The neurophysiological effects of a single session of spinal joint mobilization: does the effect last?

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Studies detailing the neurophysiological effects of spinal manual therapy have fueled a paradigm shift away from a strict biomechanical model. However, a recent systematic review of the temporal nature of a single session of spinal thrust manipulation found that the neurophysiological effects were only temporary. The objective of this review was to examine the temporal nature of neurophysiological effects after one session of spinal mobilization. Studies eligible for this review had to report on the temporal component of the neurophysiological effects of a single session of joint mobilization of the spine in human subjects. In order to be sure that the temporal nature of these effects was captured, the studies had to monitor neurophysiological effects for a time beyond the immediate post-treatment period. This systematic review followed the methodology for preferred reporting items for systematic reviews and meta-analyses. In order to assess the quality, strength, and importance of the included studies, the grading of recommendations assessment, development and evaluation system was used. Results of this review showed that the neurophysiological effects of a single session of spinal mobilization are mostly 5 minutes or less. An exception to these findings is hypoalgesia which may last up to 24 hours, based on one study. Continued research on small samples of healthy subjects with irrelevant immediate outcomes like salivary rate, skin conductance, and skin temperature should give way to randomized controlled trials on subjects with pain and decreased function.

Keywords: Manual therapy, Mobilization, Neurophysiological, Spine, Temporal

Introduction

Passive non-thrust manipulation or ‘joint mobilizations’ of the spine, defined as a low-amplitude, low-velocity sustained or oscillatory motion to the spinal vertebrae either with or without movement, is used routinely in clinical practice to successfully treat patients with pain and dysfunction.^{1–4} Theories about the mechanism by which joint mobilizations affect pain and dysfunction in patients range from physical (biomechanical) to psychological.⁵ Recently, a paradigm shift has taken place in manual therapy as an increasing number of studies support a predominantly neurophysiological mechanism of benefit with joint mobilizations.^{5,6}

Neurophysiological effects can be found at the site of treatment and at areas remote to the local area of treatment.^{7,8} These effects include improved pain-related measures (increased pressure pain threshold, decreased visual analogue scale pain rating, and

increased pain-free grip),^{9–11} changes in skin conductance (SC),¹² changes in skin temperature (ST),¹³ and improvements in range of motion with neural tensioning.^{14,15}

The implication of the term ‘paradigm shift’ is that the discovery of the neurophysiological effects of mobilization is important enough to cause a categorical and substantial change in how clinicians and scientists understand the benefits of mobilization. However, are these effects important to patients? Despite there being little correlation between impairments and functional limitations, assessments of impairments, signs, or symptoms are more commonly used as indicators of patient progress on a daily basis because we accept them as proxy measures for more complex constructs like function and ability in which improvement may take weeks.¹⁶ If this statement is true, then alleviating impairments is of critical importance for two reasons: (1) impairments are often the reason patients seek care at all; and (2) the alleviation of impairments is used as an indicator that the intervention(s) being used is/are correct or that

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treatment is effective. With such heavy clinical importance placed on neurophysiological-mediated changes in key impairments such as pain and lost motion, understanding the effect of a commonly used intervention like spinal mobilization on these impairments is paramount.

A recent systematic review by Coronado *et al.*¹⁷ reported that a single session of high-velocity, low-amplitude thrust (HVLAT) spinal manipulation had demonstrable neurophysiological effects but that the effects were short-lived. These authors concluded that although the clinical effectiveness of HVLAT is apparent, the unique contribution of HVLAT within a multimodal treatment was less clear. Similarly, the beneficial effects of mobilization as part of a multimodal strategy have been documented.^{18–20} The lasting and unique contribution of a single session of spinal joint mobilization has not been reviewed. Therefore, the purpose of this systematic review was to examine the temporal nature of the neurophysiological effects of passive joint mobilizations when used in isolation on the spine in human subjects.

Methods

This systematic review followed the methodology for preferred reporting items for systematic reviews and meta-analyses²¹ generally, and for the quality, strength, and importance assessment of individual studies included in the review, grading of recommendations assessment, development and evaluation (GRADE) system was used.²²

Inclusion/exclusion criteria

Studies eligible for this review had to report on the temporal component of the neurophysiological effects of a single session of joint mobilization of the spine in human subjects. In order to be sure that the temporal nature of these effects was captured, the studies had to monitor neurophysiological effects for a time beyond the immediate post-treatment period. Studies were excluded if they reported on the effect of manipulation, HVLAT, or were not specific as to the type of manual therapy used in treatment. Also, those studies that used other types of non-thrust manual therapy like neural mobilization, massage, myofascial release, and craniosacral therapy, to name a few, were excluded from the study. Finally, case study and case series designs as well as non-human studies and conference proceedings were excluded from review.

Search strategy

A systematic search for articles was performed in the electronic databases of the Cumulative Index to Nursing and Allied Health Literature (Table 1) (beginning to November 2010) and Medline (1960 to November 2010) using search terms related to mobilization and manual therapy. When the more specific terms ‘neurophysiological’, ‘temporal’, or ‘spine’ were added

to the search, the strategy became too specific with a great many false negatives (missed articles that would have been appropriate) when compared to the hand search. The hand search consisted of a review of the author’s (EJH) personal collection which included systematic reviews and original articles reporting outcomes related to mobilization of the spine.

Review process

The title and abstract of each article from the computer search were reviewed by two of the authors (EH and ES) and a consensus decision was reached about which articles to acquire and read in full. Also, the reference lists of the reviews and original articles from the author’s collection were scanned for additional potential articles. These potential articles were read in full by the same two authors and determined relevant or not based on their content regarding the established *a priori* inclusion/exclusion criteria.

Quality, strength, and importance assessment

In order to comment on the quality and strength of each article, the GRADE system was used.²² GRADE classifies the quality of an article as ‘high’, ‘moderate’, ‘low’, or ‘very low’ with the ability to combine the ‘low’ and ‘very low’ categories. We elected to combine these last two categories for this review. High quality evidence is identified when further research is unlikely to change the effect size of the intervention.²² Moderate quality evidence is defined as a confidence that the effect may change with further, better research.²² Finally, low quality research is defined by a confidence that further research is likely to change the reported effect.²² In order to assist us in determining the quality of an article, we modified a scoring sheet used by Gross *et al.*²³ which in itself was a modification of a quality tool recommended by the Cochrane Back Review Group.²⁴ Our scoring sheet had nine items designed to assess bias and included a range of desirable design and reporting features from the presence of randomization to evidence of an acceptable dropout rate. For each desirable trait, 1 quality point was awarded with a maximum score of 9. Studies of high quality had scores of 8 or 9; moderate quality had scores of 4–7; and low quality had scores of 0–3. Two authors (EH and ES) performed the quality scoring and resolved differences in scoring through discussion. In

Table 1 Cumulative Index to Nursing and Allied Health Literature search strategy

	Search term
1.	(mobilization or mobilization).ti
2.	Manual therapy.txt
3.	1 and 2
4.	3 and not manipulation
Total	237 results

Figure 1 Flow diagram for article selection.

the final analysis, high quality studies were indicated by an 'A', moderate quality with a 'B', and had there been any low quality studies, they would have been indicated by a 'C' grade. The 'A', 'B', and 'C' grades were used to make it easier for the reader to differentiate the quality score from the strength score.

Beyond research quality, GRADE also makes use of a strength grade. The strength grade is dichotomous: 'strong' or 'conditional (weak)'. The strength of the research is dependent upon the extent to which the positive effects of an intervention outweigh the negative effects and confidence in those effects.²⁵ We used '1' to indicate strong evidence and '2' to indicate conditional evidence.

Finally, GRADE requires an evaluation of the outcomes of each study and a comment on the importance of those outcomes to the patients who will be affected by the specified treatment modality. We elected to use the following scale to quantify importance: I=critical; II=important; III=not important. The purpose of combining strength, quality, and clinical importance ratings is to be as transparent as possible regarding the available evidence for those who will use the results of this review in their evidence-based practice. Our final scoring system was meant to simplify presentation of the studies and allow a succinct determination of strength, quality, and clinical importance. For example, an article receiving an overall score of II-A-1 would be an important (but not critical) study of high quality where the intervention detailed in the study would be strongly recommended.

Results

Literature search

All of the searches resulted in the title and abstract review of 346 articles (Fig. 1). The application of inclusion/exclusion criteria resulted in 10 articles being reviewed: 6 pertinent to the cervical spine, 3 to the thoracic spine, and 1 to the lumbar spine. After reading the titles and abstracts, the majority of the remaining articles were eliminated either because

more than one session of mobilization was performed or the neurophysiological effects were not monitored beyond the immediate post-treatment period.

Study characteristics

A summary of each of the articles included in the review can be found in Table 2. Eight of the studies examined asymptomatic subjects while one study examined patients with neck pain and one study examined patients with lateral elbow pain. The majority of the studies on asymptomatic subjects found that SC increased but that ST did not change significantly after mobilization. Further, the change in SC lasted 10 minutes at maximum and 5 minutes or less predominantly. Both studies involving symptomatic subjects demonstrated a significant reduction in pain with oscillatory mobilizations to the cervical spine,^{26,27} although mobilization at the correct level may not be a requisite for pain relief, at least locally. Mobilization of the spine seems to have an immediate effect on pain that lasts for up to 24 hours while the effect on other neurophysiological measures is less dramatic.

Quality and strength of evidence and importance of outcomes

The quality and strength of the evidence as well as the importance of the outcomes is summarized in Table 3. Six of 10 studies^{7,12,26-29} were of high quality, and the remaining four studies^{8,13,30,31} were of moderate quality. Most of the moderate quality studies were downgraded due to a lack of subject randomization and either questionable or absent allocation concealment. Of the six high quality studies, only one study²⁶ had both strong evidence and is classified as having important clinical outcomes. In addition to the Kanlayanphotporn *et al.*²⁶ study, only one other study²⁷ had important clinical outcomes by our rating. Therefore, the majority of studies in this review were rated as having a conditional or weak strength of evidence and unimportant outcomes making the overall body of work as reviewed here unimportant with respect to clinical decision-making. No studies had a grade of I-A-1, which would be interpreted as critical outcomes with high quality and strong evidence for use of the intervention.

Discussion

The implication for studies of neurophysiological effects is that if spinal mobilization produces a sympathetic nervous system (SNS) response demonstrated by many proxy measures but mostly SC and ST, then this SNS response must be because the dorsal peri-aqueductal (dPAG) matter of the mid-brain is stimulated. Stimulation of the dPAG produces analgesia, sympathoexcitation, and motor facilitation.¹¹ If the dPAG is stimulated by manual

Table 2 Article summary

Authors (maximum time after Rx. that effects were measured)	Participants	Research design	Intervention group(s)	Control group	Outcomes measures of interest	Results
Kanlayanaphotporn et al. ²⁶ (5 minutes)	60 with mechanical neck pain (42 females and 18 males) randomized to either CPA or random mobilization, aged 23–68 years	RCT. Both patient and treating therapist/ outcomes assessor were blinded to group allocation	1. Placebo: one of three mobilizations: CPA at wrong level; right UPA at wrong level; left UPA at wrong level 2. Treatment: 2, 1-minute CPA's at appropriate level	None	Pain at rest and with the most painful movement rated on a 0–100 mm VAS	Both intervention groups showed a statistically significant change in pain at rest after treatment. The treatment group showed a statistically significant difference in pain with the most painful movement versus the placebo group. Treatments (CPA's) were the only intervention to show a clinically relevant change of 20 mm
Henderson et al. ²⁸ (10 minutes)	14 asymptomatic (9 female and 5 male) of aged 30.9 years on average	RCT	1. Placebo: light touch 2. Treatment: costotransverse mobilizations 'rib raising'	None	alpha-amylase secretion in saliva as a measure of sympathetic activity, salivary flow rate as a measure of parasympathetic activity, and salivary cortisol as a measure of HPA axis activity	A statistically significant decrease in salivary alpha-amylase immediately after and for up to 10 minutes after mobilization. Rib raising appears to stimulate the activity of the parasympathetic nervous system. No significant change in either flow rate or salivary cortisol levels with placebo.
Jowsey and Perry ²⁹ (5 minutes)	36 asymptomatic (23 females and 13 males), aged 18–35 years	RCT. Double-blind, placebo controlled	1. Placebo: T4 pressure without mobilization 2. Treatment: right T4 'screw' mobilization	None	SC as a proxy measure for increased sudomotor activity	Statistically significant change in SC from baseline to 5 minutes post-Rx. in the right hand after a right-sided T4 mobilization. Questionnaire to subjects after study showed that placebo was appropriate although expectancy was greater in the placebo group.
Perry and Green ⁷ (5 minutes)	45 asymptomatic males, aged 18–25 years	Double-blind, matched subjects	1. Placebo: light pressure to left L4–5 facet, no oscillation 2. Treatment: Grade III UPA to left L4–5 facet	Subject laid prone as in other groups with no manual contact.	SC as a proxy measure for increased sudomotor activity	Statistically significant change in SC of the ipsilateral limb during the treatment with UPA oscillatory mobilization. This change did not last 5 minutes. Questionnaire to subjects after study showed that subjects were unaware as to whether they were in treatment or placebo but control subjects were aware of their assignment.

Table 2 Continued.

Authors (maximum time after Rx. that effects were measured)	Participants	Research design	Intervention group(s)	Control group	Outcomes measures of interest	Results
Moulson and Watson ⁸ (2 minutes)	16 asymptomatic (11 females and 5 males), aged 18–37 years	Single blind, placebo, within subject repeated measures	1. Placebo: C5–6 contact without SNAGS while rotating right 2. Treatment: C5–6 SNAGS into right rotation	Subject sat for the entire time with researcher/therapist behind them. No contact from the therapist.	ST and SC as proxy measures for SNS-mediated vasoconstriction and increased sudomotor activity, respectively	No left to right difference in ST or SC under any treatment condition. No significant change in ST with either intervention versus control. Significant increase in SC with both treatments versus control and from pre-test to 2 minutes post-test in treatment versus placebo. Post-Rx questionnaire showed that 13/16 could identify the SNAG as the treatment.
Chiu and Wright ³⁰ (10 minutes)	17 asymptomatic (6 females and 11 males), aged 18–30 years	Double-blind, placebo, within subject repeated measures	1. Placebo: C5 contact without mobilization 2. Treatment A: Grade III CPA at C5 3. Treatment B: Grade III lateral glide to C5	Subject lay prone for the entire time with researcher/therapist behind them. No contact from the therapist. Each patient served as their own control and received all three interventions	SC as proxy measures for SNS-mediated vasoconstriction and increased sudomotor activity, respectively	No significant change in either ST or SC in any of the treatment groups. Authors hypothesized that the failure to show significance in this study may be related to the slow rate of mobilization or the low power of the current study.
Vicenzino et al. ²⁷ (24 hours)	15 with chronic lateral epicondylagia (8 females and 7 males), aged 22.5–62 years	Double-blind, placebo, within subjects, repeated measures	1. Placebo: C5–6 contact without oscillation 2. Treatment: Grade III lateral glide at C5–6 away from the side of pain while the arm was in a position of shoulder abduction, shoulder internal rotation, and elbow extension	No contact from the therapist.	Many were measured immediately pre-post but of interest was VAS pain ratings of worst pain at 24 hours post	A decrease in worst pain rating of 1.9 cm on a 10 cm VAS in treatment group. Questionnaire to subjects after study showed that 13/15 subjects were unaware that they were in the treatment group.
Chiu and Wright ¹² (10 minutes)	16 asymptomatic males, aged 18–25 years	Double-blind, within subject repeated measures	1. Treatment A: C5 CPA, Grade III, rate of 2 Hz 2. Treatment B: C5 CPA, Grade III, rate of 0.5 Hz	Subject laid prone as in other groups with no manual contact.	ST and SC as proxy measures for SNS-mediated vasoconstriction and increased sudomotor activity, respectively	Study compared SC and ST changes with a 2 Hz (120/minute) compared to a 0.5 Hz (30/minute) oscillatory mobilization at C5. The 2 Hz mobilization produced a significant increase in SC values but not ST values. The time for maximum SC in the 2 Hz group ranged from 50 to 100 seconds.

Table 2 Continued.

Authors (maximum time after Rx. that effects were measured)	Participants	Research design	Intervention group(s)	Control group	Outcomes measures of interest	Results
Slater <i>et al.</i> ³¹ (10 minutes)	22 asymptomatic (8 females and 14 males) of age 24 years, seven months on average	Double-blind, placebo, within subject repeated measures	1. Placebo: light touch 2. Treatment: thoracic sympathetic slump with right T6 PA mobilization	Subject laid supine for the entire time with the researcher/therapist behind them. No contact from the therapist.	ST and SC as proxy measures for SNS-mediated vasoconstriction and increased sudomotor activity, respectively	Right-sided SC values were higher than left under all conditions immediately post-Rx. but not at 10 minutes post-Rx. The authors explain this finding by noting an orthostatic adjustment as the subject moved from supine to the position of the test (long sit). Further, SC mean values showed a significant difference among all conditions (Rx.>placebo>control). ST values showed inconsistent effects.
Petersen <i>et al.</i> ¹³ (5 minutes)	16 asymptomatic males, aged 18–35 years	Double-blind, within subject repeated measures	1. Placebo: light pressure to C5, no oscillation 2. Treatment: Grade III CPA to C5	Subject laid prone as in other groups with no manual contact.	ST and SC as proxy measures for SNS-mediated vasoconstriction and increased sudomotor activity, respectively	There was a statistically significant change in SC in the right upper extremity in the treatment group for up to 5 minutes post-Rx. This same finding was reported with ST, but only in treatment groups when compared to placebo group. With a Grade III mobilization, SC increases 50–60% but placebo itself showed a 30% increase.

Note: Rx. =treatment; VAS=visual analogue scale; ST=skin temperature; SC=skin conductance; SNS=sympathetic nervous system; RCT=randomized controlled trial; SNAGS=sustained natural apophyseal glides; PA=posteroanterior.

Table 3 Summary of findings

Study	Clinical outcome	Importance of outcomes in clinical decision-making (I= critical; II=important; III=not important)	Quality of evidence (A=high; B=moderate; C=low)	Strength of evidence for using intervention [1=strong; 2=conditional (weak)]	Intervention
Kanlayanphotporn <i>et al.</i> ²⁶	Neck pain relief with most painful motion and at rest lasting 5 minutes	II	A	1	CPA mobilization at correct level or CPA/UPA at incorrect level
Henderson <i>et al.</i> ²⁸	Decreased alpha-amylase secretion in saliva lasting 10 minutes	III	B	2	Costotransverse joint mobilizations: 'rib raising'
Jowsey and Perry ²⁹	Increased SC lasting 5 minutes	III	A	2	Right T4 'screw' mobilization
Perry and Green ⁷	Increased SC lasting less than 5 minutes	III	A	2	Grade III, oscillatory UPA mobilization to left L4–5 facet
Moulson and Watson ⁸	Increased SC and no change in ST lasting up to 2 minutes	III	B	2	Sustained natural apophyseal glide to C5–6 to facilitate right rotation
Chiu and Wright ³⁰	No significant change in either ST or SC for up to 10 minutes	III	B	2	Grade III CPA at C5 and Grade III lateral glide to C5
Vicenzino <i>et al.</i> ²⁷	Decreased VAS worst elbow pain rating for up to 24 hours	II	B	2	C5–6 contact without oscillation and Grade III lateral glide at C5–6 away from the side of pain while the arm was in a position of shoulder abduction, shoulder internal rotation, and elbow extension
Chiu and Wright ¹²	Increased SC and no change in ST lasting 50–100 seconds but not lasting 10 minutes	III	A	2	Treatment A: C5 CPA, Grade III, rate of 2 Hz; treatment B: C5 CPA, Grade III, rate of 0.5 Hz
Slater <i>et al.</i> ³¹	Increased SC and no change in ST immediately after Rx. but not lasting 10 minutes	III	B	2	Thoracic sympathetic slump with right T6 PA mobilization
Petersen <i>et al.</i> ¹³	Increased SC and ST for up to 5 minutes	III	B	2	Light pressure to C5 without oscillation and Grade III CPA to C5

Note: Rx.=treatment; ST=skin temperature; SC=skin conductance.

therapy, then perhaps manual therapy can also produce pain relief via its influence on the dPAG. While some have questioned this assumption,^{6,8} there appears to be ample evidence that spinal mobilization produces an extrasegmental effect based on proxy measures of SNS function. However, the temporal nature of this SNS effect, with the exception of analgesia produced by cervical mobilizations in one study of moderate quality,²⁷ appears to be mostly 5 minutes or less.

Nevertheless, the studies cited in this review and others^{6,17} have undoubtedly been important in driving a paradigm shift in manual therapy away from a strict

biomechanical model and toward a more comprehensive model that recognizes peripheral, spinal, and supraspinal neurophysiological effects.^{5,6} How then can we rate the overall body of work on the temporal effects of spinal mobilization as unimportant? As an outcomes measure, changes in functional limitations may be a more important indicator of patient progress than impairment relief since impairments are poorly correlated with function. However, impairments are used more often clinically to measure progress.¹⁶ Tuttle¹⁶ suggests that one answer to this paradox is to select an impairment that is important to the patient. A major component

of GRADE that differentiates this quality assessment system from others is that authors are asked to judge the importance of outcomes to patients.³² In our judgment, changes in ST and SC are less important to patients than pain reduction and range of motion improvement which is why only two studies^{26,27} were rated as 'important'. Further, these same two studies were the only ones in our review that examined the effect of mobilizations on patients who were actually in pain. Finally, only the study by Kanlayanaphotpran *et al.*²⁶ was given a strength grade of 'strong' due to their report of a significant effect of mobilization on cervical pain, their report of no adverse effects on any patient in the study, and the strength of the study design.

One recent randomized controlled trial²⁶ examined the temporal nature of a single session of cervical mobilization showing significant pain relief of up to 5 minutes. At this time, practitioners of manual therapy should be uncertain that a single session of spinal mobilization, by itself, has any meaningful, lasting benefit. The majority of the studies that qualified for this review have sampled less than 25, primarily asymptomatic subjects assessing the outcomes of SC and ST. These are less than inspiring criteria upon which to base a clinical decision for clinicians working with patients with spinal pain. Clearly, additional randomized trials are warranted with primary outcomes such as the lasting effect of a single session of spinal mobilization on range of motion and pain while taking into account non-specific responses like expectation, placebo, and fear.⁵ Understanding the meaningful neurophysiological effects of spinal mobilization is important since mobilization is a low-cost, non-invasive intervention that is used frequently by clinicians as part of a comprehensive management plan for patients with spine-related pain.

Limitations

The results of this systematic review should be interpreted in light of some limitations. The neurophysiological effects reported were confined to studies examining a single session of spinal mobilization only. The strength of the evidence comprising this review was mostly conditional. The lumbar spine as a region was under-represented and asymptomatic subjects were over-represented. Finally, meta-analysis enabling pooled statistics of effect was not possible due to the heterogeneous nature of the studies.

Conclusions

Only two studies^{26,27} examined the temporal nature of the neurophysiological effects of a single session of isolated spinal joint mobilizations which makes the enduring nature of clinically important outcomes difficult to judge. Research showing demonstrable

neurophysiological effects of a single session of spinal mobilization has been highly important in contributing to the paradigm shift in how clinicians view the technique, application, and outcomes related to manual therapy.^{5,6} However, now that the paradigm has shifted, continued research on small samples of healthy subjects with irrelevant immediate outcomes like salivary rate, SC, and ST should give way to randomized controlled trials on subjects with pain and decreased function so that the product is an enhanced, more robust paradigm that leads to clinical guidelines that will benefit our patients.

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References

- 1 Dhondt W, Willaers T, Verbruggen LA, Oostendorp RA, Duquet W. Pain threshold in patients with rheumatoid arthritis and effect of manual oscillations. *Scand J Rheumatol* 1999; 28:88-93.
- 2 McClatchie L, Laprade J, Martin S, Jaglal SB, Richardson D, Agur A. Mobilizations of the asymptomatic cervical spine can reduce signs of shoulder dysfunction in adults. *Man Ther* 2009;14:369-74.
- 3 Teys P, Bisset L, Vicenzino B. The initial effects of a Mulligan's mobilization with movement technique on range of movement and pressure pain threshold in pain-limited shoulders. *Man Ther* 2008;13:37-42.
- 4 Willett E, Hebron C, Krouwel O. The initial effects of different rates of lumbar mobilisations on pressure pain thresholds in asymptomatic subjects. *Man Ther* 2010;15:173-8.
- 5 Bialosky JE, Bishop MD, Price DD, Robinson ME, George SZ. The mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. *Man Ther* 2009; 14:531-8.
- 6 Schmid A, Brunner F, Wright A, Bachmann LM. Paradigm shift in manual therapy? Evidence for a central nervous system component in the response to passive cervical joint mobilisation. *Man Ther* 2008;13:387-96.
- 7 Perry J, Green A. An investigation into the effects of a unilaterally applied lumbar mobilisation technique on peripheral sympathetic nervous system activity in the lower limbs. *Man Ther* 2008;13:492-9.
- 8 Moulson A, Watson T. A preliminary investigation into the relationship between cervical snags and sympathetic nervous system activity in the upper limbs of an asymptomatic population. *Man Ther* 2006;11:214-24.
- 9 Coppieters MW, Stappaerts KH, Wouters LL, Janssens K. The immediate effects of a cervical lateral glide treatment technique in patients with neurogenic cervicobrachial pain. *J Orthop Sports Phys Ther* 2003;33:369-78.
- 10 Sterling M, Jull G, Wright A. Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. *Man Ther* 2001;6:72-81.
- 11 Vicenzino B, Collins D, Benson H, Wright A. An investigation of the interrelationship between manipulative therapy-induced hypoalgesia and sympathoexcitation. *J Manip Physiol Ther* 1998;21:448-53.
- 12 Chiu TW, Wright A. To compare the effects of different rates of application of a cervical mobilisation technique on sympathetic

- outflow to the upper limb in normal subjects. *Man Ther* 1996;1:198–203.
- 13 Petersen N, Vicenzino B, Wright A. The effects of a cervical mobilization technique on sympathetic outflow to the upper limb in normal subjects. *Physiother Theory Pract* 1993;9:149–56.
 - 14 Coppeters MW, Stappaerts KH, Wouters LL, Janssens K. Aberrant protective force generation during neural provocation testing and the effect of treatment in patients with neurogenic cervicobrachial pain. *J Manip Physiol Ther* 2003;26:99–106.
 - 15 Saranga J, Green A, Lewis J, Worsfold C. Effect of a cervical lateral glide on the upper limb neurodynamic test 1: a blinded placebo-controlled investigation. *Physiotherapy* 2003;89:678–84.
 - 16 Tuttle N. Is it reasonable to use an individual patient's progress after treatment as a guide to ongoing clinical reasoning? *J Manip Physiol Ther* 2009;32:396–403.
 - 17 Coronado RA, Bialosky JE, Cook CE. The temporal effects of a single session of high-velocity, low-amplitude thrust manipulation on subjects with spinal pain. *Phys Ther Rev* 2010;15:1–7.
 - 18 Bautmans I, Van Arken J, Van Mackelenberg M, Mets T. Rehabilitation using manual mobilization for thoracic kyphosis in elderly postmenopausal patients with osteoporosis. *J Rehabil Med* 2010;42:129–35.
 - 19 Leaver AM, Maher CG, Herbert RD, Latimer J, McAuley JH, Jull G, et al. A randomized controlled trial comparing mobilization with manipulation for recent onset neck pain. *Arch Phys Med Rehabil* 2010;91:1313–8.
 - 20 Ko T, Jeong U, Lee K. Effects of the inclusion of thoracic mobilization into cranio-cervical flexor exercise in patients with chronic neck pain. *J Phys Ther Sci* 2010;22:87–91.
 - 21 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;339:332–6.
 - 22 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
 - 23 Gross A, Miller J, D'Sylva J, Burnie SJ, Goldsmith CH, Graham N, et al. Manipulation or mobilisation for neck pain: a Cochrane Review. *Man Ther* 2010;15:315–33.
 - 24 van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. *Spine (Phila Pa 1976)* 2003;28:1290–9.
 - 25 Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations. *BMJ* 2008;336:1049–51.
 - 26 Kanlayanaphotporn R, Chiradejnant A, Vachalathiti R. Immediate effects of the central posteroanterior mobilization technique on pain and range of motion in patients with mechanical neck pain. *Disabil Rehabil* 2010;32:622–8.
 - 27 Vicenzino B, Collins D, Wright A. The initial effects of a cervical spine manipulative physiotherapy treatment on the pain and dysfunction of lateral epicondylalgia. *Pain* 1996;68:69–74.
 - 28 Henderson AT, Fisher JF, Blair J, Shea C, Li TS, Bridges KG. Effects of rib raising on the autonomic nervous system: a pilot study using noninvasive biomarkers. *J Am Osteopath Assoc* 2010;110:324–30.
 - 29 Jowsey P, Perry J. Sympathetic nervous system effects in the hands following a grade III postero-anterior rotatory mobilisation technique applied to T4: a randomised, placebo-controlled trial. *Man Ther* 2010;15:248–53.
 - 30 Chiu TW, Wright A. Comparing the effects of two cervical mobilisation techniques on sympathetic outflow to the upper limb in normal subjects. *Hong Kong Physiother J* 1998;16:13–8.
 - 31 Slater H, Vicenzino B, Wright A. 'Sympathetic slump': the effects of a novel manual therapy technique on peripheral sympathetic nervous system function. *J Man Manip Ther* 1994;2:156–62.
 - 32 Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Schunemann HJ. GRADE: what is 'quality of evidence' and why is it important to clinicians? *BMJ* 2008;336:995–8.