies with no serious limitations[60;80]. There was some indirectness as 1 study included only female participants[60]

[a] Unclear if there is prognostic imbalance[60;80]
[b] Different populations studied
[c] Both studies had adequate sample size

Results for publication bias are not presented, but were judged unlikely for all outcomes and did not influence evidence quality grades

Table 2.11 Quality assessment of evidence across studies: in individuals with mechanical neck pain of non-traumatic aetiology, is performance in the cervico-cephalic kinesthesia test impaired?

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: IMPAIRED MEAN ERROR BETWEEN VISUAL TARGET AND HEAD POSITION						
1	Cross-sectional[80]	A single study with no serious[a] limitations[80]	N/A	N/A	No[b]	Low quality evidence – a single study with no serious limitations reported an effect of non-traumatic onset neck pain on error[80].

[a]Unclear if there is prognostic balance[80]
[b]study had adequate sample size[80]

Results for publication bias are not presented, but were judged unlikely for all outcomes and did not influence evidence quality grades

Outcome: impaired mean error between visual target and head position

Kristjansson et al (2010) evaluated the effect of neck pain of non-traumatic aetiology on performance in 'The Fly' test, reporting greater errors compared with healthy controls[80]. The study had a moderate sample size and no serious limitations but did have potential age and gender distribution imbalance between groups.

Evidence summary - in individuals with mechanical neck pain of non-traumatic aetiology, is cervico-cephalic kinesthesia in 'the fly' test impaired?

There is limited low quality evidence for deficits in neck pain of non-traumatic aetiology, compared with asymptomatic control participants in performance in 'The Fly' test for cervico-cephalic kinesthesia.

2.4.7 Evidence appraisal - in individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired?

Seven studies have compared SP velocity gain with the head in neutral position and also in a neck torsion position between individuals with mechanical neck pain resulting from whiplash injury and healthy controls[90;91;98;99;101;193;194]. There was indirectness in outcomes reported with some reporting only SP gain with and without neck torsion[193;194], some reporting only the SPNT difference[98] and others reporting both[90;91;99;101]. Diferent outcomes within the studies are considered separately[1]. Appendix 4 provides results of appraisal of risk of bias and limitations in individual studies. Table 2.12 provides assessment of quality of evidence across studies that is further explained below.

Outcome: impaired smooth pursuit velocity gain

A study by Kongsted et al (2007) compared 34 individuals with chronic WAD (> 6 months, unspecified grade) with a healthy control group (n = 60) and found no difference in SP velocity gain in either a head neutral, left or right torsion postions[101]. The study had no serious risk of bias and, in adition, used analysis methods that minimised the risk of prognostic imbalance. However, testing was carried out in 2 sessions with a break between and no analysis of systematic effects or reliability was presented. Ocular motor performance was measured using an EOG system and a visual target with a maximum velocity of 38 degrees sec^{-1}. There was indirectness, with other studies using slower maximum target velocities of approximately 20 degrees sec^{-1}. In addition, the methodology in the study included supporting the participants head with a chin rest, while other studies manually stabilised the head[101].

There were inconsistent findings among the remaining 5 studies. In accordance with the results of Kongsted et al (2007), Dispenza et al (2011) reported no effect of WAD on SP velocity gain among a patient group with more variable duration of symptoms ranging from 1-12 months[193]. This was the only study to use a video-graphic system to measure SP gain in neutral and torsion positions. The study had no serious limitations, although there was some lack of reporting of data processing methods and some potential for prognostic imbalance. Other studies that evaluated SP gain with and without neck torsion did report deficits in chronic WAD[90;91;99;194]. Studies with no serious limitations byTreleavan et al (2005)[91]

Table 2.12 Quality assessment of evidence across studies: in individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired?

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: IMPAIRED SMOOTH PURSUIT VELOCITY GAIN						
6	Cross-sectional[90;91;99;101;193;194]	2 studies with no serious limitations and additional methodoligcal features that that minimised risk of bias[91;101], a further 2 studies had no serious[a] limitations[193;194] while 2 had serious[a] limitations[90;99]	Yes[b]	Yes[c,d]	No[e]	Low quality evidence -for an effect of WAD on SP gain, 1 study with no serious limitations that minimised bias[101] found no impairment. There was however inconsistency among the remaining studies, with most reporting a deficit[90;91;99;194] while1 did not[193]. Indirectness in outcome measurement methods and in populations studied may account for the inconsistency.
OUTCOME: IMPAIRED SMOOTH PURSUIT NECK TORSION DIFFERENCE						
5	Cross-sectional[90;91;98;99;101]	1 study with no serious limitations and additional methodoligcal features that that minimised risk of bias[101], a further 2 studies had no serious [a]limitations[91;98], while 2 had serious[a] limitations[90;99]	Yes[b]	Yes[c,d]	No[e]	Low quality evidence – for an effect of WAD on the SPNT difference, 1 study with no serious limitations that minimised bias found no impairment. There was however inconsistency among the remaining studies, with some reporting a deficit[90;91;98], while 1did not[99]. Indirectness in outcome measurement methods and in populations studied may account for the inconsistency.

[a]Unclear if there is prognostic imbalance[90;98;193;194], unclear eligibility criteria[99] or unclear risk of examiner bias[90;99]
[b]Differences in findings
[c]Differences in outcome measurement methods[101]
[d]Differences in populations studied
[e]All had adequate sample size

and with serious limitations by Tjell et al (1998)[90], evaluated WAD (grade II[90;91] or above[90]) both with and without associated dizziness, finding significantly reduced SP gains in both WAD groups compared with healthy controls. In chronic WAD (>6 months duration), A study with no serious limitations by Gimse et al (1996)[194] and a further study by Prushansky et al (2004)[99] both reported reduced SP gain, although the latter study had serious limitations.

Outcome: impaired smooth pursuit neck torsion difference

Reports of the effect of WAD on the SPNT difference, compared with healthy controls, are inconsistent. Kongsted et al (2007) found no difference (chronic WAD > 6 months, unspecified grade) in a study with no serious limitations, that used analysis methods that minimised risk of bias. The study however utilised a faster target velocity than other studies, resulting in some indirectness[101]. Prushansky et al (2004) similarly found no difference(grade II or III WAD > 6 months), although the study had serious limitations. Two studies with no serious limitations[91;98] and a further study with serious limitations[90;98] however did report differences in the SPNT difference in WAD of >3 or >6 months duration[90;91;98]. BothTjell et al (1998)[90] and Treleavan et al (2005)[91] included both WAD groups with and without dizziness, finding deficits in both, compared with healthy controls and also a significant difference between the WAD groups, with a greater SPNT difference associated with dizziness.

Evidence summary - in individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired?

There are inconsistent findings with some low quality evidence that SP velocity gain is impaired in the SPNT test in individuals with WAD. Similarly, for the SPNT difference, there are inconsistent findings and low quality evidence of ocular motor

dysfunction in WAD. Indirectness in the tasks (different target velocities) populations studied (different chronicity and grades of WAD) and in the outcomes reported (SP gain or the SPNT difference) make comparisons difficult.

2.4.8 Evidence appraisal - In individuals with mechanical neck pain of non-traumatic aetiology, is ocular motor function in the SPNT test impaired?

No studies were found that compared individuals with neck pain of non-traumatic aetiology with healthy controls in the SPNT test.

Evidence summary - In individuals with mechanical neck pain of non-traumatic aetiology, is ocular motor function in the SPNT test impaired?

No evidence exists for comparison of SP velocity gain or the SPNT difference between individuals with non-traumatic neck pain and healthy controls.

2.4.9 Review 2 evidence catalogues and appraisal

The catalogue for Review 2 is provided in Appendix 3 and tabulated results of appraisal of risk of bias in individual studies are presented in Appendix 4. Results of the appraisal of evidence, for each question within Review 2, are detailed in section 2.4.1. The findings and limitations of individual studies are provided for each outcome separately[151]. This is followed by a summary of the quality of evidence across the outcomes addressing the review question.

2.4.10 Evidence appraisal - In individuals with mechanical neck pain, is there correlation in performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests

Initial literature searches identified a single study by Treleaven et al (2006)[55], however updated searches in 2012 also identified the methodological study by Swait et al (2007)[195] that was conducted as part of this thesis (Chapter 3, Appendix 5). Table 2.13 provides assessment of quality of evidence in both studies, that is further explained below.

Outcome: correlation between performance in the SPNT test and cervical JPE

A study,with no serious limitations, by Teleaven et al (2006) evaluated correlation in performance between the cervical JPE test and the SPNT test in individuals with WAD and in healthy controls[55]. 100 participants with WAD grade II of at least 3 months duration were sub-grouped into 50 with dizziness and 50 without dizziness, a group of 40 healthy controls was also included[55]. No significant correlation was found between cervical JPE and the SPNT difference within either WAD sub-group, the whole WAD group or the healthy control group. A weak, but significant correlation at the .05 level of r = .23 was found between right rotation JPE and the SPNT difference, but only when both the WAD and healthy control participants were analysed as a single group. No results were reported for correlation between SP gain and cervical JPE. Various parameters of balance also had weak-moderate correlation with both JPE and SPNT differences when the WAD with dizziness group were included in the analyses. Additional analyses indicated that in the whole WAD group abnormal performance in the cervical JPE test (JPE > the upper 95% confidence interval for the control group) had high positive prediction value (88%), but low sensitivity (59.7%) or specificity (53.8%) in determining either abnormal SPNTdifference and/or balance.

Outcome: correlation between performance in cervical JPE and the cervico-cephalic kinesthesia test

A single study with no serious limitations, by Swait et al (2007)[195] (Chapter 3), evaulated association in performance between cervical JPE and the cervico-cephalic kinesthesia test. In a group of 16 healthy participants who were asymptomatic for neck pain, no significant correlation was found. While sources of bias were minimised in the study, the sample size was small.

Outcome: correlation between performance in the cervico-cephalic kinesthesia test and the SPNT test

No studies were identified that analysed correlation in performance between the cervico-cephalic kinesthesia test and the SPNT test.

Evidence summary - In individuals with mechanical neck pain, is there correlation in performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests

There is very low quality evidence, limited to a single study[196], for weak correlation between performance in the cervical JPE test and the SPNT difference, only when analysis included a group containing both individuals with WAD as well as healthy controls. No studies evaluated correlation between cervical JPE and SP gain.

No evidence was found in support of correlation between the cervico-cephalic kinesthesia and the cervical JPE tests. Rather, a single study did not find correlation[195]. No evidence exists for correlation between the cervico-cephalic kinesthesia and SPNT tests in mechanical neck pain.

Table 2.13 Quality assessment of evidence across studies: is there correlation in performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests

NO. OF STUDIES	DESIGN	LIMITATIONS	INCONSISTENCY	INDIRECTNESS	IMPRECISION	SUMMARY ACROSS STUDIES
OUTCOME: CORRELATION IN PERFORMANCE BETWEEN THE CERVICAL JPE AND SPNT TESTS						
1	Cross-sectional[55]	Single study with no serious[a,b] limitations	N/A	N/A	No[c]	Low quality evidence – for association between performance in the cervical JPE test and the SPNT difference weak correlation was demonstrated in a single study with no serious limitations, but only when healthy controls were included with WAD in the analysis.
OUTCOME: CORRELATION IN PERFORMANCE BETWEEN THE CERVICAL JPE AND cervico-cephalic kinesthesia TESTS						
1	Cross-sectional[195]	Single study[195] with no serious limitations[195]	N/A	N/A	Some[d]	Low quality evidence – *no association* in performance between cervical JPE and the cervico-cephalic kinesthesia test in healthy individuals. A single study with no serious limitations, but some imprecision, indicated no significant correlation
OUTCOME: CORRELATION IN PERFORMANCE BETWEEN THE cervico-cephalic kinesthesia AND SPNT TESTS						
0						No evidence – non exists for correlation between the cervico-cephalic kinesthesia test and the SPNT test.

[a]Unclear if there is confounding[55]

[b] poor reliability of outcome measurement protocol for repositioning following extension

[c]Study had adequate sample size[55]

[d]Study had small sample size[195]

2.5 DISCUSSION

2.5.1 Outline of what was achieved

The first review evaluated whether and how mechanical neck pain is associated with altered cervical spine proprioceptive function in WAD and non-traumatic neck pain. A comprehensive understanding of the current level of evidence for cervical proprioception impairment in mechanical neck pain, as measured by the cervical JPE test, cervico-cephalic kinesthesia test and the SPNT test was provided. A second review evaluated evidence for the construct validity[197] of these tests by examining studies that analysed convergence in correlation between performance in each. No previous reviews existed that utilised systematic approaches to identifiying evidence and appraising quality of individual studies or of the evidence across studies, therefore this is the first systemtically approached review on this subject. Relevant literature was identified and appraised using the relevant steps of GRADE[1;151].

2.5.2 Discussion of results of Review 1 – evaluation of whether and how mechanical neck pain is associated with altered cervical spine proprioceptive function in WAD and non-traumatic neck pain

<u>The effect of mechanical neck pain on cervical JPE</u>

Research questions 1 and 2 evaluated the evidence for impairment in cervical JPE, for participants with mechanical neck pain resulting from whiplash injury and of non-traumatic aetiology respectively, compared with healthy controls. More studies of the effect of mechanical neck pain on proprioception had utilised the cervical JPE test[10;51-54;58;59;68;98;140;145;150;164;165;181-184;187;189-191] than any other measure of cervical proprioception. Overall, more studies included groups with WAD (17)[10;51-54;58;68;98;140;145;150;165;181-184;187] than with non-traumatic neck pain (n = 9)[10;52;59;68;164;182;189-191]. Most of the reviewed evidence was of low to very low quality,

with indirectness due to heterogeneity of participants included in different studies (including chronicity, severity of symptoms or level of disability) and also due to methodological differences, including the head repositioning tasks used (head-to-neutral and/or head-to-target, in different planes of motion) the number of trial repeats in each task and the metric of cervical JPE used (RMSE, VE, CE or AE). There were however a few studies[53;165;184] (all utilising participants with WAD) that contributed to upgrading from the initial low quality evidence level (specified by the GRADE approach for observational studies) to moderate quality evidence, on the basis of methodological features that addressed factors that increase risk of bias particularly well.

For head-to-neutral repositioning moderate quality evidence was found for impaired cervical JPE in WAD when repositioning follows movement in the transverse plane and low quality evidence for impairment following movement in the sagittal plane. No studies included repositioning to neutral in the frontal plane among WAD participants. Studies of participants with non-trauma neck pain similarly suggested deficits in head-to-neutral repositioning, however since studies had overall greater risk of bias, with greater inconsistency in findings, the quality of evidence was low for impaired cervical JPE in the sagittal plane and very low for the transverse plane. Very few studies included repositioning following movement in the frontal plane[59;181], with low quality evidence indicating no impairment in non-traumatic neck pain and no evidence existing for WAD.

A few studies[52;58;59;68;140;145;181] utilised a variation on the cervical JPE test where the head is repositioned to a previously determined mid-range position. Among participants with WAD there was very low quality evidence found for JPE deficits with

movement to targets in the sagittal, transverse and frontal planes. In non-traumatic onset neck pain, low quality evidence indicated no deficits in head-to-target repositioning in any plane of motion[52;59;68].

Overall the greatest level of evidence for deficits is for repositioning the head to the neutral position, particularly following movement in the transverse plane and among participants with WAD.

The review identified evidence for impaired cervical JPE both for participants with WAD and neck pain of non-traumatic origin. This finding is supported by several studies that compared cervical JPE between WAD and non-traumatic neck pain groups, with most reporting no significant difference for head-to-neutral repositioning in the transverse plane[10;52;182] and head-to-target repositioning in the sagittal plane[68] or transverse plane[52;68]. However, a recent study by Treleaven et al (2011) did report greater cervical JPE in WAD compared with non-traumatic neck pain, but only among a sub-group of WAD with upper cervical pain, suggesting that interaction between both aetiology and region of pain may influence cervical JPE[198].

The review identified inconsistency in findings of cervical JPE deficits in mechanical neck pain. One explanation may be the existence of clinical heterogeneity within (as well as between) neck pain groups studied. In addition to the possible influence of the region of neck pain described above[198], this is further supported by reports that cervical JPE may be associated with frequency of symptoms (in non-traumatic onset neck pain)[163] and that cervical JPE may follow a pattern of either improving or worsening over time (in WAD)[165;199]. This suggests that division of mechanical neck pain into sub-populations of either WAD or non-traumatic onset neck pain may be an

over simplification, with considerable heterogeneity possible within each group, making generalisations problematic. The rationale for selecting study populations based only on whether neck pain follows a whiplash injury or is of non-traumatic aetiology is also questioned.

Limitations in study design and indirectness in methodology between studies (detailed in the risk of bias tables in Appendix 4 and indicated in evidence appraisal Tables 2.8 and 2.9) might also contribute to the inconsistency in findings of cervical JPE deficit identified by the review. These include differences in the metrics of error used (detailed in Appendix 3), in the equipment used (computerised motion tracking systems versus manual measurements made with a laser pointer) and in the protocols followed for evaluation of cervical JPE. Variations in protocols included the number of trial repeats over which a mean JPE was calculated, with some utilising methods demonstrating poor reliability[144;195] and also differences in the velocity of the movement instructed and whether or not repositioning was carried out with the eyes open or closed.

<u>The effect of mechanical neck pain on performance in the cervico-cephalic kinesthesia test</u>

The cervico-cephalic kinesthesia test was developed to try and overcome limitations in the cervical JPE test and has acceptable reliability established[166] but has to date been less widely utilised[60;166;200]. Review questions 3 and 4 evaluated the evidence for greater errors compared to healthy controls when participants, with WAD and non-traumatic onset neck pain respectively, track a moving visual target by moving their head. Impairment was consistently reported in both WAD and non-traumatic neck pain. However, evidence was limited in quantity and the quality of individual studies and of the evidence overall was low. Evidence was not upgraded from low

quality due to increased risk of bias associated with possible prognostic imbalances between the neck pain and control groups.

Findings of the review were the same for both comparison of WAD and non-traumatic neck pain with healthy controls. A single study comparing both groups of neck pain with each other reported poorer performance in the cervico-cephalic kinesthesia test in WAD, compared with non-traumatic origin neck pain[201]. This contrasts with the cervical JPE test, where most (but not all[192]) studies found no significant difference[10;52;68;182] between neck pain groups and, while evidence is limited in quantity, questions the validity of the cervical JPE and cervico-cephalic kinesthesia tests as equivalent measures of proprioception. A single study has also reported different courses of either worsening or improving performance in the cervico-cephalic kinesthesia test over time (and also in cervical JPE) in WAD[202], suggesting likely heterogeneity within study groups. Association between individual participants performance in cervical JPE and the cervico-cephalic kinesthesia test was not evaluated, therefore it is not known whether the same individuals within the group either improved or worsened in both tests.

<u>The effect of mechanical neck pain on ocular motor function in the SPNT test</u>

All studies that compared ocular motor performance in the SPNT test between mechanical neck pain and healthy control groups were in participants with WAD[90;91;98;99;101;193;194]. Studies were of variable quality, with inconsistency in findings. Indirectness in methodology included studies that used targets moving at different velocities and different performance measures, with some reporting the difference in SP gain between the neutral and the neck torsion head positions (SPNT difference), while others reported actual SP gain in each position. Clinical

indirectness between studies included different chronicity or grades of WAD in the populations studied. The review identified overall low quality evidence for both impairment in SP gain in neutral and torsioned neck positions and in the SPNT difference in mechanical neck pain, that was limited to participants with WAD.

The review found no studies that compared a group with non-traumatic onset neck pain to healthy controls. It has been reported that participants with WAD may be discriminated from those with non-traumatic neck pain based on the magnitude of the SPNT difference[203]. However, a recent study found that differences in SPNT test performance between WAD and non-traumatic onset neck pain were dependent on which region of the cervical spine was involved[192]. Others report that SP gain (with the head in neutral position) may following a worsening or improving course over time following WAD[175;204] or that the predictive ability of the SPNT difference for symptoms at one year following whiplash injury changed over time[146]. As for the cervical JPE and cervico-cephalic kinesthesia tests, heterogeneity within WAD groups is thus likely. Despite a reasonable number of studies evaluating ocular motor function in WAD, there are no reports of the reliability of the SPNT test.

2.5.3 Discussion of results of Review 2 – evaluation of correlation between performance in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests

Review 2 found very low quality evidence for correlation between performance in the cervical JPE test and the SPNT test. Only 1 study was identified that reported only a low level of correlation and only when the group analysed included both participants with WAD and healthy controls[55]. For correlation between cervical JPE and performance in the cervico-cephalic kinesthesia test, no evidence was found, with a single study reporting no significant correlation among healthy individuals[195]. The

review found no studies that evaluated correlation in performance between the SPNT test and the cervico-cephalic kinesthesia test.

The lack of evidence for correlation in performance between different tests questions the construct validity[197] of the cervical JPE and the SPNT test and cervico-cephalic kinesthesia tests as comparable measures of cervical proprioception, since if they were measuring the same underlying construct (cervical spine proprioception) individuals would be expected to perform at a similar level in all of them. It is possible that they are each dependent upon different neurophysiological processes, or upon other factors such demographic or symptom-related characteristics. Some studies evaluated associations of these characteristics with performance in the tests. Summarised findings are provided in Table 2.14.

Evaluation of studies using GRADE did not address risk of bias in measurement of demographic and symptom-related characteristics, and not all studies were eligible for Review 1 or Review 2. Therefore, study limitations identified in those reviews were not used to grade the evidence. However, studies where high risk of bias was identified in the measurement methods used for the cervical JPE, cervico-cephalic kinesthesia and SPNT tests are indicated.Table 2.14 indicates that within tests there are some conflicting reports for associations between demographic and symptom-related characteristics and performance in the test. Pain intensity is the only factor that has been evaluated across all 3 tests. Findings indicated that SPNT test performance was associated with pain intensity in WAD, however, no associations

Table 2.14 Summary of associations reported between demographic and symptom-related characteristics and performance in the cervical JPE, cervico-cephalic kinaesthesia and SPNT tests

FACTOR	CERVICAL JPE	SPNT TEST	CERVICO-CEPHALIC KINESTHESIA TEST
AGE	Yes[59] (WAD) Yes[51] (WAD) No[191](non-traumatic neck pain)*		
GENDER			Yes[51] (WAD)
ACTIVE CERVICAL ROM	Yes/no[a,182] (non-traumatic neck pain)*	Yes[b,51] (WAD)	
PAIN/DISABILITY			
VAS	No[150] (WAD)* No[191] (non-traumatic neck pain)*	Yes[c,91] (WAD)	No[80] (WAD & non-traumatic neck pain)
NDI		Yes[c,91] (WAD)	No[80] (WAD & non-traumatic neck pain)
DURATION	No[191] (non-traumatic neck pain)*	No[101] (WAD)	
FREQUENCY	Yes [163] (non-traumatic neck pain)		
FEAR AVOIDANCE BELIEFS			
FABQ	No[68] (WAD & non-traumatic neck pain)		
TSK	No[53;165] (WAD)		No[80] (WAD & non-traumatic neck pain)

[a] Varied according to error measurement used

[b] Only evaluated SP in neutral position

[c] Greater NDI score was associated with *less* deficit in SPNT test

*Indicates high risk of bias in test measurement methods

were found with pain intensity for either the cervical JPE or cervicocephalic kinesthesia tests. This lack of convergence in associations with pain intensity questions their construct validity (1.7). However, inconsistency between the patient groups investigated and the characteristics that were measured, make comparisons across studies problematic. There are a number of gaps indicated in the literature where there have been no evaluations of association of demographic or symptom-related characteristics with performance in the tests. Future studies should fully evaluate associations with demographic and symptom-related characteristics that might influence performance across the tests within comparable patient groups and using consistent measurement methods.

2.5.4 Evaluation of the GRADE approach

Following steps of the GRADE approach that were relevant to the aims of this thesis provided a clear structure to the process of identifying priorities and questions for the review, as well as identification and appraisal of evidence. Appraisal of risk of bias following GRADE included relatively few criteria to be appraised in individual studies which were eligibility criteria, comparability of measurement/exposure, risk of prognostic imbalance/confounding and adequacy of follow-up[1]. The latter was not relevant to most studies reviewed since they were cross-sectional in design. The criteria enabled assessment of risk of bias in individual studies to be made consistently across studies.

The criteria for summarising the contribution that individual studies make to the quality of evidence overall were generally clear[1]. There were occasions when upgrading or downgrading decisions had to be made that were deemed to be

borderline. However, GRADE specifically recognises this difficulty[1;151] and the transparent way in which evidence appraisal is presented meant that such instances can be identified in the results and their impact on subsequent evidence quality summaries is clear. In a systematic review, agreement between reviewers would further increase confidence in judgements made that was not possible here.

Some studies were either upgraded or downgraded from the initial low quality evidence level specified by GRADE for observational studies[178]. In line with GRADE recommendations, downgrading only took place where there was substantial and limitation in study designs. It is possible that upgrading of evidence was made more readily than recommended by GRADE. This was an instance where GRADE did not address the characteristics of studies, that were relevant to this review, so well. The reason for this is that GRADE is intended for systematic review for the purpose of clinical guideline development[151], and as such would most often be applied to intervention and diagnostic studies, neither of which were included here. Risk ratios that could indicate the large effect size needed for upgrading, as stipulated by GRADE, were not relevant to the studies included in the review. A decision was made to upgrade individual studies to moderate quality if they had adequate sample size to increase confidence in the effects observed and addressed the inherent weakness in cross-sectional studies as well as possible. Upgraded studies reduced the likelihood of prognostic imbalance (since group allocation cannot be random)[1] between participants in neck pain and control groups either by analysis to confirm that there were no differences in factors that might be expected to influence performance, such as age and gender, or by controlling for imbalances with their statistical analysis method. Outcome measurement methods also needed to minimise the risk of experimenter bias, for example by using blinding or automated methods of

measurement and/ or data analysis. This approach to allowing upgrading evidence enabled differentiation between the quality of evidence found for different review questions, for example moderate quality evidence for cervical JPE deficits following repositioning in the sagittal plane among participants with WAD versus low quality evidence among participants with neck pain of non-traumatic origin, and was thus useful for the purposes of this review. Any likelihood of misrepresenting (overestimating) the quality of evidence is avoided by the transparent presentation of reasons for any decisions of upgrading or downgrading evidence.

In summarising evidence for each review question across studies, the GRADE criteria proved easy to apply, so it was felt that decisions could generally be clearly judged. In particular, the recommendation to focus on findings of the highest quality studies available provided clarification where studies were more variable in quality and less consistent in findings. Judgements on quality of evidence are transparently presented with reference to the specific GRADE criteria.

2.5.5 Strengths and limitations of both reviews

The decision was made to divide the review into 2 components, Review 1 and Review 2, and to address 6 narrowly focussed review questions within Review 1. The separate consideration of evidence for the cervical JPE test, cervico-cephalic kinesthesia test and SPNT test and also for neck pain following whiplash and neck pain of non-traumatic aetiology enabled a comprehensive appraisal of the evidence so that the broad aims of the review were met i.e. whether and/or how (i.e. which aspects of head or ocular sensorimotor control are affected) mechanical neck pain is associated with altered cervical spine proprioceptive function.

The narrowly specified review questions excluded some related studies, including those where the neck pain group consisted of both participants with WAD and non-traumatic onset neck pain and also studies that compared deficits between WAD and non-traumatic neck pain, but did not make a comparison with a healthy control group. Considering this retrospectively, including evidence from neck pain groups of unspecified or varied aetiology would have increased the difficulty of drawing conclusions (introducing greater heterogeneity among studies) and would not have added to the understanding of the effects of mechanical neck pain gained.

The literature search strategy appeared effective. While electronic searches initially returned a large number of studies that were subsequently found to be not relevant, there was no apparent means of narrowing the search results without risking exclusion of relevant studies. A few additional studies were identified through hand-searching bibliographies, but saturation was reached whereby no further new studies were identified. Therefore it seems likely that the evidence database contains all of the relevant studies, at least in the English language journals.

Limitations of both reviews include the fact that one researcher carried out all parts of the review. Thus selection of studies for eligibility and data extraction was not independently checked, which would increase the likelihood of errors being detected. In addition, judgements on risk of bias in individual studies and of the quality of evidence across studies were not based on consensus.

A further limitation resulted from paucity of studies available for some components of the reviews. In addition, within many eligible studies, poor reporting whereby relevant

information was omitted, led to uncertainty regarding the risk of bias. This contributed to downgrading of evidence in some instances.

2.5.6 Indications for future research

The results indicate gaps in the literature and limitations both in the evidence for deficits in performance in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests in individuals with mechanical neck pain and also in evidence relating to the validity of these tests as measures of proprioception.

Evaluation of the construct validity[197] of these tests should be a priority, since factors that determine their performance by individuals with mechanical neck pain are poorly understood. Without comprehensive examination of associations between performances in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests alongside demographic and symptom characteristics, it is unclear whether any of the sensorimotor function impairments documented in neck pain studies utilising them are attributable to proprioceptive impairment. Demonstration of convergence in correlation between performance in all 3 tests would contribute to establishing their construct validity[50], to date this has not been evaluated and should thus be a focus for subsequent studies that should use reliable outcome measurement protocols for each test.

Within WAD and non-traumatic neck pain groups, clinical heterogeneity is likely (section 2.5.2).This, combined with the fact that different combinations of outcome measures were used in different studies, makes it difficult to compare performance across the different tests of proprioception. A study utilising all 3 tests in a single mechanical neck pain group would further elucidate how these measures of

proprioception are associated with each other. However, in comparing neck pain groups with healthy controls, the review results provide little rationale for dividing study groups into either WAD or non-traumatic neck pain.

The cervico-cephalic kinesthesia test was developed as a more complex test for proprioception, aiming to reduce the possible role of vestibular contribution or motor learning in test performance[60]. The SPNT test similarly possesses limitations. There is evidence that rapid motor learning contributes to predictive timing of smooth pursuit eye movements. This is proposed to include memory of target velocity and reversals of the target during sinusoidal stimuli[93]. The fact that the sinusoidal target presented in the SPNT test is highly predictable and readily learned might limit the influence of cervical proprioception on SP gain during the test. Development of a more complex smooth pursuit task using a less-readily predictable ocular target would enable a more detailed evaluation of the neurophysiological processes underlying ocular motor function (1.5.3) and how these might be affected in mechanical neck pain.

Reliability has generally been reported as acceptable for the cervical JPE test[15;144;145], although ICC values for different measures of error and for repositioning following different movements vary considerably[144], with some demonstrating poor[49] reliability. Differences in measurement systems used, protocols followed, error measurement and analysis methods result in uncertainty over reliability and over optimal methods and protocols to use, that need to be evaluated further. Reliability for these different factors is considered during development of measurement methods and is detailed in Chapter 3. For the cervico-cephalic kinesthesia test acceptable between day reliability was reported (ICC = .60 - .86)[60], although the

sample size (n = 10) was smaller than the recommended number[205] and the ICC model that was used was not specified, so it is unclear whether suitable analysis methods were used. There are no reports of evaluation of the reliability of SP gain with neck torsion, or of the SPNT differences, therefore the reliability of the SPNT test is not known. Acceptable reliability of data is a prerequisite for validity of the measures[50], thus future studies need to establish, as a priority, reliable methods for measurement of the cervical JPE, cervico-cephalic kinesthesia and SPNT tests, using adequately powered sample sizes.

2.6 CONCLUSION

This is the most comprehensive and detailed review of evidence for impairment of cervical proprioception in mechanical neck pain to date and the first to include appraisal of the quality of evidence. It was also the first to take a systematic approach to evaluating evidence for correlation between performance in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests. The GRADE approach was utilised and this is the first appraisal of use of this method in evaluation of evidence from observational studies of cross-sectional design that are not related to clinical intervention or diagnosis.

A substantial number of relevant studies were identified. However, observational study design, limitations and poor reporting in individual studies resulted in low or very low quality evidence being provided. A few studies however possessed particular methodological features that reduced the risk of prognostic imbalance that is inherent in studies of cross-sectional design, which resulted in upgrading of the evidence to moderate quality in one instance.

In evaluation of the evidence for impaired proprioception in mechanical neck pain, moderate quality of evidence was identified for greater JPE among participants with WAD for head-to-neutral repositioning in the transverse plane in the cervical JPE test. Evidence for participants with non-traumatic origin neck pain and for other cervical JPE tasks was of low to very low quality. There was low quality evidence for impaired performance in the cervico-cephalic kinesthesia test ('the fly') in both WAD and neck pain of non-traumatic origin. In the SPNT test there was low quality evidence for impairment in participants with WAD, but no evidence existed for participants with non-traumatic onset neck pain.

The second component of the review addressed the question of validity of cervical proprioception tests by evaluating evidence for correlation between performance in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests. Limited, low quality evidence was found to indicate little correlation between performance in the JPE and SPNT tests among individuals with mechanical neck pain.

Areas identified for subsequent research include, first establishing reliable methods for measurement of the cervical JPE, cervico-cephalic kinesthesia and SPNT tests, followed by further evaluation of test validity. Studies utilising a fuller range of proprioception tests would further elucidate how participants with mechanical neck pain perform, compared with healthy controls. More complex ocular motor tasks would eliminate the predictable nature of the visual target in the SPNT test, contributing to understanding of the neurophysiological processes that underlie performance. Future studies should address factors that reduced the quality of evidence reviewed, including using methods that reduce measurement bias and risk of prognostic imbalance, as well as properly defining and describing eligibility criteria.

3 DETERMINATION OF OCULAR TRACKING, CERVICO-CEPHALIC KINESTHESIA AND CERVICAL JPE TEST METHODS

The studies included in the literature review used a variety of different systems for measurement of ocular movements in the predictable ocular tracking test and of head position and motion in the cervical JPE and cervico-cephalic kinesthesia tests, respectively. It was necessary to establish which of the available measurement systems were most appropriate for use in subsequent investigations of differences in non-predictable ocular tracking between participants with mechanical neck pain and healthy controls (Research Aim 4, 1.9.4) and to establish the construct validity of predictable and non-predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests (Research Aim 5, 1.9.5). The literature review indicated that studies of the effect of WAD or neck pain of non-traumatic aetiology on ocular tracking had all used visual targets with a high level of predictability, limiting understanding of the processes that might be impaired. An aim of the research was to evaluate ocular tracking in a more complex test, designed to reduce the contribution of prediction to ocular tracking performance (Research Aim 4, 1.9.4). This necessitated the design of a novel ocular motor test (Research Aim 2, 1.9.2). The specification of individual tests varied across studies included in the literature review, including differences in protocols, the number of trial repeats that were performed and the parameters analysed. It was necessary first to review the existing methodological studies of measurement systems, tests and protocols to determine the methodology of the planned study (described above). Further studies were then conducted to establish the reliability of methods selected for the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests (Research Aim 3, 1.9.3). The content of these reliability studies (excluding the reliability of the non-predictable

ocular tracking test) was included in two publications[206;207] (which each also contained some additional analyses). These are provided in Appendix 5.

Determination of the ocular tracking, cervico-cephalic kinesthesia and cervical JPE test methods thus had the following specific aims:-

1. Determine the measurement systems to be used for measurement of ocular movements and of head position and motion (cervical JPE and cervico-cephalic kinesthesia tests)

2. Design a novel test of ocular motor function that overcomes limitations of the predictable ocular tracking test (Research Aim 2, 1.9.2)

3. Determine task specification for the predictable and non-predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests

4. Establish the reliability of outcome measures (Research Aim 3, 1.9.3)

3.1 DETERMINATION OF MEASUREMENT SYSTEMS FOR OCULAR MOVEMENTS AND FOR HEAD AND NECK POSITION AND MOTION

3.1.1 System for measurement of ocular movements

The catalogue of studies included in the literature review (Appendix 3) indicated that most previous studies had used electro-oculographic (EOG) systems to record ocular movement in the predictable ocular tracking test, while only a single study had used a video-graphic system. Other systems also exist. Table 3.1 provides criteria that were required of the measurement system for this thesis.

Table 3.1 Criteria to be met by ocular movement measurement system

	CRITERION
1	Able to record horizontal, vertical and oblique smooth pursuit movements over an adequate angle of ocular excursion, at a velocity of 20 degrees sec^{-1} (determined by predictable and non-predictable target trajectories)
2	Acceptable measurement accuracy[208]
3	Acceptable test-retest reliability[209;210]
4	Demonstrated validity[211]
5	Non-invasive and feasible to use in study participants

Table 3.2 provides details of available systems and the results of appraisal of their properties against the criteria specified in Table 3.1.

Inconsistent and incomplete literature available that evaluated properties of available systems led to difficulty in establishing their suitability for the study. Table 3.2 indicates that only video-graphic systems met all criteria detailed in Table 3.1, thus ocular movements in this thesis were measured using a desk mounted, pan/tilt ASL 504 remote video-graphic eye tracker. This measures eye line of gaze with a precision of greater than .5 degree and with a measurement error of less than 1 degree[212]. A 360mm x 260mm (1280 pixels x 1024 pixels) PC screen formed the visual display for presentation of the ocular target for the predictable and non-predictable tests (and also for presentation of the head target for the cervico-cephalic kinesthesia test).

Table 3.2 Properties of available systems for measurement of ocular movements

MEASUREMENT SYSTEM	PROPERTIES	CRITERION 1	2	3	4	5
Scleral Search Coil[213] - eye position signalled by induction currents in copper wire coil mounted in the eye when subject is placed in an a.c. electromagnetic field	• High spatial and temporal resolution recordings with low level of noise[214]					
	• Records 3-dimensional movements[215]	√				
	• High accuracy		√			
	• Reliability of measurement of smooth pursuit gain not reported			X		
	• Considered the gold standard for recording ocular position[214;215]				√	
	• Invasive procedure, discomfort limits duration of recording[215]					X
	• May influence saccadic movement[214]					
Electro-oculography (EOG) [216] - pairs of cutaneous electrodes measure corneo-retinal potential from which eye motion can be inferred	• High sampling rate enables recording of high velocity eye motion [216]					
	• High level of noise					
	• Non-linearity of measurement[216]					
	• Prone to artefacts[216]					
	• Limitations in measurement of vertical eye movements, does not allow recording of oblique eye movements[216]	X				
	• Accuracy not reported		X			
	• No reports of reliability of measurement of smooth pursuit gain			X		
	• no reports of evaluation of validity				X	
	• Relatively long set-up and calibration procedure					?

Table 3.2 continued

MEASUREMENT SYSTEM	PROPERTIES	CRITERION 1	2	3	4	5
Infra-red[216] - Infrared illumination of the eye is used and reflection of the light by the "limbus" or from within the pupil is detected	• Less suitable for recording vertical movements, or eye movement of greater angular deviation	X				
	• Accuracy not reported		X			
	• Slight[209] reliability (ICC_{2k} = .31) at 24 degrees sec^{-1} (2 month inter-test interval)[217]			X		
	• Comparable to gold-standard for saccades[218], not reported for smooth pursuit movement				?	
	• Relatively easy to set-up					√
Video-graphic [219] - use corneal reflection of bright light or complex pattern recognition algorithms to detect pupil, iris or both[216]	• Longer inter-sample interval, lower spatial and temporal resolution and greater high frequency noise than SSC systems[216;214]					
	• Linearity of measurement[216]					
	• Suitable for recording horizontal, vertical, oblique and in some-cases torsional eye movements[216]	√				
	• good accuracy for smooth pursuit[220]		√			
	• Substantial[209] reliability (ICC_{2k} = .96 - .94) for measurement of smooth pursuit velocity gain at 10 degrees sec^{-1} in healthy participants[221]			√		
	• Comparable to gold-standard[215;220] (except for torsion ocular movement)				√	
	• Non-invasive, relatively easy to set-up					√

√, X or ? indicate criterion (Table 3.1) met, not met or unclear, respectively

3.1.2 System for measurement of head and neck position and motion

Data extracted into the catalogue of studies included in the literature review indicated different methods used for measurement of cervical spine position and motion (Appendix 3). These range from manual measurement of cervical JPE using a head-mounted laser pointer, as originally described by Revel et al (1991)[15], to fully automated data recording and processing using electronic sensors and systems[222]. Table 3.3 provides criteria that were required of the measurement system for this thesis.

Table 3.3 Criteria to be met by cervical spine position and motion measurement system

	CRITERION
1	Minimise potential examiner bias in recording and processing of data[1]
2	Acceptable measurement accuracy[208]
3	Acceptable test-retest reliability[209;210]
4	Demonstrated validity[211]
5	Non-invasive and feasible to use in study participants

Table 3.4 provides details of available systems and the results of appraisal of their properties against the criteria specified in Table 3.3. Inconsistent and incomplete evaluation of properties of all tests led to difficulty in establishing their suitability for the research, however electronic and ultrasound motion sensing sytems met the most criteria. Of the electronic motion sensing systems, electromagnetic systems met all criteria and have been used previously for the cervical JPE and cervico-cephalic kinesthesia tests. Thus a Polhemus 3 space Fastrak electromagnetic tracking system (model 3S0002) was used to record head position and motion.

Table 3.4 Properties of available systems for measurement of cervical spine position and motion

MEASUREMENT SYSTEM	PROPERTIES	CRITERION 1	2	3	4	5
Head-mounted laser pointer[15] - position of laser beam manually recorded on a wall-mounted target	• Used for measurement of cervical JPE[15]					
	• High potential for bias in measurement	X				
	• Accuracy not evaluated		X			
	• No statistical analysis reported for reliability			X		
	• Validity not reported				X	
	• Low cost, easily implemented in a clinical setting					√
Goniometers/inclinometers/Cervical range of motion instrument (CROM)[223] - Angles of head excursion manually recorded	• CROM widely used for measurement of cervical JPE[145] and ROM[224,225]					
	• High potential for bias in measurement	X				
	• Accuracy not evaluated		X			
	• Moderate-substantial[209] intra -examiner reliability for cervical ROM (ICC_{2k} = .75 - .98)[224,225]			√		
	• Substantial[209] intra- and inter-examiner reliability reported for head repositioning to mid-range in the cervical JPE test ($ICC_{?}$ = .972-.985)[145]. Reliability for head-to-neutral repositioning not reported)			√		
	• Strong correlation with electromagnetic system for active ROM (Pearson correlation coefficient = .93-.98)[225]				√	
	• Criterion validity of CROM established (compared with radiographic gold standard) for measuring cervical ROM[223]				√	
	• Easily implemented in a clinical setting					√

Table 3.4 continued

MEASUREMENT SYSTEM	PROPERTIES	CRITERION 1	2	3	4	5
Image-based systems (e.g. optoelectric, video, photogrammetric)[226]	• Used for cervical JPE[68], ROM tests[227]					
- Light-eflective markers or light emitting diodes captured by cameras or optoelectric sensing units	• Automated measurement recording	√				
	• Accuracy not reported		X			
	• For ROM reliability moderate-substantial[209] ($ICC_?$ = .74-.95)[227]			√		
	• Validity unclear, only evaluated as reference for goniometer/inclinometers (Pearson r = .74-.95)[227]				?	
	• Lengthy set-up pocedures[226]					?
Electronic positional sensors[a] and systems[226]	• Used for cervical JPE[55], kinesthesia[60] and ROM[227] tests					
- Miniaturised low power electrical sensors attached the body. Advanced electrical circuit technology signals position and motion	• Automated measurement recording	√				
	• Electromagnetic system considered the 'gold standard'[228], high accuracy reported (±.2°)[229]		√			
	• For ROM intra-and inter-examiner reliability moderate-substantial[209] ($ICC_?$ = .64-.96)[227]			√		
	• For head-to-neutral cervical JPE reliability moderate-substantial[209] (ICC_{2k} = .69-.82) for electromagnetic system[166]			√		
	• For cervico-cephalic kinesthesia reported reliability moderate-substantial[209] ($ICC_?$ = .6-.86) for electromagnetic system[60]			√		
	• Good validity concluded for all electronic sensor types in most studies[227]				√	
	• Easy to apply and set up. Some limitations for all sensor types. For electromagnetic sensors no limitations other than exclusion of metal objects within 100mm of transmitter or receivers[226]					√

Table 3.4 continued

MEASUREMENT SYSTEM	PROPERTIES	CRITERION				
		1	2	3	4	5
Ultrasound motion sensing systems[230] • Ultrasound transmitters fixed to head and shoulder. Signal received by remote transducer	• Used for cervical JPE[144] and cervical ROM[227] tests					
	• Automated measurement recording	√				
	• Accuracy not reported		X			
	• Moderate-substantial reliability for cervical ROM ($ICC_{?}$ = .78-.96)[227]			√		
	• Low-substantial intra-examiner reliability ($ICC_{1,k}$ .29-.84) reported for head-to-neutral cervical JPE[144]			?		
	• Good validity reported[227]				√	
	• Easy to apply and set up					√

[a]Include accelerometers, gyroscopes, flexible angle sensors and electromagnetic sensors

√, X or ? indicate criterion (Table 3.3) met, not met or unclear, respectively

3.2 DESIGN A NOVEL TEST OF OCULAR MOTOR FUNCTION THAT OVERCOMES LIMITATIONS OF THE PREDICTABLE OCULAR TRACKING TEST

Findings of the literature review indicated that all studies investigating ocular tracking in participants with WAD had used a simple smooth pursuit test with a visual target following a predictable periodic trajectory in 1-dimension (2.5.6). However, in real life visual targets often change direction and/or velocity[93], thus the predictable ocular tracking test is limited in the extent to which it may indicate the impact of mechanical neck pain on performance of day-to-day tasks, or the underlying neurophysiological processes that may be impaired. To overcome this limitation a novel test was designed to enable evaluation of more complex ocular tracking function (Research Aim 2, 1.9.2).

It has been shown that humans are able to learn anticipatory responses to directional displacement and velocity changes of visual targets[231]. It is proposed that a number of levels of visual target information can be held in short-term memory simultaneously, that can be modified quickly when trajectories change[93]. To generate a complex visual target trajectory either the direction and/or the velocity could be varied during the ocular tracking test. It was decided to vary the direction of the target but to maintain constant velocity in the horizontal plane, since this would enable comparison with the constant velocity predictable ocular tracking test. Furthermore, the cervico-cephalic kinesthesia test that was developed to overcome limitations of the cervical JPE test used a target that varied in direction in 2-dimensions for the head to track and it was decided to use an ocular target with comparable spatial characteristics, enabling comparison with that test. Thus, the novel test consisted of ocular tracking of a visual target following a trajectory in 2-dimensions that varied in direction non-periodically, with constant velocity in the horizontal plane and variable

velocity in the vertical plane. Specifications for the ocular targets in both the predictable and non-predictable tests are discussed in 3.3.1.

Smooth pursuit velocity gain is the most widely used parameter of smooth pusuit performance[216] and is the measure that has previously been used in studies that report smooth pursuit impairment in mechanical neck pain[55;90;91]. An alternative parameter is phase error, which provides a measure of the latency of smooth pursuit responses and indicates the ability of the ocular motor system to utilise prediction of target motion in order to reduce delays (phase lags) in ocular tracking[93]. Since the focus of this thesis is on the effect that cervical proprioception may have on the ability to track visual targets when prediction cannot be utilised, rather than on evaluation of prediction itself, SP gain is thus the parameter used in this instance. Note that for the predictable constant speed component of the trajectory, phase error may only be pooly estimated at the turn around points of each triangular sweep (3.3.1, Figure 3.1). The reliability of SP gain measured in the novel task is evaluated in 3.4.1.

3.3 DETERMINE TASK SPECIFICATION FOR THE PREDICTABLE AND NON-PREDICTABLE OCULAR TRACKING, CERVICO-CEPHALIC KINESTHESIA AND CERVICAL JPE TESTS

3.3.1 Specification of predictable and non-predictable ocular tracking tests

Consideration of existing literature, provided in table 3.5 informed specification for the predictable ocular tracking test. No neck pain studies have previously reported a non-predictable trajectory in 2 dimensions.

Table 3.5 Existing literature for specification of target motion parameters

TARGET VELOCITY (horizontal trajectory)	SUMMARY
<u>Reliability of SP velocity gain</u> • Substantial[209] intra-examiner reliability at 10 degrees s^{-1} (ICC_{2k} = .96am and .94 pm). Tested weekly over 4 weeks. Video-graphic ocular tracker[221] • Moderate[209] intra-examiner reliability ($ICC_{?}$ = .71 to .9) at mean velocity 16 degrees s^{-1} (range = 0-22 degrees s^{-1}). Tested at 4 weeks. Schizophrenic patients.Infra-red oculography[232] • Moderate[209] intra-examiner reliability at 36 degrees s^{-1} (ICC_{2k} = .77) and 48 degrees sec^{-1} (ICC_{2k} = .70). 2 month inter-test interval. Infra-red ocular tracker[217] • No-slight[209] intra-examiner reliability at 12 degrees s^{-1} (ICC_{2k} = .10) and 24 degrees sec^{-1} (ICC_{2k} = .31). 2 month inter-test interval. Infra-red ocular tracker. Task duration decreased with increasing velocity (8.25-33.0 seconds)[217]. SP gain calculated differently to other studies[216]	• Most studies report moderate or substantial reliability at 10-48 degrees s^{-1} • Inconsistency in reported reliability at lower velocity may reflect different ocular tracking systems, test re-test interval, SP gain calculation or task duration variation • Fewer superimposed saccades with target velocities of 10-30 degrees s^{-1}. Frequency of small saccades increases over this velocity range • SP velocity gain decreases with increasing target velocity • 20 degrees s^{-1} discriminated WAD from healthy control participants in most studies
<u>Number of superimposed saccades</u> • Increasing numbers of anticipatory and catch-up saccades interrupt SP as velocity increases from 12-48 degrees s^{-1} [217] • Increasing number of superimposed saccades, decreasing velocity gain, and decreasing smooth pursuit amplitude as velocity increases from 10-60 degrees sec^{-1}. With velocities >30 degrees s^{-1}, larger saccades (> than 10 degrees s^{-1}) occurred[233]	
<u>Discriminative ability of SP velocity gain for neck pain</u> • Maximum velocity of 20 degrees s^{-1} discriminates WAD/healthy controls (EOG)[90;91;99,91;194] • Maximum velocity of 18 degrees s^{-1} did not discriminate WAD /healthy controls (video-graphic ocular tracker)[193] • Maximum velocity of 37 degrees s^{-1} did not discriminate WAD/healthy controls (EOG)[101]	

Table 3.5 continued

TARGET VELOCITY PROFILE	SUMMARY
• Triangular[a] /trapezoid[b] waveforms are recommended due to difficulties computing velocity gain with sinusoidal[c] waveforms[216] Reliability (see above for ICC values and test methods) • Moderate-substantial[209] reliability reported with trapezoid/triangular waveforms[221;232] • No-moderate reliability[209] reported for sinusoidal waveforms[217] Studies in neck pain • Used velocity profiles reported as sinusoidal[55;90-92;100], although some of these close to triangular[55;91] NB triangular/trapezoid velocity profiles have been widely used to measure steady state SP velocity gain in psychiatric research[216]	• Triangular or trapezoid waveforms are recommended • Moderate-substantial reliability. Widely used in psychiatric research
VISUAL ANGLE	**SUMMARY**
Reliability (see above for ICC values and test methods) • Moderate-substantial[209] reliability for horizontal visual angle 20-30 degrees[221;232] • No-moderate reliability[209] for 24 degrees (increases with increasing velocity/decreasing duration)[217] Studies in neck pain • EOG studies used horizontal visual angle of 40 degrees[90;91;99;91;194] or 55 degrees[101] • Video-graphic eye tracker study used 30 degrees[100] (optimum range recommended by manufacuter < 30 degrees[212]) • NB most studies in schizophrenia or in healthy participants used visual angle < 30 degrees[216]	• Most studies report moderate-substantial reliability for 20-30 degrees • Visual angles < 30 degrees have been widely used

[a] target moves with constant speed and changes direction abruptly at the end of each run
[b] target moves with constant speed as in the triangular pattern but stops at each of the two end locations
[c] target speed varies continuously in a sinusoid fashion determined by a single frequency

Table 3.5 continued

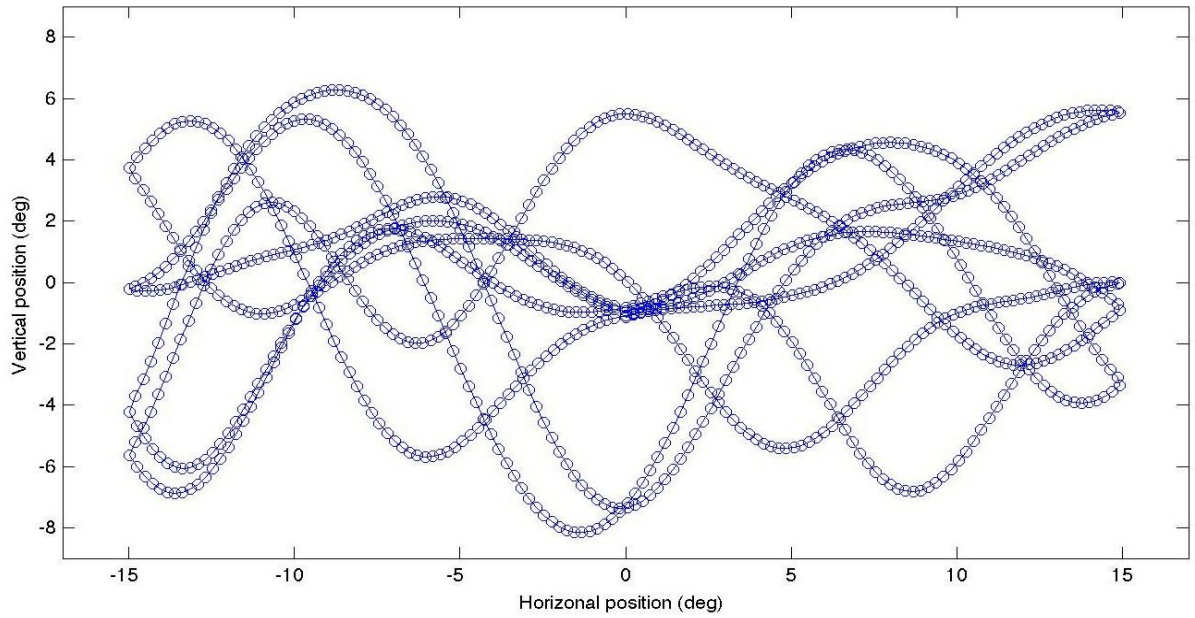
CYCLES AND TRIAL DURATION	SUMMARY
<u>Reliability (see above for ICC values and test methods)</u> • Substantial[209] reliability for 7 cycles[d] (duration not reported, but estimated 42 seconds)[221] • No-moderate[209] reliability for 8 cycles[d], decreasing duration with increasing target velocity (duration not reported, but estimated 33 seconds/12 degrees s^{-1} – 8.5 seconds/48 degrees s^{-1})[217]	• Substantial reliability reported for approximately 7 cycles/42 seconds • Great inconsistency in methods and reporting between studies
<u>Studies in neck pain</u> • 4 cycles at .2 Hz (duration not reported, but estimated 20 seconds)[55;90;91] • 60 seconds (12 cycles at .2 Hz)[101] • NB studies in schizophrenia or in healthy participants report ranges from 4-60 cycles[d,216] Inconsistent reporting and variations between studies in proportion of each cycle included in SP gain analysis prevents evaluation of the number of cycles and/or duration of SP tracking that should be used.	

[d]1 cycle = 1 leftward and 1 rightward target display traversals

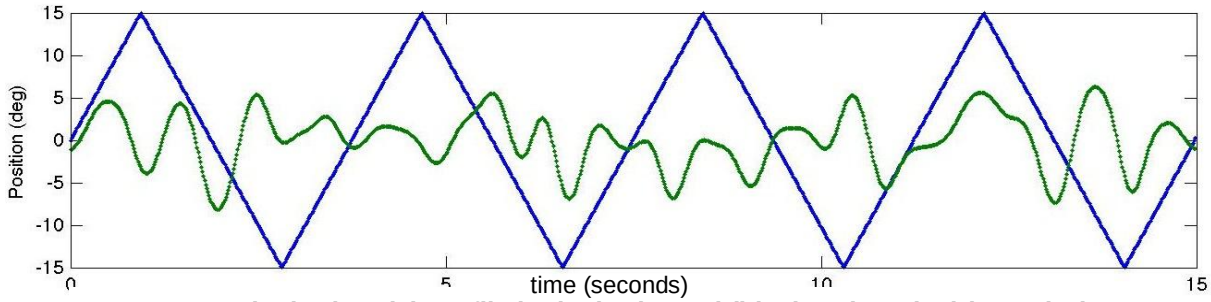
Participants were required to track a white, circular target moving against a black background. Programmes were written in MatLab (The MathWorks Inc., Natick, MA), to generate two types of ocular target motion trajectory. For the SPNT test a horizontal triangular velocity profile was generated (the target moves with constant speed, changing direction abruptly at the end of each run[216]). Non-predictable target tasks were generated from a random number sequence determining the vertical position of the target on the screen that was then low pass filtered to have an upper frequency of 1.75Hz. The vertical velocity was variable, while the horizontal position followed a constant speed ramp, starting and stopping mid-screen and sweeping left and right at a constant 20 degrees sec^{-1}. The specifications for the predictable and non-predictable ocular target motion trajectories are provided in Table 3.6. The position and velocity profiles for the non-predictable ocular target motion trajectory is further illustrated in Figure 3.1.

Figure 3.1 (a-c) Illustration of the construction of the non-predictable ocular target motion trajectory

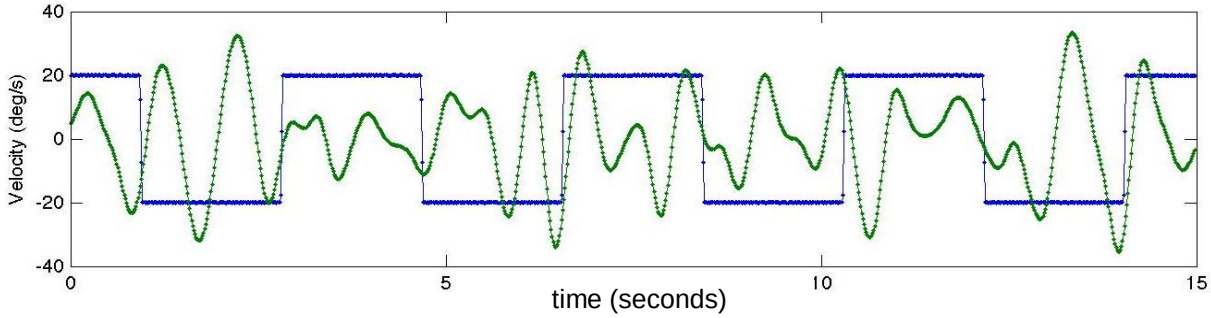
a) Horizontal (x axis) and vertical (y axis) screen display position within a single trial



b – Screen display position (y axis) in the horizontal (blue) and vertical (green) planes accross the duration of a single trial (x axis)



c – Target velocity (y axis) profile in the horizontal (blue) and vertical (green) planes accross the duration of a single trial (x axis)



Screen display position (a and b) is given in degrees of visual angle. Target velocity (c) is given in degrees of visual angle sec^{-1}. Time (b and c) is accross the duration of a single 15 second trial

Table 3.6 Ocular motor task specification

SPECIFICATION	HORIZONTAL TARGET	NON-PREDICTABLE TARGET	JUSTIFICATION
Target trajectory	Horizontal, predictable	Horizontal and vertical, non-predictable	
Target velocity	+/- 20 degrees sec^{-1}	Horizontal: +/-20 degrees sec^{-1} Vertical: Variable between +/- 30 degrees sec^{-1}	Acceptable reliability[232;221], challenges SP control systems while minimising breakdown of SP and superimposition of saccades[217]. Previously used in neck pain studies[55;90;91]
Target velocity profile	triangular	Constant horizontal and variable vertical velocity	Acceptable reliability, recommended for computing SP gain[216],? used previously in neck pain studies[a]
Visual angle	30 degrees horizontally	30 degrees horizontally, 15 degrees vertically	Horizontal angle acceptable reliability[221], within optimum specification for video-graphic ocular tracker[212]. This dictates the vertical visual angle.
Number of cycles	5 per trial (repeated 3 times)	1 per trial (repeated 3 times)	No clear indication from literature. Relatively short trials to reduce likelihood of fatigue[216]. Repeating trials enables a reliable mean to be calculated[209] and also enables trials in different head positions to be interspersed, so as to avoid order effects
Duration of each trial	15 seconds	15 seconds	Determined by velocity, visual angle and number of cycles

[a]previously described as sinusoidal waveform[55;91], however, waveform appeared triangular. Personal correspondence confirmed that steady state tracking, with constant velocity, was analysed, while portions of sinusoidal waveform (resulting from motor driving laser target) were excluded (Treleaven J, June 2013)

3.3.2 Specification of cervical JPE tests and cervico-cephalic kinesthesia tests

Consideration of existing literature, provided in table 3.7 and 3.8 informed specification of the tasks used for the cervical JPE and cervico-cephalic kinesthesia tests, respectively. Table 3.9 provides the specifications and their justification**.**

For the cervico-cephalic kinesthesia tests participants were required to track a white, circular head target moving against a blue background. Programmes were written in MatLab (The MathWorks Inc., Natick, MA) by CM to generate a series of non-predictable target trajectories, in 2 dimensions. Motion in the major dimension (for example vertical) was at a constant velocity of 1 degree sec $^{-1}$, as the target followed a constant velocity ramp, starting and stopping mid-screen, with a sweep duration of 15 seconds. In the other dimension (for example horizontal), a unique trajectory was generated for each trial from a random number sequence that was then low pass filtered to have an upper frequency of .5Hz.To ensure that the required head motion would not be so large as to provoke neck pain in the symptomatic group, the target motion subtended a maximum distance on the screen that was equivalent to 45 degrees of head motion. The position of the head-mounted sensor was projected to the visual display screen, appearing as a green circular cursor. Head movements in 2 dimensions (frontal plane and sagittal plane) were thus represented by horizontal and vertical motion respectively of the head position cursor on the screen. A 1:1 relationship was maintained, by controlling the head sensor-screen distance, between actual angular head motion and angular deviation of the cursor visible on the screen.

Table 3.7 Existing literature for specification of the cervical JPE test

HEAD-TO-NEUTRAL OR HEAD-TO-TARGET REPOSITIONING	SUMMARY
Studies in neck pain • Repositioning to the neutral position is widely reported[10;51-55;58;59;98;150;164;165;181-184;189-191]. Moderate quality evidence for deficits in WAD (2.4.3), low quality evidence for deficits in non-trauma neck pain (2.4.4) • Repositioning to mid-range targets also reported[52;58;68;140;145;181]. Very low quality evidence for impairments in WAD(2.4.3), low quality evidence of no impairment in non-trauma neck pain (2.4.4) Reliability • Variable reliability reported for both head-to-neutral(ICC(1,3) = 0-.84)[a] and head-to-target repositioning(ICC(1,3)= 0 -.90)[a] (3 trial repeats)[144]. Incorrect ICC model[b] used for intra-examiner reliability[210]. Conflicting[c] report of substantial[209] intra- ($ICC_?$ = .975-.985) and inter-examiner ($ICC_?$ = .972) reliability for head-to-target repositioning (3 trial repeats)[166]	• Impaired head-to-neutral JPE is widely reported. • Evidence for impaired head-to-target JPE in neck pain is very limited • Heterogeneity of methods (planes of motion, number of trial repeats and metrics of error) make comparison between studies difficult
CERVICAL JPE PLANES OF MOTION	**SUMMARY**
Studies in neck pain • Neck pain studies used sagittal plane[181;189], transverse plane[10;190], both sagittal and transverse plane[51-55;58;98;150;165;183;184;191] or also included frontal plane [140;145;59;164] repositioning motion Reliability • Variable reliability for all planes of motion with different measures of error (see above)[144]. For head-to-neutral JPE extension was least reliable (ICC(1,3) = 0 - .38)[a]. For head-to-target JPE transverse plane motion was least reliable (ICC(1,3) = 0 - .57)[a.] 3 trial repeats [144] • Substantial[209] within-day intra- and inter-examiner reliability for transverse and frontal plane head-to-target JPE[c] (see above)[145] • Fair-moderate[209] between day intra-examiner reliability for transverse plane head-to-neutral JPE (ICC(2,*k*) = .35 - .44) head-to-target JPE (ICC(2,*k*) = .62 - .82)[166]	• Reported reliability varies from none-substantial reliability[209] according to repositioning test used, plane of motion, number of repeats and measure of error • Sagittal and transverse plane repositioning has been most widely reported

Table 3.7 continued

NUMBER OF TRIALS	SUMMARY
<u>Studies in neck pain</u> • Studies used either 3[53-55;58;98;165;181;184;189], 4[181], 5[68], 8[182] or 10[51;150;164;190;191] trial repeats <u>Reliability</u> • Conflicting reliability reported[b] for 3 trial repeats (see above)[144;145;166]	• No concensus on how many trials to use for reliable measurement
METRIC OF ERROR	**SUMMARY**
<u>Studies in neck pain</u> • Spinal repositioning 3-dimensional error used[208], most studies of the cervical JPE test[234-236] reported JPE in the primary plane of motion • During test development observed motion and errors in non-primary planes were small • Different error measures were used in neck pain studies: - Absolute error (AE)[10;51-55;68;150;164;165;181;184;191;237]. AE = absolute value of constant error (CE) = root squared error (RSE))[144] - CE[59;68;182;184;189] accounts for directional bias in repositioning[144] - Variable error (VE)[68;182;184;189;190] accounts for variability in repositioning[144]. - Root mean squared error (RMSE)[59;184;189] is mathematical combination of CE and variable error (i.e. total error). RMSE approximates absolute CE/RSE if VE is small[144] • Recommended to consider both accuracy (AE,CE or RSE) and precision (VE) in JPE studies[208] • Different results for different metrics of error found within single studies[59;68;182;184;189;190]. • No error measure uniquely detected or defined differences between WAD and healthy controls[184] <u>Reliability</u> • Comparative reliability study reported RMSE ICC(1,3) = .29 - .9, CE ICC(1,3) = 0 - .84[a] and VE ICC(1,3) = 0 - .83)[a] (3 trial repeats)[144]. Incorrect ICC model used[b]	• JPE in primary plane of motion widely reported in neck pain studies and may provide better measure of repositioning error • It is recommended to use metrics of both repositioning accuracy and precision • There is no concensus on the best metric of error for reliable measurement

[a] Negative ICC values are theoretically not possible[238], indicate no reliability and thus are reported as zero
[b] ICC model 2,1 or 2,k should be used for intra-examiner reliability[210]
[c] Methodological differences may account for discrepancy. Metric of error not specified[145]. ICC model not specified[145]. ? mean of transverse and frontal plane JPE used[145]. Within[144;145] or between-day[166] reliability

Table 3.8 Existing literature for specification of the cervico-cephalic kinesthesia test

TARGET VELOCITY	SUMMARY
<u>Studies in neck pain</u> • Previous reports of the test used a target velocity of 16.2mm second^{-1}. Head rotation velocity to track this is unknown as centre of head-to-target distance was not recorded, but is less than 9.2 degrees second^{-1} (calculated from distance to back of chair) • Estimates of velocity threshold for self-motion perception with vestibular stimulation vary but have been reported as 1.5 degrees second^{-1} for whole body rotation[239], increasing at lower stimulus frequencies. Single vestibular neuronal recordings in macacques indicate thresholds of 3.7-.12.4 degrees second^{-1}[240] <u>Reliability</u> • Moderate – substantial[209] reliability (ICC? = .60 - .86) reported @ 16.2 mm sec$^{-1.}$ Small sample (n = 10)[60]	• Slow head rotation velocity of 1 degree second^{-1} is less likely to activate vestibular system • Moderate-substantial reliability reported but unclear head velocity
TRAJECTORY	**SUMMARY**
<u>Studies in neck pain</u> • Previous studies used 3 pre-determined non-predictable target trajectories (each repeated 3 times)[60;166;241]. <u>Reliability</u> • Moderate-substantial[209] reliability reported[166]	• Due to repetition whole trajectories could be learned
TRIAL DURATION AND NUMBER OF REPEATS	**SUMMARY**
<u>Studies in neck pain</u> • Previous studies used trial duration of 20-40 seconds[60;80], <u>Reliability</u> • Moderate-substantial reliability (see above)[166]. 3 non-predictable target trajectories were each tracked 3 times (9 trials in total)	• Unclear optimum number/duration of trials
METRIC OF ERROR	**SUMMARY**
• Previous studies used mean absolute error[60;80]	• Moderate-substantial reliability reported

Table 3.9 Task specification for the cervical JPE and cervico-cephalic kinesthesia tests

TASK SPECIFICATION		JUSTIFICATION
Cervical JPE test		
Test	Head-to-neutral repositioning	Higher quality evidence exists that head-to-neutral repositioning JPE is impaired in neck pain than for head-to-target repositioning 3.4.3f, 3.4.4g
Plane of motion	Sagittal plane (flexion and extension) & transverse plane (left and right rotation)	To prevent unduly long testing protocol only repositioning in two cardinal planes was included, these were the most widely reported in neck pain studies[181;189;10;190;51-55;58;98;150;165;183;184;191]
Number of trials	10 repeats of each repositioning motion (40 trials in total)	Enables analysis of optimum number of repeats for stable and reliable estimates
Metric of error	RSE mean and SD in primary plane of motion	Includes both accuracy and precision (recommended[208])
Cervico-cephalic kinesthesia test		
Velocity of target motion	1 degree second^{-1}	Reduces likelihood of useful vestibular system activation[239],
Target trajectory	Both pre-determined trajectories & unique non-predictable trajectory for every trial	Moderate-substantial[209] reliability reported[166] for pre-determined trial. Inclusion of unique trajectories (reducing possibility of any learning from previous presentation of target trajectory) enables evaluation of reliability of both methods
Duration of trials/number of repeats	15 seconds duration, repeated 9 times (each trajectory type)	Short duration prevents unduly long testing protocol and likelihood of fatigue. 9 repeats repoduces previous method[166]. Enables analysis of optimum number of repeats for stable and reliable estimates
Metric of error	RSE per trial	Substantial[209] reliability demonstrated in preliminary study[195]

3.4 ESTABLISHING THE RELIABILITY OF OUTCOME MEASURES

Performance based outcome measures should demonstrate test-retest reliability[242]. Tables 3.5, 3.7 and 3.8 indicate that there are limitations in the literature available for reliability of the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests. Two methodological studies were thus conducted to establish intra-examiner reliability of the underlying constructs, the measurement systems (3.1) and test specification (3.3) used, as well as the technical arrangement, protocols followed and data processing methods. The studies are described separately.

3.4.1 Establishing the reliability of the predictable and non-predictable ocular tracking tests

Background

Evaluation of reliability of smooth pursuit (SP) gain in studies reviewed in Table 3.3 was limited by heterogeneity of methods, including different equipment, ocular target specifications and test re-test interval. There had been no previous evaluation of the reliability of horizontal SP gain with neck torsion, or of ocular tracking of a non-predictable target. A preliminary study was conducted to establish the within-day intra-examiner reliability of measurement of SP gain using the video-graphic ocular measurement system, ocular task specification and protocols selected for this thesis. Evaluation of the reliability of the predictable ocular tracking test with neck torsion formed the basis for a poster presentation (Appendix 5)[207], while a further aim was evaluation of the reliability of the non-predictable ocular tracking test.

Methods

Study design

A test-retest design was used to evaluate within day reliability.

Participants

Twenty one healthy volunteers (9 men, 10 women), with a mean (SD) age of 31.2 (7.4), gave informed consent and participated in the study. Each participant was tested on 2 occasions, separated by a 10 minute interval. The same examiner performed all tests.

Equipment and Technical arrangement for measurement of ocular movements

Smooth pursuit gain was measured with an ASL 504 videographic tracking system (Bedford, MA). Participants were seated on an adjustable height swivel chair that was modified to restrict rotation to a maximum of 45 degrees.The predictable ocular tracking test has previously been reported using a maximum neck torsion angle of 45 degrees (or less if this caused too much neck discomfort)[243]. Their head was immobilised by a chin rest and bite bar to optimise recording accuracy. Some previous studies used a head restraint[101], while in others the examiner manually stabilised the participants head[100;109].The possibility that proprioceptive cues could be obtained from the chin rest or bite bar during neck torsion was considered, however it was thought that such cues would be negligible relative to the role of cervical afferent inputs, and would be the same for both controls and neck pain participants. By maintaining the head in the straight-forward position likelihood of asymmetric orbital deviation of the eye being required to track the target in opposing directions would also be minimised. The bite bar was introduced during test development, since participants sometimes rotated their head position in the sagittal plane during ocular

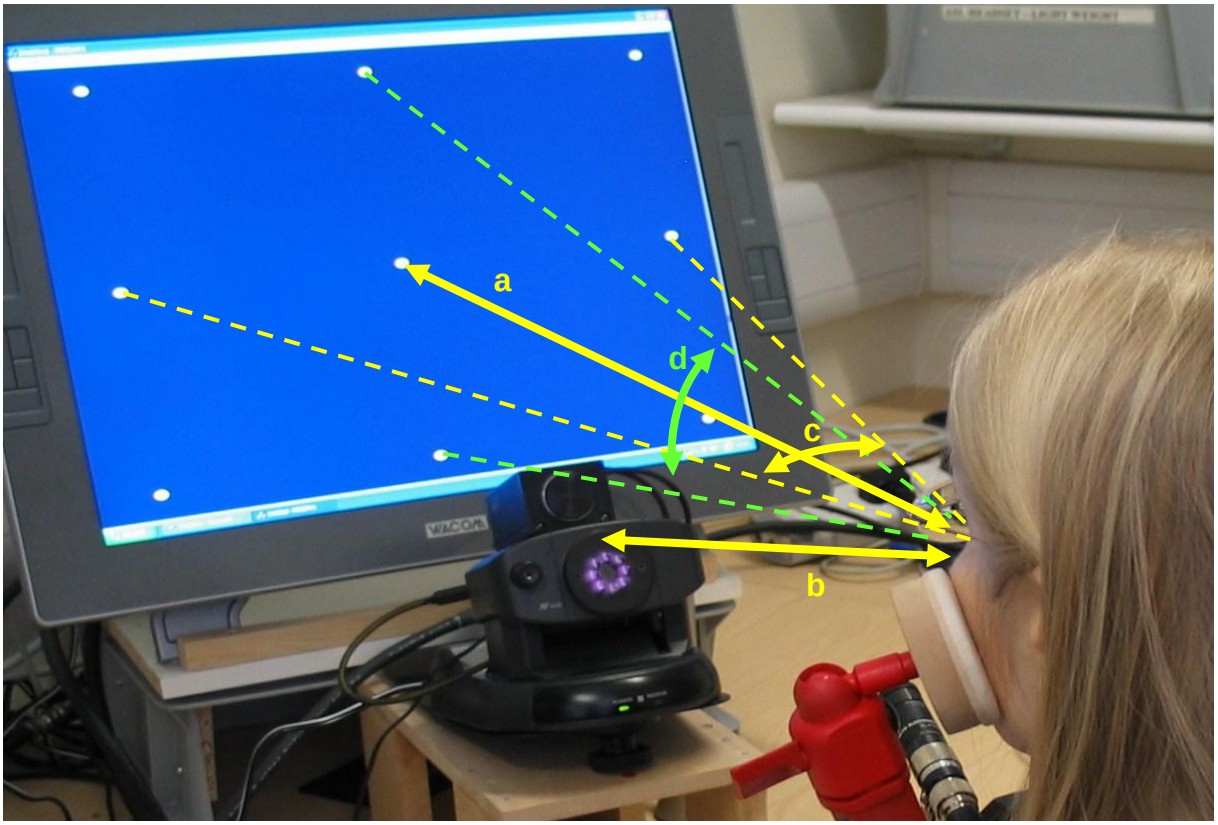
tracking, altering the vertical level of their point of gaze on the screen. The use of the bite bar eliminated this. Height of the chin rest, bite bar and seat were adjusted so that the participant's eyes were level with the screen centre. Participants maintained a comfortable neutral spine alignment in the vertical axis, without leaning against the back rest of the seat.

Previously the SPNT was carried out with EOG using a 1200mm visual display, giving a maximum visual angle of 40 degrees horizontally[90;243] although Roy-Byrne et al (1995) used a visual angle of 30 degrees[221]. Equipment was positioned so as to optimise performance of the ocular tracker (according to manufacturers guidelines[212]) providing a maximum ocular target excursion across the screen subtending a visual angle of 30 degrees horizontally and 15 degrees vertically. Relative positions of equipment to the participant are illustrated in Figure 3.2. These were identical for every participant.

Ocular motor test specifications

The predictable and non-predictable ocular target trajectories were as specified in Table 3.6.

Figure 3.2 Technical arrangement for measuring ocular movements



The video-graphic ocular tracker is located under the visual display screen. The 9-point calibration pattern is seen on the display. The eye to screen centre distance (a) = 616mm, eye to ocular tracking unit distance (b) = 480mm, the maximum horizontal visual angle across the visual display (c) =30° and the maximum vertical visual angle across the screen (d) = 15°

Calibration procedure and training protocol

To optimise the quality of data obtained from the video-graphic ocular tracker all ocular recording was performed in the dark. A 9-point calibration procedure was carried out according to the manufacturer's instructions[212], followed by a short training protocol. Previous studies of SP gain have either given no training[221] or have excluded the first part of each trial from analysis[55;90;91;217]. The purpose of including training here was to familiarise participants with the 2 different types of ocular target trajectory (since the non-predictable target was more complex than those used in previous studies) and to practise changing position for ocular tracking with neck torsion. Training consisted of one initial familiarisation trial for each of the predictable and non-predictable ocular target trajectories, with the head in a neutral position.

Each trajectory was then repeated once more with the neck in either right or left torsion (4 training trials in total). Adequacy of the training protocol was subsequently evaluated by analysis of systematic effects across trials.

Protocol for individual trials

Each trial lasted 15 seconds. Participants were instructed to fixate the stationary visual target, which was visible at the centre of the display window preceding each trial for 2 seconds, before attempting to follow its motion with their eyes as accurately as possible.

Sequence of trials

Previous studies with neck torsion collected all data in one position before a change occurred[55;90;91], raising the possibility of test performance being influenced by the preceding neck position. This possibility is supported by the fact that different findings were reported for different neck positions[55;90;91]. To avoid excessive numbers of neck torsion movements, trials were presented in blocks of 2 (one predictable and one non-predictable target task) before a position change took place. Participants were directed verbally to change position, and helped to rotate their chair 45 degrees to do so. Each neck position (neutral, left and right torsion) was repeated 3 times (resulting in a total of 18 trials) in a sequence that varied to counterbalance potential neck position order effects. The sequence of tests performed in each position was also varied across the protocol to avoid order of target trajectory type presentation effects. This pseudo-randomised (appeared random, but was not) sequence of tests was predetermined and identical for each participant. One previous study used an alternative method where different participants were pseudo-randomly allocated

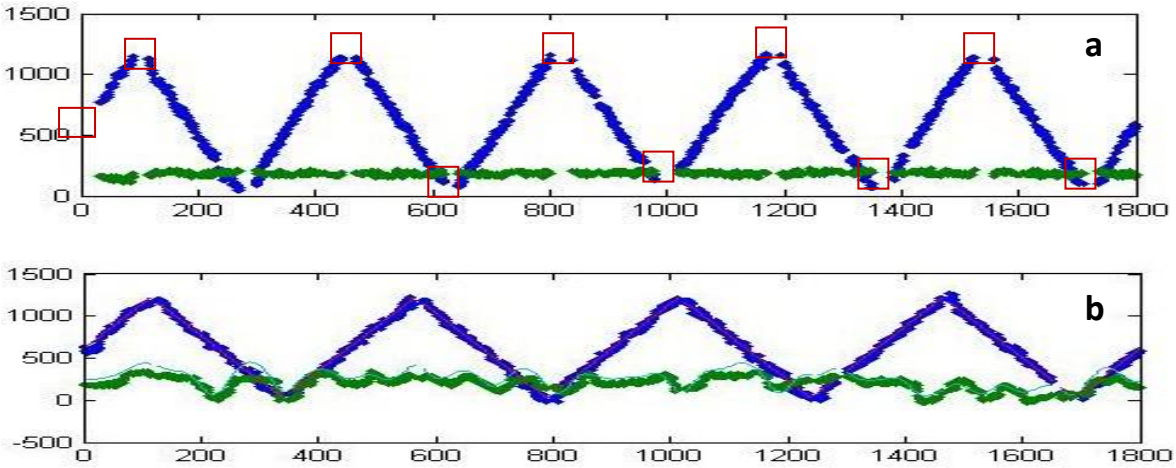
different sequences of neck position trials[101]. However this was not used in the present study, since variation in procedure between participants could result in greater within-sample[244] variance, that would in turn influence the correlation analysis that was planned[174] (Research Aim 5, 1.9.5).

Eye position over time was recorded with proprietorial E(5000) software and stored on an interface PC, according to manufacturer's instructions[212]. Non-predictable ocular target trajectory data was recorded as MATLAB files. An analysis programme was written in MATLAB. This enabled initial automated data processing. Raw eye data was passed through a 70 Hz low pass filter, blinks and other recording artefacts were excluded, according to manufacturers instructions[212]. To enable extraction of smooth pursuit eye movement data, saccades were automatically excluded where ocular velocity exceeded a threshold of 30 degrees $sec^{-1.}$ Ocular and target motion over time was then plotted for each trial, enabling further manual editing of data, details of which are provided in Table 3.10. For predictable ocular tracking trials data were excluded according to criteria specified in previous studies, enabling the SPNT test to be reproduced[55;90;91]

Mean and standard deviation SP velocity gains accross the duration of each trial were computed as the ratio of eye velocity to target velocity for all included data following editing (eye velocity divided by target velocity). For predictable ocular tracking, SP gain in the horizontal plane (hSP gain) was calculated. For non-predictable ocular tracking, hSPgain, SP gain in the vertical plane (vSP gain) and in both horizontal and vertical planes combined (cSP gain) was calculated. Mean and standard deviation of error (degrees sec^{-1}) was also calculated in horizontal and vertical planes and both combined accross the duration of each trial. This enabled

evaluation of the reliability of both temporal and spatial measures of SP performance. Figure 3.3 illustrates data that were included in the gain and error calculations accross each trial.

Figure 3.3 Illustration of data accross each trial that were included in mean and standard deviation SP gain and error calculations



The vertical axis indicates target position on the display screen (fine lines) and simultaneous ocular gaze position (heavy lines) in both horizontal (blue) and vertical (green) coordinates. The horizontal axis indicates time (msecs). Traces (a) and (b) demonstrate performance in the predictable ocular target task and the non-predictable ocular target task respectively. Trace (a) has been manually edited (indicated by red boxes) to exclude the initial open loop tracking and portions where the eye changed direction.

Data cleaning

Boxplots were generated separately for each group and for each task enabling the distribution of data to be inspected and outlying or extreme values to be identified[62]. Where these were found, all data for that participant was inspected to ascertain whether they consistently performed at similar levels or not. Data points were only removed where they appeared clearly inconsistent and not representative of that participants actual performance ability[245].

Table 3.10 Data manually excluded from the ocular tracking tests

Predictable ocular tracking test
• The initial open-loop[93] ocular tracking period (approximately 100 ms, prior to retinal feedback of target position) • Portions of data where the eye accelerated and decelerated as the target direction reversed (velocity was momentarily zero degrees sec^{-1}), leaving steady state SP tracking • Square waves[233] (saccadic shifts of the gaze between prolonged fixations) • Portions of non-tracking by participants[55;90;91]
Non-predictable ocular tracking test
• Square waves[233] • Portions of non-tracking by participants[55;90;91] NB Target velocity was constant, therefore there was no requirement to edit direction changes

Processing of data across trials

Data from the Matlab processing were exported to Excel (Microsoft). For individual participants mean SP gain and error parameters were then calculated across the 3 trials in each neck position for both predictable and non-predictable ocular tracking. The overall mean torsion (both left and right torsion) SP gains were calculated, followed by the absolute SPNT difference (the difference between mean neutral and mean torsion neck positions), as described in previous studies[55;90;91].

Analysis methods

Data were analysed for systematic differences across trials within test occasion 1 and test occasion 2, and also between tests 1 and 2, with a series of repeated measures 1-way ANOVAs. Reliability was evaluated using the intraclass correlation coefficient (ICC (2,k)[210], with 95% confidence intervals. Analysis was performed using IBM SPSS statistics.

Results

For both the predictable and non-predictable ocular tracking tests, results indicated a similar pattern whereby repeated measures ANOVAs indicated no significant effects for any SP gain or error measure, over the course of either the first or second test occasions. There was however a significant effect ($p<.01$) between occasions for hSP gain (predictable and non-predictable ocular tracking tests) and vSP and cSP gain (non-predictable ocular tracking test) with left cervical torsion or the mean of left and right torsion. During the first test occasion all SP gains in positions of neck torsion were lower than in the second test occasion.

Results of the reliability analysis for both ocular tracking tests are provided in Table 3.11.

Results indicate substantial reliability[210] for hSP gain (predictable and non-predictable ocular tracking tests) and cSP gain (non-predictable ocular tracking test) in all neck positions (ICC(2,*k*) = .853-.980), with lower bound 95% confidence intervals within the fair-substantial reliability range (ICC(2,*k)* =.471-.950). For non-predictable ocular tracking, with the exception of mean torsion, vSP gain and all error measures had reliability in the slight-moderate range (ICC(2,*k)* = .267-.651), however lower bound 95% confidence intervals were only in the virtually none-slight range ((ICC(2,*k*) = 0 -.172). For hSP and cSP parameters that had demonstrated substantial reliability, ICCs were also calculated for the differences and for the

Table 3.11 Intraclass correlation coefficients (model ICC(2,*k*)) and 95% confidence intervals for predictable and non-predictable ocular tracking

Neck position	Horizontal SP gain		Vertical SP gain		Combined SP gain		Horizontal error		Vertical error		Combined error	
	ICC	95% CI	ICC	95% CI	ICC	95% CI	ICC	95% CI	ICC	95% CI	ICC	95% CI
PREDICTABLE OCULAR TRACKING												
Neutral	.924	.811 - .969										
Right	.853	.633 - .941										
Left	.910	.471 - .973										
Torsion	.897	.639 - .963										
Difference	0*	0* - .404										
Absolute difference	.444	0* - .775										
NON-PREDICTABLE OCULAR TRACKING												
Neutral	.921	.808 - .968	.557	0* - .821	.940	.854 - .975	.635	.088 - .853	.589	.043 - .829	.431	0* - .758
Right	.919	.803 - .967	.267	0* - .704	.868	.677 - .946	.609	.007 - .843	.471	0* - .773	.326	0* - .710
Left	.965	.747 - .990	.386	0* - .727	.973	.928 - .989	.632	.101 - .850	.651	.172 - .856	.499	0* - .799
Torsion	.974	.936 - .989	.783	.465 - .912	.980	.950 - .992	.620	.064 - .846	.611	.040 - .842	.726	.467 - .877
Difference	.534	0* - .805			.582	0* - .831						
Absolute difference	.332	0* - .721			.356	0* - .729						

Green indicates substantial reliability (ICC (2,*k*) > .800), with lower bound 95 % CI in fair -substantial reliability range (.410-1.000)†

Yellow indicates moderate reliability (ICC (2,*k*) = .610-.800), with lower bound 95% CI in fair reliability range (.410-.600)†

Unshaded indicates lower bound 95% CI in virtually none-slight range (.000-.400)†

* Negative ICC values are theoretically not possible[238], they indicate no reliability and thus are reported as zero

†Categorisation of reliability according to Shrout (1998)[209]

absolute differences between neutral and mean torsion positions. For predictable and non-predictable ocular tracking these had reliability in the none-fair range, (ICC(2,*k*) = 0 -.534) however lower bound 95% confidence intervals all indicated no reliability (ICC (2,*k)* = 0).

Discussion

Substantial test-retest reliability of predictable ocular tracking with a neutral cervical position using a video-graphic ocular tracking measurement system had been previously reported once using a target velocity of 10 degrees sec^{-1} in healthy participants[221]. The results of the study similarly demonstrated substantial reliability using a target of 20 degrees sec^{-1}. There had been no previous reports of the reliability of predictable ocular tracking with cervical rotation or of non-predictable ocular tracking in any cervical position. The level of reliability considered acceptable varies widely in the literature with lower levels ranging from moderate to substantial (ICC = .610-.800)[209;246-248], however some sources recommend that only 'substantial' reliability (ICC = .810-1.000) should be considered adequate[209]. Estimation of confidence intervals around ICCs is advocated to avoid making false inferences about reliability[209]. Here, substantial reliability for all hSP and cSP gain parameters in both ocular tracking tests was established. Furthermore, lower bound 95% confidence intervals indicated moderate to substantial reliability for most hSP and SP gain parameters excepting predictable ocular tracking with left cervical torsion (ICC(2,*k*)= .471). Thus hSP and cSP gain provided acceptable measures in terms of reliability. However, for most cervical positions vSP and all error parameters had only slight-to-moderate reliability. Furthermore, lower bound 95% confidence intervals indicated virtually none- to-slight reliability. Thus these parameters did not have acceptable reliability for smooth pursuit ocular tracking.

The finding of systematic effects between test occasions for both predictable and non-predictable ocular tracking with cervical torsion, but the absence of systematic effects within either test occasion, suggests that a step-improvement in performance occurred during the interval between tests. One possible explanation is that free head and neck movements during the break, following performance of the test with the head restrained, enables increased gain of cervical proprioceptive, relative to vestibular cues to occur (i.e. enhanced use of proprioception by ocular movement systems). Similar increased gain of cervical proprioceptive cues have been reported in the cervico-ocular reflex with vestibular pathologies[170] as well as in WAD[130].

For the acceptable parameters (hSP and cSP gain), reliability of the differences and absolute differences computed between ocular tracking in neutral and torsion cervical positions was also evaluated, however these all fell below the acceptable reliability ranges described above. Furthermore, most lower bound 95% confidence intervals indicated virtually no reliability. The lack of acceptable reliability could reflect the observed systematic effects of improved performance in cervical torsion relative to the neutral cervical position in the re-test condition compared with the test condition. The literature review indicated low quality evidence of altered neutral-torsion differences in WAD(2.4.7)[91;92;98], however the finding here of inadequate reliability make this an unsuitable parameter for measurement of ocular tracking function.

Conclusions

Acceptable test-retest intra-examiner reliability was demonstrated for measurement of predictable ocular tracking and also of non-predictable ocular tracking, in neutral or torsion cervical spine positions, when hSP or cSP gain are the parameters used. This indicates that the constructs underlying performance, the video-graphic measurement system used, test specification, procedures and analysis methods used have acceptable reliability for the subsequent planned study (Research Aims 4 and 5, Chapter 4).

3.4.2 Establishing the reliability of the cervical JPE and cervico-cephalic kinesthesia tests

Background

Evaluation of reliability of the cervical JPE and cervico-cephalic kinesthesia tests in studies reviewed in Tables 3.7 and 3.8 was limited. For cervical JPE there was heterogeneity of methods and inadequate reliability had been reported for repositioning following extension in a study that used an incorrect ICC model[144]. Evaluation of reliability of cervico-cephalic kinesthesia was limited by inadequate sample size[205;249] in a single previous reliability study[60]. A second methodological study thus established the within- and between-day intra-examiner reliability of measurement of cervical JPE and cervico-cephalic kinesthesia using the equipment, technical arrangement, task specifications and procedures selected for this thesis The study also established the number of trial repeats needed to obtain stable measures with optimum reliability. Results of the study were published (Appendix 5), with the additional inclusion of a preliminary evaluation of the construct validity of the cervical JPE and cervico-cephalic kinesthesia tests by making comparisons between them[195].

Methods

Study design

A test-retest design was used to evaluate combined within and between day reliability.

Participants

Sixteen healthy volunteers (6 men, 10 women), with a mean (SD) age of 26.5 (9.4), gave informed consent and participated in the study. Each participant was tested on 3 occasions. The first 2 tests took place consecutively on the same day, with a 10 minute interval between them. The third test took place 5-7 days later, at the same time of day. The same examiner performed all tests.

Equipment and technical arrangement for measurement of cervical JPE and cervico-cephalic kinesthesia

Head position and motion was assessed using a Polhemus 3 space Fastrak electromagnetic tracking system (Colchester, VT). Participants were seated, with their back against the seat rest to prevent trunk movement. Two receivers recorded motion of the head and of the cervico-thoracic region of the spine in relation to a transmitter unit behind the chair. The head-mounted receiver, positioned over the vertex, was fixed to a plastic head strap. The second receiver was positioned over the spinous process of the T2 vertebra enabling monitoring of trunk motion. This position enabled motion at the cervico-thoracic junction to be included in measurements and minimised measurement errors due to skin slippage across the spinous process during cervical movements (anticipated to be greater at segmental levels above T2 where greater motion occurs). The sensor was attached to the skin with an adhesive Velcro pad, and secured using Micropore tape. Relative positions of

equipment to the participant are illustrated in Figure 3.4. These were identical for every participant.

Figure 3.4 Technical arrangement for measuring head position and motion

Electromagnetic sensors are mounted on the vertex of the head and over the spinous process of the second thoracic vertebra. The distance from the head-mounted sensor to the screen centre is 80cm. The yellow cursor provides the visual target, and the green, ring-shaped cursor displays head position

Cervical JPE and cervico-cephalic kinesthesia test specifications

Detailed specifications are provided in Table 3.9.

Calibration procedure and training protocols

For consistency with ocular tracking tests all cervical spine position and motion tests were also carried out in the dark. Prior to commencing data collection a calibration procedure was carried out. A miniature laser pointer was attached to the head mount. The participant was asked to move their head to point the laser consecutively towards four calibration target points appearing on the screen. The head receiver position was recorded for each point and these data were used to enable head position to be projected onto the screen for the head tracking task. The laser pointer was then removed.

A brief training protocol preceeded each test enabling task familiarisation. The justification for training protocols is provided in table 3.11. Data from these trials were not included in subsequent analyses.

Table 3.12 Justification for training protocols for the cervical JPE and cervico-cephalic kinesthesia tests

TEST	TRAINING PROTOCOL	JUSTIFICATION
Cervical JPE	1 trial of each repositioning motion (4 in total)	Previous studies used brief familiarisation training[54;55;144] or did not describe any training[52;53;59;150;164;181]
Cervico-cephalic kinesthesia	6 practice trials (3 pre-determined trajectory + 3 randomly generated trajectories)	Previous studies used a single familiarisation trial[60;250] During task development jerky head movements were initially observed as participants learned how to control the head position cursor motion

Protocol for individual trials

All trials were cued by a 2-second auditory tone, with recording commencing at the end of the tone.

For the cervical JPE test, participants located their head in their perceived neutral position. They then made a full active movement in left rotation, right rotation, flexion or extension, with direction instructed verbally before each trial. Immediately afterward, they attempted to return to the initial neutral position. Vision was occluded throughout. Start and finish positions were electronically marked. Participants were allowed to move their head prior to the start of each trial. Each of the 4 repositioning directions of motion was repeated 10 times (40 trials in total)

The cervico-cephalic kinesthesia test was carried out with the participants eyes open. During the auditory cue, participants moved their head to position the cursor over the target. Each trial then lasted for 15 seconds, during which the participants moved their heads to track the target with the head position cursor as it followed a non-predictable trajectory. Two types of trajectory were presented. Firstly, in accordance with Kristjansson et al (2004)[60], 6 curved, non-predictable trajectories with constant velocity of 1 degree sec-1 were generated. Three were presented during pretest training and 3 as test trials (each of these was presented 3 times). Secondly, to evaluate whether the test could be carried out without preselection and repetition of trajectories, a unique trajectory was generated for each of 9 trials. These had variable velocity, with a maximum of 1 degree sec^{-1}. There were 18 trials in total.

Sequence of trials

Requirements for the cervico-cephalic kinesthesia test were deemed the most complex to understand, but were more easily explained when participants had already been required to attend to static head position in the cervical JPE test.

Cervical JPE was thus evaluated first, followed by the cervico-cephalic kinesthesia tests.

Within the cervical JPE test previous studies collected all data for motion in one plane before proceeding to the next plane of motion. This raises the possibility of performance in a particular plane of motion being influenced by the order of presentation of preceding trials. Some studies of neck pain have reported different findings (within each study) for cervical JPE when repositioning followed different movements[51;53;54;59;98;165;184;191] and it is unclear whether this indicates differential effects of neck pain on specific movements, or reflects the order of testing. To counterbalance possible order effects within participants, a pseudo-randomised sequence of trials (3.4.1) was generated for the cervical JPE test that was identical for every participant. Similarly, within the cervico-cephalic kinesthesia test pre-determined and randomly generated unique trajectories were also pseudo-randomised. The same sequence of tests was presented for each of the 3 test and retest occasions.

Recording and processing data from individual trials

Position and motion (in sagittal, transverse and frontal planes) of each sensor, recorded over time, was stored on a PC. For the cervico-cephalic kinesthesia test visual target trajectory data was recorded as MATLAB files. An analysis programme was written in MATLAB that extracted the relevant parameters for each trial in each test. For the cervical JPE test, root-squared error (RSE) (degrees) was calculated for the primary plane of motion as the difference between head sensor position at the start and end of the recorded segment of data, with any difference in the T2 sensor position subtracted. For the cervico-cephalic kinesthesia test, mean RSE (degrees)

between the visual target and head position cursor was calculated across the duration of each trial.

Data cleaning

Data cleaning was performed as described for the ocular tracking tests (3.4.1).

Processing data across trials

Data from the Matlab processing were exported to Excel (Microsoft) for processing of data across trials. For individual participants accuracy (mean) and precision (SD) for RSE was calculated across trials of each cervical JPE test movement (left rotation, right rotation, flexion and extension). Mean and SD of the mean RSE for the cervico-cephalic kinaesthesia test was also calculated across trials for each participant, for both the pre-determined and the randomly generated trajectories. To enable evaluation of the influence of the number of trial repeats on performance in each test, a series of mean and SD values for each participant, were calculated with the inclusion of data from increasing numbers of trials, on each of the 3 test and retest occasions.

Analysis methods

Data were analysed for systematic differences across trials within test occasions 1, 2, and 3, and also across tests 1,2 and 3, with a series of repeated measures 1-way ANOVAs. Reliability was evaluated using the intraclass correlation coefficient (ICC (2,k)[210], with 95% confidence intervals. To enable evaluation of the effect on reliability of the number of trial repeats, a series of ICCs were calculated with the inclusion of data from increasing numbers of trials. Analysis was performed using IBM SPSS statistics.

Results

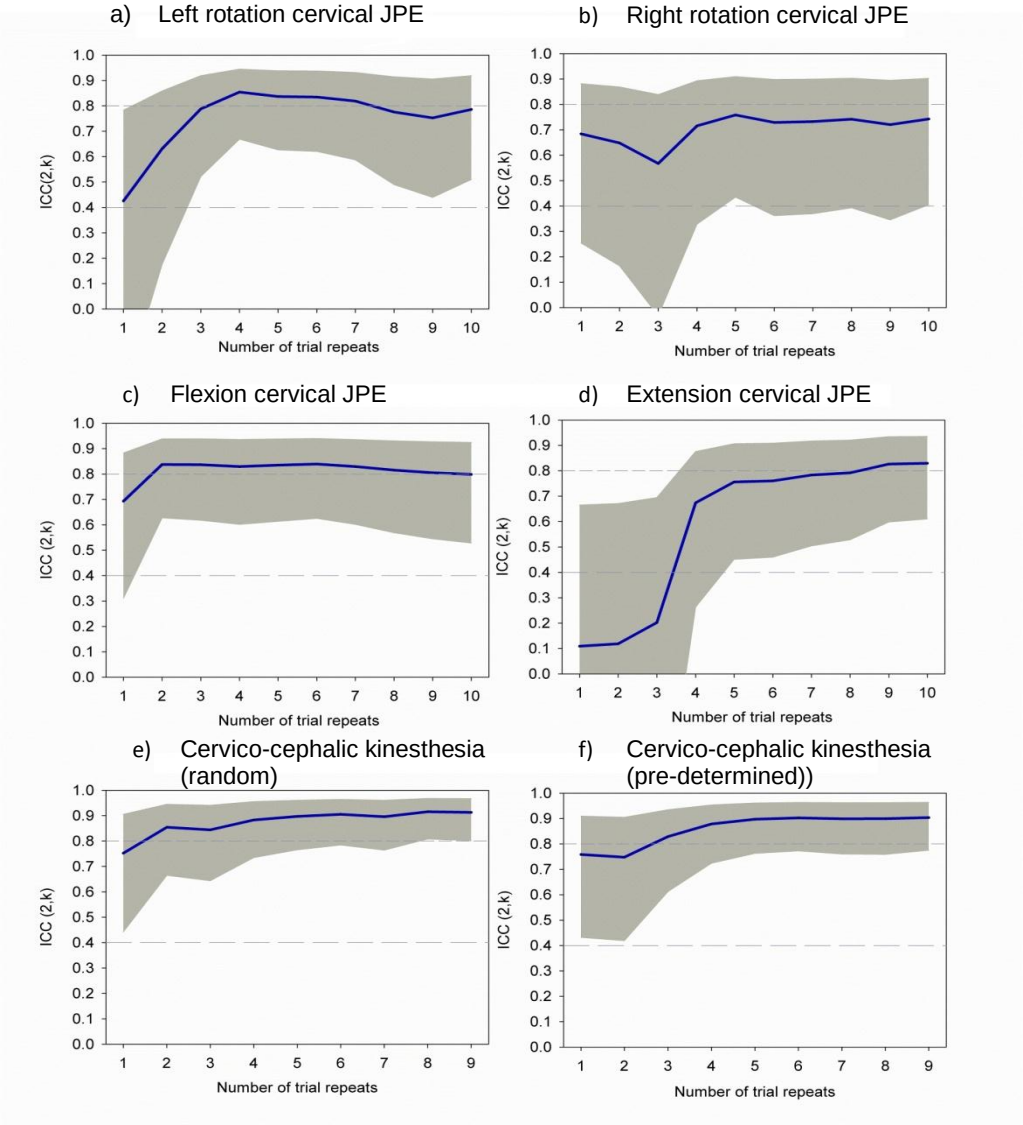
For cervical JPE and cervico-cephalic kinaesthesia tests, repeated measures ANOVAs indicated no systematic differences in group performance across trials within, or across test occasions 1 to 3 ($P > .05$)

The effect on the reliability of JPE accuracy (mean RSE) of calculating ICCs from increasing numbers of trials is shown in Figure 3.5. With 3 or fewer repeats, ICCs are lower for repositioning following extension than following flexion and rotation. For all movements, 5 or more trial repeats resulted in the highest, most stable reliability estimates of between ICC (2,k) = .730 - .840. Taking ICC = .410 as a threshold minimum for 'fair' reliability[49], consideration of the lower bound of the 95% confidence interval for ICC values shows that all exceed .410 with 5 or more trial repeats. In addition, the test-retest reliability of the precision (SD) of cervical JPE was also analysed, indicating moderate[49] reliability with 5 or more repeats for repositioning following flexion, extension and left cervical rotation (ICC (2,k) = .621 - .766), but with lower bound 95% confidence intervals only in the slight-fair reliability range (ICC (2,k) = .120 - .473). For repositioning following right rotation, precision of cervical JPE had fair reliability (ICC (2,k) = .599), but the lower bound 95% confidence interval was in the range of virtually no reliability (ICC (2,k) = 0 - .066).

For the cervico-cephalic kinaesthesia test, ICC values of over .800, indicating 'substantial'[49] reliability, were obtained for both pre-determined and randomly generated trajectories with 3 trial repeats. The highest estimates of ICC (2,k) = .900 -

.970 were derived with 5 or more repeats. The lower bound CI threshold of .410 was exceeded with a single trial.

Figure 3.5 The effect of different numbers of trials on test-retest reliability for the cervical JPE and cervico-cephalic kinaesthesia tests



The number of trial repeats from which each estimate is calculated is plotted against the ICC value obtained from the mean RSE in each cervical JPE task (a-d) and mean of the mean RSE in the cervico-cephalic kinesthesia tests for both randomly generated (e) and pre-determined (f) target trajectories. 95% confidence intervals are indicated by the gray-shaded areas. The dotted lines indicate the minimum threshold values of .041 for 'fair' reliability and .81 for 'substantial' reliability

In addition, the test-retest reliability of the precision of cervical JPE was also analysed, indicating moderate[209] reliability for repositioning following flexion, extension and left cervical rotation (ICC(2,*k)* = .621-.766), but with lower bound 95%

confidence intervals only in the slight-fair reliability range (ICC(2,*k*) = .120-.473). For repositioning following right rotation precision of JPE had fair reliability (ICC(2,*k)* = .599) but the lower bound 95% confidence interval was in the range of virtually no reliability (ICC(2,*k)* = .066).

Discussion

The aim of the present study was to test the reliability of the cervical JPE and cervico-cephalic kinesthesia tests.

Systematic error effects should be investigated before interpreting reliability analyses, because high ICC scores are possible even with significant systematic effects present[251]. The absence of systematic effects indicated that the practice protocol was sufficient to remove potential effects on performance of learning. Similarly, it can be assumed that no fatigue effects occurred.

For the cervical JPE test, poor reliability has previously been reported for head repositioning following cervical extension using 3 trials[144].In the present study, extension repositioning similarly showed poor reliability (ICC (2,k) = .200) with 3 trials, but with 5 trials this increased to .760, illustrating how the test protocol can directly influence the reliability of the outcome measurement. Test protocols and their effect on reliability of the outcome measure thus should be important considerations for clinical studies.

Levels of reliability that are considered acceptable and the consideration of estimation of confidence intervals around ICCs were discussed in 3.4.1 (in the discussion of the results of the ocular tracking reliability study). In the present study,

5 or more trial repeats resulted in estimates of the accuracy of cervical JPE with good-substantial[49] reliability *(ICC (2,k) = .730 - .840), however 95% confidence intervals revealed that even with good ICC values obtained, lower confidence interval bounds ranged only from fair to moderate reliability (ICC (2,k) = .360 - .620).* Estimates of the precision of cervical JPE had lower reliability (ICC (2,k) = .599 - .766) than for accuracy of JPE, although excepting cervical JPE following right rotation, precision was within the acceptable 'moderate' range[209]. Sample size for the reliability analysis (n = 16) was in accordance with recommendations, however a larger sample size may have resulted in narrower confidence intervals with greater lower bound of reliability values[205;249].

In the cervico-cephalic kinesthesia test substantial reliability (ICC (2,k) = .900 - .970) was demonstrated with 5 or more trials both for tracking predetermined target trajectories (that were repeated in the retest occasion) and for tracking randomly generated trajectories that were unique in every trial across the test and retest occasions. The latter would provide an advantage for longitudinal studies, since there would be no risk of improved performance due to having previously encountered the trajectories. All 95% confidence interval lower bounds fell within the 'good' range (ICC (2,k) = .780 - .770). The reliability of the cervico-cephalic kinesthesia test has only been reported once previously, using pre-determined trajectories and a 9 trial protocol[60]. The findings of the present study indicate that a shorter trials protocol produces highly reliable results. Comparable performance between randomly generated and pre-determined target trajectories indicated that the preselection and repetition of trajectories are not necessary.

Conclusion

Acceptable test-retest intra-examiner reliability was demonstrated for measurement of cervical JPE and of error in the cervico-cephalic kinesthesia tests when protocols included 5 or more trials in each test. This indicates that the constructs underlying performance, measurement system used, test specification, procedures and analysis methods used have acceptable reliability for the subsequent planned study (Research Aim 5 (1.9.5), Chapter 4).

3.5 CONCLUSION OF DETERMINATION OF METHODS FOR THE OCULAR TRACKING, CERVICAL JPE AND CERVICO-CEPHALIC KINESTHESIA TESTS

Review of existing literature identified video-graphic systems for measuring ocular movements and electro-magnetic motion measurement systems as the most appropriate for measurement of performance in the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests for this thesis (3.1).

To meet Research Aim 2 (1.9.2) a novel test of ocular tracking performance was designed to overcome limitations in the existing predictable ocular tracking test. This requires participants to track with their eyes a visual target following a complex trajectory in 2-dimensions that varies directionally, but has constant velocity (3.2). The novel test is included in subsequent studies investigating the effect of mechanical neck pain on ocular tracking of a non-predictable target (Research Aim 4, 1.9.4) and the construct validity of proposed tests of cervical proprioception (Research Aim 5, 1.9.5).

Review of existing literature informed detailed specification for the novel ocular tracking test as well as for the existing predictable ocular tracking, cervical JPE and

cervico-cephalic kinesthesia tests (3.3). These specifications informed the methodology of 2 subsequent studies evaluating reliability of these tests.

The first methodological study (3.4.1) demonstrated that for both the predictable and also the novel non-predictable ocular tracking tests, hSP and cSP gains have substantial test-retest intra-examiner reliability when ocular movements are measured with a video-graphic system, using the test specifications determined in 3.3. The second methodological study identified optimum protocols for the cervical JPE and cervico-cephalic kinesthesia tests, using an electromagnetic motion measurement system and the test specifications determined in 3.3. Moderate-substantial test-retest intra-examiner reliability was demonstrated for most cervical JPE measures using 5 or more trials repeats of each repositioning movement. Optimal, substantial reliability was identified for the cervico-cephalic kinesthesia test using 5 or more trials repeats using either predetermined or randomly generated target trajectories. Identification of protocols and parameters for the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests with acceptable reliability determined the outcome measures to be used for subsequent investigations. This fulfilled Research Aim 3 (1.9.3).

4 STUDY DESIGN & METHODS: EVALUATION OF NON-PREDICTABLE OCULAR TRACKING AND OF THE VALIDITY OF TESTS OF CERVICAL SPINE PROPRIOCEPTION IN PARTICIPANTS WITH MECHANICAL NECK PAIN AND HEALTHY CONTROLS

4.1 INTRODUCTION

Literature reviewed in Chapter 2 provides evidence, ranging from very low to moderate quality, suggesting impaired performance in participants with mechanical neck pain in tests that are proposed to measure cervical proprioception. These include tests of cervical JPE, cervico-cephalic kinesthesia and ocular motor function however all possess limitations in their ability to isolate the contribution of proprioception from other neurophysiological processes underlying test performance (1.5.1 – 1.5.3). The cervico-cephalic kinesthesia test was developed to overcome limitations in the cervical JPE test associated with possible vestibular contribution and with the predictable nature of the task. The SPNT test also uses a predictable ocular motor task. The literature review identified no studies that investigated the effect of mechanical neck pain on ocular tracking of non-predictable visual targets (2.5.6).

The review also identified limited, low quality evidence suggesting little or no convergence in correlation between performance in the cervical JPE, cervico-cephalic kinesthesia and SPNT tests and there were gaps in the existing evidence (2.4.10, 2.6). The contribution of demographic and symptom-related characteristics to their performance is also unclear (2.4.10). The construct validity (1.6) of the tests is thus questioned and it is unclear whether any of the deficits reported in their performance in mechanical neck pain indicate impaired cervical proprioception.

The present study evaluated whether non-predictable ocular target tracking reveals effects of mechanical neck pain (Research Aim 4, 1.9.4). Furthermore, the validity of both the non-predictable ocular tracking test and existing tests that have been proposed to measure proprioception was investigated (Research Aim 5, 1.9.5). Findings of the literature review (Chapter 2) and of two methodological studies (Chapter 3) informed the protocol for the study.

4.2 STUDY AIMS

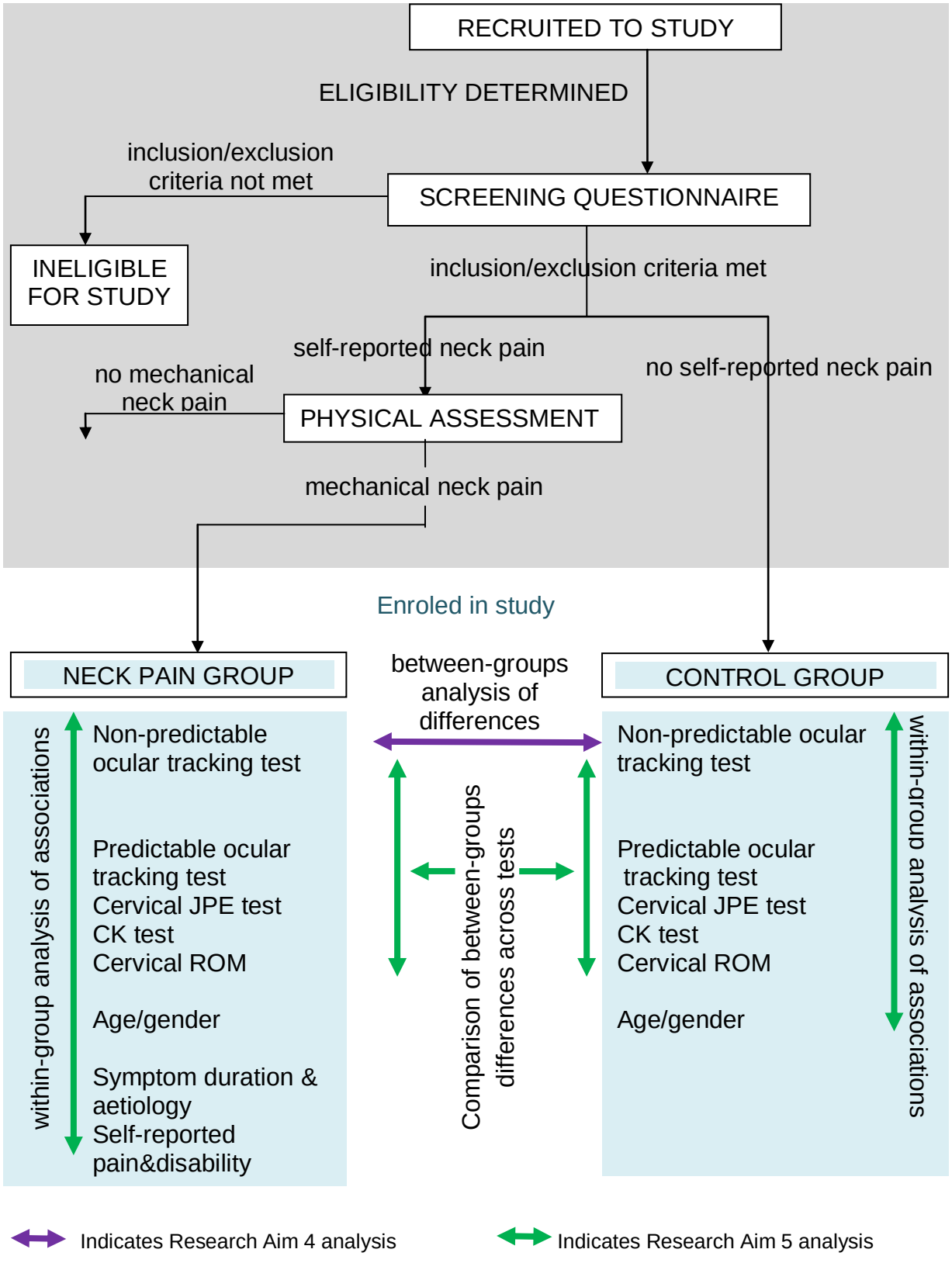
The study addresses Research Aim 4 (1.9.4) and Research Aim 5 (1.9.5).

4.3 STUDY DESIGN

A cross-sectional, controlled study with between-groups analysis of participants with mechanical neck pain compared with healthy controls evaluated the effect of mechanical neck pain on performance in the non-predictable ocular tracking task (Research Aim 4, 1.9.4). The study also investigated the construct validity of the cervical JPE, cervico-cephalic kinesthesia, predictable and non-predictable ocular tracking tests (Research Aim 5, 1.9.5) as measures of cervical proprioception, taking 3 approaches to examining convergence of the oucome measures (1.6). Firstly, comparison across tests of the between-groups analysis of performance enabled evaluation of whether mechanical neck pain had a comparable effect on performance in each test. If they were all measures of cervical proprioception, findings should be consistent across the tests (i.e. all impaired, or all not impaired). Secondly, within each group, analysis of correlation with demographic and symptom-related factors enabled evaluation of convergence of associations across the tests. Finally, within each group, analysis of correlations between performance in the cervical JPE, cervico-cephalic kinesthesia, predictable and non-predictable ocular tracking tests

enable a direct examination of convergence in the constructs measured. Figure 4.1 illustrates the study design.

Figure 4.1 Flow chart of study design



Many investigations represent a mixture of both exploratory and confirmatory aspects (providing definitive proof of a predefined hypothesis for final decision making)[252]. The present study is explanatory (addresses pre-defined questions using hypothesis testing)[62], yet possesses some exploratory features (e.g. seeks to build theory)[62] and therefore is not strictly confirmatory. Some aspects of study design were determined by the fact that there is no (non-predictable ocular target tracking) or little (correlation between tests) information available from existing evidence. Firstly, with no existing evidence for impaired ocular tracking of a non-predictable ocular target in neck pain, random sampling of large numbers of participants was not feasible within the resources for the study, or ethically justified based on the ratio of likely study value to participant burden[253]. A convenience sampling method was used, with target sample sizes of 20-30 participants per group estimated from consideration of previous studies using the SPNTtest[55;90], cervical JPE[10;51;54;58;59;163;164;182-184;189;191;254], cervico-cephalic kinesthesia[60;80] and cervical ROM[53;60;255] tests. The use of multiple outcome measures necessitated careful consideration of analysis methods (4.4.6).

A further aspect of the design that was influenced by the lack of existing evidence was the selection of outcome measures for each test. There was no evidence to indicate which measures of non-predictable target ocular tracking might or might not be impaired in neck pain, therefore multiple outcome measures (e.g. horizontal and overall smooth pursuit gain in various neck positions in the non-predictable ocular tracking test) were evaluated, informed by preliminary studies of their measurement properties[195;207] (Chapter 3).

In addition to factors related to the purpose of the study (above), design features were also determined by the requirement to minimise the risk of bias (2.2.2)[1]. Table

4.1 provides the GRADE[1] criteria for evaluation of risk of bias and quality in individual studies, along with features within the study design that address each of these.

Table 4.1 Limitations in observational studies specified by GRADE and study design features that address these

	STUDY LIMITATION	FEATURES IN STUDY DESIGN TO MINIMISE RISK OF BIAS
1)	Failure to develop and apply appropriate eligibility criteria	• Inclusion and exclusion criteria ensure correct allocation to either neck pain or healthy control groups (4.4.1) • Eligibility of neck pain participants is further established by including a physical assessment to ensure that neck pain is mechanical in nature (4.4.2)
2)	Flawed measurement of both exposure and outcome	• Tools for collection of data potentially susceptible to recall bias had validity and reliability established (e.g. self-reported neck pain and function questionnaires) (4.4.4) • Blinding of the examiner to group allocation during data collection was not feasible (4.4.4). Likelihood of experimenter and/or measurement methods bias was minimised by standardization of protocols, instructions to participants, automated data recording and largely automated processing of data. Experimenter was blinded to group allocation during all data processing (4.4.4). • Ensure that outcome measurement methods have acceptable reliability established (Chapter 3, Appendix 5)
3)	Failure to adequately control confounding (measurement and control of prognostic factors/imbalances)	• Recruitment methods increase likelihood of comparable demographic backgrounds between neck pain and control groups (socioeconomic, age, gender, medical and treatment history etc) (4.4.1) • Data collected to screen for factors other than neck pain that might influence test performance (e.g. uncorrected vision impairment, eye movements or vestibular dysfunction) (4.4.1, 4,4.2) • Between-group analysis evaluates differences in potential prognostic factors (e.g. age or gender distribution) (4.4.6)
4)	Incomplete follow-up	• Not applicable to cross-sectional study

4.4 METHODOLOGY

4.4.1 Participants

Eligibility criteria

Eligible participants were individuals with unresolving mechanical neck pain of at least 2 weeks duration and healthy individuals with no neck pain. More recent onset neck pain and also participants receiving treatment (other than usual medications) or introducing new medication within 2 weeks prior to enrolment were excluded due to difficulty determining if the condition was resolving. Changes occurring between undergoing physical examination and physical function measurements could confound findings in the mechanical neck pain group. Mechanical neck pain of any aetiology was included since the literature review (2.5.6) indicated no clear rationale for studying only WAD or only non-traumatic neck pain (there is likely to be considerable clinical heterogeneity within either group and evidence that test performance is impaired is boadly similar for each). Other musculoskeletal pain conditions were not excluded from either group if they did not impair cervical mobility, since coexistence of more than one condition is common, therefore likely among the neck pain group[256]. Prognostic imbalance[1] could arise if these were excluded from the control group and exclusion would limit generalisability of findings. Data were collected on other musculoskeletal pain conditions in both groups and compared to minimise risk of prognostic imbalance between groups. Detailed Inclusion and exclusion criteria are provided in table 4.2.

Table 4.2 Eligibility criteria for inclusion and exclusion in the study

CRITERIA FOR PARTICIPANT INCLUSION	CRITERIA FOR PARTICIPANT EXCLUSION
• Age 18-55 years [a] • Had self-reported neck pain[3] of at least 2 weeks duration, with or without radiculopathy or cervicogenic headaches[b] OR Were healthy individuals who were asymptomatic for neck pain • Were naïve to the physical function tests[h]	• Had known congenital anatomical anomalies of the cervical spine or serious underlying pathology[c] • Had vestibular pathology or reported symptoms of dizziness[d] • Had history of head trauma[d], neurological disease or reported potential neurological symptoms[e] • Had uncorrected visual impairment or history of eye surgery[f] • Had any medical condition contraindicating physical examination of the neck or sustained neck torsion[g] • Had self-reported neck pain, but mechanical pain not elicited during the physical examination[i] • Were healthy individuals without self-reported neck pain but reported history of prior neck pain, trauma or surgery[j]

[a] limits were chosen to reflect the adult target population of interest, while minimising the likelihood of significant age-related degenerative joint disease being present in the cervical spine[257]
[b] broad criteria to improve generalisability
[c] excluded according to the definition of mechanical neck pain[3]
[d] risk ofinjury to the CNS or otoliths that could influence performance in the tests[175]. WAD-associated dizziness is difficult to confirm and may be due to other pathologies[170], thus dizziness was excluded from both groups to ensure prognostic balance
[e] risk of impaired sensorimotor function that could influence performance in the tests[175]
[f] could impair visual target tracking tasks
[g] Would be unable to undergo examination to confirm eligibility for neck pain group or would be unable to peform SPNT test
[h] Risk of prognostic imbalance[1] if groups contained individuals with differing experience levels
[i] definition of mechanical neck pain[3]
[j] risk of altered mechanical function of cervical spine

Justification for criteria is indicated below table

Recruitment of participants

Participants with neck pain and healthy participants without neck pain were recruited from two chiropractic clinics by display of advertisements requesting participants and by asking prospective new patients whether they wished to participate prior to commencing treatment. Participants with neck pain were offered a written report of findings of the physical examination. Financial rewards were not offered. Healthy participants were recruited from among friends or family of the neck pain participants. This strategy was determined to increase the likelihood of both groups comprising individuals with comparable demographic characteristics., thus reducing the risk of prognostic imbalance (Table 4.1) between groups[1].These included age and gender (since limited evidence indicated that there could be associations of these with some of the tests (2.5.3), as well as socioeconomic factors and the existence of other musculoskeletal disorders that might theortically influence performance in the tests (although effect of these on performance in the cervical JPE, cervico-cephalic kinaesthesia and ocular tracking tests is unknown).

4.4.2 Procedure determining eligibility for neck pain and healthy control groups

Participant questionnaire

A letter explaining the study and an initial screening questionnaire were issued on enquiry. The screening questionnaire captured information necessary to determine eligibility (all inclusion and exclusion criteria) for both neck pain and healthy control participants (Table 4.1). In addition, data were collected on demographic characteristics, history of musculoskeletal conditions and treatment preferences. For neck pain participants, data were also captured regarding aetiology, duration and nature of neck pain and associated symptoms. Information provided enabled analysis

of likely prognostic balance[1] between groups (Table 4.1) and also provided data for the analysis of association between demographic and symptom-related characteristics and performance in the tests (Research Aim 5, 1.9.5). Volunteers reporting no neck pain and who met all eligibility criteria were enrolled in the study and assigned to the healthy participant group.

Physical assessment of neck pain

Volunteers reporting a current neck pain condition underwent a physical assessment prior to enrolment in the study. The purpose of this was to confirm eligibility[1] for the mechanical neck pain group by establishing that pain was elicited by mechanical factors[3]. A protocol was designed that included tests routinely used in manual therapy practice.

A number of techniques for identification of mechanical neck pain were considered. Studies evaluating individual techniques provide conflicting evidence on their validity and reliability when the aim is identification of specific dysfunctional spinal segments or sources of pain (e.g.zygapophyseal joint, osseous or soft tissue pain) [258-264]. Techniqes for rating the broader classification of mechanical neck pain have not been evaluated. Existing literature however suggests that pain provocation techniques have better intra- and inter-rate reliability than motion palpation for identifying dysfunction[264]. There is also indication that using more than one examination technique improves reliability for detecting segmental dysfunction [261;264]. Therefore a protocol was developed that used a range of movement/position-induced pain provocation techniques (provided in Table 4.3). Additional techniques were carried out including palpation and assessment of neurological function, depending on presenting symptoms, for the purpose of providing a report of the clinical

impression to participants, but were not used for determining eligibility for the study. The protocol is provided in Appendix 6. Neck pain elicited in at least one part of the examination was rated as a current mechanical neck pain condition.

Following training in the protocol, assessment of all volunteers was carried out by a chiropractor who did not participate in subsequent data collection or analysis. A sub-set of volunteers (n = 18)[265] were also assessed by a second chiropractor on the same occasion, enabling analysis of the inter-examiner reliability of ratings using Cohen's kappa coefficient[265]. Perfect agreement between examiners was achieved (k= 1.00). Volunteers rated as having mechanical neck pain were enrolled in the study within the neck pain group

Table 4.3 Techniques included in the physical assessment protocol

TECHNIQUE	CERVICAL MOVEMENT/POSITION	POSITIVE SIGN
Whole neck active ROM with overpressures[266]	- Whole neck , upper cervical, cervico-thoracic movements - Primary planes, combined planes	Pain provocation indicates mechanical neck pain[3].
Passive accessory intervertebral movements[266]	- Individual segments C1-T2 - Combined extension/rotation flexion/rotation	Pain provocation indicates mechanical neck pain[3].
Passive intervertebral movements (Bischoff protocol)[267]	- Individual segments - Neck in neutral position	Pain provocation indicates mechanical neck pain[3].

4.4.3 Ethical Considerations

Ethical considerations addressed principles for medical research involving human subjects specified in the World Medical Association Declaration of Helsinki (2008)[268]. Broadly, in medical research the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects should be protected. Appendix 8 provides the principles that were relevant to the study and indicates how each was addressed. Only competent adults[268] were eligible for the study. A letter to participants informed them of the aims, methods, sources of funding, and institutional affiliations of the researcher and the anticipated benefits and potential risks of the study and the discomfort it might entail[268]. Use of clinical or technical terminology was avoided to ensure comprehension by a lay person[269]. Participants were informed of their right to refuse to participate in the study or to withdraw consent to participate at any time[268] and were given the opportunity to seek further information[268] prior to providing consent in writing[268;269].

Risks or burdens to participants[269] were assessed and measures to prevent or minimise these were included in the study design and procedures. Appendix 7 provides details of the risks and burden identified and measures taken to reduce these

Participants personal information and all data collected was stored and managed in accordance with the Data Protection Act (1988)[270]. All information collected was stored securely. All data included and reported within the study was anonymised and identifiable only by coded reference number (4.4.4). No information was included that might enable identification of individual participants.

The study was conducted as part of a PhD, registered at the University of Birmingham.There were no conflicts of interest. Ethics approval was given by the ethics committee of the School of Psychology, Uiversity of Birmingham. Sources of financial support were a research fellowship provided by the Royal College of Chiropractors, a grant provided by the Chiropractic Patients Association and payment of university registration fees by the McTimoney College of Chiropractic. No funding organization had any role in the design, conduct or reporting of findings of the study.

4.4.4 Data collection

Following enrolment into the study, all participants attended a data collection session. For neck pain participants this took place 1-3 days after their physical assessment. This interval was determined by the need to both reduce the likelihood of physical assessment procedures influencing performance in the cervical JPE, kinesthesia, predictable or non-predictable ocular tracking tests (this could introduce prognostic imbalance between groups[1]) if the interval was too short, while in contrast, reducing the likelihood of mechanical neck pain having resolved subsequent to the physical assessment if the interval was too long. All participants completed a short form confirming that the data provided in their screening questionnaire was still accurate, neck pain participants were asked about any change in neck pain condition since physical assessment, while healthy participants confirmed no new neck pain condition or injury had occurred.

All participants confirmed that they had read the standardised written information provided on volunteering about the purpose of the study and the procedures involved in data collection. Participants had the opportunity to ask questions, prior to giving

written consent to data collection. Neck pain participants were given self-reported functional outcome measures questionnaires to complete just prior to performing the cervical JPE, kinesthesia, predictable and non-predictable ocular tracking and ROM tests.

Self-reported function measures

Self-reported measurement scales were used in the present study for two purposes. Firstly, characterisation of pain-related factors in the neck pain group would indicate the generalisability of findings of the study, thus scales needed to be widely used and measure items relevant to clinical settings in the neck pain population. Secondly, evaluation of association of neck pain-related factors with performance in the cervical JPE, kinesthesia, predictable and non-predictable ocular tracking test would contribute to establishing the validity of these tests (Research Aim 5, 1.9.5). Since the tests are proposed measures of cervical proprioceptive function, scales needed to enable measurement of neck-specific pain-related traits and to capture the breadth of these. In addition psychometric properties of scales used needed to be established and questionnaires needed to be reasonably quick to complete.

Many widely used scales focus on the constructs of cervical pain and perceived disability in performance of everyday activities[271-275]. It is, however, argued that outcome measures for neck pain should include psychological factors (such as low mood, anxiety, fear-avoidance beliefs, coping strategies, and poor self-efficacy) as well as pain and disability[276] . There may be overlap in scales designed to measure individual psychological constructs. This overlap has not been evaluated in a neck pain population, but has been indicated in low back pain, where most psychological

constructs fell within the category of 'pain-related emotional distress' [277]. Thus, there is no clear indicator for measurement of any specific psychological constructs in neck pain. It has been recommended that psychological constructs may be combined within multidimensional scales to provide measures that capture the breadth of relevant traits[277]. One particular aspect of psychological factors is pain-related fear and avoidance of activity[278]. As the cervical JPE, cervico-cephalic kinaesthesia and ocular tracking tests require movement, a more specific measure of the psychological construct of fear-avoidance (kinesiophobia)[279;280] was included. Table 4.4 provides the scales that were considered for inclusion in the study.

Four neck pain-specific scales were identified in use, whose psychometric properties had been evaluated (Table 4.4). The quality of evidence is limited due to indirectness[1] in analysis methods reported and also which versions of the scales were evaluated. A number of studies evaluated translated versions and reported reliability or validity that may not be comparable to English versions[281]. The NDI had been investigated the most[197;273;282]. Acceptable reliability is reported[283] and it has been validated against multiple measures of function, pain and clinical signs and symptoms, and in different populations of neck pain patient[283]. The NDI was thus selected as a measure of pain and disability. However, the NDI does not include psychological constructs.

The Neck Bournemouth Questionnaire (neck BQ) was developed to overcome the limitation of scales that did not measure psychological aspects of neck pain[284]. It's psychometric properties have been evaluated and compared to the NDI, the CNFDS, and the generic health status measure the short form of the US Medical Outcomes Survey Questionnaire (SF-36). External and longitudinal construct validity were

acceptable[284]. Moderate test-retest reliability was shown (ICC = .65 for the total score). The neck BQ was thus used alongside the NDI due to its inclusion of items measuring a range of psychological aspects of neck pain.

The existing scales specific to fear-avoidance are the TSK and its shortened version (TSK-II), and the FABQ. Although a recent study reported better reliability of the FABQ in neck pain patients[285], an earlier study reported a possible 'floor' effect whereby high proportion of zero scores occurred[286]. This might explain the weak-moderate concurrent validity reported between the two. Based on this observation, the TSK was selected over the FABQ. In addition one study has included the TSK among a range of measures aimed at characterising acute whiplash-associated disorders, showing significantly higher scores in groups of patients that scored higher in the NDI[287].

A subsequent study evaluated and compared similar psychometric properties between the TSK and a shortened version, the TSK-II, demonstrating very similar internal consistency, reliability, validity and responsiveness[278]. Therefore it was decided to utilise the shortened version, both for brevity and since it was observed that the omitted items in the TSK-II, where the response scale was reversed, were more often not completed by participants. Consent was obtained to use the NDI, neck pain BQ ad TSKII from groups that developed them[273;278;284].

Table 4.4 Self-reported outcome measurement scales considered for inclusion

SCALE	CONSTRUCTS MEASURED	PSYCHOMETRIC PROPERTIES (TEST-RETEST RELIABILITY & VALIDITY)
Neck Disability Index (NDI)[273]	Pain and disability	Reliability: Widely evaluated, ICC = .500-.980[283]. Validity: Widely validated in different settings strongly correlated to range of neck-specific & generic pain and disability measures (r>.700)[283],
Copenhagen Neck Functional Disability Scale(CNFDS)[271]	Pain and disability	Reliability: Limited evaluation in English translation[281] (ICC = .930 in Polish version)[288]. Validity: Limited literature on validation, strongly correlated to .830-.890 pain and disability and patient global assessment scores[197]
Northwick Park Scale[272]	Pain and disability	Reliability: ICCs not reported for English version. Kappa coefficient .62[197]. ('high' reported in modified Chinese version[289]). Validity: Limited literature in English version[197] (Chinese version correlated well to sub-scales of SF-36 (r= -.43 to - .71) and to NRS (r = .069))
Neck Pain and Disability Scale[275]	Pain and disability	Reliability: High reliability reported, but ICCs were not used[290]. Validity:face validity reported[197]
Modified Bournemouth Questionnaire[284]	Pain, disability, psychological aspects[a]	Reliability: ICC = .650[284]. Validity: Acceptable external and longitudinal construct validity against a range of other measures[284]
Tampa Kinesiophobia Scale (TSK/TSK-II)[278;279]	Psychological aspect[b]	Reliability: ICC = .820/.81. Validity: weak-moderate concurrent validity of TSK with FABQ (r=.33-.59)[286].
Fear Avoidance Beliefs questionnaire (FABQ)[280]	Psychological aspect[b]	Reliability: In back pain, r = .64-0/84[286], no ICCs reported. Recently In neck pain substantial reliability reported[285]. Validity: weak-moderate concurrent validity of FABQ with TSK(r=.33-.59)[286]

[a]Pain intensity; functional status in terms of day-to-day activity/social activity; affective domains (anxiety and depression); and cognitive/behavioral domains (fear-avoidance beliefs about work activity and pain locus of control)

[b]Fear-avoidance of movement beliefs (kinesiophobia)

Neck pain participant's scores for the NDI, neck BQ and TSKII questionnaires were extracted and entered in a spreadsheet in Excel (Microsoft). Demographic and additional symptom-related characteristics were also entered into the spreadsheet, enabling analysis of distribution of demographic characteristics between the neck pain and healthy control groups, and also the analysis of association between these, along with symptom-related characteristics, with performance in the cervical JPE, cervico-cephalic kinaesthesia and ocular tracking tests. Demographic and symptom-related characteristics (identified in 2.5.3) were age, gender, symptom duration and aetiology of neck pain, in addition to the NDI, neck BQ and TSKII scores.

Measurement of ocular tracking, cervical JPE, performance in the cervico-cephalic kinaesthesia test and cervical ROM

All participants followed a standardised procedure for measurement of performance in the novel test for ocular tracking of a non-predictable target (Research Aim 4) as well as the predictable ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests (Research Aim 5). Active cervical ROM was also measured (since limited literature indicated a possible influence of cervical ROM on performance in the tests (2.5.3)), enabling correlation to be evaluated (Research Aim 5). Acceptable reliability of tests was established (discussed for each test below).

Measurement of predictable and non-predictable ocular tracking

Smooth pursuit velocity gain was measured during ocular tracking of a visual target following a triangular trajectory, in the horizontal plane, at a constant steady-state velocity of 20 degrees sec^{-1} (predictable test) and also during ocular tracking of a visual target following a non-predictable trajectory in 2-dimensions at a speed of 20

degrees sec^{-1} (non-predictable test). For both tests ocular tracking was performed with a neutral head position and also with both left and right neck torsion. For each of the 2 tests, 3 trials were performed in each head position (a total of 18 trials). A video-graphic ocular tracking system was used for measurement of performance in the ocular tracking tests (3.1.1). Specification of the non-predictable and predictable ocular tracking tasks was determined in Chapter 3 (3.3.1). The technical arrangement of equipment, calibration and training procedures, protocol for individual trials, sequence of trials, procedures for data cleaning and processing of data both within and across trials were the same as those for the methodological study (3.4.1). Acceptable proportions of data that may be excluded from analysis as a result of cleaning are unclear, however it is suggested that prior knowledge of performance and measurement properties of outcomes should inform cleaning and that the influence of such data points on analysis results may be examined[245]. Proportions of data (<.5%) excluded from the preliminary study[207], where substantial reliability of performance and measurement was established (3.4.1), therefore provided a threshold above which both edited and unedited data sets were analysed.

The parameters measured were determined by the reliability that was established in the methodological study (3.4.1). In both the non-predictable and predictable ocular tracking tests hSP gain was measured, while in the former, overall cSP gain was also measured. These all had substantial[209] reliability (ICC2,*k* =.853-.980). Neutral-torsion differences had none-fair[209] reliability (ICC2,*k* = 0-.534) and were therefore not included 1.6). In relation to evaluation of the between-group differences in non-predictable ocular tracking (Research Aim 4) multiple outcome measures were thus analysed, constituting a family of primary outcomes[252;291] (i.e. hSP and cSP gain in

neutral, left and right rotated cervical positions). These determined the significance level applied in the analysis of data (4.4.6).

Measurement of cervical JPE and performance in the cervico-cephalic kinesthesia test

An electromagnetic motion tracking system was used to measure performance in the cervical JPE and cervico-cephalic kinesthesia tests (3.1.2). Specification of the tasks within each test was determined in Chapter 3 (3.3.2). The technical arrangement of equipment, calibration and training procedures, protocol for individual trials and sequence of trials, procedures for data cleaning and processing of data both within and across trials were the same as those for the methodological study (3.4.2). The number of trial repeats for each task was determined by the methodological study, whereby 5 or more repeats optimised stability and reliability. Proportions of data (<.03%) excluded from the preliminary study[195], where substantial reliability of performance and measurement was established (3.4.2) for cervical JPE and cervico-cephalic kinesthesia tests, provided a threshold above which both edited and unedited data sets were analysed[245].

In the cervical JPE test accuracy of JPE had moderate-substantial[209] reliability (ICC2,*k* = .730-.840). Precision of JPE had fair-moderate[209] reliability (ICC2,*k* = .599-.766). In the cervico-cephalic kinesthesia test a randomly generated target was used to prevent learning and prediction of the trajectory. This had substantial reliability (ICC2,*k* = .900-.970) (3.4.2). In both tests 6 repeats of each task were used to allow for possible loss of trials as a result of data cleaning.

Measurement of cervical ROM

The electro-magnetic motion tracking system used for measurements in the cervical JPE and cervicocephalic kinesthesia tests was also used to measure cervical ROM, since moderate-substantial[209] test-retest reliability has been reported (ICC2,1 = .61-.97) for measurements of cervical mobility[246;247]. The technical arrangement of equipment and calibration procedure was the same as for the cervical JPE and cervicocephalic kinesthesia tests (3.4.2).

Consideration of existing literature, provided in Table 4.5, informed specification for the cervical ROM test. Table4.6 provides the specifications for the cervical ROM test and their justification. Full-plane active cervical ROM was measured in each of the 3 cardinal planes. Moderate-substantial[209] reliability (ICC(2,*k)* = .64-.93) has been reported for this method[292].

A single training trial was given in each full plane motion. Previous studies used no training[61;247] or brief familiarization training[246;292]. Moderate-substantial reliability was demonstrated following 1 familiarisation trial of each motion[292].

Prior to each trial the required direction of movement was signalled verbally by the examiner. The start of each trial was cued by an auditory tone, of 2 seconds duration. Off-set of the tone provided the command for participants to begin the movement. Participants were required to actively move their neck as far as possible in the direction indicated, followed by a movement as far as possible in the opposite direction (i.e. full-plane ROM), before returning to neutral position. ROM (degrees) was calculated in the primary plane of motion as the difference between the

maximum angular excursion of the head sensor in each direction with motion of the T2 sensor subtracted. A brief pause enabled participants to rest between trials.

The cervical ROM trials in different planes of motion were pseudo-randomised, as described in 3.4.1, to counterbalance possible order of presentation effects.

Data cleaning was carried out, as described in 3.4.1. Since there was no data to indicate the threshold for acceptable quantities of data lost during cleaning, where any trials were edited out, both edited and unedited data sets were analysed[245].

Data were exported to Excel (Microsoft). For individual participants, mean cervical ROM was calculated across trials for sagittal, transverse and frontal plane motion[292].

Table 4.5 Existing literature for specification of the cervical ROM test

CERVICAL RANGE OF MOTION (ROM) TEST	SUMMARY
<u>Active or passive ROM</u> • Passive ROM investigates total possible ROM and shows less variability than active ROM[247] • Active cervical movements are required for both the cervical JPE and cervico-cephalic kinesthesia tests. Literature review identified no studies of these tests using passive motion (chapter 3) • Moderate-substantial[209] reliability reported for evaluation of active cervical ROM in both neck pain participants and healthy controls using Fastrak (ICC (2,*k*) = .64-.93)[292] <u>Full plane or half plane movements</u> • Both full plane[247] and half plane[246] movements have been previously used • Full plane movements are more reliable than half plane movements[61;247] <u>Number of repeats</u> • Moderate-substantial[209] reliability reported using 6 repeats in each plane[61;247;292]	• Active and passive ROM evaluate different aspects of cervical motion • Active cervical ROM is relevant to current study • Moderate-substantial[209] reliability indicated with 6 repeats of full plane motion (in each of the 3 cardinal planes)

Table 4.6 Task specification for the cervical ROM tests

TASK SPECIFICATION		JUSTIFICATION
ROM	Active cervical ROM	Replicates active ROM requirement of cervical JPE and cervico-cephalic kinesthesia tests. Moderate-substantial[209] reliability reported[292]
Plane of motion	Full plane motion 3 cardinal planes	Enables full evaluation of ROM. Lateral flexion included (not evaluated in cervical JPE or cevicocephalic kinesthesia tests) to enable association with altered coupled motion patterns to be evaluated. Moderate-substantial[209] reliability reported[292]
Number of trials	6 trials in each plane of motion	Moderate-substantial[209] reliability reported[292]

4.4.5 Procedure for enrolment in the study and data collection

Figure 4.1 summarises the overall procedure for enrolment into and progression though the study. Volunteers received a letter explaining the nature of and requirements for participation in the study. They also received a participant screening questionnaire (4.4.1, 4.4.2) for completion.This was administrated by clinic staff, who assigned a study participant coded number to returned questionnaires that was used for identification of all subsequent anonymised records. Questionnaires were screened for eligibility for the study against inclusion and exclusion criteria (Table 4.1). Eligible participants were contacted to arrange attendance for both the physical assessment (neck pain participants) and subsequent data collection (all eligible participants) visits.

The physical assessment (4.4.2) was carried out by an independent chiropractor. Results of the assessment were recorded on an assessment form (Appendix 6), identified by the participants coded number. These were checked to determine eligibility for the neck pain group.

The data collection visit took place either at the University of Birmingham or at a chiropractic clinic. On arrival participants completed a form indicating their consent to take part in data collection and whether any change in or new neck pain symptoms had occurred since return of the screening questionnaire. Neck pain participants then completed the NDI, neck BQ and TSKII questionnaires (4.4.4) which were returned in a sealed envelope identified by the participant coded number. The non-predictable and predictable ocular tracking tests were carried out, followed by measurement of cervical ROM, the cervical JPE, and cervicocephalic kinaesthesia tests. The sequence of tests was determined by the fact that non-predictable ocular tracking

was the primary outcome for analysis of between group differences (4.4.6), thus ocular tracking tests wre performed first. For evaluation of correlation between tests, it was preferable for every participant to follow the same protocol (3.4.1), as opposed to block randomisation of the cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests across participants. The order of presentation of these tests was thus pragmatic, determined by the observation that participants more easily learned the task requirements when cervical ROM was performed first, followed by the cervical JPE and finally the cervcico-cephalic kinesthesia tests.

Procedures to minimise experimenter and outcome measurement bias

Blinding of group allocation during data collection was not feasible since during development of the tests it was observed that presence of neck pain was identifiable during the chair rotation to induce neck torsion in the ocular motor tests. However, the standardised procedures, automated data recording and largely automated data processing minimised potential bias (Table 4.1). In addition, while there was some manual processing of ocular tracking data, the experimenter was blinded to participant's group allocation throughout all data processing. The experimenter had no knowledge of participants self-reported questionnaire responses until after completion of data processing.

4.4.6 Data Management and statistical analysis

Demographic and neck pain symptom characteristics were analysed first. Following the analysis methods of the methodological studies in Chapter 3, all data for the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests and cervical ROM were tested for normality using the Kolmogorov-Smirnov test and were

evaluated for systematic effects over the course of the testing protocols for each task[62;293] (3.4.1, 3.4.2).

Ocular motor data analysis enabling evaluation of the effect of mechanical neck pain on performance in the, non-predictable visual target test (Research Aim 4, 1.9.4) was then completed. Finally the analyses for evaluation of the validity of the ocular tracking, cervical JPE and cervicocephalic kinethesia tests were performed (Research Aim 4, 1.9.5).

All analyses were carried out using IBM SPSS statistics version 19.

Descriptive analysis of demographic and symptom-related characteristics within groups

Within both groups demographic characteristics were analysed descriptively. Within the mechanical neck pain group duration, aetiology, nature of symptoms associated with neck pain and self-reported functional disability (scores in the NDI, neck BQ and TSKII questionnaires) were analysed descriptively to inform the generalisability of findings of the study[62].

Comparison of demographic data between the mechanical neck pain and healthy control groups

Analysis of between-group dfferences in distribution of demographic characteristics enabled evaluation of prognostic balance between the groups in various factors that might introduce bias[1] in performance in the tests (i.e. factors other than neck pain that might influence performance in the tests of cervical proprioception, and that could be unevenly distributed across the groups). Age and gender were identified as

potentially relevant (2.5.3). Other factors that theoretically might influence performance were the coexistence of headaches or musculoskeletal conditions (these are reported to be common in neck pain and could potentially influence performance of the tests), and manual therapy having been received previously (firstly this might theoretically influence cervical proprioception through articular or muscular effects, and secondly, imbalance could reflect different socioeconomic characteristics across the groups). The independent t-test[62] was used to compare age distribution and Fisher's exact test[62] compared frequency distributions of gender, coexistence of other musculoskeletal conditions besides neck pain and manual therapy having been received previously.

Research aim 4 - evaluation of the effect of mechanical neck pain on ocular tracking of a non-predictable visual target

Between and within group differences were analysed using mixed model ANOVAs or their non-parametric versions[294], determined by distribution. Significant effects were further examined using the independent t-test or the Mann-Witney U test for between-group differences or the paired samples t-test or Wilcoxon signed rank test for within-group differences[62].

To avoid inflating the risk of Type I error, statistical adjustments are recommended for multiple testing in confirmatory studies where results are combined into a final conclusion and decision (e.g. clinical intervention studies)[252;291], although there are conflicting opinions on this[295-297]. Adjustments for multiple outcome measures (e.g. Boneferroni adjustments or reducing alpha/significance level) can however increase Type II error rate, with loss of power and increased sample size requirement[291]. The decision not to apply adjustments for multiplicity of primary outcomes and to use a

significance level of .05 was justified by by consideration of existing literature (provided in table 4.7) and the need to balance these opposing effects. Following a hierarchical strategy for determining importance of outcomes and their influence on study design[291] analysis methods were determined by the primary outcomes.

The primary analysis was for the difference between the mechanical neck pain and healthy control groups in performance of the non-predictable ocular tracking test (Research Aim , 1.9.4). Secondary analyses were also performed for both the difference between groups in performance of the predictable ocular tracking test (enabling comparison of the new, to the existing test) and for differences within groups in performance of both tests when the head was in different positions (to evaluate the effect of neck torsion on performance).

Table 4.7 Justification for the analysis method regarding multiplicity of outcomes

1. This was not strictly a confirmatory study, therefore adjustments were not necessary[252]
2. Correlation was anticipated between outcome measures within the family (e.g. hSP gain is a component of overall cSP gain)
    a. There is no formula for determining familywise error rate where tests are correlated[252]
    b. Multiplicity is not an issue where there is correlation between variables (they are thus expected to yield similar results)[291]

Research Aim 5 – Evaluation of the construct validity of the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests as measures of cervical proprioception

Three approaches to analysis were performed in relation to the obectives of Research Aim 5 (1.9.5).

Comparison of between group differences across the predictable ocular tracking, the cervical JPE, cervicocephalic kinesthesia and cervical ROM tests

Between groups differences were analysed for the Cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests (as described above). In relation to between-groups differences, as for the predictable ocular tracking test (above) these were secondary outcomes, thus analysis methods were determined by the primary outcome[291] (non-predictable ocular tracking) and were as described above. Comparison of between group differences across the tests was analysed descriptively.

Association between demographic data and neck pain symptom characteristics with performance in the ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

The distributions of age and self-reported physical function scores were tested for normality with the Kolmogorov Smirnov test and where no significant departures were found Pearson correlation coefficient was subsequently used[62]. Correlation between duration of symptoms and other outcomes was analysed with both Kendall's tau and Spearman's rho b, since this was ordinal data[62]. Post hoc linear regression was performed, if correlations were indicated, to further explore the nature of associations. Since it was not known whether there was likely to be

correlation between the oucomes analysed, there was no clear rationale for either adjusting or not adusting the significance level for multiplicity of outcomes (Table 4.7). Thus significant associations are reported at both the .01 and .05 levels. If significant associations of more than one factor were found for a test, further analysis for associations between factors were performed to evaluate their likely independence from each other by examination of scatter plots and histograms, and utilising Mann-Witney U test (ordinal data) or Chi-square test of association (nominal data).

Correlation within and between performance in the non-predictable and predictable ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

Correlations between the ocular motor and cervical spine function tests were then evaluated with Pearson correlation coefficient. Significant associations are reported at both the .01 and .05 levels (justified above). Convergence in correlation was evaluated descriptively.

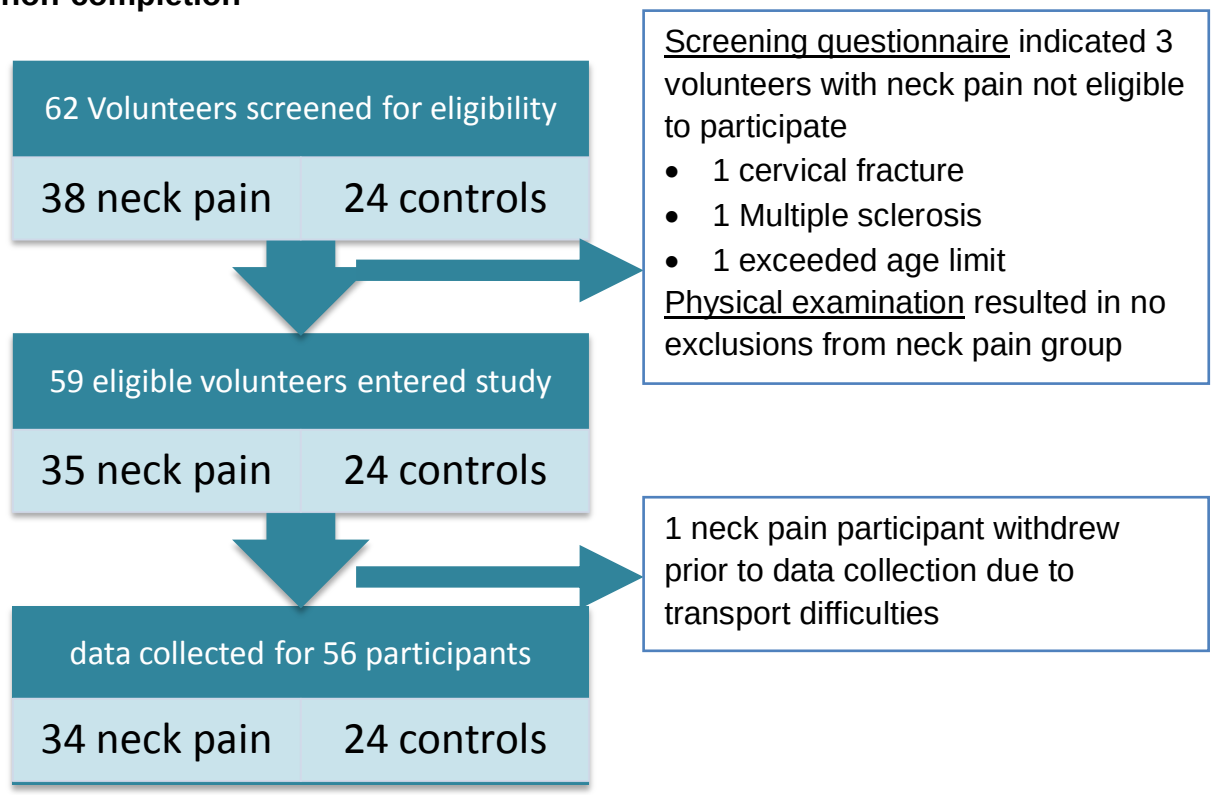
5. RESULTS: EVALUATION OF NON-PREDICTABLE OCULAR TRACKING AND OF THE VALIDITY OF TESTS OF CERVICAL SPINE PROPRIOCEPTION IN PARTICIPANTS WITH MECHANICAL NECK PAIN AND HEALTHY CONTROLS

5.1 PARTICIPANTS

5.1.1 Participant eligibility

62 individuals (38 with neck pain and 24 healthy controls) volunteered for the study and were screened for eligibility (4.4.2). Three volunteers with neck pain did not meet the inclusion/exclusion criteria (see fig 5.1). 35 volunteers with neck pain proceeded to be physically examined (4.4.2), which confirmed that they all had mechanical neck pain. In total, 59 eligible participants (35 participants with neck pain and 24 healthy controls) consented and entered the study. Subsequently 1 neck pain participant withdrew from the study (see figure 5.1).

Figure 5.1 Flow chart of recruitment to the study and reasons for exclusion or non-completion



Of the 56 participants who completed the study, technical problems prevented any data collection in the ocular tracking, cervical JPE, cervicocephalic kinesthesia and cervical ROM tests for 2 participants in the neck pain group. There was some further partial loss of data for other participants due to several technical problems. Details are provided in Table 5.1.

5.1.2 Descriptive analysis of demographic and symptom-related characteristics within groups

Demographic characteristics

Demographic characteristics of participants in both the neck pain and control groups are provided in Table 5.2. Within both groups participants spanned the range specified in the inclusion criteria. Gender mix was approximately equal in each group. Approximately half of each group reported the existence of at least 1 other musculoskeletal condition in addition to neck pain. Migraine and non-migrainous headaches were also reported in both groups. Each category of headache and musculoskeletal disorders were reported slightly more frequently in the neck pain group. Within both groups, the majority of participants had used manual therapy in the past.

Table 5.1 Data set size obtained for participants in each test

GROUP	ROM TEST	JPE TEST	CERVICO-CEPHALIC KINESTHESIA TEST	PREDICTABLE OCULAR TRACKING TEST	RESEARCH AIM 4 NON-PREDICTABLE OCULAR TRACKING TEST	RESEARCH AIM 5 FULL DATA SETS
NECK PAIN (n = 34)	28 [a,b]	28 [a,b]	28 [a,b]	29 [a,c,d]	31 [a,c]	26
CONTROLS (n = 24)	20 [e]	20 [e]	20 [e]	22 [c,f]	23 [c]	18
TOTAL	48	48	48	51	54	44

[a]Computer faults prevented any data collection (n = 2)
[b] Faults with electro-magnetic motion tracking system (n = 3) or sensor detachment (n = 1)
[c] contact lenses prevented any ocular data collection (n = 1)
[d]Failure to track predictable target, non-predictable target adequately tracked (n = 2)
[e]Faults with electro-magnetic motion tracking system (n = 4)
[f]Failure to track predictable target, non-predictable target adequately tracked (n = 1)

Pink shading indicates numbers of participants included in analysis for Research Aim 4 and blue shading indicates numbers included in the correlation analysis for Research Aim 5

Table 5.2 Demographic characteristics of participants within groups and results of the analysis of differences between groups

CHARACTERISTIC		NECK PAIN GROUP n = 34	CONTROL GROUP n = 24	WITHDREW n = 1	p
Age	Mean	40.78	38.88	38	.459[a]
	SD	9.48	9.43	N/A	
	range	19-55	26-55	38	
Gender (M/F)		15/17	12/12	0/1	1.000[b]
Coexisting conditions					
Low back pain n(%)		18 (56)	11 (46)	1	.590[b]
Migraine n(%)		5 (16)	2 (8)	0	.690[b]
Other headaches n(%)		8 (25)	4 (17)	1	.530[b]
Other joint problem n(%)		13 (41)	5 (21)	0	.150[b]
Manual therapy received[c] n(%)		23 (72)	18 (75)	1	1.000[b]

[a] analysed with independent t-test - not significant (p> .01)
[b] analysed with Fisher's Exact test - not significant (p> .01)
[c] participants used manual therapy in the past. None had received treatment within 3 weeks prior to participation

Results are given for the analysis of differences between the neck pain and control groups. Characteristics of the volunteer who withdrew from the study are also presented to enable comparison with participants who completed data collection

Neck pain symptom characteristics

Symptom characteristics and summaries of the self-reported functional outcome questionnaires are provided in Table 5.3. 91% (n = 29) of participants experienced daily neck pain. The majority (72%, n = 23) reported chronic symptoms of ≥ 3 months duration, and 35% (n = 19) reported neck pain of ≥ 12 months duration.

Table 5.3 Symptom characteristics for the neck pain group and neck pain participant who withdrew from the study

CHARACTERISTIC		NECK PAIN GROUP n = 32	WITHDREW n =1 [b]
SYMPTOM DURATION n (%)[a]	Less than 3 months	9 (28%)	0
	3-12 months	4(13%)	1
	Longer than 12 months	19 (59%)	0
AETIOLOGY n (%)[a]	Idiopathic onset	13 (41%)	1
	Following a whiplash injury	12 (38%)	0
	Following other trauma/injury	5 (16%)	
SYMPTOMS ASSOCIATED WITH NECK PAIN n (%)[a]	Restricted neck movement	23 (72%)	1
	Crepitus	24 (75%)	0
	Headache	18 (56%)	1
	Dizziness	1 (3%)	0
	Upper limb symptoms	12 (38%)	0
SELF-REPORTED QUESTIONNAIRE SCORES Mean (SD) range	NDI % score	41.63 (1.44) 34.00-82.00	Not completed
	Neck BQ % score	31.34 (19.21) 8.57-84.29	Not completed
	TSK II % score	51.99 (9.56) 32.35-77.94	Not completed
	NRS score out of 10	3.56 (1.00) 1-8	Not completed

41% (n = 13) of neck pain participants reported idiopathic neck pain (1 previously experienced a whiplash injury, but reported this was not the cause of their neck pain). 38% (n = 12) reported that whiplash injury following an RTA was the cause of neck pain (n = 3 sustained their injury 2 weeks-3 months previously, n = 9 sustained their injury ≥ 12 months previously).16% (n = 5) reported other forms of trauma as the cause, including falls, heavy lifting and sports injuries.

Almost all participants (94%, n = 30) reported restrictions and/or crepitus on neck movements. 56% reported headaches associated with their neck pain (n = 18). One participant, with neck pain resulting from an RTA, reported associated dizziness.

38% (n = 12) reported radicular-type symptoms of arm pain, numbness or tingling. Of 12 participants with neck pain following whiplash injury 5 experienced arm symptoms, indicating probable Whiplash Associated Disorder grade III (WAD III), while the remainder were WAD II[56].

Mean scores for self-reported functional disability were 31.40% and 41.63% measured with the Neck BQ and the NDI respectively. Mean TSKII score indicating fear-avoidance behaviour was 51.99%. Mean pain level indicated by the 10-point Numeric Rating Scale (NRS), included in the NDI, was 3.56.

5.1.3 Comparison of demographic data between the mechanical neck pain and healthy control groups

Table 5.2 provides the results of statistical analysis of differences between groups in factors that might theoretically influence performance in the tests (4.4.6). No significant difference between groups was found for any factor. This suggests that there was not prognostic imbalance[1] between the groups, thus potential bias was minimised. Data are included for the volunteer who withdrew from the study. The small number precluded statistical comparison with the neck pain group however visual analysis did not indicate differences.

5.2 PROCESSING, CLEANING AND EVALUATION OF DISTRIBUTION AND SYSTEMATIC EFFECTS IN THE OCULAR TRACKING, CERVICAL JPE, CERVICOCEPHALIC KINESTHESIA AND CERVICAL ROM DATA

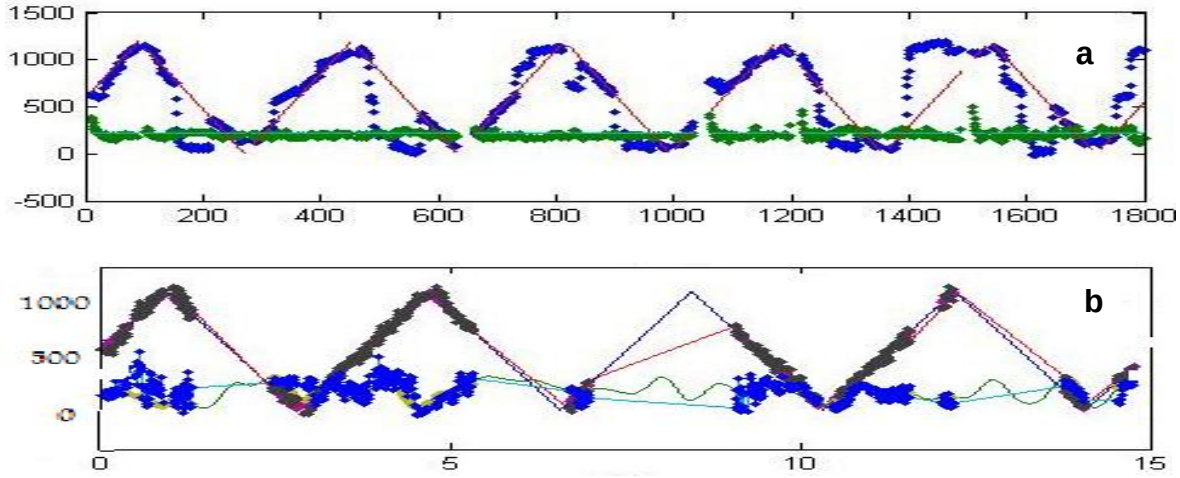
Ocular tracking data

Data processing and cleaning

Following automated processing of raw eye data, visual inspection and manual editing of ocular tracking traces (3.4.1, 4.4.4), a small number of trials were excluded from further analysis. Figure 5.2 provides examples of these. For data cleaning of remaining valid trials, visual inspection of boxplots indicated that in most instances outlying values corresponded to the same few participants, who consistently performed at similar levels, therefore it was decided that these values did represent the actual tracking ability of those participants and they were retained[245]. Appendix 9 provides an example of data handled in this way and also provides the quantity of data excluded following data processing and cleaning.

Subsequent to data cleaning, only 1 trial was excluded for a single participant. It has been suggested that the influence of excluded data points can be examined by subsequently analysing both edited and unedited data sets[298], however this was not deemed necessary with such a small reduction in data quantity and therefore only the cleaned data set was included in further analyses.

Figure 5.2 a-b Examples of trials that were excluded following ocular data processing



The vertical axis indicates target position on the display screen (fine lines) and simultaneous ocular gaze position (heavy lines) in both horizontal (blue) and vertical (green) coordinates. The horizontal axis indicates time (msecs). Trials that were excluded due to non-tracking of the predictable ocular target (a) and an insufficient amount of ocular signal obtained during a non-predictable ocular target task (b) are indicated

Evaluation of distribution and of systematic effects through the testing protocol

The Kolmogorov-Smirnov test indicated no significant departures from normality (minimum p =.117) for hSP or cSP gains in either the non-predictable or predictable ocular tracking tests.

The results of repeated measures ANOVAs (provided in Appendix 9) indicated that no significant systematic effects were present as a result of repeated measures through the testing protocol within either the neck pain ($F = .179 – 2.313$, $p \geq .109$) or the control groups ($F = .291 – 3.146$, $p \geq .057$).

<u>Cervical JPE, cervico-cephalic kinesthesia and cervical ROM data</u>

Data processing and cleaning

Following automated processing of raw data and manual checking, a small number of trials were excluded from further analysis, as a result of technical problems or

incorrect test performance by participants. For data cleaning of remaining valid trials, visual inspection of boxplots indicated that in most instances outlying values corresponded to the same few participants, who consistently performed at similar levels, therefore it was decided that these values did represent the actual tracking ability of those participants and they were retained[245]. A small amount of cervico-cephalic kinesthesia trials data, however, appeared inconsistent with paticipant's performance otherwise and was excluded. Appendix 9 provides the quantity of data excluded following data cleaning. To examine the influence of excluded data points subsequent analyses were carried out for both edited and unedited data sets[245]. For the cervical ROM test there were few outlying values and none of these were inconsistent with individual subjects performance. However, with lateral flexion, negative ROM values were achieved by 2 neck pain group participants. Inspection of data confirmed that this was due to greater motion of the electromagnetic sensor on the T2 spinous process than of the sensor mounted on the head. This indicates reduced cervical ROM relative to thoracic motion, representing an abnormal motion pattern, but it does not enable accurate evaluation of how much cervical lateral flexion actually occurred. Subsequent analyses for lateral flexion ROM were therefore carried out with both the complete data set and the edited set with those participants trials excluded.

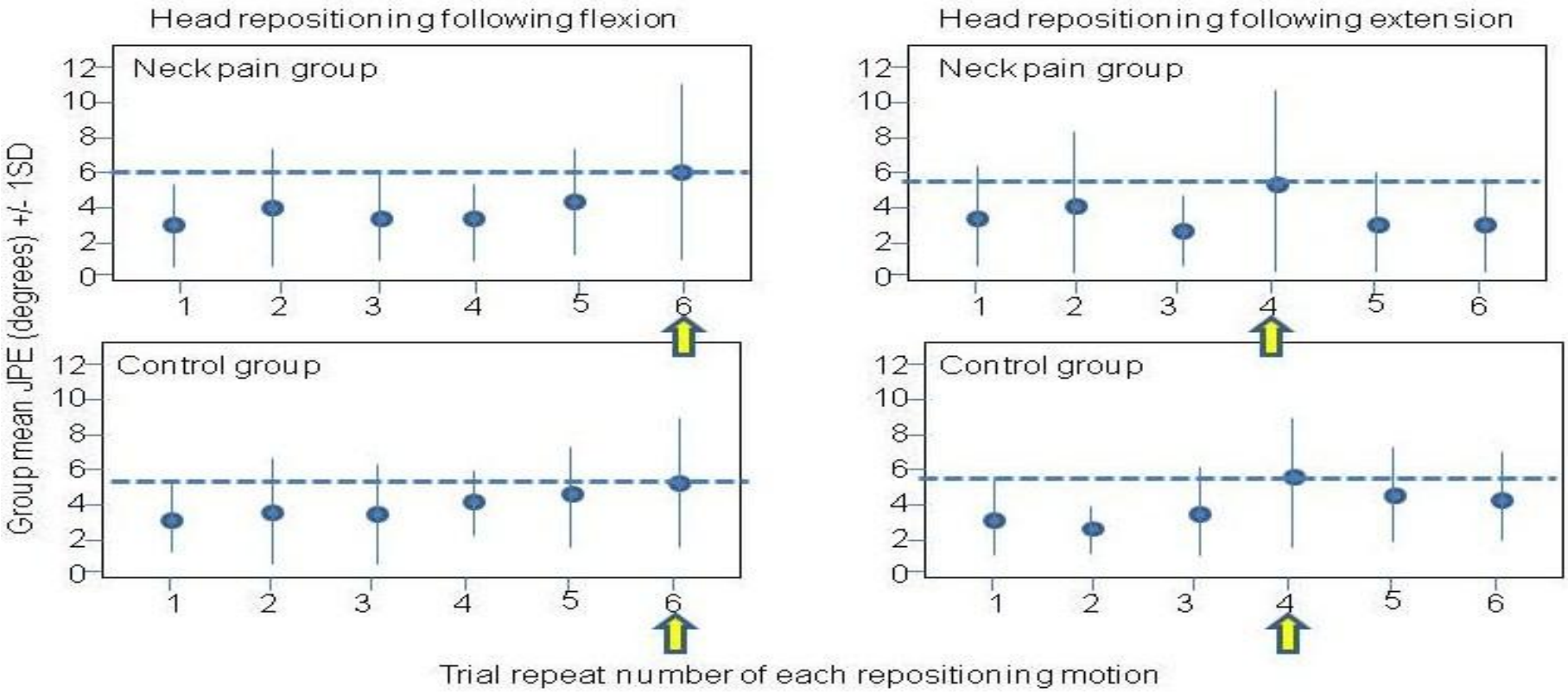
Evaluation of distribution and of systematic effects through the testing protocol

The Kolmogorov-Smirnov test indicated no significant departures from normality (minimum p =.200) for data in the cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests.

The results of repeated measures ANOVAs (Appendix 9) indicated that in the control group no systematic effects were present through the testing protocol for the cervical JPE ($F = .769 – 3.712$, $p \geq .069$), cervico-cephalic kinesthesia ($F = 1.095 – 1.350$, $p \geq .252$) or cervical ROM ($F= .420 – 1.288$, $p \geq .292$) tests. In the neck pain group, no systematic effects were present for mean horizontal or total error in the cervico-cephalic kinesthesia ($F = .473 – 2.271$, $p \geq .053$), cervical ROM ($F = .524 – 3.961$, $p \geq .052$), or cervical JPE following rotation movements ($F = 1.001 – 3.077$, $p \geq .090$). Significant systematic effects were present for cervical JPE following flexion and extension movements ($F = 4.252 – 5.134$, $p = .000$-$.049$) and for mean vertical error in the cervico-cephalic kinesthesia test ($F = 3.039$, $p = .014$).

In order to further evaluate systematic effects, error plots were obtained across trial repeats for all cervical JPE tasks. Figure 5.3 provides the error plots for head repositioning following flexion and extension motion, as examples. Visual inspection of these did not indicate overall improving or deteriorating performance through the testing protocol. However, visual analysis of plots for the neck pain group compared with the control group indicated similar patterns of fluctuations for all 4 cervical JPE tasks, suggesting order effects. In each task the trial repeat with the greatest JPE mean and variability corresponds to the occasion where that particular repositioning motion followed a trial of repositioning motion in the opposite direction.

Figure 5.3 Error plots comparing performance of the neck pain and control groups through the testing protocol for head repositioning following flexion and extension



Error bars indicate group mean +/- 1SD cervical JPE (RMSE) for each trial. Dotted blue lines indicate the greatest mean cervical JPE. Yellow arrows indicate the trial with the greatest mean and SD JPE, each following a trial with repositioning movement in the opposite direction

5.3 RESEARCH AIM 4 - EVALUATION OF THE EFFECT OF MECHANICAL NECK PAIN ON OCULAR TRACKING OF A NON-PREDICTABLE VISUAL TARGET

5.3.1 Analysis of difference between the mechanical neck pain and healthy control groups in performance of the non-predictable ocular tracking test

A primary aim of the study was to evaluate whether performance in a novel, non-predictable ocular motor test is impaired in participants with mechanical neck pain, compared with healthy controls. For both predictable and non-predictable ocular target tracking, all mean hSP and cSP gains for the neck pain group were lower than corresponding values for the control group, indicating poorer performance (Table 5.4). Standard deviations and coefficients of variation indicated greater variability in the mechanical neck pain group, compared with the healthy control group. This is also illustrated in error plots, provided in Appendix 9.

Table 5.4 Performance in the non-predictable and predictable ocular tracking tests of participants with mechanical neck pain and healthy controls

OCULAR TARGET	NECK POSITION	NECK PAIN GROUP (n = 31)			CONTROL GROUP (n = 22)		
		mean	SD	cv	mean	SD	cv
NON-PREDICTABLE	Neutral hSP gain	.775	.085	.109	.829	.071	.085
	Left hSP gain	.773	.079	.102	.807	082	.102
	Right hSP gain	.765	.084	.110	.817	.077	.094
	Torsion hSP gain	.769	.078	.102	.813	.077	.095
	Neutral cSP gain	.798	.085	.106	.864	.065	.075
	Left cSP gain	.799	.079	.099	.840	.077	.091
	Right cSP gain	.789	.083	.105	.854	.073	.085
	Torsion cSP gain	.794	.078	.098	.848	.073	.086
PREDICTABLE	Neutral hSP gain	.827	.120	.145	.879	.095	.108
	Left hSP gain	.828	.123	.148	.871	.096	.111
	Right hSP gain	.819	.134	.163	.857	.107	.125
	Torsion hSP gain	.823	.126	.153	.864	.096	.112

Mean, SD and coefficient of variation (cv) are given for velocity gain (velocity of ocular SP tracking/velocity of ocular target motion) in each neck position. Torsion = the mean of trials in left and right neck torsion. Most mean hSP or cSP gains are lower, with greater cv in the neck pain group than in the healthy control group

Results of ANOVAs for differences between the neck pain and healthy control groups in ocular tracking performance (provided in Table 5.5) indicate no significant difference in hSP gain across head positions and both the predictable and non-predictable ocular target tasks. However, in the non-predictable ocular target task cSP gain across head positions was significantly lower (poorer performance) at the .01 level in the neck pain group than in the control group (p = .008). Differences were further examined with a series of independent t-tests (Table 5.6) that indicated significant reductions in cSP gain in the neck pain group for non-predictable ocular tracking with the head in neutral (p = .004) and in right torsion (p = .004) positions. No other significant differences in performance between groups were found.

Table 5.5 Results of ANOVAs of non-predictable and predictable ocular target tracking within- and between-participants in the neck pain and healthy control groups

	ANOVA[a]					
	hSP gain			cSP gain		
BETWEEN-SUBJECTS EFFECT `	DoF	F	p	DoF	F	p
Predictable Non-predictable	1.000	3.214	.079	1.000	7.536	.008
WITHIN-SUBJECTS EFFECT/INTERACTION						
Ocular tracking test	1.000	39.051	.000			
Test x group	1.000	.013	.910			
Neck position	2.000	3.401	.071	1.000*	2.807*	.100*
Position x group	2.000	.972	.329	1.000*	3.654*	.062*
Test x position	2.000	1.358	.262			
Test x position x group	2.000	1.258	.267			

[a]Results of a series of univariate mixed model ANOVAs with the between-subjects factor 'group'. For hSP gain, within subjects factors were 'head position' (neutral, left and right torsion) and 'task' (predictable or non-predictable ocular tracking). For cSP gain, ANOVA was performed across the factor 'head position' in the non-predictable task only. DoF = degrees of freedom. * where the assumption of sphericity was not met results are reported for the most conservative adjusted test (Lower-bound). Other adjusted tests also resulted in non-significant results.

Yellow shading indicates significantly reduced performance in the neck pain group at the .01 level

Table 5.6 Results of independent t-tests of differences in non-predictable and predictable ocular target tracking performance between the mechanical neck pain and healthy control group

OCULAR TRACKING TEST	NECK POSITION/GAIN VARIABLE	p
PREDICTABLE	Neutral hSP gain	.099
	Left hSP gain	.171
	Right hSP gain	.268
	Torsion hSP gain	.204
NON-PREDICTABLE	Neutral hSP gain	.019
	Left hSP gain	.140
	Right hSP gain	.025
	Torsion hSP gain	.050
	Neutral cSP gain	.004
	Left cSP gain	.063
	Right cSP gain	.004
	Torsion cSP gain	.014

Yellow shading indicates significantly reduced performance in the neck pain group at the .01 level

5.3.2 Comparison of the effect of neck pain on performance between the non-predictable and predictable ocular tracking tests

Table 5.4 indicates that in both the neck pain and control groups, mean hSP gain is reduced (poorer performance), but variability is smaller in the non-predictable, compared with the predictable ocular tracking tasks. Results of within-subjects effects from the mixed model ANOVAs are provided in Table 5.4. The main effect of 'task' is significant (p = .000), indicating differences in hSP gain between the predictable and non-predictable ocular tracking tests. Secondary analyses thus evaluated whether between-group differences were influenced by the nature of the ocular tracking test (i.e. was the effect of neck pain the same whether the ocular target followed a predictable or a non-predictable trajectory).

In contrast to the finding of a significant effect of mechanical neck pain on non-predictable ocular tracking for cSP, no significant between-group differences were found (hSP) when data from both the predictable and non-predictable ocular tracking tests were included in the analysis (Table 5.5). In addition, results of within-subjects effects from the mixed model ANOVA for hSP gain indicate no significant interaction between group (neck pain or control group) and ocular tracking task (predictable or non-predictable) (Table 5.5). This suggests that hSP gain is influenced in a similar way in both groups, irrespective of whether the ocular target follows a predictable or non-predictable trajectory.

5.3.3 Analysis within groups of the effect of neck torsion on non-predictable and predictable ocular tracking

A further secondary analysis also evaluated the effect of neck torsion on ocular tracking. Table 5.4 suggests higher mean gains (improved performance) in both the mechanical neck pain and healthy control groups in the neutral position compared with neck torsion, for both the predictable and non-predictable ocular tracking tasks. However, results of the within-subjects analysis of the mixed model ANOVAs (Table 5.5) do not indicate a significant main effect of neck position or any significant interactions of neck position with group (neck pain or healthy controls) or with the nature of the ocular tracking task (predictable or non-predictable target trajectories) ($p>.05$).. Together with the fact that a deficit in cSP gain was demonstrated both in neutral and neck torsion positions in the neck pain participants (5.3.1), this suggests that neck position does not influence ocular tracking performance and that neck pain impairs non-predictable ocular tracking independently of any effect of neck torsion.

5.4 RESEARCH AIM 5 – EVALUATE THE CONSTRUCT VALIDITY OF THE NON-PREDICTABLE AND PREDICTABLE OCULAR TRACKING, CERVICAL JPE AND CERVICO-CEPHALIC KINESTHESIA TESTS AS MEASURES OF CERVICAL PROPRIOCEPTION

5.4.1 Comparison of the effect of neck pain on performance across tests

Descriptive data provided in Table 5.4 and Table 5.7 enable comparison to be made across tests of differences in performance between the neck pain and control groups. This is also illustrated by error plots provided in Appendix 9. For all ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests mean performance was reduced for the neck pain group. Tables 5.4 and 5.7 indicate that the coefficient of variation (enabling the dispersion of data within each group to be compared between groups and also between different tests[62]) is greater in the neck pain group for data from most tasks within all tests, indicating greater variability. Coefficients of variation were greater in both groups for the cervical JPE test compared with the cervico-cephalic kinesthesia and most cervical ROM tests (excepting lateral flexion).

Results of analysis of between groups differences in non-predictable and predictable ocular tracking tests are provided in Table 5.5. Results of statistical analysis of differences in cervical JPE, cervico-cephalic kinesthesia and cervical ROM are provided in Table 5.8. These indicate significantly greater errors in the horizontal plane in the cervico-cephalic kinesthesia test and reduced range of flexion-extension and rotation motion (poorer performance) at the .05 level in the neck pain group. No other differences were found between groups. Findings were the same for edited and unedited data sets, indicating that data cleaning did not influence the results obtained in the cervico-cephalic kinesthesia or ROM tests.

Table 5.7 Comparison of performance between groups in the cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

TEST	TASK	NECK PAIN GROUP			CONTROL GROUP		
		mean	SD	cv	mean	SD	cv
CERVICAL JPE	Flexion	4.203	2.177	.518	3.508	1.81	.516
	Extension	3.926	2.692	.686	3.369	1.499	.445
	Left rotation	4.011	2.494	.622	3.695	2.327	.630
	Right rotation	3.543	2.175	.614	3.306	1.583	.479
	Mean flexion-extension	4.056	2.094	.516	3.435	1.408	.410
	Mean Rotation	3.789	2.109	.557	3.511	1.703	.485
CERVICO-CEPHALIC KINESTHESIA	Horizontal	.247	.079	.318	.198	.052	.262
	Vertical	.235	.070	.297	.218	.056	.257
	Combined	.383	.100	.260	.329	.081	.245
	Horizontal	.235	.062	.265	.196	.047	.239
	Vertical	.231	.069	.297	.214	.049	.231
	Combined	.369	.093	.251	.324	.070	.217
CERVICAL ROM	Flexion-extension	97.625	19.48	.200	114.626	15.995	.140
	Left-right rotation	123.787	23.728	.192	138.096	17.219	.125
	Left-right lateral flexion	55.75	34.079	.611	67.201	19.888	.296
	Left-right lateral flexion	61.559	27.584	.448	67.201	19.888	.296

Group mean, SD and coefficient of variation (cv) for performance in each task. Cervical JPE = mean RMSE (degrees) cervico-cephlic kinesthesia error = mean error $msec^{-1}$ (degrees), ROM = mean full plane cervical ROM (degrees). Purple shading indicates edited data sets

Table 5.8 Statistical analysis of differences in cervical JPE, cervico-cephalic kinesthesia and cervical ROM performance between the neck pain and control group

TEST	TASK	Independent t-test p
CERVICAL JPE	Flexion accuracy	.246
	Flexion precision	.059
	Extension accuracy	.407
	Extension precision	.626
	Flexion-extension accuracy	.646
	Flexion-extension precision	.207
	Left rotation accuracy	.680
	Left rotation precision	.857
	Right rotation accuracy	.253
	Right rotation precision	.159
	Rotation accuracy	.627
	Rotation precision	.484
CERVICO-CEPHALIC KINESTHESIA	Horizontal	.022
	Vertical	.382
	Combined	.055
	Horizontal	.026
	Vertical	.368
	Combined	.078
CERVICAL ROM	Flexion-extension	.002
	Rotation	.025
	Lateral flexion	.183
	Lateral flexion	.441

Yellow shading indicates significantly reduced performance in the neck pain group at the .05 level. Purple shading indicates results for edited data sets

5.4.2 Association between demographic data and neck pain symptom characteristics with performance in the ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

The Kolmogorov-Smirnov test indicated no significant departures from normality (minimum p = .137) for the distribution of data for age of participants, scores in the Neck Disability Index (NDI), Neck Bournemouth Questionnaire (BQ), Numeric Rating Scale (NRS) or Tampa Kinesophobia Scale (TSK), Assumptions for Pearson correlation analysis for these continuous variables were met.

All necessary assumptions were met for linear regression analysis that further explored patterns of association indicated by the correlation analysis.

Association between age and gender with performance

For age, the results of analysis of correlation and linear regression with performance in the ocular tracking, head repositioning, head tracking and cervical ROM tests are provided in Table 5.9 and 5.10 respectively for both the neck pain and control groups. Table 5.10 also provides the results of addition of participant's gender to the linear regression model, since the influence of this categorical variable could not be analysed with correlation[62].

Different patterns of association between age and test performance were indicated between the neck pain and the control groups. In the neck pain group, age was significantly correlated at the .01 level with head repositioning following flexion (r= .599, p = .001) indicating greater cervical JPE with increasing age. Simple linear regression indicated that age had significant predictive power at the .01 level for head repositioning accuracy following flexion (R^2.359, p = .001). A significant negative correlation at the .01 level with lateral flexion cervical ROM (r= -.540 - -.556, p = .003) indicated reduced mobility with increasing age (for edited and unedited data sets), only in the neck pain group. Simple linear regression indicated that age had a significant predictive power at the .01 level for lateral flexion cervical ROM (R^2 = .291-.309, p =.003).

Table 5.9 Results of correlation analyses between ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM with age (neck pain and control groups) and symptom characteristics (neck pain group)

TEST	OUTCOME MEASURE/TASK	AGE control group r	AGE neck pain group r	SYMPTOM DURATION τ	SYMPTOM DURATION rs	NDI score r	NRS score r	BQ score r	TSK score r
SELF-REPORTED PAIN/DISABILITY	NDI score		-.178	.274	.339				
	NRS score		-.255	.197	.245	.508			
	BQ score		-.059	.220	.278	.649	.782		
	TSK score		-.098	.126	.173	.017	.202	.197	
PREDICTABLE OCULAR TRACKING	Neutral hSP gain	.037	-.076	-.197	-.257	-.306	-.241	-.323	-.279
	Left hSP gain	-.133	-.059	-.230	-.309	-.183	-.098	-.204	-.437
	Right hSP gain	-.039	-.115	-.203	-.248	-.246	-.137	-.226	-.391
	Torsion hSP gain	-.088	-.089	-.236	-.303	-.217	-.120	-.215	-.414
NON-PREDICTABLE OCULAR TRACKING	Neutral hSP gain	-.030	-.260	-.247	-.319	-.124	.014	-.046	-.297
	Left hSP gain	-.188	-.005	-.164	-.206	-.255	.020	-.071	-.320
	Right hSP gain	-.228	-.246	-.092	-.127	-.226	-.031	-.071	-.264
	Torsion hSP gain	-.213	-.136	-.130	-.180	-.251	-.004	-.073	-.304
	Neutral cSP gain	-.126	-.205	-.147	-.185	-.027	.003	.062	-.343
	Left cSP gain	-.251	.043	-.125	-.181	-.095	-.008	.047	-.316
	Right cSP gain	-.295	-.150	-.119	-.163	-.140	-.075	.018	-.293
	Torsion cSP gain	-.277	-.058	-.125	-.183	-.123	-.043	.033	-.315

Table 5.9 continued

TEST	OUTCOME MEASURE/TASK	AGE control group r	AGE neck pain group r	SYMPTOM DURATION Ƭ	SYMPTOM DURATION rs	NDI score r	NRS score r	BQ score r	TSK score r
CERVICAL JPE	Flexion accuracy	-.105	.599	-.270	-.342	-.093	-.059	-.018	-.168
	Flexion precision	-.208	.278	-.140	-.181	.062	-.052	-.116	-.188
	Extension accuracy	.099	.008	-.221	-.287	.070	-.003	-.042	-.285
	Extension precision	.280	-.038	-.364	-.482	.144	.232	.203	-.102
	Flexion-extension accuracy	-.012	.317	-.339	-.404	-.002	-.034	-.038	-.272
	Flexion-extension precision	.077	.071	-.333	-.402	.120	.071	.013	-.173
	Left rotation accuracy	.005	.335	-.146	-.170	-.328	-.215	-.322	.290
	Left rotation precision	.064	.176	-.233	-.286	-.319	-.139	-.302	.240
	Right rotation accuracy	.241	.141	-.065	-.089	-.040	-.205	-.171	.049
	Right rotation precision	.267	.155	-.003	.009	.089	-.036	-.017	.053
	Rotation accuracy	.119	.277	-.103	-.131	-.221	-.237	-.283	.203
	Rotation precision	.145	.169	-.121	-.139	-.105	-.093	-.176	.178
CERVICO-CEPHALIC KINESTHESIA	Horizontal	-.003	.204	.319	.412	-.096	.035	.004	.262
	Vertical	-.119	.141	.109	.132	.297	.181	.310	-.087
	Combined	-.283	.211	.292	.369	.092	.123	.172	.151
CERVICAL ROM	Flexion-extension	-.227	-.351	-.376	-.462	.019	-.244	-.181	-.188
	Rotation	-.258	-.196	-.239	-.305	-.224	-.064	-.160	.138
	Lateral flexion	-.367	-.540	.140	.188	.017	-.141	-.288	-.095

r = Pearson correlation coefficient, Ƭ = Kendall's tau, rs = Spearman's rho b. Shading indicates significant association at the .01 level (red) or .05 level (yellow). Results are shown for edited data sets, which were comparable to findings for unedited data set

Table 5.10 Results of linear regression analyses between ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM with age, gender , symptom duration and aetiology of neck pain

TEST	OUTCOME MEASURE	CONTROL GROUP		NECK PAIN GROUP			
		AGE R^2	+ GENDER R^2 change	AGE R^2	+ GENDER R^2 change	DURATION R^2	+ AETIOLOGY R^2 Change
PREDICTABLE OCULAR TRACKING	Neutral hSP gain	.001	.223	.006	.112	.077	.023
	Left hSP gain	.018	.148	.003	.086	.089	.004
	Right hSP gain	.002	.065	.013	.078	.077	.011
	Torsion hSP gain	.008	.112	.008	.080	.086	.008
NON-PREDICTABLE OCULAR TRACKING	Neutral hSP gain	.001	.143	.044	.049	.140	.095
	Left hSP gain	.035	.147	.000	.042	.126	.025
	Right hSP gain	.052	.074	.060	.066	.028	.143
	Torsion hSP gain	.045	.113	.018	.058	.088	.043
	Neutral cSP gain	.016	.087	.019	.018	.069	.024
	Left cSP gain	.063	.105	.029	.000	.099	.002
	Right cSP gain	.087	.043	.023	.037	.058	.003
	Torsion cSP gain	.077	.073	.002	.004	.085	.003

Table 5.10 continued

TEST	OUTCOME MEASURE	CONTROL GROUP		NECK PAIN GROUP			
		AGE R^2	+ GENDER R^2 Change	AGE R^2	+ GENDER R^2 Change	DURATION R^2	+ AETIOLOGY R^2 Change
CERVICAL JPE	Flexion accuracy	.011	.008	.359	.000	.159	.181
	Flexion precision	.043	.000	.077	.002	.095	.109
	Extension accuracy	.010	.002	.006	.007	.167	.083
	Extension precision	.078	.017	.000	.002	.211	.047
	Flexion/extension accuracy	.000	.005	.101	.001	.220	.166
	Flexion/extension precision	.006	.000	.005	.004	.214	.086
	Left rotation accuracy	.000	.234	.112	.021	.029	.008
	Left rotation precision	.004	.235	.031	.187	.239	.005
	Right rotation accuracy	.058	.228	.020	.003	.025	.008
	Right rotation precision	.071	.292	.065	.000	.000	.002
	Mean rotation accuracy	.014	.307	.077	.014	.034	.011
	Mean rotation precision	.021	.323	.029	.000	.004	.013
CERVICO-CEPHALIC KINESTHESIA	Horizontal	.000	.266	.042	.156	.141	.019
	Vertical	.041	.268	.020	.462	.058	.034
	Combined	.014	.295	.045	.386	.144	.000
CERVICAL ROM	Flexion-Extension	.052	.150	.123	.010	.203	.000
	Rotation	.066	.005	.038	.064	.076	.091
	Lateral flexion	.135	.004	.291	.007	.001	.036

For R^2 and R^2 change shading indicates significant ANOVA or t-test, respectively, at the .01 level (red) or .05 level (yellow). R^2 change indicates the influence on predictive power of adding gender into the regression model for age and of adding aetiology of neck pain (traumatic or non-traumatic onset) into the regression model for duration of symptoms. Results are shown for edited data sets, which were comparable to findings for unedited data sets

The addition of gender to the linear regression model for age also resulted in some differences between the neck pain and control groups, as indicated by significant R^2 change values inTable 5.14. In the control group, gender significantly increased the predictive power of the regression model at the .05 level for hSP gain with the head in neutral position in the predictable ocular target tracking test (R^2 change = .223, p = .021), at the .05 or .01 level for all measures of cervical JPE with head repositioning in the transverse plane (R^2 change = .234 - .323, p = .036 - .01) and at the .05 level for all error measures in the head tracking test (R^2 change = .231 - .295, p = .034 - .019).

In the neck pain group, gender similarly significantly increased the predictive power of the regression model at the .05 or .01 level for all error measures in the head tracking test (R^2 change = .156 - .487, p = .037 - <.0005). However, in the head repositioning test gender only significantly increased the predictive power of the model at the .05 level for cervical JPE precision following left rotation (R^2 change = .187, p = .022). Gender did not significantly influence predictive power of the regression model for any other test in the neck pain group.

<u>Association between neck pain duration, aetiology of neck pain and self-reported pain and disability with performance</u>

For the neck pain group Tables 5.11 and 5.12 provide results of correlation analysis and linear regression analysis respectively, of the association between symptom duration and self-reported pain and disability measures with performance in the ocular tracking, head repositioning, head tracking and cervical ROM tests. Table 5.10 also provides the results of addition of aetiology of neck pain (traumatic or non-

traumatic) to the linear regression model for duration of symptoms, since the influence of this categorical variable could not be analysed with correlation.

Duration of symptoms was not significantly correlated with ocular tracking of either a predictable or non-predictable visual target, however a predictive association was indicated for non-predictable target ocular tracking hSP gain with the head in neutral position (R^2 = .140, p<.05). Negative correlation coefficients (ז = -.014 – .247, rs = -.015 - -.319, p> .05) suggest decreasing hSP or cSP gain (poorer performance), with increasing duration of symptoms. In the cervico-cephalic kinesthesia test, significant correlation at the .05 level also indicates greater horizontal plane error (poorer perfomance) associated with increasing duration of symptoms (ז= .305-.319, p = .043-.034; rs = .397-.412, p = .037-.03) for edited and unedited data sets. Linear regression indicated that duration of symptoms had significant predictive power at the .05 level for both horizontal and combined cervico-cephalic kinesthesia error (R^2 = .141-.167, p = .049-.031). Duration of neck pain symptoms was also significantly negatively correlated at the .05 level with head repositioning JPE following movements in the sagittal plane (precision following flexion and accuracy and precision following flexion/extension). However, in contrast to findings for ocular tracking and cervico-cephalic kinesthesia, this indicates greater JPE (poorer performance) with *shorter* duration of symptoms(ז = -.339, p = .021; rs = -.404, p =.030). Simple linear regression indicated that duration of symptoms had significant predictive power at the .05 or .01 level for most measures of sagittal plane repositioning JPE (R^2 = .159 - .220, p = .032 - .01) and also for precision of repositioning following left rotation (R2 = .239, p = .010). Similarly, duration of symptoms was significantly negatively correlated at the .05 level with sagittal plane cervical ROM (ז = -.376, p = .01; rs = -.462, p = .012), indicating reduced ROM with

shorter duration of symptoms. Linear regression indicated that duration of symptoms had significant predictive power at the .05 level for cervical ROM in the sagittal plane.

The addition of aetiology of neck pain (traumatic or non-traumatic) did not significantly increase the predictive power of the multiple regression model for most tests. However, significant R^2 change values at the .05 level in Table 5.14 did indicate predictive power of aetiology of neck pain for random target ocular tracking hSP gain with the head in right rotation (R^2 change = .143, p = .044) and accuracy of head repositioning JPE following flexion and the mean of flexion and extension (R^2change = .166-.181, p = .013),

Scores for the NDI, BG and NRS were all significantly correlated with each other at the .01 level (r=.508-.782, p <.0003), but not with the Tampa kinespophobia scale.

For ocular tracking of a predictable target, significant negative correlations at the .05 level were indicated for hSP gain with TSK scores(r = -.391- -.437, p = .033- .016). Reduced hSP gain (poorer performance) was associated with greater TSK scores (greater fear avoidance behaviour) when the head was in a position of torsion (left, right or mean).

No significant associations were found for head repositioning, head tracking or ROM tasks with scores of any self-reported pain, disability or fear avoidance behaviour questionnaire.

Evaluation of independence of associations with age, gender, duration and aetiology of neck pain indicated in correlation and linear regression analyses

Mann Witney U test indicated a significant difference in age distribution between the traumatic and non-traumatic aetiology of neck pain sub-groups ($p = .009$), with older ages in the non-traumatic aetiology sub-group. This casts doubt on the independence of age and aetiology in their associations with performance in some tests, particularly head repositioning in the sagittal plane among the neck pain group, where both age and aetiology of neck pain contributed significantly to prediction of accuracy of JPE following flexion.

Histograms suggested that duration of symptoms may be longer among females than males and among traumatic versus non-traumatic onset neck pain. Chi-squared test indicated no significant association between aetiology of neck pain and gender. There were no indications of association in either group between any other of the variables.

5.4.3 Correlation within and between performance in the non-predictable and predictable ocular tracking, cervical JPE, cervico-cephalic kinesthesia tests

Consideration of convergence in correlations within and between each test enabled evaluation of their construct validity as measures of cervical proprioception (1.7). Correlation between cervical ROM and performance in each test was also evaluated.

The results of correlation analysis are provided separately for the neck pain and control groups, enabling comparison, in Tables 5.11 – 5.1 6

Table 5.11 Results of correlation analyses between ocular tracking with cervical JPE, cervico-cephalic kinesthesia and cervical ROM within the neck pain group

TEST		PREDICTABLE OCULAR TRACKING hSP gain				NON-PREDICTABLE OCULAR TRACKING hSP gain				cSP gain			
		N	L	R	T	N	L	R	T	N	L	R	T
PREDICTABLE OCULAR TRACKING	Left hSP gain	.927											
	Right hSP gain	.957	.925										
	Torsion hSP gain	.963	.977	.984									
NON-PREDICTABLE OCULAR TRACKING	Neutral hSP gain	.778	.824	.773	.814								
	Left hSP gain	.840	.875	.849	.881	.843							
	Right hSP gain	.817	.784	.817	.820	.908	.839						
	Torsion hSP gain	.863	.863	.867	.885	.914	.956	.961					
	Neutral cSP gain	.727	.809	.738	.788	.946	.774	.870	.858				
	Left cSP gain	.785	.819	.825	.844	.799	.916	.812	.898	.828			
	Right cSP gain	.754	.761	.774	.786	.883	.780	.947	.903	.928	.867		
	Torsion cSP gain	.796	.817	.827	.843	.872	.876	.912	.933	.910	.965	.968	
CERVICAL JPE	Flexion accuracy	.040	.184	-.009	.074	-.081	.115	-.213	-.061	-.085	.085	-.150	-.040
	Flexion precision	-.036	.150	-.007	.056	-.040	.019	-.194	-.098	-.098	-.033	-.166	-.107
	Extension accuracy	.066	.228	.128	.172	.108	.183	-.048	.063	.034	.090	-.063	.010
	Extension precision	.057	.223	.098	.151	.143	.185	.025	.104	.071	.080	.002	.040
	flexion-extension accuracy	-.037	.009	-.053	-.024	-.066	-.105	-.098	-.106	.050	-.015	.008	-.004
	flexion-extension precision	-.341	-.224	-.283	-.261	-.279	-.291	-.329	-.325	-.106	-.110	-.157	-.140
	Left rotation accuracy	.062	.241	.076	.148	.025	.176	-.145	.006	-.025	.099	-.122	-.018
	Left rotation precision	.014	.197	.044	.109	.063	.111	-.069	.016	-.005	.009	-.085	-.042
	Right rotation accuracy	-.365	-.376	-.380	-.386	-.502	-.314	-.470	-.413	-.441	-.282	-.411	-.361
	Right rotation precision	-.164	-.160	-.142	-.153	-.259	-.059	-.218	-.149	-.225	-.022	-.182	-.110
	Rotation accuracy	-.237	-.221	-.254	-.244	-.341	-.239	-.337	-.303	-.244	-.175	-.247	-.220
	Rotation precision	-.299	-.244	-.236	-.244	-.367	-.225	-.357	-.307	-.242	-.087	-.239	-.173
CERVICO-CEPHALIC KINESTHESIA	Horizontal	-.543	-.556	-.537	-.555	-.539	-.352	-.497	-.443	-.596	-.459	-.554	-.524
	Vertical	-.383	-.210	-.350	-.286	-.269	-.123	-.290	-.217	-.172	-.058	-.189	-.129
	Combined	-.569	-.482	-.549	-.524	-.499	-.296	-.486	-.409	-.481	-.330	-.466	-.412
CERVICAL ROM	Flexion-extension	.233	.265	.208	.237	.210	.103	.109	.109	.223	.138	.142	.144
	Rotation	.062	.005	.030	.014	.043	-.052	.096	.026	-.039	-.157	.001	-.078
	Lateral flexion	.347	.333	.268	.307	.500	.213	.479	.367	.464	.211	.441	.342

Predictable ocular tracking/ transverse plane JPE, most measures are not significantly correlated (r = -.014 - -.386)

Non-predictable ocular tracking/transverse plane JPE, most measures are not significantly correlated (r = -.005 - -.502)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Table 5.12 Results of correlation analyses between ocular tracking with cervical JPE, cervico-cephalic kinesthesia and cervical ROM within the control group

TEST		PREDICTABLE OCULAR TRACKING hSP gain				NON-PREDICTABLE OCULAR TRACKING hSP gain				cSP gain			
		N	L	R	T	N	L	R	T	N	L	R	T
PREDICTABLE OCULAR TRACKING	Left hSP gain	.898											
	Right hSP gain	.870	.793										
	Torsion hSP gain	.933	.941	.952									
NON-PREDICTABLE OCULAR TRACKING	Neutral hSP gain	.785	.707	.770	.782								
	Left hSP gain	.809	.885	.737	.852	.871							
	Right hSP gain	.729	.747	.794	.815	.900	.923						
	Torsion hSP gain	.785	.829	.783	.850	.904	.980	.981					
	Neutral cSP gain	.813	.784	.836	.857	.869	.790	.801	.812				
	Left cSP gain	.822	.908	.755	.874	.735	.880	.778	.847	.884			
	Right cSP gain	.780	.833	.833	.880	.780	.836	.853	.863	.935	.940		
	Torsion cSP gain	.812	.880	.807	.889	.768	.868	.827	.866	.923	.985	.985	
CERVICAL JPE	Flexion accuracy	.067	-.006	.072	.037	.148	.082	.159	.117	.104	-.021	.076	.022
	Flexion precision	.136	.170	.114	.148	.226	.266	.253	.261	.267	.231	.275	.252
	Extension accuracy	.025	.039	.016	.028	.059	-.020	-.005	-.019	.135	.057	.037	.044
	Extension precision	.158	.047	.258	.167	.109	.003	.075	.043	.208	.081	.108	.099
	Fflexion-extension accuracy	.059	.019	.059	.042	.125	.042	.100	.065	.132	.012	.065	.033
	Flexion-extension precision	.247	.150	.277	.229	.235	.161	.210	.188	.284	.144	.209	.177
	Left rotation accuracy	-.678	-.672	-.406	-.561	-.475	-.617	-.478	-.557	-.435	-.588	-.483	-.537
	Left rotation precision	-.640	-.657	-.358	-.527	-.423	-.560	-.410	-.491	-.429	-.551	-.450	-.500
	Right rotation accuracy	-.210	-.331	-.138	-.242	-.398	-.458	-.318	-.397	-.262	-.351	-.252	-.304
	Right rotation precision	-.484	-.548	-.545	-.577	-.585	-.584	-.540	-.577	-.592	-.601	-.549	-.584
	Rotation accuracy	-.579	-.630	-.353	-.511	-.523	-.649	-.485	-.578	-.431	-.580	-.459	-.522
	Rotation precision	-.768	-.780	-.600	-.723	-.575	-.682	-.562	-.634	-.620	-.717	-.628	-.678
CERVICO-CEPHALIC KINESTHESIA	Horizontal	-.656	-.636	-.435	-.561	-.438	-.436	-.315	-.382	-.530	-.591	-.507	-.555
	Vertical	-.639	-.621	-.368	-.516	-.373	-.404	-.213	-.316	-.480	-.544	-.431	-.493
	Combined	-.678	-.656	-.413	-.559	-.418	-.435	-.269	-.359	-.516	-.583	-.480	-.537
CERVICAL ROM	Flexion-extension	-.166	.063	-.184	-.071	-.043	.036	-.061	-.015	.098	.211	.157	.186
	Rotation	.148	.311	.191	.262	.139	.240	.094	.174	.311	.406	.312	.367
	Lateral flexion	.400	.522	.363	.462	.012	.251	.188	.219	.247	.400	.365	.383

Predictable ocular tracking/ transverse plane JPE - most measures are significantly correlated (r = - .138 - -.780)
Non-predictable ocular tracking/transverse plane JPE, most measures are significantly correlated (r = -.-252 - -.717)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Table 5.13 Results of correlation analyses between cervical JPE with cervico-cephalic kinesthesia and cervical ROM in the neck pain group

TEST		CERVICAL JPE											
		Flexion		Extension		flexion-extension		Left rotation		Right rotation		Rotation	
		Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.
CERVICAL JPE	Flexion precision	.691											
	Extension accuracy	.472	.692										
	Extension precision	.541	.575	.782									
	Flexion-extension accuracy	.822	.805	.889	.782								
	Flexion-extension precision	.628	.810	.875	.891	.888							
	Left rotation accuracy	.230	.179	.104	-.058	.189	.099						
	Left rotation precision	.069	.108	.185	-.048	.157	.059	.878					
	Right rotation accuracy	.143	.350	.176	-.025	.191	.184	.584	.483				
	Right rotation precision	.135	.239	.087	-.089	.129	.075	.691	.570	.791			
	Rotation accuracy	.214	.289	.154	-.050	.214	.151	.908	.786	.870	.822		
	Rotation precision	.106	.155	.114	-.108	.131	.037	.879	.874	.683	.865	.886	
CERVICO-CEPHALIC KINESTHESIA	Horizontal	.004	-.078	-.197	-.193	-.132	-.131	.340	.074	.042	.238	.227	.184
	Vertical	.221	.135	.094	.069	.177	.109	.134	.083	.148	.384	.162	.248
	Combined	.115	.015	-.086	-.101	.000	-.041	.303	.102	.115	.371	.245	.264
CERVICAL ROM	Flexion-extension	.208	.231	.351	.317	.331	.387	-.080	.010	-.027	-.083	-.064	-.027
	Rotation	.042	.300	.046	.140	.048	.284	.108	.086	.184	.022	.155	.035
	Lateral flexion	-.245	.136	.174	.058	-.016	.205	-.196	-.118	.242	.016	-.003	-.113

Transverse plane cervical JPE/cervico-cephalic kinesthesia - most measures are not significantly correlated (r = .042 - .384)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Table 5.14 Results of correlation analyses between cervical JPE with cervico-cephalic kinesthesia and cervical ROM in the control group

TEST		CERVICAL JPE											
		Flexion		Extension		Flexion-extension		Left rotation		Right rotation		Rotation	
		Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.	Acc.	Prec.
CERVICAL JPE	Flexion precision	.847											
	Extension accuracy	.481	.545										
	Extension precision	.426	.432	.723									
	Fflexion-extension accuracy	.888	.822	.830	.649								
	Flexion-extension precision	.795	.824	.696	.823	.871							
	Left rotation accuracy	.121	.136	.270	.357	.219	.256						
	Left rotation precision	.046	.045	.200	.327	.136	.189	.957					
	Right rotation accuracy	.271	.131	.315	.602	.344	.492	.495	.516				
	Right rotation precision	.229	.140	.042	.174	.171	.237	.395	.411	.742			
	Rotation accuracy	.210	.154	.328	.523	.309	.403	.914	.894	.805	.620		
	Rotation precision	.115	.088	.156	.253	.157	.191	.893	.919	.622	.704	.902	
CERVICO-CEPHALIC KINESTHESIA	Horizontal	.382	.349	.036	.214	.251	.315	.733	.729	.402	.562	.689	.792
	Vertical	.374	.351	.185	.237	.326	.314	.793	.773	.371	.358	.712	.753
	Combined	.391	.366	.130	.248	.305	.332	.805	.792	.397	.458	.734	.804
CERVICAL ROM	Flexion-extension	-.318	-.247	-.123	-.293	-.271	-.394	.055	.103	-.019	.005	.028	.114
	Rotation	-.441	-.297	-.147	.006	-.361	-.195	.067	.111	-.022	-.317	.029	-.053
	Lateral flexion	-.252	-.228	-.190	-.169	-.258	-.202	-.303	-.324	.057	-.185	-.185	-.391

Transverse plane cervical JPE/cervico-cephalic kinesthesia - most measures significantly correlated (r = .358 - .805)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Table 5.15 Results of correlation analyses between cervico-cephalic kinesthesia and cervical ROM in the neck pain group

TEST		CERVICO-CEPHALIC KINESTHESIA			CERVICAL ROM		
		Horizontal	Vertical	Combined	Flexion-extension	Rotation	Lateral flexion
CERVICO-CEPHALIC KINESTHESIA	Vertical	.478					
	Combined	.862	.794				
CERVICAL ROM	Flexion-extension	-.505	-.032	-.359			
	Rotation	-.043	-.331	-.220	.427		
	Lateral flexion	-.297	-.262	-.343	.342	.391	

Cervico-cephalic kinesthesia/cervical ROM – significant correlation for sagittal plane ROM (r = -.032 - -.505)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Table 5.16 Results of correlation analyses between cervico-cephalic kinesthesia and cervical ROM in the control group

TEST		CERVICO-CEPHALIC KINESTHESIA			CERVICAL ROM		
		Horizontal	Vertical	Combined	Flexion-extension	Rotation	Lateral flexion
CERVICO-CEPHALIC KINESTHESIA	Vertical	.812					
	Combined	.944	.958				
CERVICAL ROM	Flexion-extension	-.143	-.128	-.139			
	Rotation	-.257	-.150	-.193	.604		
	Lateral flexion	-.427	-.262	-.357	.169	.392	

Cervico-cephalic kinesthesia/cervical ROM – no signifcant correlation (r = -.128 - -.427)

Coloured shading indicates values of Pearson's r that were significant. For analysis of correlations within each test, pink and light yellow shading indicate values that were significant at the .01 and .05 level respectively. For analysis of correlations between different tests red and yellow shading indicate values that were significant at the .01 and .05 level respecitively. Dotted lines indicate patterns of convergence that were different between the neck pain and control group (differences are summarised below each table)

Correlation within the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests

Table 5.11 and Table 5.12 indicate that within both the non-predictable and predictable ocular tracking tests, hSP and cSP gain were significantly correlated at the .01 level, in all neck positions, in both the neck pain ($r = .828 - .984$, $p < .0005$) and control groups ($r = .735 - .985$, $p < .0005$). This indicates strong association between each participant's smooth pursuit performance across tasks within each ocular motor test.

Results of correlation analysis between different tasks within the cervical JPE test for the neck pain and control groups are provided in Tables 5.13 and 5.1 4. Correlations between all parameters of cervical JPE in the sagittal plane were significant at the .01 level in the neck pain group ($r = .472- .891$, $p = .01 - <.0005$). Most were significant at the .05 or .01 level for the control group ($r = .426 – .847$, $p = .061 – <.0005$). For cervical JPE in the transverse plane, all correlations were significant at the .01 level in the neck pain group ($r = .483 – .908$, $p = .008 - <.0005$) and were mostly significant in the control group ($r = .395 – .957$, $p = .085 - <.0005$). For comparison between saggital and transverse plane cervical JPE, however, there were no significant correlations in the neck pain group. In the control group, there were a few significant correlations ($r = .042 - .602$, $p = .870 - .005$). This indicates that while association between participants' performance in cervical JPE in the sagittal and transverse planes is overall weak, there are some stronger associations within the control group than the neck pain group.

Results of correlation analysis between different error measurements within cervico-cephalic kinesthesia test for the neck pain and control groups (unedited data set) are

provided in Tables 5.15 and 5.16. In both groups horizontal plane, vertical plane and overall combined error were all significantly correlated with each other t the .05 or .01 level, although correlations were overall stronger in the control group (neck pain group r = .478 – .862, p = .047 - <.0005; control group r = .812 – ..958, p <.0005). Results for the edited data set were similar.

Correlation between performance in the non-predictable and predictable ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests

Summarised correlations (Tables 5.11 - 5.16) are presented below for each possible combination of pairs of tests. Figures 5.4 and 5.5 summarise key patterns of association between all of the tests, enabling convergence in correlation to be evaluated:

- *Non-predictable/Predictable ocular tracking test*

  cSP and hSP gain in all neck positions were significantly correlated (r = .727 - .908, p< .0005) between performance in the non-predictable and predictable ocular tracking tests in both the neck pain (Table 5.11) and control groups (Table 5.12). Due to their strong correlation, the non-predictable and predictable ocular tracking tests are considered together below, unless there were differences between them in correlations with other tests.

- *Ocular tracking tests/Cervical JPE*

  For associations between smooth pursuit performance (hSP or cSP gain) and cervical JPE following sagittal plane movements, no significant correlations were indicated in either group. In contrast, some significant correlations were found between smooth pursuit performance and cervical JPE following

transverse plane movements. Negative correlation coefficients indicated greater JPE with reduced (poorer) gain. Comparison of Tables 5.11 and 5.12 indicates some differences between the neck pain and control groups. In the neck pain group, most correlations were not significant, with the exception of JPE accuracy (mean) following right rotation, which was significantly correlated at the .05 or .01 level, with smooth pursuit perfomance for predictable target tracking with left, right or mean neck torsion and also for non-predictable target tracking with the head in neutral, right or mean torsion positions (r = -.376 - -.502, p =.048 - .006). In contrast, in the control group most correlations were stronger than in the neck pain group. The majority of negative correlations were significant at the .05 or .01 level, indicating poorer smooth pursuit performance with poorer JPE following transverse plane movements (r = -.431- -.780, p = .074 - <.0005).

- *Ocular tracking/cervico-cephalic kinesthesia tests*

  Negative correlations indicate poorer predictable and non-predictable target ocular tracking (reduced hSP or cSP gain) with poorer cervico-cephalic kinesthesia test performance (greater mean error) for both the neck pain and control groups. The majority of correlations were significant at the .05 or .01 level in both the neck pain group (r = -.383 - -.596, p = .048 – .001) and the control group (r = -.493- -.678, p = .044-.003). The edited cervico-cephalic kinesthesia test data set provided similar results.

- *Cervical JPE/ cervico-cephalic kinesthesia tests*

  For the neck pain and control groups a distinctly different pattern of correlation was indicated. In the control group the majority of correlation coefficients

between performance in the tests were significant at the .05 or .01 level (r = .458 - .805, p = .048 - ≤.00005), indicating greater cervical JPE with greater cervico-cephalic kinesthesia test errors. However, in the neck pain group correlations were mostly not significant, with the exception of precision of right rotation cervical JPE that was significantly correlated at the .05 level with vertical plane cervico-cephalic kinesthesia test error (r = .384, p = .043).

Correlation between cervical ROM and performance in each of the tests of proprioception was also evaluated (Tables 5.11-5.16). In both groups, correlations between ocular tracking and cervical ROM were mostly not significant. However, significant correlation at the .05 or .01 level was indicated in the neck pain group between lateral flexion ROM (unedited data set) and predictable and non-predictable target hSP and cSP gain with the head in neutral or right torsion positions (r = .441 - .500, p = .019 - .007). For the control group lateral flexion ROM was significantly correlated at the .05 level with predictable target hSP gain with the head in left torsion position (r = .522, p = .026).

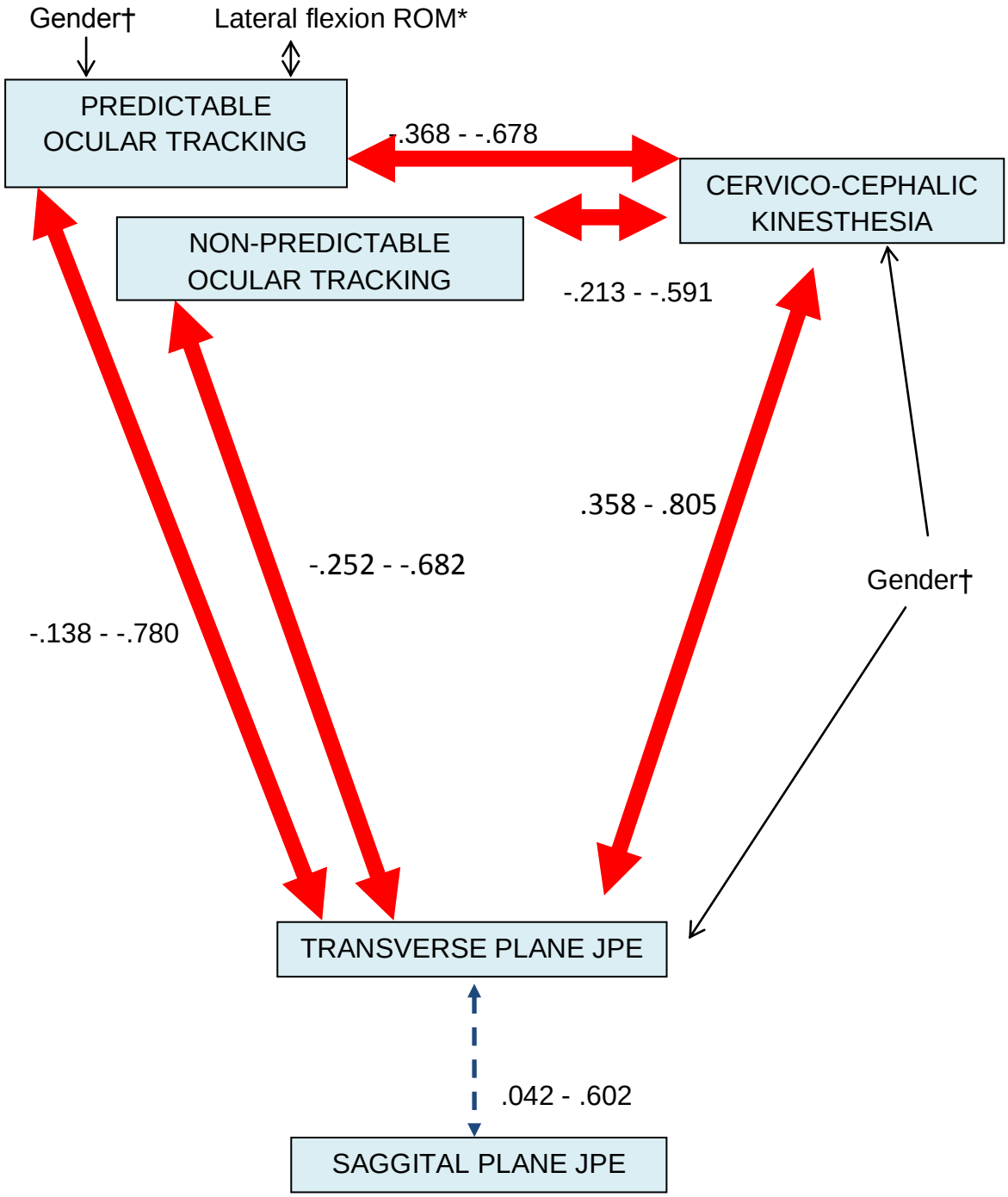
Correlations between cervical JPE and cervical ROM in both groups were mostly not significant. In the neck pain group there were two exceptions. Accuracy of JPE following flexion was significantly negatively correlated at the .05 level with lateral flexion cervical ROM (edited data set only) (r = -.403, p = .037), indicating greater cervical JPE with reduced ROM, however precision of repositioning following the mean of flexion and extension in the neck pain group was significantly *positively* correlated at the .05 level with flexion-extension cervical ROM (r = .387, p = .083), indicating reduced cervical JPE with reduced ROM.

Correlations between cervico-cephalic kinesthesia test error and cervical ROM in both groups were mostly not significant, with the exception in the neck pain group of horizontal plane cervico-cephalic kinesthesia test error that was significantly negatively correlated at the .01 level with flexion-extension cervical ROM ($r = -.505$, $p = .006$), indicating greater error with reduced ROM.

Summary of convergence in correlation between the non-predictable and predictable ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests

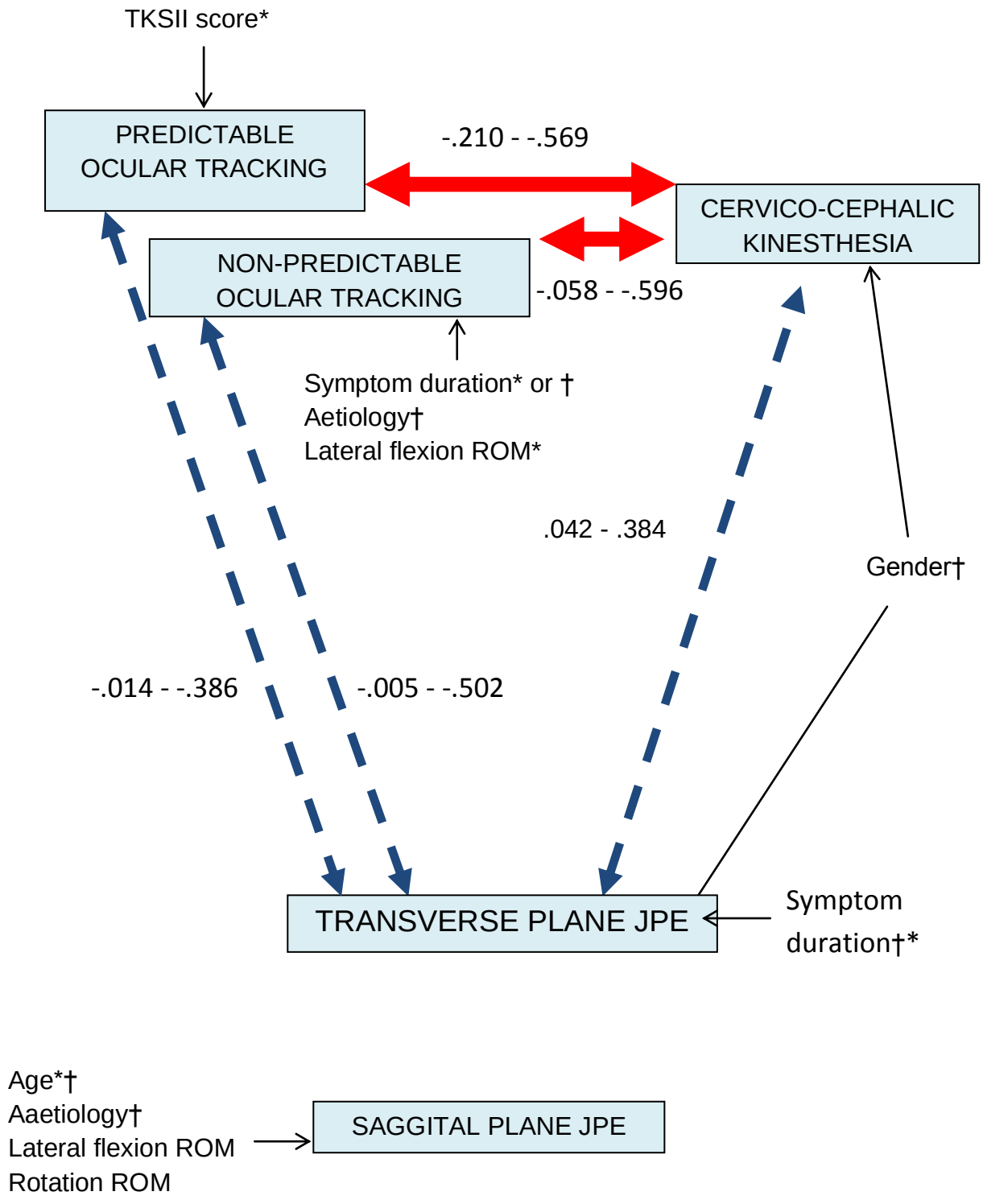
Figures 5.4 and 5.5 provide summarised key patterns of association for each test in the control group and the neck pain group respectively. Comparison indicates differences between the groups. In particular, in the control group there was extensive convergence of significant correlations between ocular tracking, transverse plane cervical JPE and cervico-cephalic kinesthesia tests, with improving performance in each one associated with improving performance in the others. However, in the neck pain group, performance in transverse plane head repositioning is relatively disassociated from performance in the ocular tracking and cervico-cephalic kinesthesia tests (i.e. the majority of correlations were not significant), despite the fact that no difference in performance level was indicated between groups for transverse plane repositioning JPE (5.4.1). Another key difference between tests in the neck pain group was the association of symptom duration with performance whereby longer duration was associated with greater deficits for the non-predictable ocular tracking and cervico-cephalic kinesthesia tests, but with reduced deficits for transverse plane cervical JPE.

Figure 5.4 Summarised key patterns of association within the control group for the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests



Bold red lines indicate extensive correlations (the majority of measures are significantly correlated, with some significant at the .01 level). Blue dashed lines indicate few correlations (the majority are not significant). Values given are ranges of Pearson's r. * indicates significant correlation, † indicates significant predictive association

Figure 5.6 Summarised key patterns of association within the neck pain group for the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests



Bold red lines indicate extensive correlations (the majority of measures are significantly correlated, with some significant at the .01 level). Blue dashed lines indicate few correlations (the majority are not significant). Values given are ranges of Pearson's r. * indicates significant correlation, † indicates significant predictive association

6 DISCUSSION

6.1 OVERVIEW

The characteristics of the mechanical neck pain and the healthy control groups comprising the study samples are discussed. Results are then discussed in relation to Research Aim 4 and Research Aim 5 (1.9.4, 1.9.5). First the effect of mechanical neck pain on performance in the novel ocular motor test using a non-predictable visual target trajectory is discussed. Secondly the construct validity of the existing smooth pursuit neck torsion test (SPNT), cervical joint position error (JPE) and cervico-cephalic kinesthesia tests is evaluated. Theoretical explanations for findings of the study in terms of the neurophysiological effects of neck pain and the constructs influencing performance in the tests are proposed. Study limitations are considered along with their likely effect on results of the study. Clinical implications of the results and Indications for future research are then discussed.

6.2 CHARACTERISTICS OF THE STUDY PARTICIPANTS

31 participants with mechanical neck pain and 23 healthy control participants were included in the evaluation of the effect of mechanical neck pain on ocular tracking of a non-predictable target. This was within the target sample size of 20-30 participants per group (4.3). Slightly fewer full data sets were obtained (5.1.1) for the correlation analysis evaluating construct validity of the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests (26 neck pain and 18 healthy controls). It is reported in the literature that sample sizes of 10-30 are common in correlation studies[174], however there is no clear recommendation on sample size. Decreasing sample size has been shown not to affect the Pearson Correlation Coefficient[174], thus samples achieved in the present study were sufficient to establish Pearson's r values. There is increasing

risk of Type II error with decreasing sample sizes[62] and as a function of increasing variability[174]. In addition, it is reported that increased variability can reduce Pearson's r[174]. Examination of the coefficients of variation for the outcome measures (Table 5.4 and Table 5.7) indicate relative differences in their variability, with the lowest variability for SP gain measures in ocular tracking (cv = .075 - .163) and the highest variability for cervical JPE (cv = .410 - .686). Thus it is possible that some correlation coefficients might have been reduced or may not have been detected as significant, as a consequence of greater variability in some outcome measures within the given sample size.

The mean (SD) age for participants with neck pain was 40.78 (9.48) years, which is in accordance with reports that the risk and prevalence of neck pain increases to middle years before reducing[299]. Studies evaluating the role of gender in occurrence of neck pain are inconclusive; while some report greater risk and prevalence among women, others do not[299]. This is in line with the present study's findings of approximately equal numbers of males and females (15 males/17 females). Increased comorbidity with other musculoskeletal conditions and headaches is also reported for neck pain[299] and was frequently reported by the neck pain participants (low back pain n = 18 (58%), migraine n = 5 (16%), other headaches n = 8 (27%), other musculoskeletal conditions n = 13 (42%)). Most participants had chronic neck pain, with 19 (61%) reporting symptoms of over 12 months duration. NDI % scores for neck pain participants spanned the mild-severe range[53] (mean (SD) 41.63 (10.44), range 34-82). The aetiology of neck pain was varied, in accordance with previous reports[299], with the majority reporting non-traumatic onset (n = 13(42%)) or following whiplash injury (n = 12(39%)), but a few reporting other traumatic injury mechanisms (n = 5 (16%)). The neck pain group thus appears to represent the wider population in terms of age, gender, comorbidity and varied aetiology[299]. The finding

of no significant differences between the neck pain and healthy control groups for demographic factors or for the existence of other musculoskeletal conditions indicates a comparable control group and supports the recruitment method used (4.4.1).

6.3 RESEARCH AIM 4 – EVALUATION OF THE EFFECT OF MECHANICAL NECK PAIN ON OCULAR TRACKING OF A NON-PREDICTABLE VISUAL TARGET

6.3.1 Impaired ocular tracking in mechanical neck pain, independent of neck position

This was the first study to compare ocular tracking of a visual target following a non-predictable trajectory between participants with and without mechanical neck pain. This novel test was designed to reduce the predictability of the visual target trajectory that may facilitate performance in the existing SPNT test (1.5.3). Findings indicated significant deficits (p =.004 - 008) in sensorimotor processes underlying complex ocular movements in two dimensions in mechanical neck pain whereby the 2-dimensional smooth pursuit velocity gain (cSP gain) were decreased compared with the healthy control group when the neck was in neutral position and with right neck torsion (5.3.1).

The absence of significant effects of neck position, or of its interaction with group (neck pain versus healthy controls) suggests that the deficits in neck pain were independent of neck position. This is supported by the fact that the deficit in cSP gain was present both with the neck in a neutral position and with right torsion (5.3.3). There is inconsistency in the literature whereby some studies using *predictable* targets have attributed deficits to altered cervical proprioception in the neck torsion conditions[90;91], although others found no effect of neck torsion on ocular tracking[99;101;193]. Differences in neck pain groups (all previous studies used

participants with WAD), test methods and ocular target trajectories (all previous studies used predictable tagets) make comparisons with the present study difficult. Both the inadequate reliability of the SPNT difference (3.4.1)[207], and the finding in the present study that deficits occurred independently from neck torsion, favour evaluation of SP gain with or without neck torsion using a non-predictable target as a test of ocular motor function, but do not support the use of SPNT differences in studies of neck pain.

6.3.2 Absence of impairment in ocular tracking of a predictable target

In contrast to impairment found in cSP gain in neck pain in ocular tracking of a non-predictable target, no between group differences hSP gain were identified when predictable target tracking was also included in the analysis (5.3.1). The non-predictable ocular tracking task could thus have greater sensitivity to detect deficits in ocular tracking associated with neck pain when cSP gain is considered. This might be associated with the lower variability in performance, indicated by smaller coefficients of variation, in each group for the non-predictable test (Table 5.4). Reduced variability increases power[62] and might thus reduce the sample size requirement for detection of a between group difference for the non-predictable, compared with the predictable ocular tracking task. An alternative explanation for the impairment found in the non-predictable but not predictable ocular tracking test is that different neurophysiological processes underlie performance of each (discussed in 6.3.4) and only those that determine non-predictable target tracking are impaired in participants with neck pain.

An observed advantage of the non-predictable target ocular tracking test was that 3 participants who failed to perform the predictable ocular tracking test correctly (Figure

5.2) performed the non-predictable test adequately (Table 5.1). Failure to track the predictable target was unlikely to reflect smooth pursuit deficit per se since the non-predictable target could be tracked. Theoretical explanations may be either that those individuals had impaired processes related to prediction (1.5.3), that prediction was too effective enabling anticipatory saccades to be made to the target reversal position, or that the inherently more complex nature of the non-predictable target test resulted in greater attention by participants to performing it correctly. In ocular tracking of periodic stimuli prediction is most apparent at points where the target direction reverses[93] thus the possibility of either impaired or enhanced prediction in those 3 participants could be examined by analysis of those portions of data, or alternatively, by measurement of phase error in future studies.

6.3.3 Impaired ocular tracking in neck pain of non-traumatic aetiology and in WAD

This is the first report of impaired SP gain in a neck pain group that includes cases with non-traumatic aetiology. Linear regression analysis indicated that aetiology of neck pain predicted 14.3% of variability only for hSP gain with right neck torsion ($p < .05$), but was not significantly predictive for SP gain or in the neutral position, where deficits in neck pain were also found. This suggests that SP gain was impaired in both the WAD and non-traumatic neck pain participants for non-predictable target ocular tracking. However, there was a lack of independence between different predictive factors whereby, in addition to the difference in aetiology, participants with WAD had longer duration of symptoms and were also older than participants with non-traumatic neck pain, therefore indications for an association with aetiology should be considered with caution. No predictive association was indicated for aetiology with performance in predictable target ocular tracking, suggesting that the

absence of deficits was not due to the inclusion of participants with non-traumatic neck pain. Thus indications are, that impairment found in the novel test of ocular tracking of a non-predictable target in the mechanical neck pain group was not associated only with WAD. However, comparison of ocular tracking between sub-groups of neck pain participants was not an aim of the present study, thus sub-group sizes were small. Further studies with larger sub-groups are needed to evaluate whether there are differences in ocular tracking between participants with WAD versus non-traumatic neck pain.

6.3.4 Sensorimotor processes that may account for the impairment in non-predictable ocular tracking in mechanical neck pain

The non-predictable visual target tracking task used here was an example of head-restrained ocular tracking, with active trunk-under-head rotation (1.5.3). The generation of a unique trajectory for each non-predictable target trial meant that whole trajectories cannot be learned, and the method for generating non-predictable target trajectories based on random number sequence generation reduces the likelihood that prediction on a moment-to-moment basis could contribute to performance. Thus the deficits in non-predictable ocular tracking in neck pain are unlikely to result from impaired predictive ability. In the predictable ocular tracking task it is possible that predictive ability is a determining factor in test performance, and that this is not impaired in neck pain. This could be further investigated by measurement of phase errors or utilisation of ocular motor tasks such as visual target extinction, that are proposed to specifically evaluate prediction[93].

It is unclear whether cervical proprioception contributes to maintenance of smooth pursuit ocular tracking when the head is stabilised, either with or without active head-

under-trunk rotation (1.5.3). There are also limitations in the theoretical sensorimotor mechanisms by which cervical proprioception may contribute to smooth pursuit in the test paradigm used, either via influences on cortical areas governing smooth pursuit or by influencing the cervico-ocular reflex (1.5.3). The findings of the present study further question the likelihood that altered cervical poprioception in neck pain accounts for previously reported impairment in the SPNT test, as a result of alteration in the cervico-ocular reflex, since deficits found in the non-predictable ocular tracking task were independent of head-under-trunk rotation, also occurring when the head was in neutral position where no cervical stimulus would be generated. Previous studies of the SPNT test reported conflicting findings, but some studies similarly reported deficits in the neutral head position, as well as during trunk-under-head rotation[91;99;194]. Furthermore, in the present study the stationary target was fixated prior to the onset of target motion, thus cervico-ocular reflex suppression would be expected (1.5.3). In addition, the present study used a method whereby the participants head was stabilised with an immobile table-mounted bite bar that might be expected to reduce the cervico-ocular reflex by providing an earth-centred point of reference[118] (1.5.3).

While the deficit in non-predictable tracking in mechanical neck pain is likely to be independent of predictive ability, it remains unclear whether the impaired performance represents a deficit in proprioception. The fact that there was impairment in the neutral head position, where there was unlikely to be significant cervical proprioceptor activation suggests that different underlying processes may account for the impairment. An alternative explanation for the deficit in non-predictable ocular tracking found in neck pain participants in the present study, that

was not present for predictable ocular tracking, could be reduced cognitive processes that have been shown to reduce smooth pursuit performance[93].

6.3.5 Cognitive processes in smooth pursuit – the possible role of visuomotor attention, visual working memory and velocity mismatch detection and correction

Visuomotor attention has been demonstrated to influence smooth pursuit performance (1.5.3). Thus impaired attention processes during ocular tracking tasks could explain deficits found in non-predictable target tracking in neck pain.

Prediction, visual working memory and detection of mismatches between expected and actual visual target velocity contribute to smooth pursuit tracking of predictable targets (1.5.3). The non-predictable target task was designed to remove or minimise the possibility that prediction of target motion facilitates performance in the SPNT test that might thus reduce its dependence on cervical proprioception. It has been demonstrated that complex visual target trajectories place greater challenges on working memory during smooth pursuit and the lack of ability to predict motion of the target may increase the load on visual working memory and on the processes underlying mismatch detection and correction in the non-predictable, compared with the predictable ocular tracking test (1.5.3). A possible explanation for the deficit found in the non-predictable, but not the predictable ocular target tracking test is that impaired cognitive functions associated with attention, working memory or mismatch detection and correction were present in the neck pain group, but would be expected to have greater impact in the more complex non-predictable ocular tracking test, while prediction may have facilitated smooth pursuit in the predictable ocular tracking test.

6.3.6 Evidence for cognitive impairments in mechanical neck pain

Perceived deficits in cognitive functions such as concentration and memory are frequently reported in WAD patients[300;301]. There is inconsistent evidence of measurable cognitive deficits in WAD from studies that applied neuropsychological tests [125-127;300;302;303], while a meta-analysis by Kessels et al (2000) did conclude impairments in working memory, attention and immediate recall in WAD[124], a different review did not[126]. Inconsistency between exclusion criteria for studies in the reviews could account for their different conclusions. Neuroimaging tachniques have indicated hypometabolism (using positron emission tomography, or PET) and hypoperfusion (using single-positron emission tompgraphy, or SPECT) of several cortical areas in WAD patients, providing a possible mechanism for cognitive impairment, however there is some conflict in their findings, and questions over the reliability of imaging techniques to detect the changes reported[125;304]. Brain perfusion also correlated with an electrophysiological marker of cognitive ability (P300 event-related potential) in WAD, with a sub-group showing apparent deficits. However, both brain imaging and electrophysiological studies have failed to show any correlation with self-reported perceived cognitive impairment or neuropsychological measures of cognitive processes, including attention and working memory, suggesting that cognitive deficits are not associated with structural brain injury following whiplash injury, but rather with emotional aspects of pain[125-127]. This raises the possibility that cognitive impairments may not be specific to WAD, but might also apply more generally to mechanical neck pain or to other pain conditions. Cognitive processes have not been studied specifically in individuals with non-traumatic neck pain, however it has been reported that a subset of patients with chronic structural spinal pain (undefined aetiology or location) may be impaired in some parts of the Working Memory Index (a component of the Wechsler Adult Intelligence-III test)[305]. Thus it is

possible that the neck pain group in the present study had cognitive impairments in working memory, attention and/or immediate recall.

The possible association between cognitive function in neck pain and performance in the non-predictable ocular tracking test could be investigated by evaluating correlation between performance in the test and neuropsychologic tests of visuomotor attention, visual working memory and velocity mismatch detection and correction. Visuomotor attention in mechanical neck pain may be investigated by including distractors or embedding stimuli that increase attention within ocularmotor tests[306]. There is however a lack of consensus on how individual visual working memory or velocity mismatch detection and corrction may be investigated by manipulating ocularmotor paradigms. It had been suggested that measurement of the dip in smooth pursuit velocity when a target is briefly extinguished, followed by recovery prior to its reappearance, reflected velocity memory[307]. Barnes et al (2008) however propose that this phenomenon indicates mismatch detection and correction and suggest that anticipatory smooth pursuit responses to previously learned sequences of visual target perturbations[231] may provide a measure of velocity memory[93]. Deficits in performance in these tests in neck pain could nevertheless indicate impared visuomotor attention or impaired visual memory/velocity mismatch detection and correction.

6.4 RESEARCH AIM 5 – EVALUATION OF THE CONSTRUCT VALIDITY OF THE NON-PREDICTABLE OCULAR TRACKING TEST, PREDICTABLE OCULAR TRACKING TEST, CERVICAL JPE AND CERVICO-CEPHALIC KINESTHESIA TESTS

For individual tests, consideration of differences between the neck pain and healthy control groups, alongside analysis of convergence in correlation and predictive associations with demographic and symptom-related characteristics, enabled a detailed evaluation of factors associated with performance in each test. Analysis of convergence in correlation in performance across the different tests then enabled evaluation of their construct validity as measures of cervical proprioception.

6.4.1 Comparison of the effect of neck pain on performance across tests

Deficits in the mechanical neck pain group were not consistently indicated across the tests. Significant impairment was found in performance of the non-predictable target ocular tracking test ($p = .004 - .050$), cervico-cephalic kinesthesia test ($p = .022 - .026$), and in cervical ROM in the sagittal and transverse planes ($p = .002 - .025$) but no between-group differences were found in the predictable target ocular tracking test or the cervical JPE test. This disparity might indicate that different constructs are being measured by different tests, questioning their construct validity, or alternatively could result from unequal sensitivity among tests to detect a difference in a common underlying construct (e.g. proprioception) in the present study[62]. In the latter case it would be expected that correlation between performance levels across the tests would exist, and in the neck pain group this was not the case (5.4.3), which suggests that different constructs are measured.

6.4.2 Association between demographic data and neck pain symptom characteristics with performance in the ocular tracking, cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

For each test, the results are first evaluated in relation to the existing literature, followed by discussion of demographic and symptom-related characteristics associated with performance in each of them. Finally the patterns of correlation across the different tests and implications of these for test construct validity are discussed.

Non-predictable ocular tracking test

Significant between group differences (6.3.1) indicate that mechanical neck pain is associated with impaired smooth pursuit (reduced hSP and cSP gain) during ocular tracking of a non-predictable target, that is independent of neck position. Key associations of demographic and symptom-related factors with performance in ocular tracking of a non-predictable target are summarised in Figure 6.1, along with relevant results.

Association with aetiology and duration of neck pain

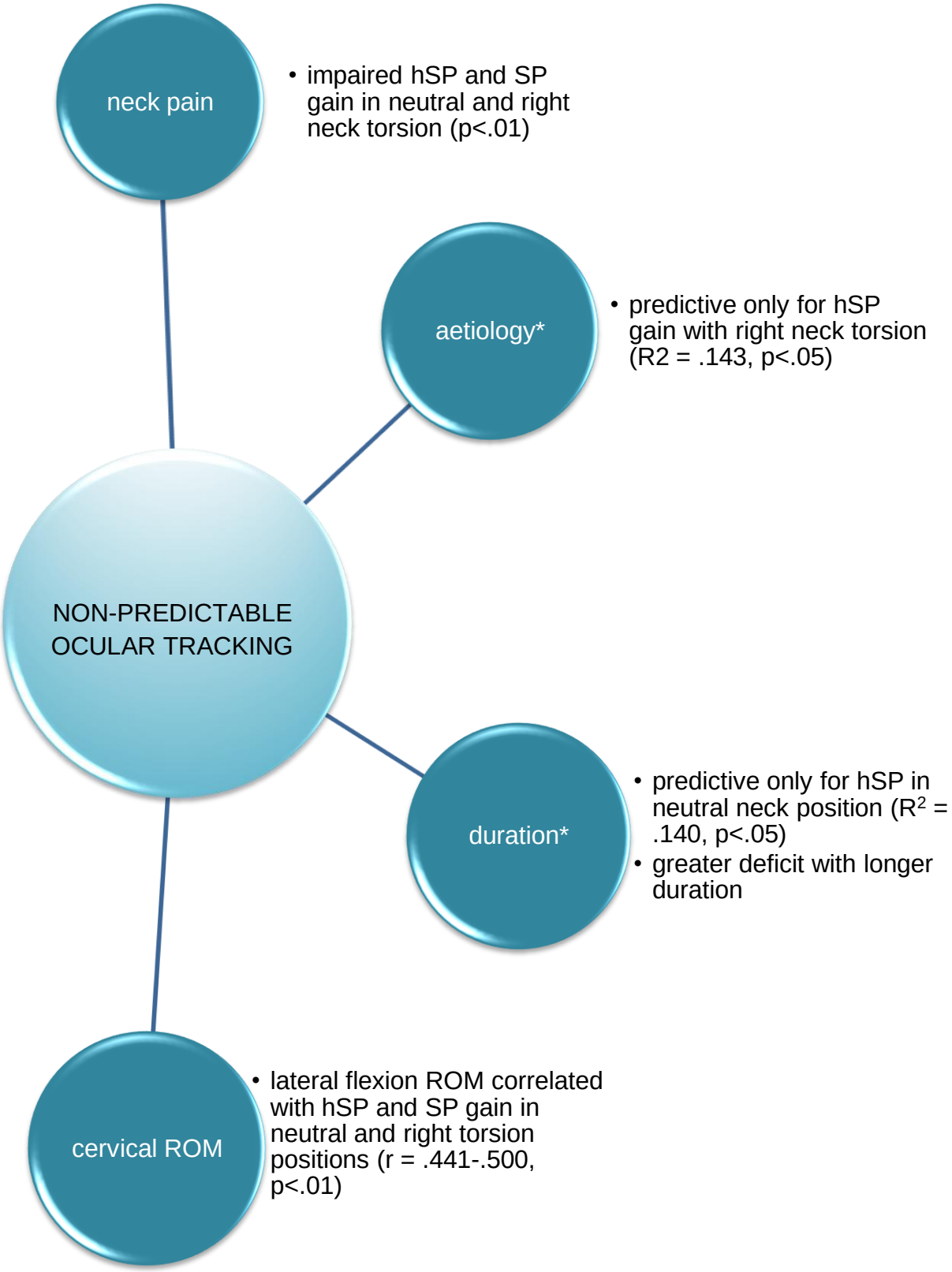
Predictive associations of aetiology of neck pain for hSP gain with right neck torsion and also of duration of symptoms for hSP gain in the neutral position should be interpreted with caution due to a lack of independence within the neck pain group between aetiology, age and duration of symptoms (5.4.2). The fact that correlation analysis did not indicate associations for age or duration of symptoms with test performance might suggest that aetiology is the relevant factor, however this could not be confirmed since the aetiological category was nominal data, and thus could not be analysed with correlation[62]. Further elucidation of the role of aetiology of neck pain in determining non-predictable ocular tracking requires studies appropriately

powered to enable comparison between sub-groups with WAD and non-traumatic neck pain.

Association with cervical ROM

Associations between lateral flexion range of motion and ocular tracking differed between the neck pain and healthy control groups. In the neck pain group deficit in ROM was correlated with impairment in hSP and cSP gain ($p<.01$) both in the neutral and right torsion neck positions. These were also the conditions in which the neck pain group were impaired compared with the healthy control group. This raises the possibility that decreased cervical spine mobility resulted in a lesser degree of neck torsion during the test that may have influenced hSP and cSP gain. This is however unlikely, since the correlation and the between group difference was present in the neutral neck position where no cervical motion was required. Thus additional factors related to lateral flexion ROM might underlie the impaired ocular tracking that occurred in the neck pain group. Age is one possible factor, that was correlated with ($r= .540$, $p<.01$) and predictive for ($R^2 =.291$, $p<.01$) lateral flexion ROM in the neck pain group. However, age is unlikely to underlie performance in the non-predictable ocular target test, since correlation and predictive associations were not identified between age and hSP or cSP gain. In the healthy control group lateral flexion ROM was not associated with hSP or cSP gain or with age (5.91). No previous studies have evaluated associations between cervical ROM, and smooth pursuit ocular movements.

Figure 6.1 Non-predictable ocular tracking: associations of demographic and symptom-related characteristics



Blue circles indicate associations in neck pain group. * indicates unclear association due to possible lack of independence between aetiology, age and duration of symptoms

Predictable ocular tracking test

The finding of no difference in hSP gain is inconsistent with results of the literature review that established low quality evidence (2.4.7) for impairment in WAD, although not all studies reported deficits[99;101]. The present study however used a different patient group that included participants with non-traumatic neck pain, which has not been previously reported upon. It is possible that predictable ocular tracking performance might be impaired in WAD, but not in non-traumatic neck pain. However, results of the linear regression analysis did not find any predictive power of aetiology of neck pain for this test, suggesting that this is not the case. Studies sufficiently powered to enable comparison between WAD and non-traumatic neck pain sub-groups are needed to evaluate this further. Methodological differences might also account for disparity of findings. Only one previous study stabilised the participants head with a chin rest[101], finding no SPNT test deficit in WAD. It is suggested that relaxation of cervical muscles in the stabilised position could account for the absence of deficits identified[101]. In the present study the head was stabilised with cheek pads and a bite bar (a wooden disposable tongue depressor) and it is unlikely that the bite bar would be strong enough to enable participants to support their head weight on it. It is possible that variation in bite forces during neck torsion could provide cues regarding posture, or influence cervical muscle activity, since both posturographic[308] and cervical muscle EMG[309] activity changes have been reported in response to biting. However this seems unlikely to explain the absence of deficits since impairment that was independent of neck position was found in the neck pain group in the *non-predictable* ocular target tracking test which used the same head stabilisation method. The present study also differed from others in terms of the measurement system and technical arrangement of equipment, which resulted in some differences in the test protocol, however it was the first study to use

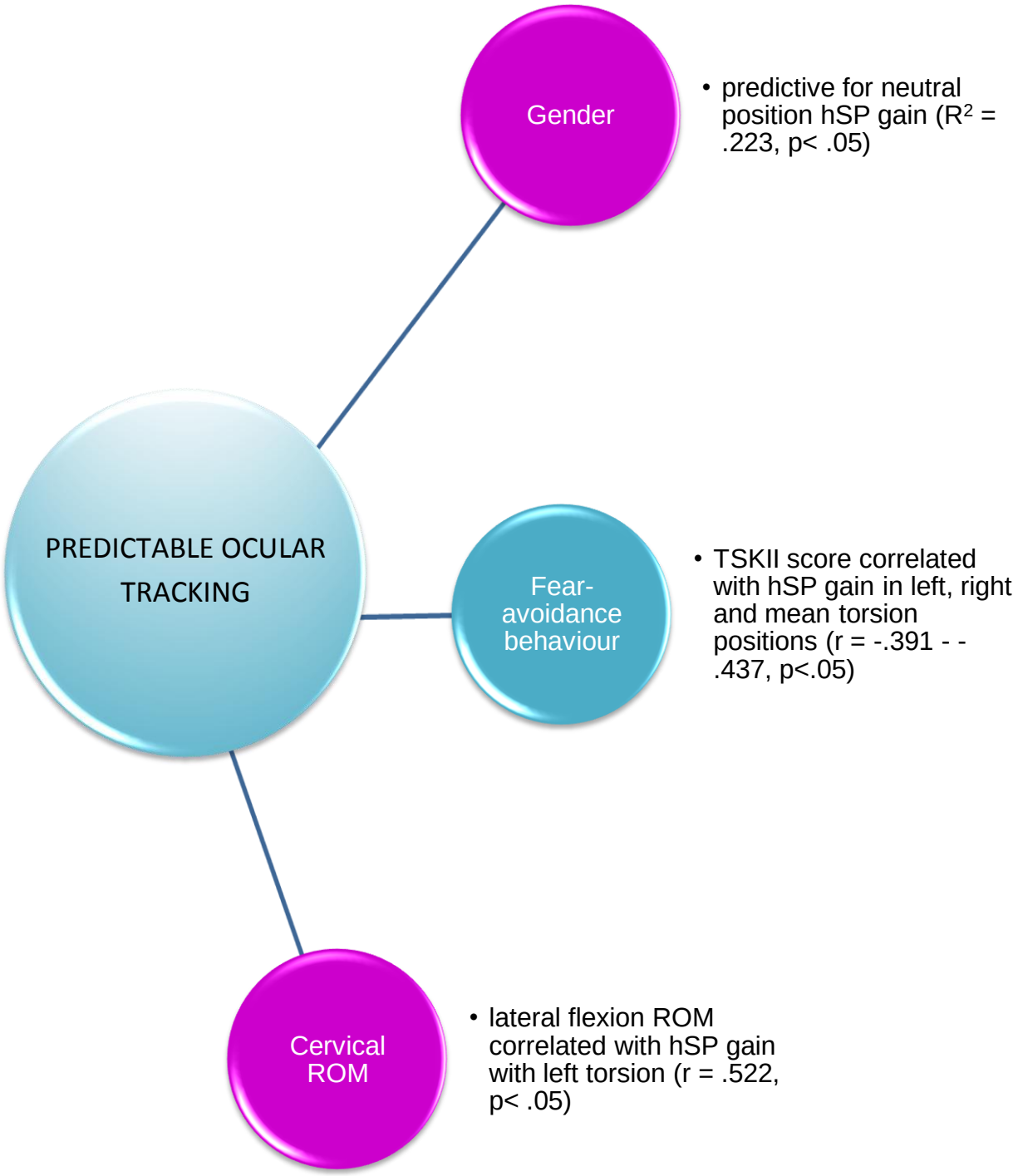
measurement and data processing methods with substantial reliability demonstrated[207], thus it is unlikely that type II error[62] resulted from the methodology.

Associations with gender, fear-avoidance beliefs and cervical ROM

Key associations of demographic and symptom-related factors with performance in ocular tracking of a predictable target are summarised in figure 6.2. Different effects of gender on performance are indicated between the neck pain and healthy control groups, whereby gender was predictive for hSP gain in the healthy control group only. This has not been previously reported. There was no effect of age on performance indicated in either group. No previous studies have evaluated the effect of age on perfomance in the SPNT test.

The absence of between group differences in performance level in the predictable ocular tracking test indicates that performance is comparable in both groups, but determined by different factors (indicated by patterns of correlation and prediction), gender and lateral flexion ROM (hSP gain) in the healthy control group and fear avoidance behaviour (hSP gain) in the neck pain group. Other studies have evaluated association of predictable ocular tracking test performance with self-reported outcome measures, reporting significant correlation with neck pain intensity (measured with visual analogue scale)[91], and with Dizziness Handicap Inventory score[91], but not with NDI score[91;98], anxiety levels[91;98] or self-reported driving habits[98] in WAD. The present study similarly found no association with NDI score, and also found no association with pain intensity.

Figure 6.2 Predictable ocular tracking test: associations of demographic and symptom-related characteristics



Blue circles indicate associations in neck pain group, purple indicates association in the healthy control group

The role of fear avoidance behaviour (measured by the TSKII) in the predictable ocular tracking test has not been previously reported but is a likely factor contributing to test performance in neck pain when the cervical spine is rotated (torsion conditions). This could explain previous reports in some studies of impairment in the predictable ocular tracking test, associated with neck torsion, in participants with WAD[90-92;98;187], since elevated fear-avoidance of movement behaviour is reported in WAD[53;165]. It is possible that neck pain participants in the present study had less fear-avoidance behaviour than those in other studies that utilised the non-predictable ocular tracking test, which could explain the absence of deficits. In contrast to the predictable ocular tracking test, association between performances in the non-predictable ocular target test with TSKII scores was not indicated, thus fear-avoidance beliefs contribute differently to the two tests.

There was some association between cervical ROM and performance in the predictable ocular tracking test in the healthy control group, whereby hSP gain (with left neck torsion) was correlated with cervical ROM (lateral flexion).The association of reduced lateral flexion ROM with reduced hSP and cSP gain in the neck pain group for non-predictable ocular tracking was not present for predictable ocular tracking. There is no clear explanation for these differences.

Cervical JPE test

The finding of no difference in cervical JPE between neck pain and healthy control participants is consistent with some other studies[10;58;59]. However, the literature review concluded that low or very low evidence existed for impaired cervical JPE in most head-to-neutral repositioning tests in both WAD and non-traumatic neck pain

and that moderate evidence existed for impaired repositioning in the transverse plane in WAD (3.5.2a). It is difficult to make comparisons between studies due to the variable participant groups, methods and measures of error used. Some studies report seemingly smaller errors than found here[52-54], others are however comparable[144]. Table 6.1 provides cervical JPE values in healthy control groups (where less heterogeneity between studies might be expected than between neck pain groups), enabling comparison between studies using the Fastrak measurement system. Standard error of the mean (SEM)[62] was calculated[144;195] to enable comparison with studies[53;54;165;184] that reported SEM rather than SD. In Table 6.1 visual comparison of cervical JPE across studies indicates that errors were greater in the present study than in most others. Gender was predictive for transverse plane cervical JPE in the present study (5.4.2), therefore differences in gender distribution might account for differences in cervical JPE magnitude across studies. However, comparison of gender distributions with JPE values in table 6.1 does not indicate any pattern of association between gender distribution and magnitude of cervical JPE within studies. Similarly, consideration of sample size or sampling error (SEM) does not indicate any association with cervical JPE magnitude. The fact that the order of repositioning movements differed in the present study and the study by Swait et al (2007)[195], compared with other studies does not explain greater magnitudes of JPE, since Lee et al (2006)[144] reported JPE values that were comparable to findings of the present study, yet used a similar order to other studies. Cervical JPE values were comparable to those obtained in the preliminary study[195] in a different group of healthy participants, thus seem representative of JPE in healthy individuals without neck pain. Different findings for magnitude of JPE might result from other studies[53;54;165;184; 144] using only 3 trial repeats, whereas it was demonstrated that this was insufficient to generate estimates of JPE that were both stable and reliable[195].

Table 6.1 Comparison of mean (standard error of mean) cervical JPE among healthy control groups in studies using Fastrak measurement system

Study	Flexion JPE	Extension JPE	Left rotation JPE	Right rotation JPE	%male	n
*Lee (2006)[144]	4.4(.5)	6.5(.6)	5.2(.7)	4.9(.6)	50	20
*Swait (current study)	3.5 (.4)	3.4 (.3)	3.7(.5)	3.3(.3)	50	24
*Swait (2007)[195]	5.2(.5)	2.5(.5)	3.3(.5)	4.0(.6)	38	16
Hill (2009)[184]		3.0(.3)	2.5(.4)	3.2(.4)	43	40
Sterling[165] (2003)		2.8(.3)	2.6(.3)	2.7(.3)	40	20
Sterling (2004)[53]		2.9(.6)	2.3(.3)	2.3(.5)	45	20
Treleaven (2003)[54]		2.4(.3)	2.0(.2)	2.5(.2)	34	44

JPE (degrees) is given to one decimal place for consistent presentation across studies. SEM [62] was calculated* to enable comparison across studies that did not report SD .Gender distribution within study samples and sample size (n) are provided. Studies are listed approximately in order of descending magnitudes of JPE. Consideration of the progression down each column of gender distribution, sample size and SEMs do not indicate any trends associated with decreasing magnitudes of JPE

Magnitude of cervical JPE in the neck pain group was also greater than that reported in other studies[53;54;165;184;], thus the absence of a between groups difference is unlikely to result from poorer performance of the healthy control group in the present study.

The finding of a systematic effect (5.1.3) across trials in the neck pain group for head repositioning following flexion and extension, whereby the preceding trial influenced performance, was previously unreported. No such effect was found in the healthy control group, which is consistent with findings in the methodological study[195]. Comparing JPE between the neck pain and control groups for each trial reveals similar patterns of fluctuation (Figure 5.3) that does not follow a progressively improving or deteriorating performance. This suggests that JPE in individual trials may be influenced by the repositioning movement in the preceding trial(s), but that this is not the result of learning or fatigue effects during testing. For each direction of repositioning movement, JPE was greatest in trials that were immediately preceeded by repositioning following head motion in the opposite direction. This might reflect a residual sensorimotor effect of each repositioning motion that persists to influence performance of the next (i.e. an order of presentation effect). Other studies utilised protocols with blocks of all trials of each movement presented together[15] enabling the possibility that mean JPE across trials for a single movement could be influenced by where in the protocol trials of that movement occur (i.e. an order effect for blocks of trials of individual repositioning movements). To reduce this likelihood, trials for repositioning following flexion, extension, left or right rotation movements were pseudo-randomised (3.4.2), thus over the course of the protocol, potential order effects should be counterbalanced. All participants followed the same trials protocol

therefore it is unlikely that the systematic effect influenced the results of the between groups analysis.

Associations with age, gender, duration and aetiology of neck pain

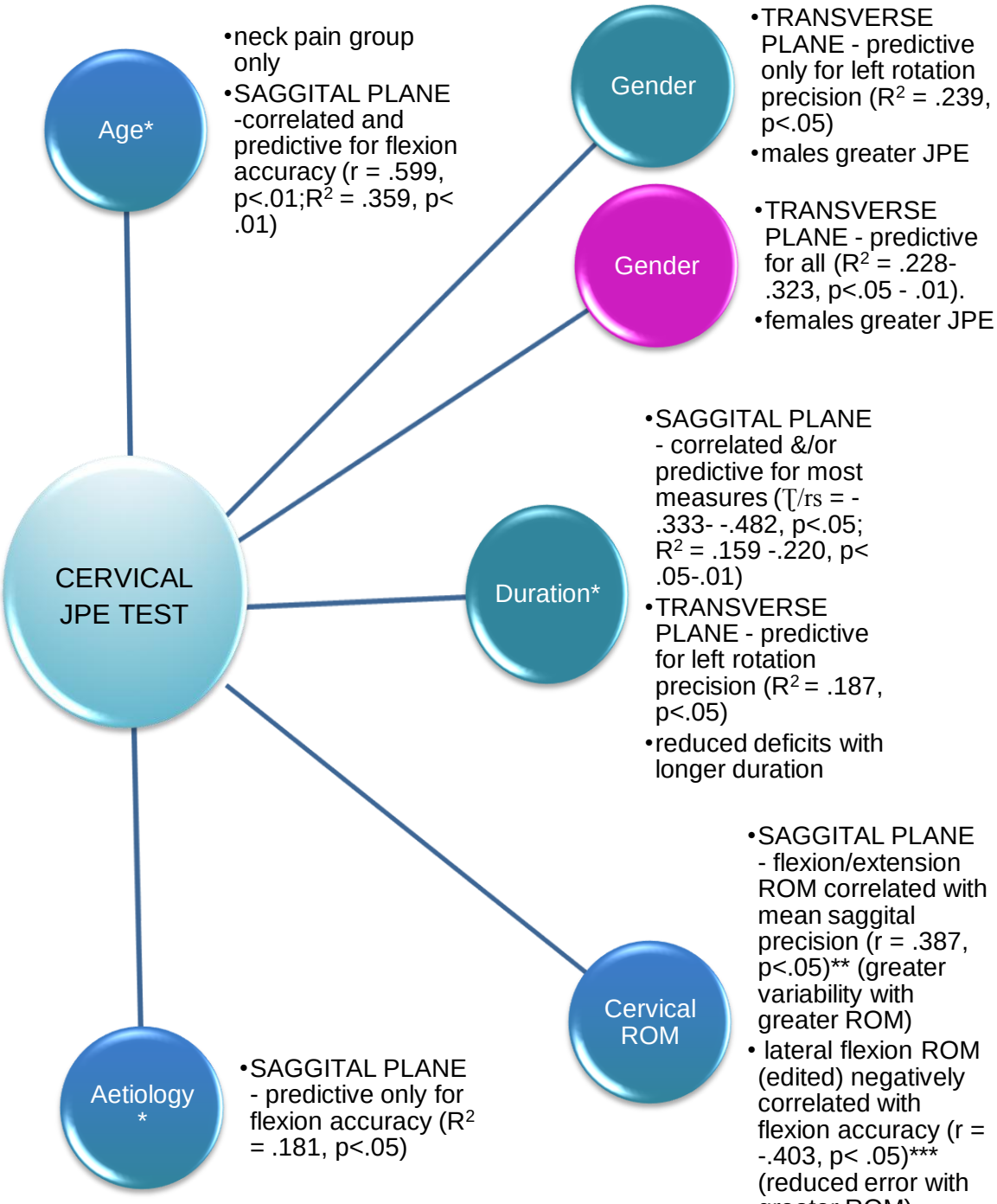
Key associations of demographic and symptom-related factors with performance in the cervical JPE test are summarised in figure 6.3.

Age was correlated and predictive only for accuracy of repositioning following flexion and only in the neck pain group. The lack of independence between age, aetiology and duration of symptoms questions the role of age in cervical JPE, particularly since aetiology is also predictive for accuracy of repositioning following flexion. However, the greater predictive power of age (R^2 = .359) compared with aetiology (R^2 = .181) suggests that age is a determining factor. Other studies of association between age and cervical JPE reported conflicting findings, with some finding no correlation for WAD[51]. These studies all utilised manual JPE measurement methods with risk of experimenter bias and unclear reliability, thus must be interpreted with caution. A further study by Teng et al (2007)[59], with reduced risk of bias associated with automated measurements, found an age-related increase in sagittal plane JPE in a middle-aged adults both with or without a history of neck pain, compared with younger healthy adults. Similarly, Lee et al (2008)[163] reported increased cervical JPE associated with older age. The neck pain participants in these studies[59;163] had non-traumatic neck pain, thus the age effect was independent of aetiology (i.e. WAD versus non-traumatic neck pain) and further supports the likelihood that the

association identified in the present study was dependent on age rather than aetiology.

Duration of neck pain was also significantly correlated and predictive for most measures of repositioning in the sagittal plane, as well as being predictive for the precision of repositioning following left rotation. Deficits in performance reduced with increasing duration of symptoms. This is in contrast to the greater impairment indicated with increasing duration in both the non-predictable ocular tracking and cervico-cephalic kinesthesia tests. The fact that age and aetiology were not associated with all of the same measures supports an influence of duration of symptoms on cervical JPE. One previous study reported no correlation between symptom duration and cervical JPE, but had high risk of bias[191]. A further study by Lee et al (2008)[163] found no effect of duration of pain, or frequency of symptoms, on cervical JPE, but this was duration of individual occurrences of neck pain, rather than the overall chronicity as measured in the present study, thus is not directly comparable. It has been reported that sub-groups of participants within a WAD group had either improved or worsened performance in the cervical JPE test over time following injury[310]. Within the neck pain group in the present study, the significant correlation and linear regression result suggests a simpler pattern only of improving over time (5.4.2). This is the first report of correlation and a predictive relationsip between duration of a mechanical neck pain condition and cervical JPE.

Figure 6.3 Cervical JPE: associations of demographic and symptom-related characteristics



**reduced ROM associated with greater precision (reduced SD)
***reduced ROM associated with reduced accuracy (greater JPE)

Blue circles indicate associations in neck pain group, purple indicates association in the healthy control group. * indicates unclear association due to possible lack of independence between aetiology, age and duration of symptoms

Gender was predictive in the healthy control group for all measures of transverse plane repositioning cervical JPE, with overall greater errors indicated in females than males. In the neck pain group, gender was only predictive for precision of left rotation JPE with males having greater errors. Thus there was a dissociation of the role of gender in determination of cervical JPE between groups, whereby different patterns of association were present in each group. One previous study[191], with high risk of bias, reported no correlation between gender and cervical JPE in healthy controls or in WAD. Lee et al (2008)[163] similarly did not find any association between gender and cervical JPE in head repositioining to neutral position, but did find greater JPE among females with non-traumatic neck pain when repositioning was to a remembered mid-range position. The finding of association of gender with cervical JPE in the present study indicates the importance of controlling for gender distribution in study design. Gender effects were unlikely to influence the results of between groups analysis in the present study, since no differences in gender distribution were present between the groups.

Correlation analyses indicated that in the neck pain group reduced accuracy of cervical JPE following flexion movement was associated with reduced lateral flexion ROM. However, reduced sagittal plane ROM (poorer performance) was associated with greater precision (better performance) of repositioning cervical JPE following sagittal plane motion. One explanation for this seemingly anomalous finding is that a reduced ROM in neck pain participants results in them making smaller flexion and extension movements during the cervical JPE tests, which in turn results in less variability (greater precision) in neutral position relocation error. Such an effect could

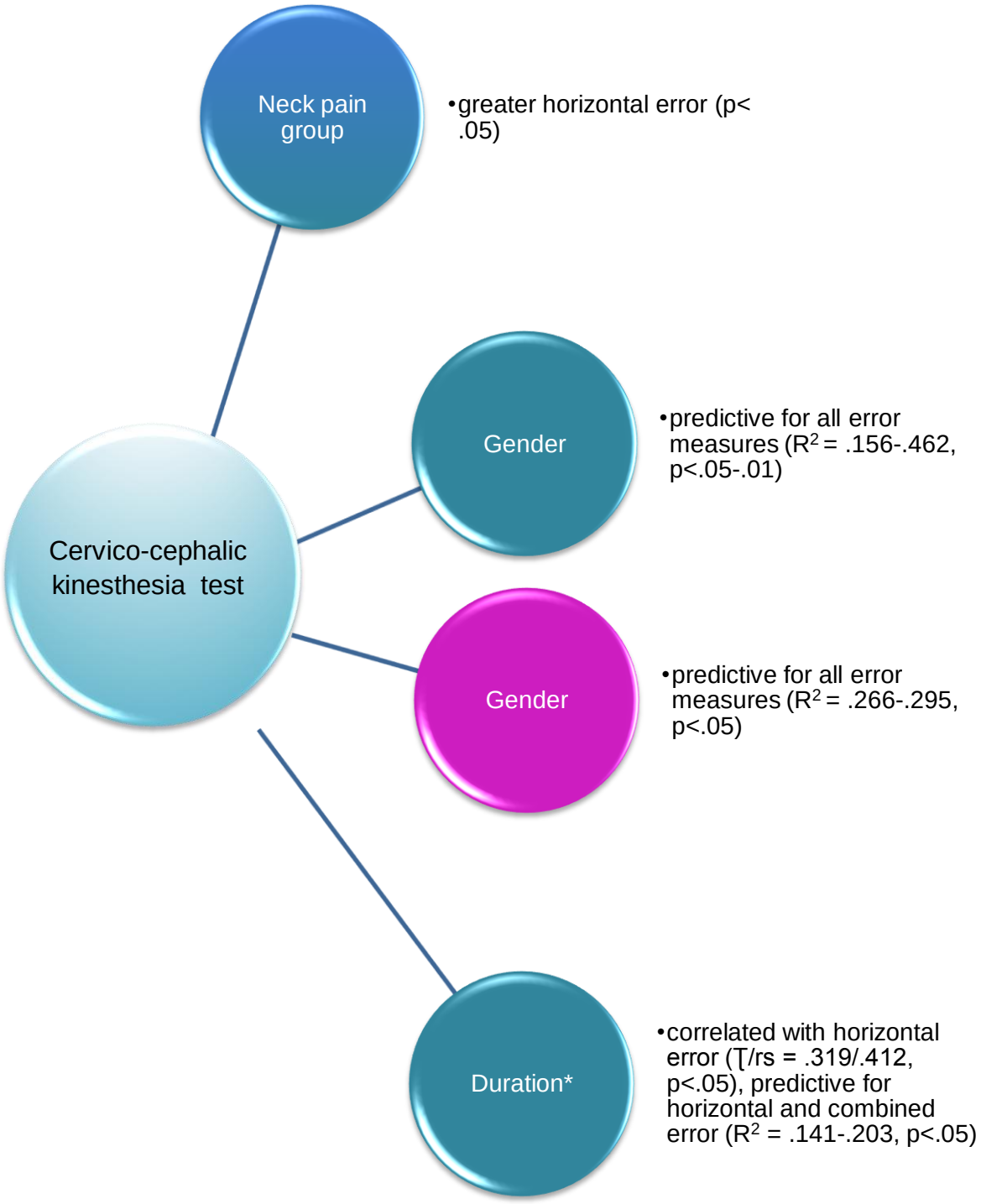
improve mean neck pain group performance in the cervical JPE test, thus resulting in no difference between neck pain and healthy control groups. This is unlikely to explain the absence of between-group differences for all cervical JPE measures in the present study, since the positive correlation with ROM only existed for mean sagittal plane cervical JPE. However, further indications of altered motion patterns in neck pain during performance of the cervical JPE test arise from findings of a more inferior axis of motion during repositioning to a mid-range position in the sagittal plane in WAD compared with healthy control participants[68]. Only one previous study[191] evaluated association between active cervical ROM and cervical JPE, reporting no correlation in either a healthy control group or in WAD, although this used methods with inadequate reliability of measurement of cervical JPE[144;195].

The finding of no association between cervical JPE and self-reported functional disability or pain intensity in neck pain was is in accordance with previous studies[15;51;58;163;191]. This was the first evaluation of association between cervical JPE and fear avoidance behaviour, indicating no relationship with TSKII scores in neck pain. This contrasts with findings that TSKII score was correlated with hSP gain with neck torsion in the SPNT test, indicating different factors influencing performance across the tests.

Cervico-cephalic kinesthesia test

Key associations of demographic and symptom-related factors with performance in the cerviico-cephalic kinesthesia test are summarised in figure 6.4

Figure 6.4 Cervico-cephalic kinesthesia test: associations of demographic and symptom-related characteristics



Blue circles indicate associations in neck pain group, purple indicates association in the healthy control group**.** * indicates unclear association due to possible lack of independence between aetiology, age and duration of symptoms

Significantly greater horizontal plane error was found in the neck pain group, compared with the control group (5.4.1). The deficit is in accordance with previous studies in participants with WAD[60;80] and chronic non-trauma neck pain[80]. In the present study a unique target trajectory was followed for every trial, which differs from previous methodologies[60;80] where a gradual improvement in performance in a control group and deterioration in a WAD group over successive trials was reported[80]. This might indicate learning (perhaps associated with the repeating target trajectories) and fatigue respectively, and could increase the difference in mean errors measured between groups. No systematic effects were detected with our methodology, thus order effects were unlikely, and furthermore a protocol with greater reliability was established[195].

Associations with gender, and duration of neck pain symptoms

Gender was predictive for all error measures in both the healthy control and neck pain groups in the cervico-cephalic kinesthesia tests. Females had greater errors than males. The underlying construct that is gender-dependent is unclear, however reduced performance in females has consistently been reported in the finger tapping test, which is a proposed measure of motor speed[311]. Since non-predictable ocular tracking, which includes many of the same underlying neurophysiological processes (Table 6.2), was not associated with gender, it is possible that motor control of cervical muscles could be slower in females than males, resulting in greater error in head tracking of the visual target. The between-groups difference in performance in the test was not dependent on gender-related factors, since there was no difference in gender distribution between the neck pain and healthy control group.This was the first evaluation of the role of gender in performance in the cervico-cephalic kinesthesia test. The role indicated for gender influencing test performance means

that gender distributions must be balanced, or imbalances controlled for in analyses, for comparisons to be made between groups.

Duration of symptoms in the neck pain group was also predictive for horizontal plane error in the cervico-cephalic kinesthesia test, with longer duration of symptoms associated with greater error. No association was indicated between age and performance in the cervico-cephalic kinesthesia test. This contrasts with findings of a relationship between age and sagittal plane JPE in neck pain, suggesting that different factors, that are affected differently by age, contribute to performance across the tests. No other symptom-related characteristics (functional disability, pain intensity or fear-avoidance behaviour) were associated with performance in the cervico-cephalic kinesthesia test. No other studies have evaluated any factors contributing to test performance.

Evaluation of construct validity: summary of associations between demographic and symptom-related characteristics with performance tests

Consideration of associations of demographic and symptom-related factors with performance in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests indicates that different combinations of factors contribute to each. The absence of convergence or divergence of correlations of different factors across the different tests (1.6) suggests that the constructs that underlie performance in each test (that are influenced by these factors) are not the same, thus challenging their construct validity for cervical proprioception. Construct validity is discussed further in 6.5.

6.4.3 Correlation between performance in the non-predictable and predictable ocular tracking, cervical JPE, cervico-cephalic kinesthesia tests

Analysis of convergence of correlation in performance across the different tests enabled evaluation of their construct validity as measures of a common underlying construct.

Comparison with findings of previous studies

Patterns of convergence in correlation between the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests differed from the findings of other studies.

In the present study all correlations with transverse plane cervical JPE were greater ($r = .358 - .805$) and most were significant ($p<.05$), within both the neck pain and healthy control groups. In healthy participants, previously no significant correlations were detected ($r = -.141 - .228$) between the cervical JPE and cervico-cephalic kinesthesia tests[195]. The same measurement methods were used and sample sizes were comparable ($n = 16$ in the earlier study versus $n = 18$), however the absence of correlation found in the earlier study may be due to its younger age of participants (26.5 (9.4) versus 38.88 (9.43)), or unequal gender distribution (more females than males versus equal proportions), particularly since gender was predictive for both the cervico-cephalic kinesthesia and cervical JPE tests in the present study.

The present study found significant correlations, mostly within the healthy control group, between cervical JPE and performance in the ocular tracking tests (hSP or cSP gain). Only one previous study evaluated correlation between cervical JPE and performance in the SPNT test. Treleaven et al (2006) found no significant correlation within a healthy control group or within a WAD group between performance in the

cervical JPE test and the hSPNT difference (r= -.20 - .11)[55], although correlation was found when both control and WAD participants were analysed together. Findings were however not directly comparable to the findings of the present study, since only the SPNT difference was analysed. The SPNT difference was not included in the present study as it was demonstrated to have inadequate reliability (3.4.1).

No previous studies evaluated correlations in any participant group for hSP or cSP gain in either predictable or non-predictable ocular tracking with any other test. Correlation between cervico-cephalic kinesthesia with any ocular tracking test had not been evaluated in any participant group, and in a neck pain group cervical JPE and cervico-cephalic kinesthesia had not been compared. Significant correlations were found in the present study, but in patterns that differed between the neck pain and control groups (5.12)

Dissociation of correlation between healthy and neck pain participants

In the healthy control group there were many correlations (5.11) that were significant between performance in the ocular tracking tests (both predictable and unpredictable targets), cervical JPE (transverse plane) and cervico-cephalic kinesthesia tests. This convergence suggests that one or more common constructs contribute to their performance. In the neck pain group comparative dissociation was found between performance in the cervical JPE (transverse plane) test and both the ocular tracking and cervico-cephalic kinesthesia tests (5.4.3), with fewer, weaker correlations indicated. This lack of convergence[50] of correlations suggests that in neck pain the constructs determining performance in the cervical JPE test differ from those determining the ocular tracking and cervical kinesthesia test performance. In 6.5 a

theoretical model is proposed to explain the conrvegence in correlation and the disassociation in the pattern between the neck pain nd healthy control groups.

6.4 A THEORETICAL MODEL FOR THE CONVERGENCE IN CORRELATION FOUND BETWEEN TESTS

6.5.1 Theoretical constructs within the model

Figure 6.5 illustrates a possible theoretical model of constructs that determine performance in the tests that may explain the patterns of correlation found.

According to the model, in healthy participants the common construct A is strongly associated with performance level in all 3 tests. There are however 4 possible explanations that might account for the disassociation of performance in the transverse plane cervical JPE test from performance in the ocular tracking and cervico-cephalic kinesthesia tests in participants with neck pain:

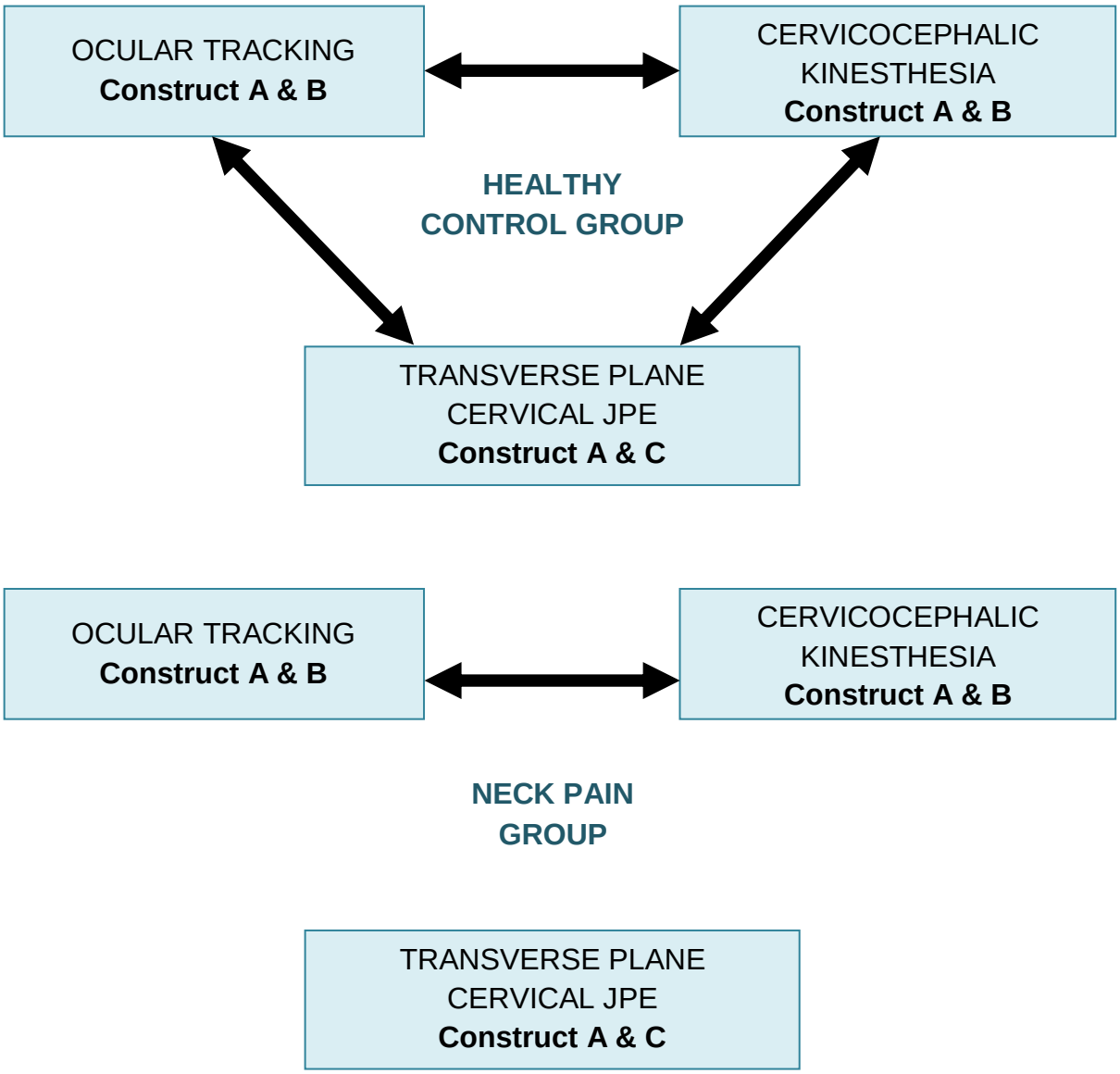
1. The common construct A is not impaired in neck pain. Construct B is impaired and is associated with performance in both the ocular tracking and cervico-cephalic kinesthesia tests, but not the transverse plane cervical JPE test

2. The common construct A is not impaired in neck pain. Construct C is impaired and is associated with perfomance in the transverse plane cervical JPE test, but not the ocular tracking and cervico-cephalic kinesthesia tests

3. The common construct A is impaired in neck pain and is associated with performance in the transverse plane cervical JPE test, however, in the ocular tracking and cervico-cephalic kinesthesia tests the unique construct B compensates for the impairment in construct A

4. The common construct A is impaired in neck pain and is associated with performance in both the ocular tracking and cervico-cephalic kinesthesia tests, however in the transverse plane cervical JPE test the unique construct(s) C compensates for the impairment in construct A

Figure 6.5 Theoretical model for construct(s) determining performance in the ocular tracking, cervico-cephalic kinesthesia and transverse plane cervical JPE tests in the healthy control and neck pain groups



Construct(s) A is common to all tests. Construct(s) B is common to the ocular tracking and cervico-cephalic kinesthesia tests, but is not shared with the cervical JPE test. Construct(s) C is unique to the cervical JPE test. Arrows indicate high levels of correlation

Explanation 2 is unlikely, since between-group analysis of performance indicated no impairment in transverse plane cervical JPE in neck pain (construct C), compared with healthy controls, while explanation 3 is unlikely since impairment was indicated (construct B) in both the non-predictable ocular tracking and cervico-cephalic kinesthesia tests. Thus either explanation 1 or 4 may account for the patterns of correlation found. These are considered further in 6.5.5. The construct validity of the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests is evaluated further by consideration of firstly, the neurophysiological processes that theoretically contribute to performance of each test (6.5.2), secondly, which may provide constructs A, B or C (6.5.3), and thirdly, evaluation of whether the findings of the study and also existing evidence supports each eligible process as providing construct A, B or C, according to explanation 1 or 4 (6.5.3)

6.5.2 Identification of neurophysiological processes that theoretically contribute to performance in each test

Neurophysiological processes that theoretically underlie performance in the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests were discussed in 1.5. These are provided in table 6.2, where each column identifies the processes involved in each individual test (indicated by either shading or a cross). Broad neurophysiological processes are further divided down into more narrowly defined processes only in the instances where there was a difference between these across tests.

Constructs A, B and C are derived from the model that accounts for different patterns in the convergence of correlations between tests in the heathy control, compared with the neck pain groups (6.5.2, figure 6.5). In Table 6.2, each row identifies the

contribution of each neurophysiological process across the ocular tracking, cervico-cephalic kinesthesia and transverse plane cervical JPE tests. This indicates that those that were common to all tests and are thus candidates for construct A are non-task dependent processes (this broad definition includes cognitive, psychological or physiological factors that could influence performance in sensory motor function tests in general), and cervical poprioception, or transformation of proprioceptive signals into ocular motor output. Those that were common to the non-predictable and predictable ocular tracking tests and to the cervico-cephalic kinesthesia test, but not to the cervical JPE test, are candidates for construct B. These were processes of visual target localisation and motion computation, transformation of visual target information for the purpose of guiding ocular movement, detection and correction of mismatches between visual target and ocular position and motion, attentional processes that are specific to visuomotor performance, transformation of proprioceptive information for the purpose of guiding ocular movement and motor control of extraocular muscles that generate horizontal ocular movements. Neurophysiological processes that were unique to the cervical JPE test, that are thus candidates for construct C, were vestibular processes or motor efference copy processes.

Table 6.2 Neurophysiological processes that theoretically may underlie performance in ocular tracking, cervico-cephalic kinesthesia and transverse plane cervical JPE tests

PROCESS	NON-PREDICTABLE OCULAR TRACKING	PREDICTABLE OCULAR TRACKING	CERVICO-CEPHALIC KINESTHESIA	CERVICAL JPE (TRANSVERSE PLANE)
Non-task dependent factors (cognitive/psychological/physiological)				
VISUAL SENSORY & VISUOMOTOR PROCESSES				
Visual target localisation in space[97;103], velocity/direction computation				
Visuomotor transformation (for ocular movement)				
Visuomotor transformation (for head movement)			X	
Gaze pursuit (combined head and eye tracking)[312;313]			X	
Visuomotor predictive processes[93;313]				
Continuous retinal error feedback, mismatch detection and correction[93]				
Visuomotor attention[93]				

Table 6.2 continued

PROCESS	NON-PREDICTABLE OCULAR TRACKING	PREDICTABLE OCULAR TRACKING	CERVICO-CEPHALIC KINESTHESIA	CERVICAL JPE (TRANSVERSE PLANE)
NON-VISUAL SENSORY & SENSORIMOTOR TRANSFORMATION PROCESSES				
Cervical proprioception[83;107;239;314]				
Propriomotor transformation (for ocular motion)[85]				
Propriomotor transformation (for head motion)[85]			X	X
Vestibular processing and transformation[63;64]				
MOTOR & ARTICULAR PROCESSES				
Motor efference copy (head motion)[63]				
Motor control of extraocular muscles[94] – medial and lateral recti				
Motor control of extraocular muscles[94] -superior & inferior recti and obliques	X		X	
Motor control of cervical rotators[82]			X	X
Motor control of cervical flexors/extensors/lateral flexors[82]			X	
Cervical articulation[82]			X	X

Shading indicates processes that may provide constructs A, B and C in the model (on the basis of convergence found in correlation between tests) - orange shading indicates construct A, purple indicates construct B, green shading indicates construct C. Crosses indicate processes that would not provide constructs A,B or C

6.5.3 Evaluation of neurophysiological processes identified as candidates for constructs within the model

Construct A

According to the model, construct A is common to the ocular tracking, cervico-cephalic kinesthesia tests and transverse plane cervical JPE. Table 6.2 indicates that only cervical proprioception, its subsequent transformation for ocular motion, or more general processes that contribute to motor performance in a non-task dependent way, are potentially common to all of these tests. It seems unlikely that common non-task dependent processes (e.g. level of alertness, motivation etc) are key determinants of performance, since they would be expected to have similar effects on sagittal plane JPE to those on transverse plane JPE and the absence of any correlation between those tests in either group argues against this. Cervical proprioception or transformation of proprioceptive signals into ocular motor commands are therefore more likely to underlie construct A, contributing to performance in non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and transverse plane cervical JPE tests in the healthy control group. In the neck pain group cervical poprioception or transformation of propioceptive signals into coluar motor commands may either be impaired or unimpaired (according to explanations 1 or 4 within the model). Each possibility is considered separately.

Construct B

According to explanation 1, cervical proprioception, or propriomotor processes are not impaired in the neck pain group. A number of neurophsyiological processes may provide construct B, that is impaired (Table 6.2). These are each considered below.

Efferent control of extra-ocular muscles

Deficits in efferent control of medial and lateral recti is unlikely to underlie correlation between the ocular tracking and cervico-cephalic kinesthesia tests. Firstly, while pontine nuclei generating output for ocular movements in smooth pursuit[94] may sustain damage during whiplash injury to the neck[175], the participants here included both those with traumatic and non-traumatic aetiology neck pain and there was no association indicated between aetiology of neck pain and either predictable ocular tracking or performance in the cervico-cephalic kinesthesia test (although aetiology was predictive for non-predictable ocular tracking hSP gain, but only with right neck torsion). Secondly, there is no apparent mechanism for a direct effect of mechanical neck pain on the extra-ocular muscles themselves. Efferent control of extra-ocular muscles is thus unlikely to provide construct B.

Visual processes

It is also unlikely that purely visual processes (processing of retinal signals) account for performance in the ocular tracking and cervico-cephalic kinesthesia tests in the neck pain group, since there is no apparent mechanism for visual dysfunction in mechanical neck pain. In addition, all participants stated that vision was normal or corrected to normal with glasses or contact lenses.

Visuomotor and/or propriomotor transformation

Several cortical and subcortical areas are activated by both head restrained and unrestrained (gaze movement) ocular tracking and also by cervical proprioceptor stimulation. This suggests common processes that may include polysensory (both visual and proprioceptive signals) transformation, perhaps into trunk or space centred coordinates (1.5.2). Impairment of these transformations in neck pain could explain

the convergence in correlation found between the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE test in the neck pain group. There is no apparent mechanism for direct impairment of thse cortical processes (in the absence of deficits in cervical proprioceptive inputs from the periphery) in neck pain. However, there is some evidence that attention may be impaired, at least in WAD (6.3.6) and fMRI has indicated attention-related modulation of areas involved in visuomotor transformation[315]. Thus an indirect effect of neck pain on polysensory transformation could underlie correlation between ocular tracking and cervico-cephalic kinesthesia test performance. Construct B is not shared with the transverse cervical JPE test, therefore in neck pain, according to explanation 1 of the model, cortical areas implicated in polysensory transformation would not be activated during that test. This could be investigated in fMRI studies to evaluate convergence in correlations between activity in different brain areas during performance in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests. In addition, establishing correlations between activity level and performance in the tests would provide evidence of brain regions where activity determines performance in each test.

Visuomotor attention, visual working memory or velocity mismatch detection and correction

In addition to polysensory transformation, common areas of brain activity (1.5.2) during head restrained or head unrestrained ocular tracking might reflect other cognitive processes that are common to both the non-predictable and predictable ocular tracking tests and also the cervico-cephalic kinesthesia test. Cognitive impairments that might affect ocular tracking may be present in mechanical neck pain (6.3.6) and could result in deficits in visuomotor attention, visual working memory or

velocity mismatch detection and correction (1.5.3), this could explain the strong association that was found between performance in non-predictable and predictable ocular tracking and cervico-cephalic kinesthesia tests. The lack of predictability could however place greater load on these cognitive processes in the non-predictable ocular tracking test and the cervicocepehalic kinesthesia tests. This could explain the fact that their performance was impaired in the mechanical neck pain group, while performance in the predictable ocular target test was not affected. The cervical JPE test does not utilise a visual target, thus visuomotor attention, visual working memory and velocity mismatch detection and correction would not be expected to contribute to performance. These cognitive processes are thus candidates for construct B, which is not shared with the cervical JPE test (Figure 6.5,Table 6.2). Evaluation of correlations between ocularmotor tests designed to evaluate visuomotor attention, visual working memory and velocity mismatch and correction (6.3.5), with performance in the non-predictable and predictable ocular tracking and cervico-cephalic kinesthesia tests could provide further evidence for these processes as providing construct B.

Construct C

According to mechanism 4, common processes (that might be cervical proprioception related processes) underlie performance in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests, accounting for correlations found in the healthy control group. These are impaired in the neck pain group, accounting for correlation between ocular tracking and the cervico-cephalic kinesthesia tests, however another process that is unique to the cervical JPE test enables compensation (construct C). Table 6.2 indicates that either vestibular processes or motor efference copy could signal the active head motion that occurs in cervical JPE test.

Vestibular processes

A number of cortical and subcortical areas are activated by vestibular stimulation and also by cervical proprioceptor stimulation and motor efference copy (1.5.1). Evidence for a role of vestibular processes in performance of the cervical JPE test comes from observations that vestibular stimulation modulates ego-centred spatial perception.In individuals with spatial neglect, the subjective straight ahead position (the target for repositioning in the cervical JPE test) in the transverse plane is impaired but is modulated by cervical proprioceptor stimulation.Neglect patients are however unimpaired in perception of the straight ahead position in the sagittal plane[67], suggesting that transverse and sagittal plane perceived straight ahead are determined by different brain mechanisms. This may also explain the absence of correlation between transverse plane and sagittal plane cervical JPE in both the neck pain and healthy control groups in the present study.

While the exact cortical location for subjective straight ahead orientation functions is unknown, the combined influence of both vestibular and cervical proprioception on this function raises the possibility that the gain of either input (i.e. the weight of its influence) could be raised to compensate for a deficit in the other. Evidence for such adaptation comes from observations that the gain of the cervical proprioceptive signal for self-motion perception is raised in association with age-related decreases in vestibular function[316]. An analogous adaptation in gain is reported for ocular stabilisation reflexes, whereby increasing age is associated with decreased gain of the vestibulo-ocular reflex and reciprocal increased gain of the cervico-ocular reflex. There is no evidence available as to whether the gain of vestibular signals for self-motion perception is raised in association with deficits in cervical proprioception. This

might be evaluated in neurological patients with selective loss of somatosensory afferent neurons. In WAD changes in the gain of the cervico-ocular reflex have been reported[86;87], however the gain is *increased* (with no reciprocal change in the vestibulo-ocular reflex) suggesting an increased sensitivity to cervical proprioceptive stimulation, rather than a deficit, a finding that has been associated with reduced cervical mobility[317]. The possibility of adaptations in gain of cervical proprioceptive and/or vestibular signals for perception of straight ahead and self-motion perception in mechanical neck pain could be investigated in several ways including:

i) Evaluation of subjective straight ahead orientation in the dark with no head rotation (excluding vestibular stimulation and motor efference copy) e.g. by participants aligning a laser pointer with their perceived mid-sagittal plane[318]. Impairment in neck pain would indicate a cervical proprioception deficit that may be present in the cervical JPE test, but compensated for by vestibular and/or motor efference copy signals

ii) Evaluation of the contribution of cervical proprioceptive and vestibular signals to self-motion perception following passive head and/or trunk rotations in the dark by relocating a visual target to the remembered pre-rotation position. This would enable evaluation of the relative gains of both signals (as has previously been reported for age-related changes[316]) and would confirm whether cervical proprioceptive contribution to self-motion perception is altered and also whether vestibular signals compensate in neck pain

iii) If deficits were found in either task, the effect of cervical proprioceptive (neck muscle vibration) or vestibular (caloric) stimulations on performance could be

further evaluated, as in studies where both compensated the deficits found in neglect patients[318]

Together these investigations could confirm whether or not mechanism 4 provides a likely explanation for the absence of cervical JPE found in the present study and whether vestibular signals compensate for cervical proprioceptive deficits. The finding that longer duration of symptoms was associated with reduced cervical JPE (Figure 6.3) might also support explanation 4, whereby an adaptive increase in vestibular gain takes place over time.

Motor efference copy

Altered proprioception in neck pain could give rise to a mismatch signal (between expected proprioceptive reafference and actual activity) that enables subsequent motor adaptation in proprioceptively guided head motion. Motor adaptation following experimentally induced sensory mismatch is well documented in relation to manual reaching and tracking[63;319;320], but not in relation to active head motion. The cerebellum is a likely site of acquisition of new sensorimotor transformations, that once learned are then stored in motor cortical areas[321].

A possible mechanism whereby the cerebellum could be involved in motor adaptation of head movements based on cervical proprioceptive signals exists. Recording studies in monkeys indicate interactions during active head movements in the vestibular nuclei between motor commands sent to the neck (efference copies) and cervical proprioceptive feedback, whereby vestibular afferent signals are cancelled out providing there is no mismatch. It is proposed that the nodulus-uvula of the cerebellum may be the origin of this cancellation signal[64;107]. In addition to enabling

neck motor adaptation to the proprioceptive signal, this could also provide a possible mechanism for increased gain of the vestibular contribution to performance of the cervical JPE test.

The role of motor efference copy in performance of the cervical JPE test could be evaluated by using passive rather than active head movements, which would eliminate generation of an efference copy for cervical mucle activity. This has been evaluated in healthy participants, with no difference found in transverse plane cervical JPE when the movement away from the neutral position was passive compared with active movement. The study also attempted to control the timing of head motion to reduce likely vestibular contribution[322]. However, the absence of reduction in performance when motor efference copy is unavailable does not preclude explanation 4, since according to the model a compensatory process contributes to cervical JPE performance only in the neck pain group. Similar investigations should therefore be conducted in participants with neck pain.

6.5.4 Research Aim 5 – conclusion of evaluation of the construct validity of the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests

The key outcome of the evaluation of the construct validity of the tests are that the non-predictable and predictable ocular tracking tests, cervico-cephalic kinesthesia tests and transverse plane cervical JPE test may be measures of cervical proprioception in the healthy control group and that this may or may not be impaired in the neck pain group. However, in the neck pain group the tests can not all have construct validity for cervical proprioception, as indicated by the dissociation in correlation that was found compared with the healthy control group, as well as the

findings of impaired performance only in the non-predictable ocular tracking and cervico-cephalic kinesthesia tests.

A model with two alternative explanations for findings of the study was proposed and evaluated. It is not possible to establish which of the two explanations underlie the construct validity of the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests, based on the evidence provided by the present study. However, in both explanations a common process that determined performance in the healthy control group may be cervical proprioception, or related processes. In the first explanation, processes most likely to be impaired in the neck pain participants that subsequently determine performance in the ocular tracking and cervico-cephalic kinesthesia tests are visual attention and processes of error detection and correction, rather than cervical proprioception. In the other explanation, either vestibular processes or motor efference copy could be utilised as an adaptation to compensate performance in the transverse plane cervical JPE test in the presence of impaired cervical proprioception. The explanations need not be mutually exclusive and it is possible that elements of both underlie the deficits found in neck pain in the non-predictable ocular tracking and cervico-cephalic kinesthesia tests as well as the patterns of correlation between tests. i.e. there could be some impairment in cervical proprioception in the neck pain group, that is compensated for in the transverse plane cervical JPE test, but performance in the ocular tracking tests may be further impaired by an effect of visual attention and/or predictive processes. Thus, although the tests give insight into whether there are deficits in sensorimotor control in neck pain, it is inappropriate to use them as specific measures of cervical proprioception. The findings and discussion above also highlight the fact that, in general, sensorimotor systems have capacity to utilise adaptive processes to compensate for

impairment associated with pathology (e.g. improvement in symptoms of neglect with vestibular or proprioceptive stimulation[318] and altered gain of the cervico-ocular reflex in patients with vestibular pathology[114]) and that this may confound attempts to understand impairment when patients are compared with healthy participants, particularly if functional tests are selected in efforts to establish the effect of pathology on motor tasks that are carried out in daily activities, that may incorporate a number of different sensorimotor processes. Suggestions are made above for further investigations that may more specifically determine the underlying constructs, impairments and adaptive processes in mechanical neck pain in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests.

6.5 STUDY LIMITATIONS

First risk of bias in the study is evaluated, followed by consideration of other limitations to the study and to interpretation of the evidence that it provides.

6.6.1 Risk of bias in the study

The GRADE criteria (2.2.2) specify four areas for the potential introduction of risk of bias in observational studies – eligibility criteria, prognostic imbalance, exposure/outcome measurement and follow-up[1].

Eligibility criteria

To minimise risk of bias introduced by eligibility criteria it was necessary to ascertain that the patient group was comprised of individuals who had mechanical neck pain and that control group participants did not have neck pain[1]. For the neck pain group the use of a physical examination enabled clear confirmation of current neck pain that was elicited by movement.The control group did not undergo a physical

examination, rather eligibility was determined based on self-reported absence of neck pain. It is thus possible that members of the control group might have had neck pain, however this is unlikely since there was no financial or other incentive for participants to inaccurately deny having neck pain. The study therefore had low risk of bias associated with group eligibility.

Prognostic imbalance

A weakness of observational study designs is that with groups drawn from different populations there is greater risk of bias due to imbalances in prognostic factors that might influence the outcome of interest, compared with randomised studies[151]. Methods to minimise risk of bias due to prognostic imbalance include analysis methods with covariates included to control for group differences[163;192], there is criticism of this approach, suggesting that it is invalid where there are high levels of cofounding or where strong correlations exist between covariates (e.g. age, gender) and independent variables (i.e. group)[323]. Age and gender have been associated with incidence of neck pain, albeit with inconsistency between reports, questioning the independence of these possible cofactors from the independent variable. There was incomplete evidence available regarding factors that covary with performance in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests, thus covariate selection[324] and checking of assumptions[62] based on their relationship with the outcomes was problematic. It was thus preferable to demonstrate that there was no imbalance between groups in factors known, or anticipated to influence the outcomes. Associations between age, gender and performance in some of the tests (5.4.2) found in the present study support the balancing of these characteristics between the neck pain and control groups. Other factors that might theoretically influence test performance were also analysed for balance between groups, including

presence of headaches, musculoskeletal conditions other than neck pain and history of having received manual therapy previously. Their inclusion enhanced the generalisablity of the study findings and controlled for potential effects of pain (not specific to neck pain), spinal function and sociodemographic factors determing treatment preferences. Between groups analysis of prognostic factors indicated that the neck pain and control groups were comparable. It is however possible that other prognostic factors could exist that were not evaluated.

The small number of neck pain participants (n = 3) that withdrew from the study were not apparently different from those that did in any measured characteristics (5.1.2), therefore this small loss was unlikely to introduce prognostic imbalance as a result of selection bias. The study therefore had low risk of bias associated with prognostic imbalance.

Measurement of outcomes

Measurement of outcomes is another aspect of study design where increased risk of bias may arise[151]. Many of the studies comparing cervical JPE in neck pain with controls used a manual method of measurement[10;15;51;140;145;183;191] that introduced a high risk of bias. Methods of reducing this include automated data collection and/or processing methods[19;53;55;68;91;98;165;181;182;189;190] and blinding of the person carrying out these processes to the group allocation of each participant[52;53;164;165;182]. In the present study effective blinding of the examiner was not considered feasible, since the inclusion of the SPNT test meant that pain or restricted ROM might be evident as neck torsion was introduced. However, data collection for all tests was automated and standardised protocols for testing were followed for all participants, reducing the potential for experimenter bias. It is possible that in the ocular tracking tests the

amount of trunk-under-head rotation could have varied between the groups, since this was not tightly controlled. Evidence for this comes from the finding that in both groups there was correlation between lateral flexion ROM and the SPNT difference (control group) or hSP and cSP gain in neutral and right torsion positions (neck pain group). However, this is unlikely to have confounded the study results for 2 reasons. Firstly, there was no between-group difference in lateral flexion ROM. Secondly, deficits found in the neck pain group were not dependent on neck motion since they occurred in the neutral head position in the neck pain group.

Processing of raw data was also largely automated, except for the necessity to include a final manual checking and editing of smooth pursuit data traces. Likelihood of bias was however reduced by blinding the data processor to the participants group. Another process where bias might be introduced was in the data cleaning and editing process. This was carried out according to standardised criteria that were applied to both groups. There was an emphasis on minimising the editing out of data and where this did occur both the edited and unedited data sets were subsequently analysed. The study therefore had low risk of bias associated with outcome measurement.

6.6.2 Other limitations to the study and the evidence it provides

Generalisability of findings

Since inclusion criteria for mechanical neck pain were broad in the study, its design limits the extent to which comparisons can be made with other studies that aimed to examine cervical proprioception in specific sub-groups, for example participants with WAD[10;51-55;58;60;68;90;91;98;145;150;165;181;183;193;194] or non-traumatic onset neck pain[10;52;59;68;163;164;189-191].

Recruitment via a chiropractic clinic limits the generalisability of the sample to individuals with mechanical neck pain who are likely to consider seeking chiropractic treatment for their condition. The control group were recruited from friends and family of the neck pain participants which has the advantage of balancing sociodemographic and healthcare preference characteristics between groups, but might limit generalisability to the wider population.

Interpretation of findings

Impaired ocular tracking in mechanical neck pain in the non-predictable visual target test and the cervico-cephalic kinesthesia test was identified in the mechanical neck pain group, however there are limitations in how this evidence may be interpreted.

The non-predictable ocular tracking test had not been utilised before in evaluation of the effects of mechanical neck pain, thus there is indirectness[151] between the evidence provided by the present study and by other studies that used only the SPNT[90;91;98;99;101;193;194]. In the cervico-cephalic kinesthesia test there was also indirectness with evidence provided by other studies, since the present study used a unique non-predictable visual target trajectory for every trial, which was not the case in other studies[60;166;325]. There is further indirectness between populations sampled, since studies included in the literature review (Chapter 2) all used more narrowly defined neck pain sub-groups. Due to limitations introduced by indirectness, caution should be exercised in making comparisons between the findings of the present study and existing evidence.

The design of the study did not enable identification of which specific underlying construct is impaired in mechanical neck pain, or the underlying pathophysiology that results in impairment in the non-predictable ocular tracking and cervico-cephalic kinesthesia tests.

While the results of the correlation analysis indicates that the ocular tracking, cervical JPE and cervico-cephalic kinesthesia do not all have construct validity for cervical proprioception in both participant groups, the study design is unable to identify the constructs that were measured. These could be investigated by comparing performance in those tests with others that more narrowly isolate the different processes that may underlie performance in the ocular tracking, cervical JPE and cervico-cephalic kinesthesia tests (as discussed, with suggestions made in 6.5.3).

6.7 CLINICAL IMPLICATIONS OF FINDINGS

6.7.1 Impaired non-predictable target ocular tracking and cervico-cephalic kinesthesia test performance

The findings of the present study indicate that patients with mechanical neck pain have impaired complex ocular and head and/or gaze motor functions. Both individuals with neck pain following whiplash injury or of non-traumatic aetiology may be impaired. These findings have implications for understanding of the effects of neck pain, rehabilitation targeted towards restoring function and methods of evaluating functional ability that are discussed below.

Whether or how individuals with mechanical neck pain experience symptoms associated with impaired ocular and head and/or gaze control is unclear. Self-reported visual symptoms have been found in studies of WAD[326;327]. It is possible that ocular motor deficits, as identified in the present study, could be perceived as visual

symptoms. Possible causes of impairments identified include reduced cognitive functions (6.3.6), which have also been reported in WAD[300;301]. There is however no evidence examining whether self-reported visual or ocular symptoms or reduced cognitive functions in mechanical neck pain are associated with impaired ocular and head and/or gaze control. No studies have evaluated visual or ocular symptoms in mechanical neck pain of non-traumatic aetiology. A further clinical implication of the findings of impaired ocular and head and/or gaze control is that these might influence the prognosis for recovery in mechanical neck pain. This has not been evaluated.

Understanding of impairments that are present in mechanical neck pain may provide a target for rehabilitation approaches. Some interventional studies in chronic non-specific neck pain used protocols including ocular and head coordination exercises, reporting improvements in cervical JPE[328-330], postural sway and jerkiness of cervical ROM[331] and pain or disability[328;329;332;333]. Findings suggest that rehabilitation of sensorimotor control of ocular and head coordination may be effective in treating mechanical neck pain, however the effect of specific tasks within exercise protocols used has not been isolated. The findings in the present study of impairment in ocular tracking of a non-predictable visual target and in the cervico-cephalic kinesthesia test indicate that the effectiveness of inclusion of these specific sensorimotor tasks in rehabilitation of neck pain should be evaluated.

In addition to rehabilitation of sensorimotor control, the effect of interventions targeting mechanical dysfunction in the cervical spine have also been evaluated using the cervical JPE test as an outcome measure, with improved performance reported following acupuncture[334], mobilisation[335], manipulation[334;336], chiropractic[57] and cranio-cervical flexion training[328]. No studies have evaluated the effectiveness of

rehabilitation or any other intervention in mechanical neck pain using non-predictable ocular tracking or the cervico-cephalic kinesthesia tests as functional outcome measures. The fact that deficits were present in performance of non-predictable target ocular tracking, but not predictable target tracking, suggest that the novel task that was evaluated in the present study for the first time is a more useful test to detect impairments in ocular motor function in patients who have mechanical neck pain. While the necessity for specialised equipment to perform the ocular tracking and cervico-cephalic kinesthesia test limits the likelihood of routine use in clinical settings, they may be utilised in more specialised clinical or research settings. The finding in the present study of deficits in performance in the non-predictable ocular tracking and cervico-cephalic kinesthesia test indicate that they provide useful measures, with acceptable reliability established (3.4.1), for future studies investigating dysfunction in mechanical neck pain and effectiveness of interventions. These should not however include evaluation of SPNT differences since impairments were not found in the present study. Furthermore, reliability of these was not acceptable (3.4.1).In addition, hSP or cSP gain with the head in neutral position, but not with cervical torsion should be the parameters measured in the non-predictable ocular tracking test, due to the finding of a systematic effect on performance in neck torsion positions upon re-test (Chapter 3).

6.7.2 Lack of construct validity of tests of cervical spine proprioception

The dissociation of convergence in correlation between the ocular tracking, cervico-cephalic kinesthesia tests and cervical JPE tests within the neck pain group in the present study (5.4.3, 6.4.3) indicates that impaired performance in either test in mechanical neck pain patients may not be attributed to altered cervical spine proprioception. Further investigation is needed of the constructs that underlie

performance of each test to provide understanding of why impairment is present in mechanical neck pain patients. As suggested (6.6.3, 6.5.4), this should include evaluation of the role of cognitive impairments in ocular and head and/or gaze control and whether adaptations in either vestibular gain or dependence upon motor efference copy occur as compensatory mechanisms during active relocation of the head to the perceived straight ahead position. Adaptations in brain strategies for performing smooth pursuit ocular tracking are reported to occur in other disorders including Parkinson's disease[94], providing evidence of the capacity for compensation for deficits in sensorimotor control. In WAD and non-specific neck pain, changes in the axis of motion during head repositioning to neutral following cervical rotation are reported[68]. In WAD activity of neck muscles is also reported to be redistributed, with increased interaction with ocular movements during gaze tasks[74]. Rather than contributing to functional deficits and clinical symptoms experienced, it is possible that such changes could represent adaptive strategies for performing motor tasks. This could be investigated further by studies that evaluate correlation between altered performance in sensorimotor tasks and reported symptoms. Thus it should be recognised that in patients with mechanical neck pain adaptive strategies may be utilised to overcome deficits, which might thus reduce their experience of movement-related symptoms.

6.6 AREAS FOR FURTHER RESEARCH ARISING FROM STUDY AIMS

The present study found that participants with mechanical neck pain exhibited impaired performance in the novel test of ocular tracking of a non-predictable visual target and also in the cervico-cephalic kinesthesia test (study aim 1, 4.1). Subsequent studies should further explore these specific deficits to enable understanding of which patients with neck pain might be impaired (including

comparison of deficits between groups with WAD and neck pain of non-traumatic aetiology), how deficits progress over time and the prognostic properties of deficits. Interventional studies should evaluate the effectiveness (in reducing symptoms and improving function) of rehabilitation programmes that specifically include and target performance in ocular tracking of non-predictable visual targets and head and/or gaze control in the cervico-cephalic kinesthesia test. Inclusion of both tests as functional outcome measures in studies of other interventions for neck pain will establish relationships between symptomatic improvements and ocular and head and/or gaze control and will contribute to understanding mechanisms of effect of interventions.

Validity of the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests as measures of cervical proprioception was not indicated across both the healthy control and the neck pain groups (Research Aim 5, 1.9). Further studies are needed to elucidate the constructs that underlie performance in the ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests, as detailed in 6.6.3. These should include, for each test, comparison of performance in that test with psychometric tasks that are designed to isolate specific potential constructs that may contribute (for example visuomotor attention, working memory, vestibular function and motor efference copy).

7. CONCLUSION

The research programme was exploratory in nature, with a number of aims (1.9) that together sought to address gaps in existing understanding of impairments in sensorimotor control in mechanical neck pain and in understanding of the construct validity of measures of sensorimotor control. A systematic approach to review of the literature, using GRADE, identified gaps in existing evidence, both for the effect of mechanical neck pain on ocular motor function and also for the construct validity of the cervical JPE, cervico-cephalic kinesthesia and the existing SPNT tests (Research Aim 1, 1.9.1). A Novel test of ocular motor function that measured smooth pursuit performance during ocular tracking of a non-predictable visual target was developed (Research Aim 2, 1.9.2, 3.2). Two methodological studies established reliable methods for measurement of performance in the non-predictable and predictable ocular tracking tests and also in the cervical JPE and cervico-cephalic kinesthesia tests (Research Aim 3, Chapter 3)

Research Aim 4 sought to evaluate the effect of mechanical neck pain on performance in a novel, complex ocular motor function test. To test the hypothesis that neck pain would disrupt sensorimotor control and thus affect ocular tracking, we demonstrated for the first time that a group of participants with mechanical neck pain had significantly poorer performance than a healthy control group when tracking a visual target following a complex trajectory that was difficult to predict, in 2-dimensions with smooth pursuit eye movements. This deficit was present both with neutral and torsion positions of the neck. It is unclear however what underlying process is impaired in neck pain to generate the reduced SP gain found and further studies were proposed that would elucidate this.

Research Aim 5 sought to evaluate the construct validity of the novel ocular motor test alongside three other tests previously reported to be effective measures of cervical spine proprioception. Three approaches were used to evaluate whether or not the non-predictable ocular tracking, predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests were measures of a common underlying construct.

First, between group differences were analysed across all four tests. In addition to reduced performance in the non-predictable ocular tracking test (Research Aim 4), a deficit was also found in the cervico-cephalic kinesthesia test in neck pain. However, no effect of neck pain was found on performance in either the predictable ocular tracking test or the cervical JPE test. These disparities suggest that either the latter two tests are measures of different underlying constructs, or that they were not sensitive to detecting differences between the neck pain and healthy control groups.

The second approach to evaluation of construct validity was to analyse correlation of performance in the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests with age, gender, cervical ROM, symptom duration and self-reported measures of pain and disability. Comparisons across tests indicated that different factors were associated with performance in each. This suggests that the constructs measured by each test are in turn influenced by different factors, which would not be expected if a common construct determined performance in all of the tests.

The third approach to evaluation of the construct validity of the tests was to analyse convergence in correlation between performance in the non-predictable and

predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests. Correlation between tests would suggest that performance was determined by one or more common underlying constructs. In healthy participants there was correlation between performance in all of the tests (excluding cervical JPE in the sagittal plane), supporting the likelihood of a common construct being measured. However in participants with neck pain, there was convergence in correlation between performance in the non-predictable and predictable ocular tracking tests and the cervico-cephalic kinesthesia test, there was disassociation (compared with findings in the healthy control group) whereby most cervical JPE measures were not correlated with any other test. These findings suggest firstly that in participants with neck pain constructs determining performance differ from those that determine performance in healthy participants, and secondly that in participants with neck pain constructs determining performance differ between the cervical JPE test compared with the non-predictable and predictable ocular tracking and cervico-cephalic kinesthesia tests. The assessment of the construct validity of the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests thus indicates that they do not all have construct validity for a single sensorimotor process. Previous reports of impairments in WAD and neck pain in the tests have been attributed to deficits in cervical spine proprioception. However the finding of lack of construct validity for a common sensorimotor process in the present study indicates that not all of the tests, if any, may be measures of cervical proprioception in neck pain.

Clinical implications of findings of the study are that people with mechanical neck pain may have impaired sensorimotor control of complex ocular and head and/or gaze control. These deficits however may not be the result of altered cervical spine proprioception. The specific tests where functional impairments were identified in

neck pain (i.e. the non-predictable ocular tracking and cervico-cephalic kinesthesia tests) may provide either a target for rehabilitation approaches (e.g. these tests could be included in rehabilitation exercise protocols) or a measure of outcome following treatments for neck pain, that should be investigated with interventional studies.

Further studies are also needed to identify the nature of constructs that underlie performance in the non-predictable and predictable ocular tracking, cervico-cephalic kinesthesia and cervical JPE tests and the processes that are impaired in mechanical neck pain, including the possible contribution of cognitive processes and vestibular adaptation.

This thesis provides the first investigation of, and report that individuals with mechanical neck pain have impaired smooth pursuit ocular movement when attempting to track a visual target following a non-predictable trajectory in 2-dimensions. It also provides the first detailed analysis of the relationship between several tests that have previously been proposed to measure cervical proprioception, with results indicating that this assumption may be incorrect.

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LIST OF APPENDICES

APPENDIX 1

SEARCH STRATEGY FOR MEDLINE AND EMBASE

Figure 1 Medline search strategy

Figure 2 EMBASE search strategy

Figure 1. Medline search strategy

#277	Add	Search **(#274) OR #276** Limits: **Humans, English**	740	12:28:51
#276	Add	Search **(#275) AND #258** Limits: **Humans, English**	174	12:13:53
#275	Add	Search **(((((#259) OR #260) OR #261) OR #262) OR #263) OR #266** Limits: **Humans, English**	16020	12:13:19
#274	Add	Search **(((((#266) OR #269) OR #270) OR #271) OR #272) OR #273** Limits: **Humans, English**	724	12:10:50
#273	Add	Search **(#268) AND #263** Limits: **Humans, English**	30	12:09:45
#272	Add	Search **(#268) AND #262** Limits: **Humans, English**	5	12:09:15
#271	Add	Search **(#268) AND #261** Limits: **Humans, English**	24	12:08:50
#270	Add	Search **(#268) AND #260** Limits: **Humans, English**	195	12:08:19
#269	Add	Search **(#268) AND #259** Limits: **Humans, English**	203	12:07:35
#268	Add	Search **(#267) OR #226** Limits: **Humans, English**	18154	12:06:39
#267	Add	Search **("Neck"[Mesh]) OR "Neck Pain"[Mesh]** Limits: **Humans, English**	16749	12:02:25
#266	Add	Search **"cervical proprioception" OR (cervical spine AND propriocept*) OR (neck AND proprioception)** Limits: **Humans, English**	661	11:44:53
#263	Add	Search **"proprioception test" OR "measure of proprioception" OR "measure proprioception"** Limits: **Humans, English**	1672	11:35:43
#262	Add	Search **"smooth pursuit neck torsion test"** Limits: **Humans, English**	5	11:33:49
#261	Add	Search **"repositioning test" OR "relocation test" OR "cervico-cephalic relocation" OR "repositioning error" OR "joint position error" OR "repositioning accuracy" OR "cervico-cephalic kinesthesia"** Limits: **Humans, English**	159	11:32:35
#260	Add	Search **propriocept* OR kinesthe* OR kinaesthe* OR "position sense"** Limits: **Humans, English**	8374	11:27:28
#259	Add	Search **("Proprioception"[Mesh]) OR "Kinesthesis"[Mesh]** Limits: **Humans, English**	13631	11:26:17
#258	Add	Search **(#255) NOT #257** Limits: **Humans, English**	7811	11:24:10
#257	Add	Search **"Case Reports" [Publication Type]** Limits: **Humans, English**	1113547	11:22:33
#255	Add	Search **(#251) NOT #254** Limits: **Humans, English**	9718	11:21:13
#254	Add	Search **"Congenital Abnormalities"[Mesh]** Limits: **Humans, English**	274974	11:20:49
#251	Add	Search **(#248) NOT #250** Limits: **Humans, English**	9879	11:18:55
#250	Add	Search **"Surgical Procedures, Operative"[Mesh]** Limits: **Humans, English**	1367544	11:18:15
#248	Add	Search **(#247) NOT #242** Limits: **Humans, English**	13273	11:13:45
#247	Add	Search **(#246) NOT #241** Limits: **Humans, English**	13777	11:11:52

#246	Add	Search **(#245) NOT #239** Limits: **Humans, English**	13943	11:11:02
#245	Add	Search **(#244) NOT #238** Limits: **Humans, English**	14005	11:10:36
#244	Add	Search **(#243) NOT #236** Limits: **Humans, English**	14225	11:10:09
#243	Add	Search **(#233) NOT #235** Limits: **Humans, English**	17399	11:09:38
#242	Add	Search **"Pregnancy"[Mesh]** Limits: **Humans, English**	384578	11:08:40
#241	Add	Search **"Cervix Uteri"[Mesh]** Limits: **Humans, English**	12621	11:07:48
#239	Add	Search **"Carotid Artery Injuries"[Mesh]** Limits: **Humans, English**	2430	11:06:47
#238	Add	Search **"Vertebral Artery"[Mesh] OR "Vertebral Artery Dissection"[Mesh]** Limits: **Humans, English**	4819	11:05:40
#236	Add	Search **"Neoplasms"[Mesh]** Limits: **Humans, English**	1521470	11:04:27
#235	Add	Search **"Fractures, Bone"[Mesh]** Limits: **Humans, English**	75826	11:03:58
#233	Add	Search **((((#224) OR #226) OR #229) OR #231) OR #232** Limits: **Humans, English**	18653	11:02:43
#232	Add	Search **"non-traumatic neck pain" OR "non traumatic neck pain" OR "idiopathic neck pain" OR "chronic neck pain" OR "acute onset neck pain"OR "acute neck pain"** Limits: **Humans, English**	533	11:01:14
#231	Add	Search **whiplash OR whiplash-associated OR "flexion extension injury" OR "flexion-extension injury* OR "flexion extension injuries" OR "flexion-extension injuries"** Limits: **Humans, English**	343	10:55:19
#229	Add	Search **(#227) AND #228** Limits: **Humans, English**	17192	10:50:51
#228	Add	Search **pain OR *algesia OR *algesic OR ache** Limits: **Humans, English**	334725	10:50:34
#227	Add	Search **neck OR cervical OR "cervical spine" OR cervicogenic OR cervicobrachial OR cervico-thoracic OR suboccipital** Limits: **Humans, English**	222257	10:49:52
#226	Add	Search **"Whiplash Injuries"[Mesh]** Limits: **Humans, English**	1813	10:47:48
#224	Add	Search **"Neck Pain"[Mesh]** Limits: **Humans, English**	3182	10:46:09

Figure 2. EMBASE search strategy

Ovid: Current Search History

Embase Classic+Embase 1947 to 2012 April 18

#	Searches	Results	Search Type
1	neck pain/	10073	Advanced
2	limit 1 to (human and english language)	8665	Advanced
3	whiplash injury/	3611	Advanced
4	limit 3 to (human and english language)	2337	Advanced
5	(neck or cervical or "cervical spine" or cervicogenic or cervicobrachial or cervicothoracic or suboccipital).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	408354	Advanced
6	limit 5 to (human and english language)	227961	Advanced
7	(pain or Salgesia or Salgesic or ache).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	697965	Advanced
8	limit 7 to (human and english language)	448945	Advanced
9	6 and 8	26306	Advanced
10	(whiplash or whiplash-associated or "flexion extension injur$" or "flexion-extension inju$").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	4156	Advanced
11	limit 10 to (human and english language)	2602	Advanced
12	("non-traumatic neck pain" or "non traumatic neck pain" or "idiopathic neck pain" or "chronic neck pain" or "acute onset neck pain" or "acute-onset neck pain" or "acute neck pain" or "subclinical neck pain").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	647	Advanced
13	limit 12 to (human and english language)	554	Advanced
14	2 or 4 or 9 or 11 or 13	27863	Advanced
15	fracture/	70396	Advanced
16	neoplasm/	207653	Advanced
17	artery dissection/	5383	Advanced
18	carotid artery/ or carotid artery injury/	44298	Advanced
19	uterine cervix/	22393	Advanced
20	pregnancy/	578700	Advanced
21	surgical technique/	252407	Advanced
22	congenital disorder/	72734	Advanced
23	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22	1228176	Advanced
24	14 not 23	24669	Advanced
25	neck/ or cervical spine/	66642	Advanced
26	limit 25 to (human and english language)	28221	Advanced
27	proprioception/ or kinesthesia/	10671	Advanced
28	limit 27 to (human and english language)	6733	Advanced
29	(proprioceptive$ or kinesthe$ or kinaesthe$ or "position sense").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	16916	Advanced
30	limit 29 to (human and english language)	9240	Advanced
31	("repositioning test" or "relocation test" or "cervicocephalic relocation" or "repositioning error" or "joint position error" or "repositioning accuracy" or "cervicocephalic kinaesthesia" or "proprioception test" or "measure of proprioception" or "measure proprioception").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	267	Advanced
32	31	267	Advanced
33	limit 32 to (human and english language)	215	Advanced
34	("smooth pursuit neck torsion" or "smooth pursuit test").mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	49	Advanced
35	limit 34 to (human and english language)	30	Advanced
36	28 or 30 or 33 or 35	9366	Advanced
37	14 or 26	51020	Advanced
38	37 not 23	44764	Advanced
39	36 and 38	348	Advanced

APPENDIX 2

STUDIES EXCLUDED FROM THE LITERATURE REVIEW

Table 1 Studies excluded from the literature review following screening of abstract or assessment of full text article

Table 1 Studies excluded from the literature review following screening of title & abstract or assessment of full text article

STUDY	EXCLUSION*	REASON FOR INELIGIBILITY
Anastasopoulos D, Nasios G, Mergner T, and Maurer C. Idiopathic spasmodic torticollis is not associated with abnormal kinesthetic perception from neck proprioceptive and vestibular afferences. J Neurol. 2003;250:546-55	abstract	participants - not mechanical neck pain
Armstrong,B.; McNair,P.; Taylor,D.Head and neck position sense. Sport Med 2008, 38 (2): 101-117	full text	study design-narrative review
Bagust J, Rix GD, and Hurst HC. Use of a Computer Rod and Frame (CRAF) Test to assess errors in the perception of visual vertical in a clinical settingGÇöA pilot study. Clinical Chiropractic 2005;8:134-9	abstract	outcome measure - perceived visual vertical
Burke JP, Orton HP, West J, Strachan IM, Hockey MS, and Ferguson DG. Whiplash and its effect on the visual system. Graefes Arch Clin Exp Ophthalmol 1992;230:335-9	full text	outcome measure - not SPNT test, clinical examination findings only
De Hertogh W, Vaes P, Beckwee D, van Suijlekom H, Duquet W, and Van Roy P. Lack of impairment of kinaesthetic sensibility in cervicogenic headache patients. Cephalalgia 2008;28:323-8	abstract	participants - not mechanical neck pain
Docherty S, Scharer R, Bagust J, and Humphreys BK. Perception of subjective visual vertical and horizontal in patients with chronic neck pain: A cross-sectional observational study. Man Ther 2012;17:133-8	abstract	outcome measure - perceived visual vertical
Fattori B, Borsari C, Vannucci G et al. Acupuncture treatment for balance disorders following whiplash injury. Acupunct.Electrother.Res 1996;21:207-17	abstract	outcome measure - posturography
Golomer E, Guillou E, Testa M, Lecoq C, and Ohlmann To. Contribution of neck proprioception to subjective vertical perception among experts in physical activities and untrained women. Neuroscience Letters 2005;381:31-5	abstract	outcome measure - perceived visual vertical
Grip H, Jull G, and Treleaven J. Head eye co-ordination using simultaneous measurement of eye in head and head in space movements: potential for use in subjects with a whiplash injury. J Clin Monit Comput 2009;23:31-40	full text	outcome measure - not SPNT test (eye fixation, saccades & head rotations)
Haavik H and Murphy B. Subclinical neck pain and the effects of cervical manipulation on elbow joint position sense. J Manipulative Physiol Ther 2011;34:88-97	abstract	outcome measure - elbow JPE, not cervical JPE

Table 1 continued

STUDY	EXCLUSION*	REASON FOR INELIGIBILITY
Haavik-Taylor H and Murphy B. Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. Clin Neurophysiol 2007;118:391-402.	abstract	outcome measure - somatosensory evoked potential
Hawk C, Cambron JA, and Pfefer MT. Pilot study of the effect of a limited and extended course of chiropractic care on balance, chronic pain, and dizziness in older adults. J Manipulative Physiol Ther 2009;32:438-47.	abstract	outcome measure - self-reported balance
Heikkila H, Johansson M, and Wenngren BI. Effects of acupuncture, cervical manipulation and NSAID therapy on dizziness and impaired head repositioning of suspected cervical origin: a pilot study. Man Ther 2000;5:151-7.	abstract	participants - no healthy control group
Hildingsson C, Wenngren BI, and Toolanen G. Eye motility dysfunction after soft-tissue injury of the cervical spine. A controlled, prospective study of 38 patients. Acta Orthop Scand 1993;64:129-32.	abstract	participants - no healthy control group outcome measure - not SPNT test (no neck torsion)
Hildingsson C, Wenngren BI, Bring G, and Toolanen G. Oculomotor problems after cervical spine injury. Acta Orthop Scand 1989;60:513-6.	full text	outcome measure - not SPNT test (no neck torsion)
Jull G, Falla D, Treleaven J, Hodges P, and Vicenzino B. Retraining cervical joint position sense: the effect of two exercise regimes. J Orthop Res 2007;25:404-12.	abstract	participants - no healthy control group
Kelders WP, Kleinrensink GJ, Van Der Geest JN et al. The cervico-ocular reflex is increased in whiplash injury patients. J Neurotrauma 2005;22:133-7.	abstract	outcome measure - cervico-ocular reflex
Kongsted A, Jorgensen LV, Leboeuf-Yde C, Qerama E, Korsholm L, and Bendix T. Are altered smooth pursuit eye movements related to chronic pain and disability following whiplash injuries? A prospective trial with one-year follow-up. Clin Rehabil. 2008;22:469-79.	full text	participants - no healthy control group
Kristjansson E and Treleaven J. Sensorimotor function and dizziness in neck pain: implications for assessment and management. J Orthop Sports Phys Ther 2009;39:364-77.	full text	study design-narrative review

Table 1 continued

STUDY	EXCLUSION*	REASON FOR INELIGIBILITY
Lee H, Nicholson LL, Adams RD, and Bae SS. Proprioception and rotation range sensitization associated with subclinical neck pain. Spine (Phila Pa 1976.) 2005;30:E60-E67.	full text	outcome measure - 'just noticeable' movement discrimination, not cervical JPE
Lee HY, Wang JD, Yao G, and Wang SF. Association between cervico-cephalic kinesthetic sensibility and frequency of subclinical neck pain. Man Ther 2008;13:419-25.	full text	participants - no healthy control group
Loose VD, Van Den OM, Burnotte F et al. Functional assessment of the cervical spine in F-16 pilots with and without neck pain.	full text	participants - unspecified neck pain classification
McNair PJ, Portero P, Chiquet C, Mawston G, and Lavaste F. Acute neck pain: cervical spine range of motion and position sense prior to and after joint mobilization. Man Ther 2007;12:390-4.	abstract	participants - no healthy control group
Montfoort I, Kelders WP, Van Der Geest JN et al. Interaction between ocular stabilization reflexes in patients with whiplash injury. Invest Ophthalmol Vis.Sci. 2006;47:2881-4.	abstract	outcome measure - not SPNT test (ocular reflexes)
Montfoort I, Van Der Geest JN, Slijper HP, De Zeeuw CI, and Frens MA. Adaptation of the cervico- and vestibulo-ocular reflex in whiplash injury patients. J Neurotrauma 2008;25:687-93.	abstract	outcome measure - not SPNT test (ocular reflexes)
Oddsdottir GL and Kristjansson E. Two different courses of impaired cervical kinesthesia following a whiplash injury. A one-year prospective study.Manual Therapy. 17 (1) (pp 60-65), 2012. Date of Publication: February 2012.	full text	participants - no healthy control group
Oosterveld WJ, Kortschot HW, Kingma GG, de Jong HA, and Saatci MR. Electronystagmographic findings following cervical whiplash injuries. Acta Otolaryngol. 1991;111:201-5.	full text	outcome measure - not SPNT test (visual suppression test)
Palmgren PJ, Sandstrom PJ, Lundqvist FJ, and Heikkila H. Improvement after chiropractic care in cervico-cephalic kinesthetic sensibility and subjective pain intensity in patients with nontraumatic chronic neck pain. J Manipulative Physiol Ther 2006;29:100-6.	abstract	participants - no healthy control group

T**able 1 continued**

STUDY	EXCLUSION*	REASON FOR INELIGIBILITY
Revel M, Andre-Deshays C, and Minguet M. Cervico-cephalic kinesthetic sensibility in patients with cervical pain. Arch Phys Med Rehabil. 1991;72:288-91.	full text	participants - unspecified neck pain classification
Revel M, Minguet M, Gregoy P, Vaillant J, and Manuel JL. Changes in cervico-cephalic kinesthesia after a proprioceptive rehabilitation program in patients with neck pain: a randomized controlled study. Arch Phys Med Rehabil. 1994;75:895-9.	abstract	participants - no healthy control group, unspecified neck pain classification
Rogers RG. The effects of spinal manipulation on cervical kinesthesia in patients with chronic neck pain: a pilot study. J Manipulative Physiol Ther 1997;20:80-5.	abstract	participants - no healthy control group
Roijezon U, Bjorklund M, Bergenheim M, and Djupsjobacka M. A novel method for neck coordination exercise--a pilot study on persons with chronic non-specific neck pain. J Neuroeng.Rehabil. 2008;5:36.	abstract	participants - no healthy control group outcome measure - novel head control task
Sterling M, Jull G, and Kenardy J. Physical and psychological factors maintain long-term predictive capacity post-whiplash injury.Pain. 122 (1-2) (pp 102-108), 2006. Date of Publication: May 2006.	full text	participants - no healthy control group
Sterling M, Jull G, Vicenzino B, Kenardy J, and Darnell R. Physical and psychological factors predict outcome following whiplash injury.Pain. 114 (1-2) (pp 141-148), 2005. Date of Publication: March 2005.	full text	participants - no healthy control group
Sterling M. Kinaesthetic exercise does not improve outcome (or kinesthesia) in patients with acute whiplash. Aust J Physiother 2001;47:67.	abstract	participants - no healthy control group
Taimela S, Takala EP, Asklof T, Seppala K, and Parviainen S. Active treatment of chronic neck pain: a prospective randomized intervention. Spine (Phila Pa 1976.) 2000;25:1021-7.	abstract	participants - no healthy control group outcome measure - not eligible (ROM & pain pressure threshold)
Tjell C, Tenenbaum A, and Sandstrom SÃ. Smooth Pursuit Neck Torsion Test-A Specific Test for Whiplash Associated Disorders? Journal of whiplash and related disorders 2002;1:9-24.	abstract	participants - no healthy control group

Table 1 continued

STUDY	EXCLUSION*	REASON FOR INELIGIBILITY
Treleaven J, Clamaron-Cheers C, and Jull G. Does the region of pain influence the presence of sensorimotor disturbances in neck pain disorders?Manual Therapy. 16 (6) (pp 636-640), 2011. Date of Publication: December 2011.	full text	participants - no healthy control group
Treleaven J. Sensorimotor disturbances in neck disorders affecting postural stability, head and eye movement control. Man Ther 2008;13:2-11.	full text	study design-narrative review
Treleaven J. Sensorimotor disturbances in neck disorders affecting postural stability, head and eye movement control--Part 2: case studies. Man Ther 2008;13:266-75.	abstract	participants - no healthy control group
Uthaikhup S, Sterling M, and Jull G. Cervical musculoskeletal impairment is common in elders with headache.Manual Therapy. 14 (6) (pp 636-641), 2009. Date of Publication: December 2009.	abstract	participants - not mechanical neck pain
Van den Oord MH, De L, V, Sluiter JK, and Frings-Dresen MH. Neck strength, position sense, and motion in military helicopter crew with and without neck pain. Aviat.Space Environ.Med 2010;81:46-51.	full text	participants - unspecified neck pain classification
Wenngren BI, Pettersson K, Lowenhielm G, and Hildingsson C. Eye motility and auditory brainstem response dysfunction after whiplash injury. Acta Otolaryngol. 2002;122:276-83.	abstract	participants - no healthy control group

*Reason for exclusion from review 1 is indicated. None of these studies analysed association between eligible outcome measures, thus did not meet inclusion citeria for review 2

APPENDIX 3

LITERATURE REVIEW DATABASE

Table 1. Evidence Catalogue for Review 1

Table 2. Evidence Catalogue for Review 2

Table 1. Evidence Catalogue for Review 1

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Armstrong 2005[58] **Focus:** Investigation of cervical JPE in WAD/control groups. Evaluation of effect of cranio-cervical flexion on cervical JPE **Study design:** Mixed (cross-sectional & randomised longitudinal) **Participants:** • **N:** 23 whiplash, 23 controls • **Age/gender:** Mean(SD) 33.9(12.1), 41.2(11.9). female/male 15/8, 13/10 • **Inclusion:** Mild-moderate disability WAD II & III, (mean NDI 24/50) . Healthy controls	**Outcome measurement:** • **JPE**: Head-to-neutral & mid-range head-to-target relocation in flexion/extension, L/R rotation (AE & VE) • **Other:** ROM**,** patient-specific functional scale(PSFS), pain scale & NDI • **Intervention:** Single cranio-cervical flexion training session (not relevant to review 1) • **Method:** Polhemus Fastrak, 3 trial repeats **Eligibility criteria:** Clearly described inclusion/exclusion. Unclear how controls were recruited **Measurement of exposure/outcome :** Clear comparability between groups **Prognostic imbalance:** Comparable between WAD & controls (cross-sectional analysis) **Other:** (longitudinal study not relevant to review 1- no blinding described, randomization not described, v small sub-groups with no characteristics presented, same-day post-intervention measures)	• No baseline JPE difference between groups • No effect of cranio-cervical flexion training • Some significant differences in ROM between WAD/controls (P<.05)

Summarised details of focus, design, methods and results are provided for each included study. Aspects of design and method relevant to subsequent appraisal of risk of bias (according to GRADE criteria for observational studies[1]) and limitations in each study are also specified

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Cheng 2010[189] **Focus:** Evaluation of JPE and correlation to EMG in young adults with non-traumatic 'work-related' neck pain **Study design:** Cross-sectional **Participants:** • **N:** 12 non-traumatic neck pain, 12 controls • **Age/gender:** Mean(SD) 25.4(2.1)/24.9(1.8), gender matched • **Inclusion:** Mild-moderate neck pain 4.4(2.2) years duration. Healthy controls	**Outcome measurement:** • **JPE**: Head-to-neutral relocation in flexion/extension (CE, VE, RMSE) • **Other:** Neck flexor/extensor EMG(3 second MVCs x2) • **Method**:Electrogoniometer. 3 repeats of each. Eyes open **Eligibility criteria:** Selected from largely comparable populations **Measurement of exposure/outcome**: Examiners not blinded, method minimises examiner measurement bias **Prognostic imbalance:** Comparable age/gender mix. Potential imbalance - work experience described for neck pain group, not controls. Vision not compared between groups, might influence JPE (eyes open) **Other:** Unclear validity as JPE tested with eyes open	• Sig. JPE difference (CE & RMSE, not VE) between groups and repositioning directions (P<.05) • Altered EMG patterns between groups

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Dispenza (2011)[193] **Focus:** Evaluation of SP and saccades in WAD (of different durations) and controls **Design:** Cross-sectional **Participants:** • **N:** 37 WAD, 23 healthy controls (WAD sub-groups 11 1-2 months, 11 2-6 months, 11 7-12 months), 23 healthy controls • **Age/gender:** Mean(range) 36.5(23-53), 3.4(19-49). (WAD sub-groups mean 34.1, 37.6, 37.6.) female/male 14/23, 11/12 (Sub-group gender balance not specified) • **Inclusion:** WAD > 12 months	**Outcome measurement:** • **SPNT:** Regular horizontal visual target, 18° sec^{-1}. Analysed SP gain in neutral, L and R torsion • **Other:** Saccade tests .4 Hz +/- 20 degrees horizontally • **Method:** Video-oculography **Eligibility criteria:** Appears adequate. Recruitment of control group not described, but inclusion/exclusion criteria adequate. Dosnt mention eye/visual function criteria. Used of vestibular testing as an exclusion criterion. Excluded 3 WAD with BPPV & 1 with hearing loss. 3 exclusions from control group were not explained **Measurement of exposure/outcome:** Comparable between groups. Measurement methods minimise bias, however raw data processing is not described **Prognostic imbalance:** Unclear how controls were recruited	• No sig. differences between groups* in any of the test parameters *Unclear whether differences were analysed across sub-groups since only t-test described in analysis method

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Feipel (2006)[181] **Focus:** Evaluation of 3-D poprioception in whiplash/controls **Study design:** Cross-sectional **Participants:** • **N:** 29 whiplash, 26 healthy controls • **Age/gender:** Mean(SD) 37(14)/35(11), 62%/54% female • **Inclusion:** Moderate-severe WAD (RTA or sports injury), 71% were WADIII.	**Outcome measurement:** • **JPE:** Head-to-neutral flex/extension & mid-range relocation L/R rotation (50 degrees), combined axial rotation/ipsilat flexion (50/20 degrees) (AE and maximal overshoot) • **Method**: Electrogoniometer.Head-to-neutral 4 repeats, eyes open and eyes closed. Head-to-target (mid-range) 3 repeats, eyes closed • **Other**: ROM **Eligibility criteria:**Recruitment method not clearly described. Inclusion/exclusion criteria appear adequate. **Measurement of exposure/outcome:** Clear comparability between groups. Examiners not blinded but method minimises examiner bias in measurements **Prognostic imbalance:** Achieved through inclusion/exclusion criteria. Comparable age & gender mix, clearly evaluated	• WADIII sig. greater head-to-neutral JPE than controls (P =.009) • WAD sig. > head-to-target rot/lat flex JPE than controls (P =.04) • Eyes closed sig. >JPE than eyes open (P =.03) • < JPE to neutral than remote targets • >JPE in primary plane of motion • Sig < flex/ext ROM in WAD

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Gimse (1993)[194] **Focus:** Comparison of reading & SP gain in WAD and healthy controls **Design:** Cross-sectional, age & gender matched control group **Participants:** • **N:** 26 WAD, 26 healthy controls • **Age/gender:** Matched control group • **Inclusion:** Unclear	**Outcome measurement:** • **SPNT:** Sinusoidal stimulus 20° sec^{-1}, .2 Hz. SP gain with and without 45° neck torsion analysed • **Other:** Eye movements during reading • **Method:** EOG **Eligibility criteria:** Clearly described. Absence of vestibular pathology confirmed with otoneurological testing **Measurement of exposure/outcome:** Not clear how much manual data processing there was **Prognostic imbalance:** Appears fair	• Sig. impaired reading in WAD • Sig impaired SPgains in neutral & with neck torsion in WAD

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Grip (2007)[68] **Focus:** Examination of variations in axis of motion, along with cervical JPE in WAD, non-trauma neck pain & controls. Also evaluation of association with pain intensity and fear avoidance beliefs **Study design:** Cross-sectional **Participants:** • **N:** 21 non-specific neck pain, 22 whiplash, 24 healthy controls • **Age/gender:** Mean(SD) 49(16), 49(15), 50(18), female/male 14/7, 17/5, 16/8 • **Inclusion:** > 3 months duration neck pain, non-trauma or WAD I or II, healthy controls	**Outcome measurement:** • **JPE:** Head-to-target **(**mid-range) flex/ext (25 degrees), L/R rot (30 degrees) (AE,CE,VE) • **Method:** ProReflex system. 5 repeats each, interspersed sequence • **Other:** Axis of motion analysed . All completed pain VAS[a] and perceived health EQ-VAS. Neck pain completed Neck pain and disability questionnaire, Disability rating and FABQ[b] **Eligibility criteria:** Clear explanation of recruitment and confirmation of neck pain or WAD. Inclusion criteria given but no specification of exclusions **Measurement of exposure/outcome:** Clear comparability between groups. Examiners not blinded but method minimises examiner bias **Prognostic imbalance:** Comparable age and gender mix. Dosnt specify exclusions e.g. Vestibular problem etc	• WAD sig > flexion JPE(CE) than controls (P =.04) • No other JPE differences • Neck pain groups axis of motion more inferior in flex, ext (P<.05), more variable in direction for left rotation (P =.01 and .05) • FABQ no difference between neck pain groups. No correlation with other outcomes

[a]Visual Analogue Scale, [b]Fear Avoidance Belief's Questionnaire

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Heikkila (1996)[150] **Focus:** Evaluated JPE in WAD compared to controls (also case-series investigating the effect of a rehabilitation programme on JPE) **Study design:** Cross-sectional (and case-series) **Participants:** • **N:** 14 whiplash, 34 healthy controls (for case-series n = 8 whiplash) • **Age/gender:** Range/mean 23-47/35, 26-53/36; female/male 7/7, 21/11 • **Inclusion:** WAD > 6 months duration	**Outcome measurement:** • **JPE:** Head-to-neutral following L & R rot, flex & ext (Global error, horizontal & vertical error) • **Method:** Laser pointer. 10 repeats each direction.WAD group tested during 1st rehab week & after 6 weeks • **Other:** Pain intensity (VAS[a]) **Eligibility criteria:** Clearly described WAD group recuitment and characteristics, little explanation for control group **Measurement of exposure/outcome:** Comparable between groups. Examiners not blinded. Manual method more likely to introduce examiner bias **Prognostic imbalance:** Comparable age and gender mix. Dosnt specify exclusions for either group e.g. Vestibular problem etc **Other notes:** Heterogenous WAD symptoms (include vertigo, HA, radicular Sx, tiredness & LBP)	• WAD sig. > proportion errors >4cm (P<.0001) • WAD sig. < accuracy JPE all directions (P<.001) • Following rehab WAD sig. Improved R rot & extension JPE • No correlation between JPE & pain intensity (VAS) No difference in VAS pre-post rehab)

[a]Visual Analogue Scale

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Heikkila (1998)[51] **Focus:** Investigation of JPE, ROM & occular motor function in WAD **Study design:** Cross-sectional **Participants** • **N:** 27 whiplash, 39 healthy controls (25 controls for occular motor function tests) • **Age/gender:** Range/mean 18-66/38.3, 26-53/35 (25-40/34); female/male 14/13, 24/15, (unspecified) • **Inclusion:** WAD II or III (RTAs) attended emergency unit for acute neck strain 1-2 years previously. (7 were pain-free). Healthy controls	**Outcome measurement:** • **JPE:** Head-neutral L & R rot, flex & ext (Global error, horizontal & vertical error) • **Other:** Smooth pursuit test without torsion (horizontal SP gain & no. superimposed saccades (20degrees sec & 30 degrees sec)) & voluntary saccades to 30,40 & 50 degrees of midline (accuracy, latency, peak velocity) • **Method:** CROM instrument, 10 repeats (JPE). EOG (occulomotor) **Eligibility criteria:** All had sustained whiplash, some asymptomatic by the time of study. Poorly defined control group, recruitment method not described. Different controls for different tests **Measurement of exposure/outcome:** Comparable between groups. Examiners not blinded **Prognostic imbalance:** Mean age comparable, unbalanced gender mix. Other factors unclear as recruitment source not explained	• WAD sig. > JPE L/R rot, flex, ext (P<.001) • dizziness &/or radiculopathy > JPE compared to WAD without these • pathologic SP & Saccades reported for WAD group (no results given for comparison to control group) • Sig association between saccades &/or SP dysfunction & JPE (P<.007) • Sig. correlation between SP/saccades & active ROM • in WAD age sig. correlated with JPE not in control group • Association between SP/saccades with age & gender reported

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Hill 2009[184] **Focus:** Comparison of WAD with & without dizziness with controls in JPE. Also compares different measures of error **Study design:** Cross-sectional **Participants:** • **N:** 50 WAD with dizziness, 50 WAD without dizziness, 50 healthy controls • **Age/gender:** Mean(SD) 35.5(8.1), 35.0(9.5) , 29.5(8.3). ?gender • **Inclusion:** Chronic WAD > 3 months	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot & ext (AE, RMSE, CE, VE) • **Method:** Polhemus Fastrak, 3 repeats of each. Analysed RMSE, AE, CE & VE **Eligibility criteria:** Clearly described recruitment, group allocation and inclusion/exclusion criteria **Measurement of exposure/outcome:** Bias minimised **Prognostic imbalance:** Controlled for possible age imbalance with analysis method **Other notes:** Data set was from a previous study (Treleaven et al, 2006)	**Results:** • WAD-dizziness sig. > JPE than healthy controls (P<.05 or <.01) for R rot (AE, RMSE, L rot (CE (AE, RMSE), ext (CE) • WAD-no dizziness sig. > JPE than healthy controls (P<.05) for R rot (CE) & ext (CE) • WAD-dizziness sig. > JPE than WAD-no dizziness (P≤ .01) for R rot (AE, RMSE) & L rot (AE, RMSE) • No single error measurement uniquely detected or defined differences between WAD & controls

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Kongsted (2007)[101] **Focus:** Evaluation of smooth pursuit in long-lasting WAD, compared with controls **Design:** Cross-sectional **Participants:** • **N:** 34 WAD, 60 healthy controls • **Age/gender:** Median(range) 28 females 38(20-51) and 6 males 46(44-51), 33 females 40(18–63) and 27 males 40(22–62). • **Inclusion:** WAD > 6 months	**Outcome measurement:** • **SPNT:** Sinusoidal stimuls .2 Hz, maximum velocity 37° sec^{-1}. Measured SP gain and SPNT difference. Chin stabilised, torsion angle generated muscle tension but pain-free • **Method:** EOG. Automated data processing. Tests performed over 2 sessions **Eligibility criteria:** Well-established, full list of inclusion/exclusion citeria presented **Measurement of exposure/outcome:** Adequately defined. Examiner bias unlikely due to computerized data processing **Prognostic imbalance:** Clear description of non-attendees between groups. Characteristics appear comparable. Analysis adjusted for age and gender	• No sig. Differences in SP gain or SPNT differences between WAD and healthy controls (P>.05) • No sig. association with pain severity, duration, symptoms of dizziness or headaches (P>.05)

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Kristjansson (2003)[52] **Focus:** Comparison of head relocation accuracy in WAD, non-trauma neckpain and asymptomatic controls using neutral head repositioning and more complex predetermined positions **Design:** Cross-sectional **Participants:** • **N:** 22 WAD, 20 non-trauma neck pain, 21 healthy controls • **Age/gender:** Mean(SD) 33.4(1.6), 30(9.1), 26.9(6.4). (male/female) 11/11, 11/9, 10/11 • **Inclusion:** Neck pain duration 3-48 months	**Outcome measurement:** • **JPE:** 5 tests – 1)head-to-neutral L/R rot 2)Head-to-target (30°) L/R rot. 3)Head repositioning following passive trunk rotation (30°). 4)Head-to-neutral relocation following figure-of-eight motion. 5)Figure-of-eight movement test (AE) • **Method:** Polhemus FASTRAK used. Repeats test 1) ?10, 2) 3, 3)?, 4)3, 5) 2x3 figure-eights **Eligibility criteria:** Clearly described recruitment, group allocation and inclusion/exclusion criteria **Measurement of exposure/outcome:** Comparable between groups. Examiner blinded **Prognostic imbalance:** A little disparity in ages. Gender mix balanced well. Difference in pain/disability between non-trauma and WAD groups	• Sig. > head-to-neutral JPE WAD & non-trauma neck pain than controls (P =.001) • Nontrauma/WAD JPE difference not significant (P =.07). • All other JPE tests no sig between-groups differences

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Kristjansson (2004)[60] **Focus:** Investigates reliability of cervico-cephalic kinesthesia ('the fly') test & descrimnative ability between WAD & controls **Design:** Cross-sectional (described as case-control) **Participants:** • **N:** 20 chronic WAD, 20 healthy controls • **Age/gender:** Range 19-49 (groups not compared). Females only • **Inclusion:** WAD I or II, 6 months-6 years duration	**Outcome measurement:** **Cervico-cephalic kinesthesia: H**ead-tracking of visual target following unpredictable trajectory • **Method:** Polhemus FASTRAK used. 3 repeats each of 3 movements patterns (20,30 and 40 seconds). Mean absolute error calculated **Eligibility criteria:** Group allocation reasonably described – 'convenience sample' **Measurement of exposure/outcome:** Comparable. Minimal likelihood of examiner bias **Prognostic imbalance:** No data presented on age ranges in each group. Fair exclusion criteria, but some details not specified e.g. Eyes/vision normal?	• WAD sig. > error (P =.02) • Acceptable between-day reliability (ICC = .6 -.81). better among WAD group

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Kristjansson (2010)[80] **Focus:** Comparison of WAD, non-trauma neck pain & controls in the 'fly' test (as an evaluation of validity), also evaluated reliability **Design:** Cross-sectional **Participants:** • **N:** 18 WAD, 18 non-trauma neck pain, 18 healthy controls • **Age/gender:** Mean(SD) 35.5(11.9), 38.0(8.3), 32.2(1.9). male/female 2/16, 7/11, 10/8 • **Inclusion:** Neck pain groups VAS min 3 in past weeks, 6-25 months duration. WADII	**Outcome measurement:** • **Cervico-cephalic kinesthesia:** Head-tracking of visual target following unpredictable trajectory • **Method:** Polhemus Fastrak used. Easy, medium & difficultpatterns, 3 repeats of each. Test-retest 1 week apart **Eligibility criteria:** Appears adequate. Inclusion/exclusion criteria rather broadly described **Measurement of exposure/outcome:** Comparable betwen groups, minimal likelihood of experimenter bias **Prognostic imbalance:** In neck pain groups disparity in pain severity. Recruitment sources are not described. Some gender imbalance that is not controlled for	• ANOVA indicated sig. differences between patterns within each group & between groups (all P<.001) • ICC = .53 -.82

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Loudon (1997)[145] **Focus:** Comparison of JPE between WAD and controls. Also evaluated reliability **Design:** Cross-sectional **Participants:** • **N:** 11WAD, 11 healthy controls • **Age/gender:** Range/mean(SD) 28-57 42(8.7); 28-57, 43(1.3). male/female 2/9, 'matched' controls • **Inclusion:** WAD 3-24 months	**Outcome measurement:** • **JPE:** Head-to-target (30° and 50°) L/R rotation, (20°) L/R lateral flexion (measured angle of active rotation from 0° to target) • **Method:** CROM, manual reading of measurement. 3 repeats of each. Eyes closed. Manually moved head to target angle, then to 0°. Intra- and inter- examiner test-retest (unspecified method) **Eligibility criteria:** Adequately defined **Measurement of exposure/outcome:** High risk of bias with manual measurement system **Prognostic imbalance:** Poorly defined exclusion criteria	• ANOVA (trial no. and position) indicated sig. Differences between groups (P<.05) • Newman-Keuls indicated sig. greater errors in WAD for 30degree rotation & 20degree lat flexion (P unspecified). Not sig. for 50 degree rotation • Tendency to overshoot. • Worsening across repeated trials (no reorienting) • ICC (intra- and inter-) = .972-.985

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Madeleine (2004)[140] **Focus:** Comparison between WAD and controls of posture, ROM and JPE with experimentally altered sensory conditions **Design:** Cross-sectional. Pilot study **Participants:** • **N:** 11 WAD, 11 healthy controls • **Age/gender:** Mean(SD) 33.3 (6.7), 33.1(6.8). Female/male 7/4, 7/4 ('matched') • **Inclusion:** Chronic WAD > 6 months	**Outcome measurement:** • **JPE:** Head-to-target (30° and 50°) L/R rotation, (20°) L/R lateral flexion (unspecified error measure) • **Other**: Cervical ROM, posturography +/- achilles vibration & eyes open/closed (healthy controls +/- experimentally induced algesia (trapezius saline injection)) • **Method:** Gravity goniometer. JPE 3 repeats. **Eligibility criteria:** Adequately defined **Measurement of exposure/outcome:** Opportunity for experimenter bias in JPE measures **Prognostic imbalance:** Little description of recruitment or inclusion/exclusion criteria for controls. Comparable age/gender	• 'Tendency' to greater JPE in WAD • No descriptive or statistical results presented for JPE • Sig. reduced cervical ROM (P =.003-<.001) • Sig. greater postural activity in patients (P =.009-<.001) • No sig. effect of experimentally induced algesia (posturography only evaluated)

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Palmgren (2009)[164] **Focus:** Evaluation of JPE & postural balance in chronic non-trauma neck pain – pilot study **Design:** Cross-sectional **Participants:** • **N:** 13 non-trauma neck pain, 16 healthy controls • **Age/gender:** mean(SD) 38(7.4), 35.1(5). Female/male 13/2, 6/10 • **Inclusion:** Neck pain > 3 months, no neck trauma	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot, L/R lat flex, flex/ext (accuracy in mm) • **Method:** Manual laser method, 10 repeats. Experimenter blinded to group **Eligibility criteria:** Well defined exclusion criteria **Measurement of exposure/outcome:** Adequately defined. Examiner blinded to group **Prognostic imbalance:** Gender imbalance. Not clear who the control group were	• Sig. JPE difference only for flexion motion ($p<.05$) • Sig. difference for 1 out of 8 parameters in posturography (elipse area in tandem stance with eyes closed) ($p<.05$)

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Pereira (2008)[98] **Focus:** Evaluation of self-reported diving habits, sensorimotor and psychologic features after WAD & of relationships between these **Design:** Cross-sectional **Participants:** • **N:** 30 WAD, 30 healthy controls • **Age/gender:** Mean(SD) 33.8(9.4), 25.6(5.1). females% 73, 73 • **Inclusion:** > 3months duration, NDI mean(S) 13.1(19)	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot & ext (AE?) • **SPNT:** Sinusoidal stimulus 20° sec^{-1}, .2 Hz. SP gain & SPNT difference. <45° torsion • **Other:** Cervical ROM, driving habits questionnaire, NDI[a], GHQ-28[b], IES-R[c], TSK[d] questionnaires • **Method:** JPE measured with FASTRAK, 3 repeats. SPNT measured with EOG **Eligibility criteria:** Well defined exclusion/inclusion criteria **Measurement of exposure/outcome:** Adequately defined. Minimal examiner bias likelihood **Prognostic imbalance:** Clearly described recruitment and characteristics. Was an age & driving experience differencethat was not controlled for in analysis	• Left JPE sig *reduced* in WAD (p =.05) • SPNT sig greater in WAD (p<.01) • ROM (all) sig decreased in WAD (p<.01) • WAD sig more driving difficulty (p<.01) • Correlation - not sig between driving and JPE, SPNT or ROM performance • Correlation sig between driving and NDI, GHQ-28 and IES-R scores (all r=.52, p<.01)

[a]Neck Disability Index, [b]28-item General Health Questionnaire, [c]Impact of Events Scale-Revised, [d]Tampa Kinesophobia Scale

T**able 1 continued**

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
<u>Pinsault (2008)</u> **Focus:** Evaluation of whether vestibular function influences performance in the cervical JPE test by comparison between chronic non-trauma neck pain, bilateral labyrinthine-defective and healthy control participants **Design:** Cross-sectional **Participants:** • **N:** 7 labyrinthine-defective, 7 non-trauma neck pain, 7 healthy controls • **Age/gender:** Mean(SD) 67(15), 56(9), 64(12). Males/females 4/3, 3/4, 4/3 • **Inclusion:** Neck pain > 3 months	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot (AE,VE) • **Method:** Laser pointer, video capture of data, automated processing. 10 repeats each **Eligibility criteria:** Well-defined inclusion/exclusion criteria. Recruitment not described. **Measurement of exposure/outcome:** Less likelihood of experimenter bias in outcome measurement with this method. Clearly confirmed labyrinthine defect. Scant description of neck pain confirmation/characteristics **Prognostic imbalance:** Younger neck pain group (however greater errors found are in opposite direction to likely effect of a younger group). Unclear where they were all recruited from.	• Horizontal error sig greater for non-trauma neck pain versus either controls or labyrinthine-defective group (AE p<.01, VE p<.05) • Global AE sig greater for neck pain than either of other groups (p<.05) • No differences between controls/labrinthine patients

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Prushansky (2004)[99] **Focus:** Evaluation of saccade and SP tests to differentiate WAD from healthy controls **Design:** Cross-sectional **Participants:** • **N:** 26 WAD, 23 healthy controls • **Age/gender:** Mean(SD) 4.3(1.6), 34.2(13.7). females/males 16/10, 16/7 • **Inclusion:** WAD II or III, > 6 months	**Outcome measurement:** • **SPNT:** Horizontal target motion (waveform not specified), target velocity .75 m/sec (not specified in degrees sec^{-1}). Measured SP gain and SPNT difference • **Other:** horizontal saccades with small (5–19˚) and large (20–30˚) amplitudes (peak velocity, accuracy & latency). Neutral and torsion positions • **Method:** EOG. 30° neck torsion. Head supported by examiner **Eligibility criteria:** Fair, not fully described how they were recruited **Measurement of exposure/outcome:** Method of raw data processing not described. Cant exclude bias if it was done manually **Prognostic imbalance:** No inclusion/exclusion criteria re the eye or vision. Slight age imbalance between groups controlled for in analysis	• Sig reduced SP gain in WAD compared to controls (p =.01) & sig lower consistency (coefficient of variation) (p =.0005) • No sig difference in SPNT difference between groups • Saccades greater latencies for WAD group (p =.001), no difference between neck positions

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
<u>Rix (2001)</u> **Focus:** Comparison of cervical JPE between chronic non-traumatic cervical spinal pain and healthy controls **Design:** Cross-sectional (described as prospective) **Participants:** • **N:** 11 non-traumatic neck pain, 11 healthy controls • **Age/gender:** Mean(SD) 41.1(13.3), 39.3(1.3). men/women = 6/5, 5/6 • **Inclusion:** Non-trauma neck pain > 7 weeks (3 months-5 years), daily or continuous pain, intensity 11-point [a]NRS 5.1(1.9)	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot, flex/ext (global error) • **Other:** Cervical ROM • **Method:** Cervical JPE measured with laser pointer, 10 repeats. ROM measured with CROM instrument **Eligibility criteria:** Adequately described inclusion/exclusion criteria, reasonably described recruitment **Measurement of exposure/outcome:** High risk of bias with manual measurement method. No blinding described **Prognostic imbalance:** Age & gender balanced. Although dizziness/vertigo is an exclusion criterion for controls, this is not specified for the neck pain group	• Greater global JPE in neck pain following flexion (p =.03) • No other sig differences • No sig correlations between JPE & age or any pain characterisitcs (intensity, frequency, localisation, painful movement etc)

[a]11-point Numeric Rating Scale

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Sjolander (2008)[182] **Focus:** Comparison of cervical motion and cervical JPE between neck pain and healthy control groups (WAD and insidious onset sub-groups) **Design:** Cross-sectional **Participants:** • **N:** 7 WAD, 9 insidious onset neck pain, 16 healthy controls • **Age/gender:** Mean(SD) 45(11), 40(9), 41(9) - mostly females • **Inclusion:** Insidious onset neck pain or WAD > 6 months duration	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot (CE, VE) • **Other:** Cervical ROM, ROM variability, peak velocity of motion, smoothness of movement (jerk index) • **Method:** Polhemus FASTRAK, 8 repeats for JPE **Eligibility criteria:** Adequately described recruitment and inclusion/exclusion criteria **Measurement of exposure/outcome:** Clear measures to ensure groups allocation correct. Method minimises experimenter bias through blinding & use of FASTRAK **Prognostic imbalance:** Some chronic neck pain participants had dizziness, but this was an exclusion criterion for control group. Age, weight, height, pain characteristics etc all demonstrated comparability between groups (ANOVAs)	• MANCOVA sig VE difference across groups ($p<.01$). Covariates (ROM) not sig • VE following R rot 1-way ANCOVA sig ($p<.01$), with covariate R rot ROM sig ($p<.05$). Sig difference between controls & both neck pain groups • VE following L rot ANCOVA sig ($p<.01$) but L rot ROM covariate not sig. Sig difference between controls & WAD • Neck pain groups both had sig greater jerk index & ROM variability than controls. • No differences between WAD & idiopathic neck pain in any test

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Sterling (2003)[165] **Focus:** Evaluation of development of motor system dysfunction over time following whipash injury **Design:** Prospective longitudinal study **Participants:** • **N:** 66 WAD, 20 healthy controls • **Age/gender:** Mean(SD) 36.27(12.69), 4.1(13.6). females/males 45/21, 12/8 • **Inclusion:** Whiplash injury < 1 month previously	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot & ext (AE) • **Others:** Cervical ROM, superficial nck flexor surface emg, NDI[a] and TSK[b] scores • **Method:**JPE (and ROM) measured with Polhemus FASTRAK, 3 trial repeats. Measurements at 1, 2 and 3 months. WAD group subdivided at 3 months into recovered, mild or moderate-severe symptoms (based on NDI score) **Eligibility criteria:** Very clearly defined **Measurement of exposure/outcome:** Clearly defined. Minimal risk of experimenter bias with electronic method and blinding **Prognostic imbalance:** Very comparable gender & ages, clearly specified & included as covariates in analysis to control for imbalance. No criteria for other disease specified e.g. Vestibular, neurological **Follow-up:** No loss to follow up, all groups re-tested at same intervals	• Sub-groups mean(SD) NDI at 3 months - recovered 3.0(3.1), mild group 18.5(5.2), moderate/severe 47.9(12.2) • Moderate/severe symptom group had sig greater R rot JPE at 1 month than all other groups, that was unchanged at 3 months (p =.002) • All WAD groups had decreased ROM & increased emg at 1 month. Emg changes persisted in all, ROM loss persisted only in moderate/severe group

[a]Neck Disability Index, [b]Tampa Kinesophobia Scale

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Sterling 2004[53] **Focus:** Characterisation of acute WAD sub-groups based on sensory and motor dysfunction **Design:** Cross-sectional **Participants:** • **N:** 80 WAD, 20 healthy controls • **Age/gender:** Mean(SD) 33.5(14.7), 39.5(14.6). females/males 56/24, 11/9 • **Inclusion:** WADII or III, < 1 month post-collision	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot & ext (AE) • **Other:** Active ROM, superfical neck flexor emg, pressure pain threshold, thermal pain thresholds, brachial stretch provocation, NDI, GHQ-28, TSK • **Method:** JPE (and ROM) measured with Polhemus FASTRAK, 3 trial repeats **Eligibility criteria:** Very clearly defined **Measurement of exposure/outcome:** Clearly defined. Minimal risk of experimenter bias with electronic method and blinding **Prognostic imbalance:** Comparable gender & ages, clearly specified & included as covariates in analysis to control for imbalance. No criteria for other disease specified e.g. Vestibular, neurological	• Sub-groups mean NDI - mild 15.6, moderate 39.5, severe 69.5 • R rot JPE sig greater in severe & moderate WAD groups than mild or control groups (p<.01).Ext JPE sig greater in severe group than others • All WAD groups had reduced ROM, increased emg and increased TSK scores compared to controls. Only moderate & severe groups had generalized hypersensitivity to pain & temp

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Teng (2007)[59] **Focus:** Evaluation of the effect of a history of mild neck pain on cervical JPE (cervico-cephalic kinesthetic sensibility) in young and middle-aged adults and of whether cervical JPE decreases with age **Design:** Cross-sectional **Participants:** • **N:** 20 middle aged adults with history of neck pain, 20 middle-aged healthy controls, 20 young adult healthy controls • **Age/gender:** Mean(SD) 58.8(5.7), 54.5(5.0),21.9(3.9). females/males 6/14, 3/17, 11/9 • **Inclusion:** History of mild chronic neck pain (≥ 6 months in past year), currently asymptomatic	**Outcome measurement:** • **JPE:** Head-to-neutral & head-to-target (65% of full ROM) L/R rot, flex/ext, L/R lat flex (CE,RMSE) • **Method:** Zebris ultrasound motion system. No. repeats unspecified. Movement at 35° sec-1 **Eligibility criteria:** Clearly defined **Measurement of exposure/outcome:** Clearly defined, minimal risk of bias in measurements **Prognostic imbalance:** Imbalances in gender and postural activities between young and midle aged groups. No explanation of recruitment methods. Clear and appropriate exclusion criteria	• Age-related decreased head-to-neutral JPE accuracy only for CE & RMSE in flexion/extension ($p<.05$) • Age-related decreased head-to-target repostioning performance only for L rot RMSE • After controlling for age as a covariate, no sig between-groups difference

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Tjell (1998)[90] **Focus:** Comparison of SPNT test in WAD and different balance disorders **Design:** Cross-sectional **Participants:** • **N:** 50 WAD-with dizziness, 25 WAD-without dizziness, 20 CNS vertigo, 20 Meniere's disease & 30 healthy controls • **Age/gender:** Mean(range) 39(18-60), ?(21-63), 52(29-69), 48(33-67), 47(29-59). Female/male 31/19, 17/?, 11/9, 12/8, 15/15 • **Inclusion:** WAD grade II or above, duration> 6 months. CNS vertigo included MS, brain stem infarcts, cerebellar infarct etc	**Outcome measurement:** • **SPNT test:** Sinusoidal stimulus 20° sec^{-1}, .2 Hz. SP gain & SPNT difference analysed • **Method:** EOG. Manual data processing. 45° torsion, manually stabilised **Eligibility criteria:** Clearly described and confirmed classification diagnoses as far as is possible **Measurement of exposure/outcome:** Described as double blind method, but blinding is not explained in the methodology. Potential for bias if manual data editing was unblinded **Prognostic imbalance:** Neck pain severity not described. Potential imbalance in age/gender distributions between groups that is not evaluated or controlled for	• Within both WAD groups torsion sig. reduced SP gain ($p<.001$), not in control groups • SPNT difference was sig different between both WAD groups and healthy controls ($p<.001$) • SPNT differences were sig. different between both WAD groups ($p<.01$) • Sensitivity of SPNT difference 90% (WAD-dizziness) & 56%(WAD-without dizziness), specificity91%

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Treleaven (2003)[54] **Focus:** Evaluation of the association between dizziness and cervical JPE in WAD **Design:** Cross-sectional **Participants:** • **N:** 76 chronic WAD+dizziness &/or unsteadiness, 26 WAD with no dizziness/unsteadiness, 44 healthy controls • **Age/gender:** Mean(SD) 39.11(1.3), 4.23(1.9), 34.1(1.8). females/males 76/29 (all WAD), 29/15 • **Inclusion:** Chronic (>3 months) WAD II or III	**Outcome measurement:** • **JPE:** Head-to-neutral R/L rot, ext (AE) • **Method:** Polhemus FASTRAK. 3 trial repeats **Eligibility criteria:** Clearly defined **Measurement of exposure/outcome:** Clearly defined. Minimal risk of experimenter bias **Prognostic imbalance:** Clearly described recruitment and exclusion criteria. Ages & gender comparable. There was a sig difference in pain index between the WAD groups	• WAD had sig greater JPEs in each primary plane (all p< .05) • No differences in non-primary planes • Dizzy WAD group sig greater R rot JPEs than non-dizzy WAD (p =.006) • Non-dizzy WAD JPEs not sig different from healthy controls

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Treleaven (2005)[91] **Focus:** Evaluation of the association between SPNTgain, anxiety & pain levels in WAD with dizziness, WAD without dizziness & healthy controls **Design:** Cross-sectional **Participants:** • **N:** 50 WAD with dizziness, 50 WAD without dizziness, 50 healthy controls • **Age/gender:** Mean(range) 35.5(19-46), 35.0(18-46), 29.9(19-45). Female/male 38/12, 38/12,30/20 • **Inclusion:** WAD II, > 3 months	**Outcome measurement:** • **SPNT:** Sinusoidal stimulus 20° sec^{-1}, .2 Hz. SP gain & SPNT difference • **Other:** VAS[a], NDI[b], STAIT[c], DHI[d] • **Method:** EOG. <45° torsion, manually stabilised head. Automated (and manual?) data processing. Examiner blinded during data processing **Eligibility criteria:** Clearly described inclusion/exclusion criteria and recruitment methods **Measurement of exposure/outcome:** Blinding minimised bias during data processing **Prognostic imbalance:** Analysed comparability between groups. Analysis compensated for potential imbalances (VAS, NDI score and age as factors)	• R & combined torsion SP gain sig. reduced & SPNTdif sig. greater in WAD with dizziness than WAD without dizziness (p<.004) • SP gain in all positions sig. reduced & SPNTdiff sig greater in WAD without dizziness than controls (p<.002) • In WAD with dizziness (DHI) was associated with SPNT difference, SPNTdiff weakly correlated with DHI score • In all WAD SPNTdiff weakly correlated with VAS (p<.05) • In WAD without dizziness, greater NDI score sig. associated with less SPNT deficit (p<.05)

[a]Visual Analogue Scale, [b]Neck Disability Index, [c]State Trait Anxiety Inventory Short Form, [d]Dizziness Handicap Inventory Short Form

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Treleaven (2008)[187] **Focus:** Comparison of sensorimotor disturbance between WAD and vestibular pathology associated with acoustic neuroma **Design:** Cross-sectional (described as repeated measures, case controlled) **Participants:** • **N:** 20 WAD, 20 acoustic neuroma, 20 healthy controls • **Age/gender:** range 40-60, 33-59, 43-59. Females/males 15/5, 9/11, 14/6 • **Inclusion:** WAD or acoustic neuroma > 3 months	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot, ext (AE) • **SPNT:** Sinusoidal 1-D target • **Other:** Postural stability, DHI[a] and STAIT[b] scores • **Method:** Cervical JPE measured with Polhemus Fastrak, 3 repeats. SPNT test measured with EOG, 45° neck torsion, manually stabilised head **Eligibility criteria:** Cearly defined inclusion/exclusions, but possibility of vestibular pathology within the WAD group (no difference in dizziness scores) **Measurement of exposure/outcome:** Comparable - method minimises likelihood of experimenter bias **Prognostic imbalance:** Analysed for diferences in age (not significant), but possible gender imbalance not analysed	• No sig differences in cervical JPE between the WAD & vestibular groups • Differences in SPNT (P =.00), selected measures of postural stability (P<.04), and reported symptoms between the WAD & vestibular groups • Greater ext & R rot JPE(p<.05) in WAD versus controls and in SPNT (p<.01)

[a]Dizziness Handicap Inventory Short Form, [b]State Trait Anxiety Inventory Short Form,

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Uremovic (2007)[183] **Focus:** Comparison of cervical JPE in WAD and healthy controls **Design:** Cross-sectional **Participants:** • **N:** 60 WAD, 60 healthy controls • **Age/gender:** Range (all participants) 20-5. Described as age & gender matched • **Inclusion:** Recent whiplash injury	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot & ext following 30° movement • **Method:** Gravity goniometer-based measurement system **Eligibility criteria:** Unclear **Measurement of exposure/outcome:** Possibility for bias with manual method **Prognostic imbalance:** Unclear NB Full text not available	• Sig. difference between WAD and controls (p<.001)

Table 1 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Woodhouse (2008)[10] **Focus:** Comparison of motor control deficits in WAD compared with chronic non-trauma neck pain **Design:** Cross-sectional **Participants:** • **N:** 59 WAD, 57 chronic non-trauma & 57 healthy controls • **Age/gender:** Mean(SD) 38.19(1.8), 43.7(12.6), 38.2(1.9). females/males 34/22, 38/19, 28/29. • **Inclusion:** WAD I-II, neck pain > 6 months	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot (AE) • **Other:** Cervical ROM • **Method:** Laser pointer, 2 trial repeats for JPE. Polhemus Fastrak for cervical ROM **Eligibility criteria:** Clearly defined **Measurement of exposure/outcome:** Possibility for bias with manual method. Unreliable JPE method **Prognostic imbalance:** Analysis method controlled for differences e.g. In age, gender	• No sig differences in JPE • Max cervical ROM sig reduced in WAD compared to others • Altered motion patterns (conjunct motion) in both WAD and non-trauma neck pain gorups

Table 2. Evidence Catalogue for Review 2

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Swait (2007)[195] **Focus:** Evaluation of optimisation of reliability and of correlation between performance in the cervical JPE and cervico-cephalic kinesthesia tests in healthy individuals **Design:** Test-retest, cross-sectional (correlation) **Participants:** • **N:** 16 healthy participants • **Age/gender:** Mean(SD) 26.5(9.4). Female/male 10/6 • **Inclusion:** No neck pain	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot, flex, ext (**Cervico-cephalic kinesthesia:** Head-tracking of visual target following unpredictable trajectory. Predetermined and randomly generated trajectories • **Method:** Polhemus Fastrak. 10 trials each JPE test, 9 trials each cervico-cephalic kinesthesia test trajectory type (correlation analysis used 6 trial repeats in each test) . Within- and between-day measurment **Eligibility criteria:** Adequate – excluded neck pain, trauma, ocular, vestibular, neurological pathology etc (limited detail described in paper) **Measurement of exposure/outcome:** Adequate – single asymptomatic group. Low risk of bias as same procedure for all participants. No blinding needed **Prognostic imbalance:** Not applicable (single study group)	• No sig correlation between cervical JPE and cervico-cephalic kinesthesia tests (p>.05 • Within cervical JPE tests sig correlation between accuracy and precision of each (p<.01) & between flexion & extension precision (p<.01) • 5 or more trials resulted in stable and reliable (ICC2k = .73-.97) estimates of all tests

summarised details of focus, design, methods and results are provided for each included study. Aspects of design and method relevant to subsequent appraisal of risk of bias (according to GRADE criteria for observational studies[1]) and limitations in each study are also specified

Table 2 continued

STUDY AND PARTICIPANTS	METHODS/STUDY LIMITATIONS	RESULTS
Treleaven (2006)[55] **Focus:** Investigation of relationship between cervical JPE, SPNT and standing balance in WAD and healthy individuals **Design:** Cross-sectional **Participants:** • **N:** 50 WAD with dizziness, 50 WAD without dizziness, 40 healthy participants • **Age/gender:** Mean(range) 35.5(19-46), 35(18-46), 29.6(19-45). Female/male 38/12, 38/12, 23/17 • **Inclusion:** WAD II > 3 months	**Outcome measurement:** • **JPE:** Head-to-neutral L/R rot, ext (AE) • **SPNT:** Sinusoidal stimulus 20° sec^{-1}, .2 Hz. SP gain & SPNT difference • **Other:** Postural stability • **Method:** Polhemus fastrak measurement for cervical JPE, 3 trial repeats. EOG measurement in SPNT test, 45° neck torsion, automated (and manual?) data processing,examiner blinded during data processing. Computerised posturography **Eligibility criteria:** Adequately described **Measurement of exposure/outcome:** Blinding at data processing stage minimises bias for SPNT data. Minimised for JPE **Prognostic imbalance:** Slight age imbalance. No inclusion/exclusion citeria for visual/eye function. No pain severity for WAD groups reported. However, no between-group analysis	• JPE & SPNT tests only weakly correlated for R rot JPE with the whole groups included ($p<.05$) • Rotation JPE & balance tests mostly weak-moderate correlations in whole sample, combined WAD and WAD with dizziness (not within no-dizziness group) Balance & SPNT tests weak-moderate correlations in whole sample and combined WAD, not individual groups • Abnormal JPE score high positive prediction value (88%), but low sensitvity (60%) and specificity (54%) to determine abnormality in SPNT or balance tests.

APPENDIX 4

RESULTS OF APPRAISAL OF RISK OF BIAS AND OTHER LIMITATIONS IN INDIVIDUAL STUDIES

Review 1

Table 1 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is cervical JPE impaired?

Table 2 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired?

Table 3 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired?

Table 4 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain of non-traumatic aetiology, is performance in the cervico-cephalic kinesthesia test impaired?

Table 5 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired?

Review 2

Table 6 Appraisal of risk of bias and study limitations: In individuals with mechanical neck pain, is there correlation in performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests?

Table 1 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is cervical JPE impaired?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Hill R (2009)[184] Head-to-neutral -sagittal plane	Adequate -clearly defined	Adequate -bias minimised	Adequate -controlled with analysis*?	poor reliability extension JPE method[144;195]	No serious limitations *? evidence upgrade (not for extension JPE)
-transverse plane	Adequate -clearly defined	Adequate -bias minimised	Adequate -controlled with analysis*?	Unclear reliability	No serious limitations *? evidence upgrade
Sterling M (2004)[53] Head-to-neutral -sagittal plane	Adequate -clearly defined	Adequate - bias minimised	Adequate -largely described & evaluated -controlled with analysis (gender)*	? poor reliability extension JPE method[144;195]	No serious limitations *? evidence upgrade (not for extension JPE)
-transverse plane	Adequate -clearly defined	Adequate - bias minimised	Adequate -largely described & evaluated -controlled with analysis (gender)*?		No serious limitations *? evidence upgrade
Sterling M (2003)[165] Head-to-neutral -sagittal plane	Adequate -clearly defined	Adequate -minimised measurement bias -ensured exposure	Adequate -largely described & evaluated -controlled with analysis (gender)*?	? poor reliability extension JPE method[144;195]	No serious limitations *? evidence upgrade (not for extension JPE)
-transverse plane	Adequate -clearly defined	Adequate -minimised measurement bias -ensured exposure	Adequate -largely described & evaluated -controlled with analysis (gender)*?		No serious limitations *? evidence upgrade

Table 1 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Feipel V (2006)[181] Head-to-neutral -sagittal plane Head-to-target -frontal plane	Adequate -largely described	Adequate - largely described.	Adequate -largely described	Unclear reliability	No serious limitations
-transverse plane	Adequate -largely described	Adequate - largely described.	Adequate -largely described		No serious limitations
Grip H, (2007)[68] Head-to-target -sagittal plane -transverse plane	Adequate - largely described	Adequate - largely describe -minimised likelihood of assessor bias	Unclear - incomplete specification of exclusions?		No serious limitations
Kristjansson E, (2003)[52] Head-to-neutral -transverse plane Head-to-target -transverse plane	Adequate - well-described	Adequate - clearly described. Examiner blinded	Unclear -largely described,some age imbalance possible?	Unclear reliability	No serious limitations

Table 1 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Pereira (2008) Head-to-neutral -sagittal plane (extension only)	Adequate -well-defined	Adequate -clearly described -bias minimised	Adequate -clearly descibed ?slight age imbalance	? poor reliability extension JPE method[144;195]	No serious limitations
Transverse plane	Adequate -well-defined	Adequate -clearly described -bias minimised	Adequate -clearly descibed ?slight age imbalance	-unclear reliability	No serious limitations
Treleaven J (2003)[54] Head-to-neutral -sagittal plane (extension only)	Adequate -clearly descibed	Adequate – bias minimised	Adequate -clearly described	? poor reliability extension JPE method[144;195]	No serious limitations
-transverse plane	Adequate -clearly descibed	Adequate – bias minimised	Adequate -clearly described	-unclear reliability	No serious limitations

Table 1 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Armstrong B (2005)[58] Head-to-neutral -sagittal plane	Adequate - largely described	Adequate - clearly described	Unclear - incompletely described	? poor reliability extension JPE method[144;195]	≈No serious limitations
Head-to-neutral -transverse plane	Adequate - largely described	Adequate - clearly described	Unclear - incompletely described	Unclear reliability	≈No serious limitations
Head-to-target -sagittal plane -transverse plane	Adequate - largely described	Adequate - clearly described	Unclear - incompletely described	Unclear reliability	≈No serious limitations
Treleaven J (2008)[187] Head-to-neutral -sagittal plane (extension only)	Unclear -possible vestibular pathology in WAD?	Adequate – bias minimised	Unclear – possible gender imbalance?	? poor reliability extension JPE method[144;195]	≈No serious limitations
-transverse plane	Unclear -possible vestibular pathology in WAD?	Adequate – bias minimised	Unclear – possible gender imbalance?	-unclear reliability	≈No serious limitations
Woodhouse A (2008)[10] Head-to-neutral -transverse plane	Adequate - clearly defined	Unclear -increased risk of bias with manual method? - effects more likely in opposite direction	Adequate - controlled for with analysis method	-unclear reliability	≈No serious limitations

Table 1 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Sjolander P (2008)[182] Head-to-neutral -transverse plane	Adequate	Adequate -clearly described -manual method -bias minimised	Inadequate - some of neck pain subjects had dizziness, this was excluded from control group?	-unclear validity (fast rotation)? -small groups?	≈Serious limitations
Uremovic M (2007)[183] Head-to-neutral -sagittal plane -transverse plane	Unclear	Unclear -manual measurement,? experimenter bias	Unclear	Unclear reliability	Serious limitations (several criteria) ? evidence downgrade
Heikkila H (1996)[150] Head-to-neutral - sagittal plane - transverse plane	Unclear	Unclear -examiner bias potential?	Unclear -incompletely described		Serious limitations (several criteria) ? evidence downgrade
Heikkila HV (1998)[51] Head-to-neutral - sagittal plane - transverse plane	Unclear -incomplete description	Unclear -examiner bias potential?	Unclear - incompletely described	Small sub-groups	Serious limitations (several criteria) ? evidence downgrade

Table 1 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Loudon JK (1997)[145] Head-to-target - transverse plane - frontal plane	Unclear -incomplete description	Unclear - manual method -examiner bias potential?	Unclear - exclusions not specified	-unclear reliability	Serious limitations (several criteria) ? evidence downgrade
Madeleine P (2004)[140] Head-to-target - transverse plane - frontal plane	Adequate	Unclear - manual method - examiner bias potential?	Unclear - little information about control group	-unclear reliability -no statistical results are described or presented	Very serious limitations (several criteria) ? evidence downgrade

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of limitations in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

Table 2 Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain of non-traumatic aetiology, is cervical JPE impaired?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Woodhouse A (2008) [10] Head-to-neutral -transverse plane	Adequate-clearly defined	Unclear ?risk of bias with manual method, however effects more likely in opposite direction to results??	Adequate - controlled for with analysis method	Unclear reliability	No serious limitations
Teng CC (2007)[59] Head-to-neutral -sagittal plane -transverse plane -frontal plane Head-to-target -sagittal plane -transverse plane Frontal plane	Adequate -clearly defined	Adequate - bias minimised	Unclear - ?gender and possible postural activity imbalances -recruitment sources not described	Unclear reliability (protocol not fully specified)	≈No serious limitations

Table 2 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Sjolander P (2008)[182] Head-to-neutral -transverse plane	Adequate	Adequate - clearly described method minimised possibility of bias	Unclear - ?dizziness possible among neck pain group, exclusion criteria for control group	? Unclear validity (performed rotation as fast as possible) -Good reliability -Small sub-groups -Highly significant results	≈No serious limitations
Cheng CH (2010)[189] Head-to-neutral -sagittal plane	Adequate	Adequate -largely described -minimal likelihood of assessor bias	Adequate - largely described	? Unclear validity (eyes open) ? poor reliability extension JPE ?small sample size	No serious limitations (≈extension JPE)
Grip H (2007)[68] Head-to-target -sagittal plane -transverse plane	Adequate - largely described	Adequate - largely described. minimal likelihood of assessor bias	Unclear - ?dosnt specify exclusions e.g. Vestibular disorders etc that might influence repositioning	Unclear reliability	No serious limitations

Table 2 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Kristjansson E (2003)[52] Head-to-neutral -transverse plane	Adequate - well-described	Adequate -clearly described -examiner blinded	Unclear ?some age imbalance possible. (pain and disability not comparable between WAD and non-trauma groups)	Unclear reliability	No serious limitations
Head-to-target -transverse plane	Adequate - well-described	Adequate -clearly described. Examiner blinded	Unclear ?some age imbalance possible. (-pain and disability not comparable between WAD and non-trauma groups)	Fair-excellent reliability reported -	No serious limitations
Palmgren PJ (2009)[164] Head-to-neutral -sagittal plane	Adequate	Adequate -examiner blinded	Unclear - ?gender imbalance	Unclear reliability	No serious limitations
-frontal plane -transverse plane	Adequate	Adequate -examiner blinded	Unclear - ?gender imbalance	Good reliability	No serious limitations

Table 2 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Pinsault N (2008)[190] Head-to-neutral -transverse plane	Unclear - ?recruitment not fully described	Adequate - experimenter bias minimised (laser method, automated data recording) -confirmation of neck pain not fully described?	Unclear - ?recruitment source not described ? age imbalance, expected to act in opposite direction to findings??	Good reliability Very small patient group size	≈Serious limitations (several criteria)
Rix GD (2001)[191] Head-to-neutral -sagittal plane	Adequate	Unclear - examiner bias potential??	Unclear - ?dosnt specify exclusion of dizziness/vertigo for neck pain goup	Unclear reliability	≈Serious limitations
-transverse plane	Adequate	Unclear - examiner bias potential??	Unclear - ?dosnt specify exclusion of dizziness/vertigo for neck pain goup	Good reliability	≈Serious limitations

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of risk of bias in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

Table 3. Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is performance in the cervico-cephalic kinesthesia test impaired?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Kristjansson E (2004)[60] -Mean error	Adequate	Adequate – bias minimised	Unclear - incompletely described?	Good-substantial reliability	No serious limitations
Kristjansson,E (2010)[80] -Mean error	Adequate	Adequate - bias minimised	Unclear - imbalance in gender? (& pain severity[a])	Good-substantial reliability	No serious limitations

[a]Pain severity imbalance between WAD and non-traumatic neck pain groups, not relevant to review question

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of risk of bias in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

Table 4. Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain of non-traumatic aetiology, is performance in the cervico-cephalic kinesthesia test impaired?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
	Appropriate eligibility criteria	Comparable exposure & outcome measurement	Control of confounding (e.g. prognostic imbalance)		
Kristjansson,E (2010)[80] -Mean error	Adequate	Adequate - bias minimised	Unclear - imbalance in gender? (& pain severity[a])	Good-substantial reliability	No serious limitations

[a]Pain severity imbalance between WAD and non-traumatic neck pain groups, not relevant to review question

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of risk of bias in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

Table 5. Appraisal of risk of bias and study limitations: in individuals with mechanical neck pain in WAD, is ocular motor function in the SPNT test impaired?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
Kongsted A (2007)[101] -Head neutral SP gain -Neck torsion SP gain -SPNT difference	Adequate -clearly defined	Adequate- method minimised bias likelihood	Adequate -controlled with analysis?	Unclear reliability	No serious limitations -good sample sizes ? upgrade
Pereira MJ(2008)[98] -SPNT difference	Adequate	Adequate	Unclear - age/experience imbalance? -effect in opposite direction to expected if bias present??	Unclear reliability	No serious limitations
Treleaven J(2005)[91] -Head neutral SP gain -Neck torsion SP gain -SPNT difference	Adequate -clearly specified	Adequate	Adequate - analysis controlled for various factors?	Unclear reliability	≈No serious limitations ?upgrade
Gimse R (1996)[194] -Head neutral SP gain -Neck torsion SP gain	Adequate	Adequate	Unclear - little information on control group recruitment and demographics?	Unclear reliability	≈No serious limitations

Table 5 continued

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
Dispenza F (2011)[193] -Head neutral SP gain -Neck torsion SP gain	Adequate -mostly defined	Adequate -bias minimised	Unclear - lacking information?	Unclear reliability	≈No serious limitations
Prushansky T (2004)[99] -Head neutral SP gain -Neck torsion SP gain -SPNT difference	Unclear ?recruitment incompletely described?	Unclear ? method not fully described so possibility of experimenter bias?	Adequate - analysis controlled for various factors	Unclear reliability	≈Serious limitations (several criteria)
Tjell C (1998)[90] -Head neutral SP gain -Neck torsion SP gain -SPNT difference	Adequate -clearly defined and verified	Unclear -'double blind' not described in method. Unclear if manual data processing was blinded?.	Unclear - ?possible age/gender imbalances not controlled for	Unclear reliability	Serious limitations

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of limitations in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

Review 2

Table 6. Appraisal of risk of bias and study limitations: In individuals with mechanical neck pain, is there correlation in performance in the cervical JPE, cervico-cephalic kinesthesia and the SPNT tests?

STUDY/OUTCOME MEASURES	GRADE RISK OF BIAS CRITERIA			OTHER LIMITATIONS	EVIDENCE APPRAISAL NOTES
Swait G (2007)[195] -Cervical JPE/cervico-cephalic kinesthesia test	Adequate	Adequate -bias minimised, single study group	Adequate -single study group, no symptoms	Good reliability JPE and cervico-cephalic kinesthesia tests demonstrated	No serious limitations
Treleaven J (2006)[55] -Cervical JPE/SPNT test	Adequate	Adequate -bias minimised	Unclear -no inclusion/exclusion criteria for visual/eye function[a] (possible age/pain imbalances,but no between-group comparison)	? poor reliability extension JPE method[144;195]	≈No serious limitations

Within each study appraisal of each outcome is provided. ? denotes points to be considered when evaluating quality of evidence across studies. Evidence appraisal notes include summaries of limitations in the study, relative to the risks inherent in the study design. Risk of bias in study follow-up was not applicable and is not included

APPENDIX 5

PUBLICATIONS

Figure 1 Conference proceedings

Swait G, Rushton AB, Miall RC and Newell D

Evaluation of Cervical Proprioceptive Function: Reliability of smooth pursuit velocity gain in cervical rotation using a video-graphic ocular tracking system[207]

College of Medical and Dental Sciences Research Gala, University of Birmingham. 2012

Figure 2 Journal article

Swait G, Rushton AB, Miall RC and Newell D

Evaluation of Cervical Propriocep[tive Function: optimising protocols and comparison between tests in normal subjects[195]

Spine. 15(32(24)), E962-701. 2007.

Figure 1

Evaluation of Cervical Proprioceptive Function: Reliability of smooth pursuit velocity gain in cervical rotation using a videographic ocular tracking system

Gabrielle Swait, Alison Beverley Rushton, Chris R Miall

BACKGROUND

- A number of tests are proposed measures of cervical proprioception (ability to sense neck position) & have been used to evaluate effects of neck pain[1-5]
- These include measures of perceived 'straight ahead' position (cervical joint position error (JPE) test)[1,2], ability to sense motion of the head on the neck (cervicocephalic kinesthesia)[3] & effects of neck rotation on smooth pursuit eye movements (SPNT test)[4,5]
- Performance based outcome measures should demonstrate test-retest reliability[6]
- Protocols optimising reliability of the cervical JPE & kinesthesia tests have been established[7]
- The SPNT test measures ability to match the velocity of smooth pursuit eye movements to the velocity of a moving visual target (smooth pursuit gain) , with the head in straight and rotated positions[4]
- Previously the SPNT test was performed using electro-oculography, which possesses limitations[8]
- Videographic eye movement measurement systems are an alternative[8] but have not been used to evaluate SPNT test performance
- Reliability of assessment of smooth pursuit gain (SP gain) in the SPNT test has not been reported

OBJECTIVE

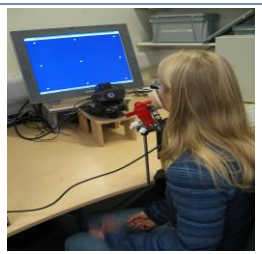
To devise and establish the reliability of a method, using a videographic ocular tracker, for evaluating SP gain with cervical rotation

STUDY DESIGN

A test-retest design evaluated within-day reliability

METHODS

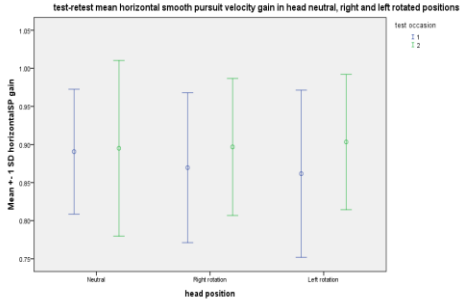
- SP gain was measured with an ASL 504 videographic tracking system in 21 healthy participants [9], tested on 2 occasions(test 1 & test 2), separated by a 10 minute interval. See DIAG 1.
- For each test occasion participants tracked a visual target following a horizontal trajectory at 20 degrees sec^{-1} with their head static in neutral position and while their trunk was rotated to the right or left. 3 trials were performed in each position.
- Mean SP gains for individual trials, and for each head position were calculated. Repeated measures ANOVAs evaluated systematic error across trials within and between the test and retest Reliability was evaluated using the intraclass correlation coefficient (ICC (2,k))[10].



DIAG 1. Participant seated in front of visual display with head stabilised & trunk rotated

RESULTS

- Repeated measures ANOVAs indicated a systematic effect on SP gain between test 1 and test 2 occasions for left cervical rotation (p = .000) and the mean of left & right rotation (combined neck torsion) (p = .005). During the first test occasion SP gains were lower than in test 2.
- No systematic effects were detected over the course of either the test 1 or the test 2 occasions
- Substantial reliability[10] was demonstrated for right, left and mean torsion positions with ICCs (95% CI) of .853 (.633-.941), .910 (.471-.973) and .897 (.639-.963) respectively.



- CONCLUSION
- Acceptable reliability was demonstrated for evaluation of SP gain with cervical rotation, however systematic effects were detected. SP gain improved in the test 2 occasion
- The absence of systematic effects within either test 1 or test 2 suggests improvement may be associated with the break between tests.
- In natural conditions both cervical proprioceptive and vestibular cues signalling head motion influence eye movements, with vestibular cues predominating. During the tests the head was held in a static position, preventing vestibular stimulation.
- One possibility is that subsequent free head and neck movements during the break enables increased gain of cervical proprioceptive , relative to vestibular cues to occur (i.e. enhanced use of proprioception by eye movement systems), that could then improve SP gain in test 2. A similar increased dependence on cervical proprioception has been reported in patients with vestibular problems [11] as well as in whiplash patients[12] for a different type of reflex eye movement
- Differences in SPgain with cervical rotation have been reported following whiplash injury in cross-sectional studies[2;4], however the systematic effect makes this test an unsuitable outcome measure for longitudinal studies e.g. Evaluating the effect of interventions on cervical proprioception with before and after treatment measurements.

1. Sterling M, Jull G, Vicenzino B, and Kenardy J. Characterization of acute whiplash-associated disorders. Spine 2004;29:182-8; 2. Treleaven J, Jull G, and LowChoy N. The relationship of cervical joint position error to balance and eye movement disturbances in persistent whiplash. Manual Therapy 2006;11:99-106; 3. Kristjansson E, Hardardottir L, Asmundardottir M, and Gudmundsson K. A new clinical test for cervicocephalic kinesthetic sensibility: 'The Fly'. Arch Phys Med Rehabil 2004;85:490-5; 4. Tjell C, Tenenbaum A, and Sandstrom S. Smooth pursuit neck torsion test - a specific test for whiplash associated disorders? J Whiplash and Associated Disorders 2003;1:9-24; 5. Treleaven J, Jull G, and LowChoy N. Smooth Pursuit Neck Torsion Test inWhiplash-Associated Disorders:Relationship to Self-Reports of Neck Pain and Disability, Dizziness and Anxiety. J Rehabil Med 2005;37:219-23; 6. Christensen HW NN. The ability to reproduce the neutral zero position of the head. J Manipulative Physiol Ther 1999;1999-1-26-28; 7. Swait G. Evaluation of cervical proprioceptive function. Rushton AB, Miall RC, and Newell D. Optimizing protocols and comparison between tests in normal subjects. Spine 32(24), E692-E701. 2007; 8. Schmid-Priscoveanu A. Infrared and video oculography--alternatives to electrooculography? Allum JH. HNO 47(5), 472-478. 1999; 9. Walter SD, Eliasziw M, and Donner A. Sample size and optimal designs for reliability studies. Statist.Med 1998;17:101-10; 10. Weir JP. Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. J Strength Cond Res 2005;19:231-40; 11. Brandt T. Cervical vertigo - reality or fiction. Audiol Neurootol 1, 187-196. 1996; 12. Montfoort I, Van Der Geest JN, Slijper HP, De Zeeuw CI, and Frens MA. Adaptation of the cervico- and vestibulo-ocular reflex in whiplash injury patients. J Neurotrauma 2008;25:687-93.

Figure 2

SPINE Volume 32, Number 24, pp E692–E701

Evaluation of Cervical Proprioceptive Function

Optimizing Protocols and Comparison Between Tests in Normal Subjects

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APPENDIX 6
PHYSICAL EXAMINATION PROTOCOL

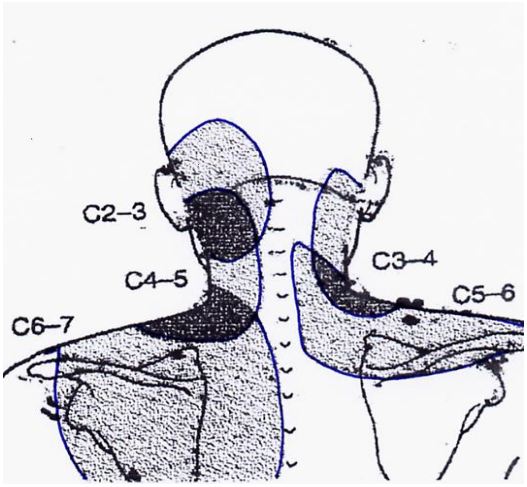
Cervical Spine Assessment **Patient ref ……**

PART 1 - Active ROM with Overpressure

Perform with patient seated. Indicate location of any pain elicited on diagram.

ROM No.	MOTION	RESTRI-CTED	PAINFUL		EASED BY SNAG
			FACET PATTERN	NON-FACET	
	example	√	*L C3/4*	√	*L C3/4*
1	Chin tuck				
2	Upper cervical extension				
3	L upper quadrant				
4	R upper quadrant				
5	L rotation (flexed)				
6	R rotation (flexed)				
7	Neck flexion				
8	Extension				
9	L rotation (neutral)				
10	R rotation (neutral)				
11	L lateral flexion				
12	R lateral flexion				
13	L rotation (extended)				
14	R rotation (extended)				
15	L quadrant				
16	R quadrant				
17	Compression				
18	Distraction				

Facet joint referral patterns



PART 2 – Passive Physiological Intervertebral Movements (motion palpation)

Perform sitting or supine. Indicate direction in which motion is restricted (+)

Segmental level						
C0/1(glide)	**L**	**R**				
	flexion	**extension**	**L rotation**	**R rotation**	**L lat flexion**	**R lat flexion**
C1/2						
C2/3						
C3/4						
C4/5						
C5/6						
C6/7						
C7/T1						

PART 3 – Passive Accesory Intervertebral Movements

Patient supine. With neck in extension/rotation apply AP pressure to each TP. Indicate aggravation or alleviation of **symptoms**(+/-)

Segmental level	**Extension/Left rotation**		**Extension/Right rotation**	
	Left TP	**Right TP**	**Left TP**	**Right TP**
C1				
C2				
C3				
C4				
C5				
C6				
C7				
T1				
T2				

Patient supine or prone. With neck in flexion/rotation apply PA pressure to each articular pillar. Indicate aggravation or alleviation of *symptoms* ***(+/-)***

Segmental level	**Flexion/Left rotation**		**Flexion/Right rotation**	
	Left pillar	**Right pillar**	**Left pillar**	**Right pillar**
C1				
C2				
C3				
C4				
C5				
C6				
C7				
T1				
T2				

PART 4 – Bischoff protocol

Patient prone, head neutral. Apply L and R transverse, and central PA pressure to SPs. Palpate for zone of tenderness around affected segments. Record increase or decrease in *symptoms* ***with SP pressures, presence of fixation or tenderness around segment.***

Segmental level	L transverse	R transverse	Central	Tender zone
C1				
C2				
C3				
C4				
C5				
C6				
C7				
T1				
T2				

(PART 5 - Additional tests for radiculopathy (depending on presentation, not included in study)

Test	*Findings*
Dejerine triad (+/-)	
Reflexes (C5-C7, 1+-4+)	
Myotomes (C5-T1, 1-5)	
Dermatomes (C5-T1, ↓)	
Brachial plexus stretch	
TOS	

APPENDIX 7
PARTICIPANT QUESTIONNAIRES

Figure 1 Participant screening questionnaire

Figure 2 Participant consent form

Figure 3 Self-reported function questionnaires (the NDI, neck BQ and TSKII)

Figure 1 – Participant screening questionnaire

1. Do you currently suffer from a neck problem?…… YES/NO

   If YES, please answer the following questions:

   a. How long have you had your neck problem for (please circle)?

Less than 7 days 1-2 weeks 2-6 weeks 6 weeks-3 months

3-6 months 6-12 months Longer than 12 months

   b. Has it during the last 2 weeks (or since onset if less than 2 weeks ago)

   got worse got better stayed the same (please circle)?

   c. Has it during the last 2 weeks (or since onset if less than 2 weeks ago) occurred every day? …..YES/NO

   d. What was the cause (if known)?…….

   ……..

   e. What symptoms do you associate with the neck problem (please circle)?

   Neck pain restricted neck movement cracking/crunching sensations

   Headache/pain dizziness arm pain/numbness/tingling other (give details)

   …….

2. Have you ever had an injury to your neck? ……. YES/NO

   If 'yes', please answer the following questions:

   a. When did the injury occur?…….

   b. Was it a whiplash injury?…….YES/NO

   c. How did the injury occur?…….

   d. What investigations or treatment did you have at the time?……

   …….

   e. What medical diagnosis was made (if any)?

   ……

   f. Do you still experience symptoms from that injury?…..YES/NO

3. Have you ever had an X-ray or scan of your neck ……..YES/NO

   a. If YES, what were the results of this?…….

4. Do you suffer from any of the following (please circle)?

Back pain Migraine Other headache Other joint pain

5. Have you ever received any chiropractic, osteopathy, other manipulation or physiotherapy?…..YES/NO

If YES, please circle the type of treatment received, then answer the following questions:

a. which of the following was it for (please circle)?

Current neck problem *Previous neck problem* *Any other problem(please specify)*

……..

b. Did the treatment help? …….YES/NO

c. When was your last visit?……..

d. Will you be receiving any of the above treatments in the next 2 weeks (during the course of this study)? ..…YES/NO

6. Are you on a waiting list for any type of treatment (please give details)?….YES/NO

…….

7. Have you ever suffered from a neurological or psychiatric condition?…. YES/NO

If YES, please give details (nature of condition, duration, current medication etc)

…….

…….

8. Have you ever suffered from any of the following medical conditions (please circle)?

Arthritis *Cancer* *High blood pressure* *Heart problems* *Stroke* *Aneurysm* *Vertigo/dizziness* *Balance problems* *Blackouts* *Thyroid problems* *Diabetes* *Other medical condition(please specify)*

……..

9. Do you currently take any prescription, or non-prescription medications?….YES/NO

If YES, please give details (names of medications)……

……..

10. How many units of alcohol do you drink, on average, per week?……..

11. Have you ever had surgery on your spine, neck, eye or brain? ……. YES/NO

If YES, please give details (when and what the procedure was)…….

……

……

12. Is your vision normal, or corrected to normal with contact lenses? YES/NO

Figure 2 – Participant consent form

Thankyou for agreeing to take part in our research. Please answer the following questions.

Do you still have a neck problem?		YES	NO
Over the last 2 weeks has this changed at all?	NO	GOT WORSE	GOT BETTER
Have you read the information about the study that was sent to you?		YES	NO
Have you received enough information about the study?		YES	NO
Have you had the opportunity to ask questions and discuss this study?		YES	NO
Do you understand that you are free to leave the study at any time, without having to give a reason for leaving?		YES	NO
Do you understand that any information collected about you will remain strictly confidential?		YES	NO

I consent to participating in the above study

Signed…… Date……..

Name (printed)……..

Please complete the following three questionnaires. Choose only one response for each question. Please complete all questions.

Figure 3 – Self-reported function questionnaires (the NDI, neck BQ and TSKII)

THE NECK DISABILITY INDEX

Patient Name _____ **File #** _____ **Date** _____

Please read instructions:

This questionnaire has been designed to give the doctor information as to how your neck pain has affected your ability to manage in everyday life. Please answer every section and mark in each section only the ONE box which applies to you. We realize you may consider that two of the statements in any one section related to you, but just mark the box which most closely describes your problem.

SECTION 1 – PAIN INTENSITY

- ☐ I have no pain at the moment.
- ☐ The pain is very mild at the moment.
- ☐ The pain is moderate at the moment.
- ☐ The pain is fairly severe at the moment.
- ☐ The pain is very severe at the moment.
- ☐ The pain is the worst imaginable at the moment.

SECTION 2 – PERSONAL CARE (Washing, Dressing, etc.)

- ☐ I can look after myself normally without causing extra pain.
- ☐ I can look after myself normally but it causes extra pain.
- ☐ It is painful to look after myself and I am slow and careful.
- ☐ I need some help but manage most of my personal care.
- ☐ I need help every day in most aspects of self-care.
- ☐ I do not get dressed; I wash with difficulty and stay in bed.

SECTION 3 – LIFTING

- ☐ I can lift heavy weights without extra pain.
- ☐ I can lift heavy weights but it gives extra pain.
- ☐ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently positioned, for example, on a table.
- ☐ Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned.
- ☐ I can lift very light weights.
- ☐ I cannot lift or carry anything at all.

SECTION 4 – READING

- ☐ I can read as much as I want to with no pain in my neck.
- ☐ I can read as much as I want to with slight pain in my neck.
- ☐ I can read as much as I want with moderate pain in my neck.
- ☐ I can't read as much as I want because of moderate pain in my neck.
- ☐ I can hardly read at all because of severe pain in my neck.
- ☐ I cannot read at all.

SECTION 5 – HEADACHES

- ☐ I have no headaches at all.
- ☐ I have slight headaches which come infrequently.
- ☐ I have moderate headaches which come infrequently.
- ☐ I have moderate headaches which come frequently.
- ☐ I have severe headaches which come frequently.
- ☐ I have headaches almost all the time.

SECTION 6 – CONCENTRATION

- ☐ I can concentrate fully when I want to with no difficulty.
- ☐ I can concentrate fully when I want to with slight difficulty.
- ☐ I have a fair degree of difficulty concentrating when I want to.
- ☐ I have a lot of difficulty concentrating when I want to.
- ☐ I have a great deal of difficulty concentrating when I want to.
- ☐ I cannot concentrate at all.

SECTION 7 – WORK

- ☐ I can do as much work as I want to.
- ☐ I can only do my usual work, but no more.
- ☐ I can do most of my usual work, but no more.
- ☐ I cannot do my usual work.
- ☐ I can hardly do any work at all.
- ☐ I can't do any work at all.

SECTION 8 – DRIVING

- ☐ I can drive my car without any neck pain.
- ☐ I can drive my car as long as I want with a slight pain in my neck.
- ☐ I can drive my car as long as I want with moderate pain in my neck.
- ☐ I can't drive my car as long as I want because of moderate pain in my neck.
- ☐ I can hardly drive at all because of severe pain in my neck.
- ☐ I can't drive my car at all.

SECTION 9 – SLEEPING

- ☐ I have no trouble sleeping.
- ☐ My sleep is slightly disturbed (less than 1 hr sleepless).
- ☐ My sleep is mildly disturbed (1-2 hrs sleepless).
- ☐ My sleep is moderately disturbed (2-3 hrs sleepless).
- ☐ My sleep is greatly disturbed (3-5 hrs sleepless).
- ☐ My sleep is completely disturbed (5-7 hrs sleepless).

SECTION 10 – RECREATION

- ☐ I am able to engage in all my recreation activities with no neck pain at all.
- ☐ I am able to engage in all my recreation activities, with some pain in my neck.
- ☐ I am able to engage in most, but not all, of my usual recreation activities because of pain in my neck.
- ☐ I am able to engage in a few of my usual recreation activities because of pain in my neck.
- ☐ I can hardly do any reaction activities because of pain in my neck.
- ☐ I can't do any recreation activities at all.

Pain Scale:

Rate the severity of your pain by checking on box on the following scale.

No Pain	0	1	2	3	4	5	6	7	8	9	10	Excruciating Pain

The following scales have been designed to find out about your neck pain and how it is affecting you. Please answer ALL the scales by circling ONE number on each scale that best describes how you feel:

1. Over the past week, on average how would you rate your neck pain?

No pain Worst pain possible

0 1 2 3 4 5 6 7 8 9 10

2. Over the past week, how much has your neck pain interfered with your daily activities (housework, washing, dressing,lifting, reading, driving)?

No interference Unable to carry out activities

0 1 2 3 4 5 6 7 8 9 10

3. Over the past week, how much has your neck pain interfered with your ability to take part in recreational, social, and family activities?

No interference Unable to carry out activities

0 1 2 3 4 5 6 7 8 9 10

4. Over the past week, how anxious (tense, uptight, irritable, difficulty in concentrating/relaxing) have you been feeling?

Not at all anxious Extremely anxious

0 1 2 3 4 5 6 7 8 9 10

5. Over the past week, how depressed (down-in-the-dumps, sad, in low spirits, pessimistic, unhappy) have you been feeling?

Not at all depressed Extremely depressed

0 1 2 3 4 5 6 7 8 9 10

6. Over the past week, how have you felt your work (both inside and outside the home) has affected (or would affect) your neck pain?

Has made it no worse Has made it much worse

0 1 2 3 4 5 6 7 8 9 10

7. Over the past week, how much have you been able to control (reduce/help) your neck pain on your own

Completely control it No control whatsoever

0 1 2 3 4 5 6 7 8 9 10

This is a list of phrases which other patients have used to express how they view their condition. Please indicate the extent to which you agree with each statement

		Strongly disagree	Somewhat disagree	Somewhat agree	Strongly agree
1	I'm afraid that I might injure myself if I exercise.	1	2	3	4
2	If I were to try to overcome it, my pain would increase.	1	2	3	4
3	My body is telling me I have something dangerously wrong.	1	2	3	4
4	My pain would probably be relieved if I were to exercise.	1	2	3	4
5	People aren't taking my medical condition seriously enough.	1	2	3	4
6	My accident has put my body at risk for the rest of my life.	1	2	3	4
7	Pain always means I have injured my body.	1	2	3	4
8	Just because something aggravates my pain does not mean it is dangerous.	1	2	3	4
9	I am afraid that I might injure myself accidentally.	1	2	3	4
10	Simply being careful that I do not make any unnecessary movements is the safest thing that I can do to prevent my pain from worsening	1	2	3	4
11	Although my condition is painful, I would be better off if I were physically active.	1	2	3	4
12	Pain lets me know when to stop exercising so that I don't injure myself.	1	2	3	4
13	It's really not safe for a person with a condition like mine to be physically active.	1	2	3	4
14	I can't do all the things normal people do because it's too easy for me to get injured.	1	2	3	4
15	Even though something is causing me a lot of pain, I don't think it's actually dangerous.	1	2	3	4
16	No one should have to exercise when he/she is in pain.	1	2	3	4

APPENDIX 8
ETHICAL CONSIDERATIONS

Table 1 Ethical considerations of relevant principles of the Declaration of Helsinki (2008)[268]

Table 2 Results of the assessment of predictable risks and burden to participants

Table 1 Ethical considerations of relevant principles of the Declaration of Helsinki (2008)[268]

PRINCIPLE AND RELEVANT ETHICAL CONSIDERATIONS
12. Must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory experimentation • Review of literature identified theoretical rationale for the research (1,3) • Preliminary studies established safe, effective methods for outcome measurements[195;207]
14. Design and performance must be clearly described in a research protocol that should contain a statement of the ethical considerations involved and indicate how principles in this Declaration have been addressed. • Design and performance described in protocol (4) • Statement of ethical considerations (4.10) • Indications of how principles in Declaration addressed (Table 4.15)
15. Protocol must be submitted for consideration, comment, guidance and approval to a research ethics committee before the study begins • Protocol submitted and ethical approval obtained from the University of Birmingham School of Psychology Ethics Committee
16. Must be conducted by individuals with appropriate scientific training and qualifications. Research on patients or healthy volunteers requires supervision of a competent and appropriately qualified physician or other health care professional • Research conducted by registered chiropractor (GS) with qualifications in physiology/neuroscience (rationale for study) who was responsible for protection of participants. Trained in use of equipment. Study supervised by post-doctoral researchers in health & population sciences/physiotherapy (AR) and psychology/neuroscience (CM)
18. Must be assessment of predictable risks and burdens to the individuals/communities involved in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation Problem of neck pain, need for better understanding based on research that may inform treatment approaches is well-defined in the literature[3;16;337-339] • Predictable risks/burdens assessed and measures taken to minimise these (Table 4.16)
2. Physicians may not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial results • Risks were assessed and measures taken to minimise these. Study would be stopped if unforeseen risk/benefit issues arose
21. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects • Importance of the objective established and outweighs minor risks/burdens identified (see also principle 18)

Table 1 continued

PRINCIPLE AND RELEVANT ETHICAL CONSIDERATIONS
22. Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees • Participation was voluntary. To prevent coercion no monetary payment to participants were offered
23. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information and to minimise the impact of the study on their physical, mental and social integrity • All information collected was handled according to clinic data protection procedures[270] • All information included in the study was anonymised and individuals were not identifiable (4.3.8)
24. In medical research involving competent human subjects, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed • Participants were informed of all required aspects of the study (participant letter , Appendix 3) • Participants were informed of their right to refuse to participate and to withdraw from the study (consent form, Appendix10) • Participants were given opportunity to ask for further information (consent form, Appendix 10) • Written consent was obtained (consent form, Appendix 10)
3. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication • It is intended to publish all findings, with the declarations required

Table 2 Results of the assessment of predictable risks and burden to participants

IDENTIFIED RISK: PHYSICAL HARM

• Pain caused by physical assessment
  ○ Nature of tests is to elicit pain, therefore high likelihood of some pain being experienced
  ○ Tests are routinely used in clinical practice
  ○ Some test procedures are also used as treatments (mobilizations)
-Training of examiner (AS) included specification to elicit minimum pain possible during provocation tests
- Participants informed that pain would be elicited during assessment procedure
- Usual advice/management by clinician available, should participants have any concerns (specified in letter to participants)
• Harm or pain caused by procedures for measurement of ocular motor or cervical spine position and motion tests
  ○ Adopting positions or carrying out movements required in tests could aggravate neck pain symptoms
- Participants positioned with care to avoid causing pain
- Limit cervical torsion to pain-free amount in SPNT test (previously reported method[91])
- Inform participants verbally that testing may be stopped should they wish. Checked that they are happy to continue at regular intervals throughout testing

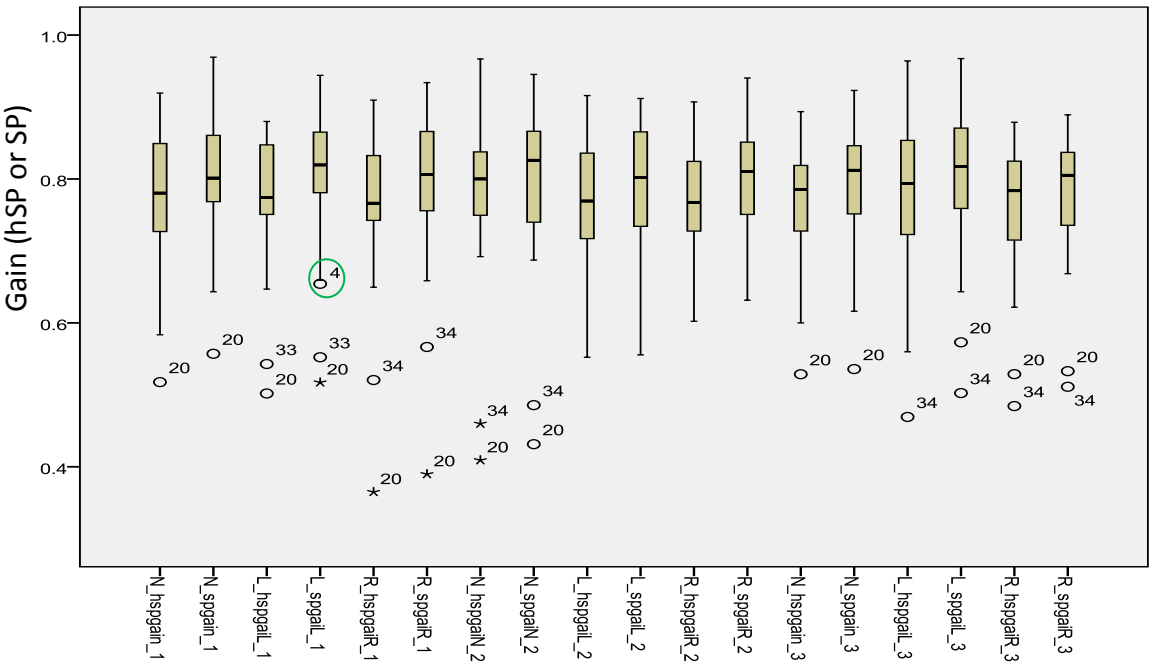
IDENTIFIED RISK: PSYCHOLOGICAL HARM
• Potential for burden on participants to feel they are beholden to complete study participation **- Participants informed that they are free to withdraw at any time, without having to give a reason and without harming study** • Potential for completing questionnaires to change patients emotional/cognitive responses to symptoms   ○ Questionnaires are widely used among neck pain patients and in research[197;273;278;279;282;284]. No such effects have been reported
IDENTIFIED RISK: SOCIAL HARM
• Information collected is not considered socially sensitive • Clinic data protection procedures are adhered to so as to ensure no disclosure of personal information[270] **- All data used in study is anonymised and individuals are not identifiable**
IDENTIFIED RISK: BURDEN ON PARTICIPANTS
• Time and expense of travel for 2 visits to clinic/laboratory • Duration of examination (30 minutes) and ocular motor and cervical spine testing procedures (90 minutes) • Requirement not to receive manual treatment for neck pain between physical assessment and laboratory visits **-Physical assessment offered at 2 clinic sites and at different days and times, including weekends** **- Laboratory visit available at different days and times, and at weekends** **-Requirements of participation clearly explained in letter to volunteers, prior to consent being sought**

Bold type provides measures in study design to address risks and burdens identified

APPENDIX 9

RESULTS OF OCULAR DATA PROCESSING, CLEANING AND EVALUATION OF SYSTEMATIC EFFECTS

Figure 1 Example of data cleaning process: Boxplots of hSP and cSP gain non-predictable ocular tracking in the neck pain group



Horizontal smooth pursuit (hSP) or combined horizontal and vertical smooth pursuit (cSP) gain is indicated on the vertical axis. Boxes indicate group data for either hSP or cSP in individual trials. Labels on the horizontal axis indicate the head position (N = neutral, L = left torsion, R = right torsion) and trial repeat number in each position (1,2, or 3). Most outlying or extreme values correspond to the same participants (participant numbers 20,33 and 34) who perform consistently in most trials. The green circle indicates a single trial where participant 4 had an outlying value, but inspection of all data values for that participant indicated that gain was consistent across trials thus the data was retained

Table 1 Comparison of quantity of ocular tracking data recorded and excluded between the neck pain and control groups

		NECK PAIN GROUP		CONTROL GROUP	
Ocular target tracking task		Predictable N = 31	Non-predictable N=31	Predictable N=22	Non-predictable N=22
Total number of trials recorded		279	279	198	198
Unedited data set - number of valid trials after data processing (% loss)		274 (1.79)	277 (.36)	192 (3.03)	192 (3.03)
Trials excluded from unedited data set following cleaning – number (% of unedited set)	hSP gain	1 (.36)[a]	0	0	0
	cSP gain		0		0
Edited data set - number of valid trials after cleaning (% of all recorded trials)		273[a] (97.85)	277 (99.28)	192 (96.97)	192 (96.97)

[a]hSP was the only parameter in the linear task therefore the whole trial was excluded

The quantities of ocular motor data excluded as a result of both data processing and cleaning are summarised. This indicates small percentage reductions only that are comparable between the neck pain and control groups and also between the predictable and random target ocular tracking trials.

Table 2 Results of repeated measures ANOVAs evaluating systematic effects through the testing protocol for predictable and non-predictable ocular tracking

OCULAR TARGET	NECK POSITION	NECK PAIN GROUP F	NECK PAIN GROUP p	CONTROL GROUP F	CONTROL GROUP p
PREDICTABLE	hSP Neutral	.864	.428	.296	.745
	hSP Left	1.880	.163	1.126	.335
	hSP Right	1.497	.234	1.215	.308
RANDOM	hSP Neutral	.273	.763	.947	.399
	hSP Left	.005	.995	.893	.420
	hSP Right	.341	.713	.692	.508
	cSP Neutral	.225	.800	.385	.684
	cSP Left	.179	.836	.291	.749
	cSP Right	2.313	.109	3.146	.057

Table 3 Comparison of quantity of cervical JPE, cervico-cephalic kinesthesia and cervical ROM data recorded and excluded between the neck pain and control groups

	NECK PAIN GROUP			CONTROL GROUP		
Test	CERVICAL JPE n = 29	CERVICO-CEPHALIC KINESTHESIA n = 28	ROM n = 29*	CERVICAL JPE n = 20	CERVICO-CEPHALIC KINESTHESIA n = 19	ROM n = 20
Total number of trials recorded	696	168	522	480	114	360
Unedited data set – number of valid trials after raw data processing (% loss)	681 (.02)	165 (.02)	505 (.03)	470 (.02)	114 (0)	352 (.02)
Trials excluded from unedited data set following cleaning – number (% of unedited set)	0 (.00)	7 (.04)	11 (.02)	1 (.01)	3 (.03)	0 (.00)
Edited data set – number of valid trials after cleaning (% of all recorded trials)	678 (97.84)	158 (94.05)	494 (94.64)	470 (97.91)	111 (97.37)	352 (97.78)

*For lateral flexion ROM n = 27 in edited data set, after removal of participants 13 and 34, whose trials all had negative values

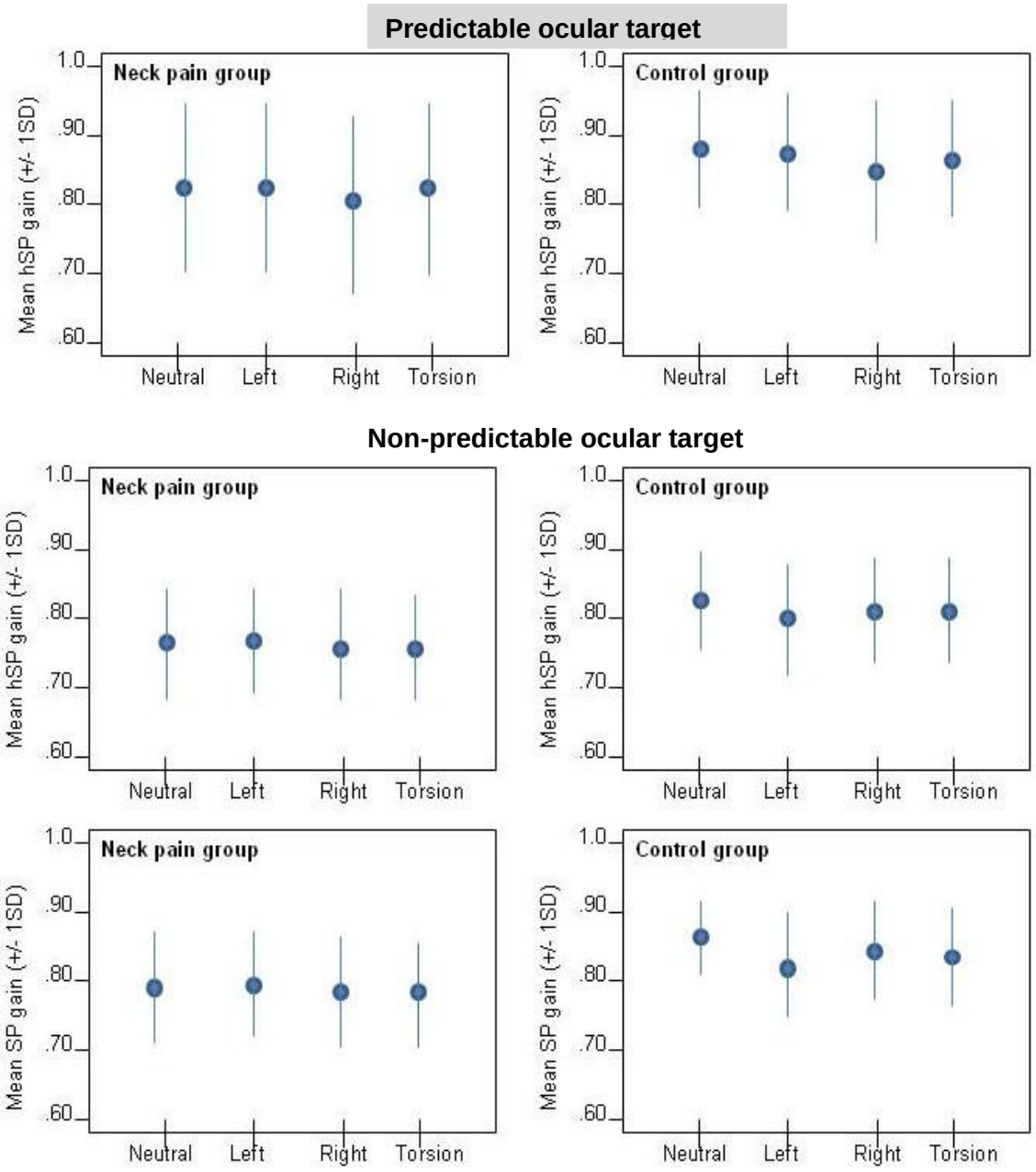
Table 4 Results of repeated measures ANOVAs evaluating systematic effects through the testing protocol for the cervical JPE, cervico-cephalic kinesthesia and cervical ROM tests

TEST		NECK PAIN GROUP		CONTROL GROUP	
		F	p	F	p
CERVICAL JPE	Flexion	5.134	.000	1.756	.129
	Extension	4.252	.004-.049[a]	3.712	.018-.069[a]
	Left rotation	1.001	.326-.412a	.769	.391-.574[a]
	Right rotation	3.077	.019-.090[a]	1.244	.279-.302[a]
	Horizontal error	.473	.499-.703[a]	1.256	.291
	Vertical error	3.039	.014	1.350	.252
CERVICO-CEPHALIC KINESTHESIA	Total error	2.271	.053	1.095	.370
	Horizontal error	.473	.499-.675[a]	1.256	.291
	Vertical error	3.039	.014	1.350	.252
	Total error	2.271	.053	1.095	.370
CERVICAL ROM	Flexion	3.721	.052-.069[a]	.216	.807
	Extension	.514	.602	1.536	.236-.237[a]
	Left rotation	3.961	.048-.061[a]	.342	.568-.609[a]
	Right rotation	2.180	.127	.140	.870
	Left lateral flexion	1.537	.228	1.288	.292
	Right lateral flexion	1.367	.257-.260[a]	.420	.661
	Left lateral flexion	1.537	.228	1.288	.292
	Right lateral flexion	1.367	.257-.260[a]	.420	.661

[a] Mauchly's test of sphericity significant at .01 level, therefore p is the range of values given by Greenhouse-Geisser, Huynh-Feldt and Lower-bound tests

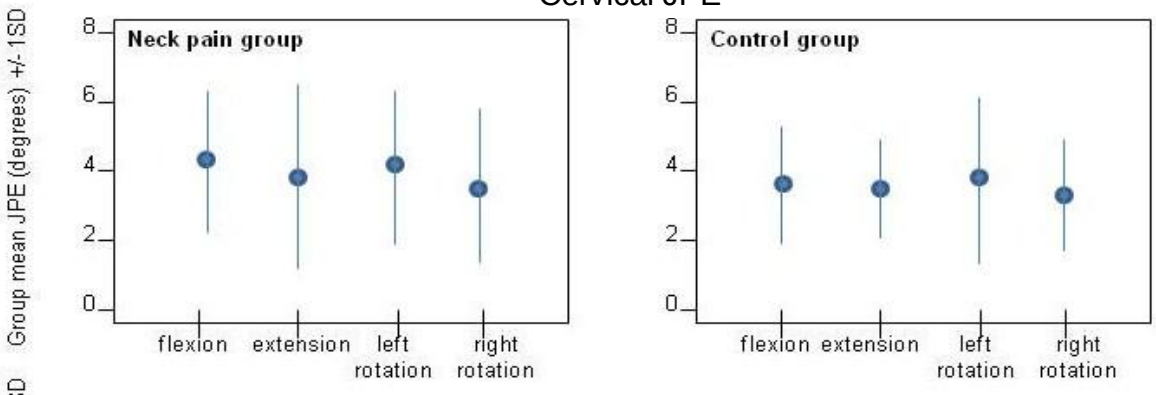
Red shading indicates p<.01: significant at 99% level. Blue shading indicates edited data sets.

Figure 2 Error plots comparing performance in ocular tracking tasks

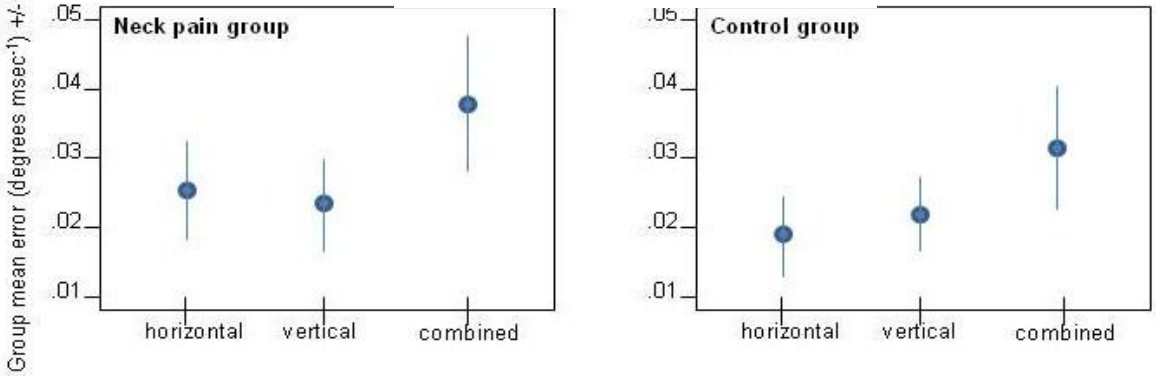


Bars indicate group mean velocity gain (+/- 1SD) for hSP or cSP(vertical axis). Horizontal axis indicates neck position (torsion = mean of right and left torsion). Lower mean hSP and cSP gains, with slightly greater SDs are apparent in the neck pain group (left hand column), compared with the healthy control group

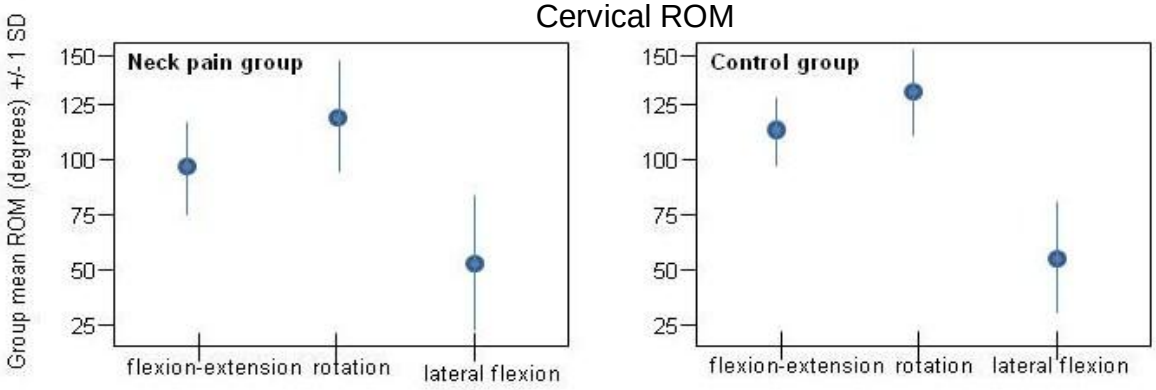
Cervical JPE



Cervico-cephalic kinesthesia



Cervical ROM



is RMSE. The horizontal axis indicates the direction of head motion that precedes repositioning for the head repositioning task, the component plane of error for the head tracking task and the full plane motion for the cervical ROM test. Edited and unedited data sets were similar; results for unedited sets are provided here