Available online at www.sciencedirect.com
ScienceDirect
Manual Therapy 13 (2008) 387–396
MANUAL THERAPY
www.elsevier.com/math

Systematic review

Paradigm shift in manual therapy? Evidence for a central nervous system component in the response to passive cervical joint mobilisation

Annina Schmid[a,*], Florian Brunner[b], Anthony Wright[c], Lucas M. Bachmann[d]

[a]Uniklinik Balgrist, Department of Physiotherapy, Forchstrasse 340, 8008 Zurich, Switzerland
[b]Uniklinik Balgrist, Department of Rheumatology, Forchstrasse 340, 8008 Zurich, Switzerland
[c]School of Physiotherapy, Curtin University of Technology, Perth, Australia
[d]Horten Center for patient-oriented research, University of Zurich, Switzerland

Received 28 February 2007; received in revised form 30 November 2007; accepted 18 December 2007

Abstract

Segmental neurological modulation, neural hysteresis and biomechanical effects have been proposed as mechanisms underpinning the effects of manual therapy. An increasing number of studies hypothesise activation of the central nervous system resulting in a non-segmental hypoalgesic effect with concurrent activation of other neural pathways as a potential mechanism of action. Whether this model is consistent with the current literature is unknown.

This systematic review aims to assess the consistency of evidence supporting an involvement of supraspinal systems in mediating the effects of passive cervical joint mobilisation.

We searched randomised trials in three electronic databases from inception to November 2007, without language restriction, and checked reference lists of included studies. We assessed study validity and extracted salient features in duplicate.

Fifteen studies met our inclusion criteria. The overall quality was high. We found consistency for concurrent hypoalgesia, sympathetic nervous system excitation and changes in motor function. Pooling of data suggested that joint mobilisation improved outcomes by approximately 20% relative to controls. This specific pattern suggests that descending pathways might play a key role in manual therapy induced hypoalgesia.

Our review supports the existence of an alternative neurophysiological model, in which passive joint mobilisation stimulates areas within the central nervous system.

Keywords: Treatment outcome; Cervical pain; Neck; Manipulation spinal; Joint mobilisation techniques; Physical therapy (speciality)

1. Introduction

Passive cervical joint mobilisation techniques (Maitland et al., 2005) are widely used among manipulative physiotherapists worldwide to treat motion restriction and pain of spinal origin. Until recently, experts believed that the interplay of local and segmental responses to the mobilisation was responsible for a clinical benefit. The concept includes activation of gate-control mechanisms (Melzack and Wall, 1965; Wyke, 1985), hysteresis effects leading to a reduced neural afferent discharge (Zusman, 1986) and biomechanical effects such as tissue lubrication or "correction of spinal joint subluxation" (Paris, 1979).

However, an increasing number of studies indicate that passive joint mobilisation might also activate various areas within the central nervous system to produce a multisystem response that extends beyond the

*Corresponding author. Tel.: +65 421 868 215;
fax: +41 44 386 15 89.
E-mail address: anninaschmid@hotmail.com (A. Schmid).

1356-689X/$ - see front matter
doi:10.1016/j.math.2007.12.007

specific joints and spinal segments stimulated. For example, Vicenzino et al. (1995) conducted passive cervical mobilisation in healthy subjects and found analgesia in multiple sites. In a randomised study of 23 healthy subjects without previous manual therapy experience, McGuiness et al. (1997) reported that application of passive cervical joint mobilisation influenced both respiratory and cardiac function.

High agreement among all published reports confirming an extrasegmental contribution to manual therapy induced pain control in humans could lay the basis for a paradigm shift in regard to mechanisms of action of passive joint mobilisation. In this systematic review we set out to assemble and appraise current evidence, assess the consistency of multisystem responses, and if found, to explore the relationships between neurophysiological response patterns.

2. Method

2.1. Literature search

We searched potentially relevant articles in CINAHL (Ovid Version), MEDLINE (Pubmed Version) from inception to November 2007 and the Cochrane Controlled Trials Register (2007 issue 4). The reference lists of all known primary and review articles were examined to further identify cited articles not captured by electronic searches. Contacting experts in order to include unpublished work complemented our searches. No language restrictions were placed on any of our searches. We used the search strategy as recommended by the Cochrane Collaboration (van Tulder et al., 1997) which we adapted for our purpose. (An example of our search strategy is available in the Appendix).

2.2. Study selection

We selected randomised controlled studies (RCTs) if they investigated the immediate effect of passive accessory cervical joint mobilisation techniques either in healthy humans or in a patient population with symptoms in the neck or upper limb. Subjects had to be older than 18 years. We excluded trials on animals, investigations of high velocity manipulation techniques, passive physiological intervertebral joint mobilisation or a combination of treatments comparing the long-term effect of manual therapy to another intervention. We also excluded studies involving the mobilisation of the lumbar spine, thoracic spine or peripheral joints.

As the aim of this study was to review all kinds of possible effects of passive accessory mobilisation techniques, the inclusion criteria were not limited to specific neurophysiological outcome measures. Only studies investigating biomechanical effects were excluded from this study.

2.3. Assessing methodological quality

After conducting the literature search, citations consisting of titles and abstract were screened by one reviewer and categorised as definitely relevant, possibly relevant and not relevant, on the basis of the inclusion criteria and study design. The complete reports of those citations that were definitely or possibly relevant were obtained and examined for compliance with selection criteria by two reviewers independently. Any discrepancies were resolved by discussion. The selected studies were assessed for methodological quality using components of study design that would ensure internal validity as recommended in the updated method guidelines for systematic reviews in the Cochrane Back Review Group (van Tulder et al., 2003). This criteria list (see Table 2) was first published in 1997 and later adapted in 2003. It has been used in several systematic reviews before. This scale includes the criteria of the Jadad scale (Jadad et al., 1996). The maximal achievable overall quality score (QS) is 11 and studies that score greater than 50% on the overall QS were considered to have acceptable validity (Verhagen et al., 2001).

2.4. Statistical analysis

We aimed at pooling results if at least five studies reported on the same outcome. We extracted differences between the intervention and control measurements and calculated population weighted mean differences. Statistical analyses were performed using the Stata Version 9.2 statistical software package (4905 Lakeway Drive, College Station, USA).

3. Results

The initial search in CINAHL yielded 60 trials and after scanning them, six of those met the inclusion criteria. Searches in MEDLINE identified 234 studies contributing two additional studies. Searching the Cochrane Controlled Trials' register did not add further articles. Scanning the reference lists identified six additional trials and expert contact revealed one unpublished article leading to a total of 15 included studies (see Fig. 1).

Table 1 provides details in respect to participants, interventions, outcome measures and results of included studies.

The overall quality of the identified studies was consistently high (Table 2) and none of the studies which met our inclusion criteria had to be excluded due to methodological issues.

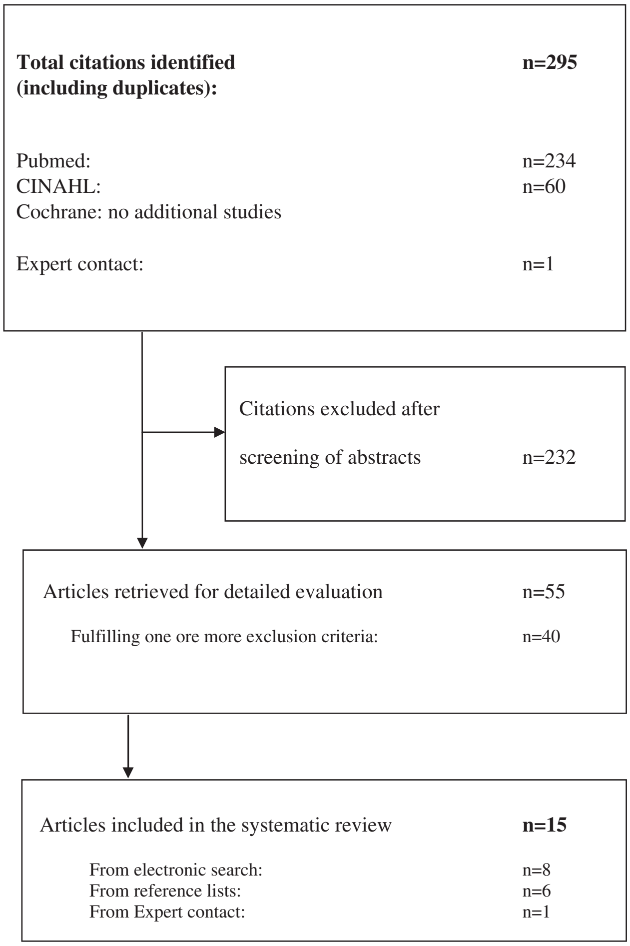

Fig. 1. Study flow.

Most studies used a double blind design consisting of an intervention condition and one or two control conditions, receiving either manual contact, no contact or therapeutic ultrasound control interventions (Petersen et al., 1993; Vicenzino et al., 1994, 1995, 1996, 1998a, b, 1999; Chiu and Wright, 1996, 1998; McGuiness et al., 1997; Sterling et al., 2001; Saranga et al., 2003). All except one (Coppieters et al., 2003b) of the included studies used a within-subject design. The studies included patient populations (lateral epicondylalgia, cervical pain, and cervicobrachial pain) as well as healthy volunteers.

3.1. Consistency and meta-analysis

We found consistency for concurrent hypoalgesia, sympathetic nervous system excitation (skin conductance (SC), blood pressure, heart rate and respiratory rate) and changes in motor function suggesting an involvement of the central nervous system in coordinating the response to manual therapy treatments (Table 3).

However, the included studies used a wide variety of outcome measures and did not consistently report individual values. Therefore, we could only include three outcome parameters in our statistical analysis. These, however, demonstrate that Manual Therapy is capable of inducing changes in indicators of sympathetic nervous system function and pain related measures that are approximately 20% greater than control conditions (Table 4).

3.2. Pain related measures

Several pain measures have been used in the included studies such as pressure pain threshold (PPT), thermal pain threshold (TPT) and visual analogue scale (VAS) ratings. Indirect measures of perceived pain included pain free grip strength (PFG) and pain free range of motion (ROM) in upper limb neurodynamic tests (Butler, 2000).

There is consistent evidence that cervical accessory mobilisation increases the PPT not only locally but in a widespread manner involving at least the forequarter on the side of treatment (Vicenzino et al., 1995, 1996, 1998b; Sterling et al., 2001). Interestingly, Sterling et al. (2001) found a significant increase in PPT isolated on the side of the applied unilateral posteroanterior mobilisation. Unlike the change in PPT, the studies consistently report no effect on TPT (Vicenzino et al., 1995, 1998b; Sterling et al., 2001). This is an interesting finding and may have some relevance for any potential mechanism of action.

There is evidence for a significant improvement in VAS at rest and 24 h after spinal manual therapy (Vicenzino et al., 1996; Sterling et al., 2001; Coppieters et al., 2003a, b). Moreover, the cervical mobilisation produced a 43.4% reduction of the symptom area (Coppieters et al., 2003a). Indirect pain measures show a consistent beneficial effect on pain free range of movement in the neurodynamic tests (Vicenzino et al., 1996, 1998b; Coppieters et al., 2003a) and an improvement of pain free grip force (Vicenzino et al., 1996, 1998b).

3.3. Sympathetic nervous system indicators

There is high evidence that passive accessory mobilisation increases SC in a widespread manner in both upper limbs (Petersen et al., 1993; Vicenzino et al., 1994, 1995, 1998b; Chiu and Wright, 1996, 1998; Sterling et al., 2001). This effect is reported to last for several minutes of post treatment (Vicenzino et al., 1994). One study observed an increased blood flux in the elbow while there was a decreased blood flux in the hand (Vicenzino et al., 1998b). In two studies, the heart rate rose 10.5% and 13% and the respiratory rate increased 36% and 44% (McGuiness et al., 1997; Vicenzino et al., 1998a). During application of an accessory mobilisation technique diastolic blood pressure also increased in two studies (McGuiness et al., 1997; Vicenzino et al., 1998a).

Table 1
Selected studies characteristics

Authors	Participants	Interventions	Outcome measures	Results
Chiu and Wright (1996)	16 Healthy subjects without previous manual therapy experience	C5 central pa III 2 Hz C5 central pa III 0.5 Hz Control	SC ST	Significant increase in SC in 2 Hz Rx compared to control and 0.5 Hz No significant difference in ST between the three conditions
Chiu and Wright (1998)	17 Healthy subjects without previous manual therapy experience	C5 unilateral pa right III C5 right lateral glide III Placebo Control	SC ST	No significant difference in SC and ST Significant increase in SC in unilateral pa compared to placebo and control
Coppieters et al. (2003a)	20 Subjects with subacute unilateral or bilateral minor peripheral upper limb nerve injury	C5/6 contralateral lateral glide, variable duration, amplitude and frequency Therapeutic Ultrasound	ULTT1: pain scale, symptom distribution and ROM elbow	Significant increase in elbow extension, decrease in pain and decrease of the symptom area after cervical mobilisation
Coppieters et al. (2003b)	20 Subjects with nonacute brachial or cervicobrachial neurogenic pain	Cervical contralateral lateral glide at 1 or more motion segments (C5-T1) with the arm in a ULTT 1 position Therapeutic Ultrasound	ULTT1: ROM elbow, pain intensity and shoulder girdle elevation force	Shoulder girdle elevation force occurred later in ROM after mobilisation and force decreased Force at end range after mobilisation increased significantly after mobilisation Significant decrease of pain intensity during ULTT Significant increase in elbow ROM during ULTT 1
McGuiness et al. (1997)	23 Healthy, nonsmoking subjects without previous manual therapy experience	C5 central pa III Placebo Control	Respiratory rate Blood pressure Heart rate	Significant increase in respiratory rate, blood pressure and heart rate in treatment group compared to control and placebo
Petersen et al. (1993)	16 Healthy subjects without previous manual therapy experience	C5 central pa III (Rx) Placebo Control	SC ST	SC: significant increase in Rx group compared to placebo and control ST: significant decrease in Rx group compared to control, no sign. Difference in placebo and Rx group
Saranga et al. (2003)	20 Healthy subjects without previous manual therapy experience	C5/6 ipsilateral lateral glide III Placebo Control	ULTT1: elbow extension	Significant increase in Elbow extension in treatment group compared to placebo and control
Sterling et al. (2001)	30 Subjects with mid or lower cervical pain lasting longer than 3 months and a dysfunction at C5/6	C5/6 unilateral pa III on symptomatic side Placebo Control	EMG: superficial neck flexors SC ST PPT TPT VAS pain in resting position and in end range of symptomatic rotation	VAS: significant decrease Treatment vs. Control, but not significant compared with placebo PPT: significant increase in treatmentcompared to placebo and control TPT: no significant effect EMG: significant decrease in superficial neck flexors activity in treatment vs. placebo and control SC: significant increase in treatment group compared to placebo and control ST: significant decrease in treatment group
Vicenzino et al. (1994)	34 Healthy subjects without previous manual therapy experience	C5/6 left lateral glide III with upper limb in ULTT1 position	SC left and right ST left and right	SC: no significant side effect, significant increase in SC in treatment condition compared to placebo and control ST: no significant difference in temperature between treatment and placebo, control

		C5/6 left lateral glide III with upper limb in ULTT2b position Placebo Control		Significant side effect: left side reached max temperature 1 minute earlier than right limb
Vicenzino et al. (1995)	24 Healthy subjects without previous manual therapy experience	C5/6 left lateral glide III Placebo Control	Pain pressure threshold (PPT) wrist extensors TPT wrist extensors SC ST	SC: significant increase in treatment compared to placebo and control ST: significant increase in Rx compared to control Time taken to achieve the maximum SC effect was sign Shorter than that for ST Significant negative correlation PPT and time taken to achieve a maximum SC PPT: sign. Increase in treatment vs. control and placebo TPT: unchanged
Vicenzino et al. (1996)	15 Subjects with lateral epicondylalgia	C5/6 lateral glide III contralateral to the symptomatic side Placebo Control	ULTT2b, PFG test, PPT Pain VAS at rest and function VAS both 24 h pre and post intervention	ULTT, PPT, PFG and 24 h pain VAS improved significantly in Rx group compared to control and placebo. No significant difference in function VAS and immediate post intervention pain VAS
Vicenzino et al. (1998a)	24 Healthy subjects without previous manual therapy experience	C5 left lateral glide III Placebo Control	Respiratory rate Blood pressure Heart rate	Significant increase in respiratory rate, heart rate and blood pressure in Rx group compared to placebo and control
Vicenzino et al. (1998b)	24 Subjects with chronic lateral epicondylalgia	C5/6 lateral glide III contralateral to the symptomatic side Placebo Control	Pain: ULTT 2b, PPT, TPT and PFG Sympathetic nervous system (SNS): SC, ST and skin blood flux in hand and elbow	Pain: significant improvement of ULTT, PPT and PFG of Rx compared to control and placebo SNS: significant changes in SC, blood flux and ST in hand, ST in elbow not significant There was a significant correlation between pain and SNS outcomes
Vicenzino et al. (1999)	24 Healthy subjects without previous manual therapy experience	C5/6 left lateral glide III Placebo Control	Stress rating scale Stress VAS Pain VAS McGill questionnaire	No significant difference in stress perception Only two patients perceived pain during intervention
Wright et al. (2007)	24 Healthy subjects without previous manual therapy experience	C5/6 unilateral pa left Placebo Control	PPT EMG superficial neck flexors	No significant change in PPT EMG: no significant change in superficial neck flexor activity

Abbreviations: C5: 5th cervical vertebra; C5/6: Facet joint between the 5th and the 6th cervical vertebrae; III: Grade three (Maitland, 1994); pa: Posteroanterior accessory mobilisation (Maitland, 1994); EMG: Electromyogram; ULTT: Upper limb tension test (Butler, 2000); ROM: range of motion.

Table 2
Description of study quality

Study	Was the method of randomisation adequate?	Was the treatment allocation concealed?	Were the groups similar at baseline regarding the most important prognostic indicators?	Was the patient blinded to the intervention?	Was the care provider blinded to the intervention?	Was the outcome assessor blinded to the intervention?	Were co-interventions avoided or similar?	Was the compliance acceptable in all groups?	Was the drop-out-rate described and acceptable?	Was the timing of the outcome assessment in all groups similar?	Did the analysis include an intention-to-treat analysis?	Overall quality score
Petersen et al. (1993)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1994)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1995)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1996)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Chiu and Wright (1996)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
McGuiness et al. (1997)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1998a)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1998b)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Vicenzino et al. (1999)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Sterling et al. (2001)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Coppieters et al. (2003a)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Coppieters et al. (2003b)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Saranga et al. (2003)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8
Chiu and Wright (1998)	Yes	Yes	Yes	D/K	No	Yes	Yes	Yes	No	Yes	No	7
Wright et al. (2007)	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	8

Items could be addressed as Yes, No, Don't Know (D/K).

Table 3
Outcome parameters

Author (Year)	Sympathetic nervous system										Analgesia									Motor function			Other effects	
	SC AUC	SC max	ST max	ST min	ST AUC	Blood flux elbow	Blood flux hand	HR	RR	BP	PPT elbow	PPT cervical	ULNT 1	ULNT 2b	VAS 24th	VAS resting	Symptom area	TPT	PFG	CCFT	Arm function VAS	PFG	Stress VAS	Stress rating scale
Vicenzino et al. (1996)	0	0	0	0	0	0	0	0	0	0		0	0	↑	↓	NS	0	0	↑	0	NS	↑	0	0
Chiu and Wright (1996)	↑	↑	0	NS	NS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
McGuiness et al. (1997)	0	0	0	0	0	0	0	↑	↑	↑	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sterling et al. (2001)	↑	↑	NS	↓	NS	0	0	0	0	0	0	↑	0	0	0	↓	0	NS	0	↑	0	0	0	0
Coppieters et al. (2003b)	0	0	0	0	0	0	0	0	0	0	0	0	↑	0	0	↓	0	0	0	0	0	0	0	0
Coppieters et al. (2003a)	0	0	0	0	0	0	0	0	0	0	0	0	↑	0	↓	0	↓	0	0	0	0	0	0	0
Vicenzino et al. (1999)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NS	NS
Saranga et al. (2003)	0	0	0	0	0	0	0	0	0	0	0	0	↑	0	0	0	0	0	0	0	0	0	0	0
Petersen et al. (1993)	↑	0	0	0	NS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chiu and Wright (1998)	NS	0	0	0	NS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vicenzino et al. (1998a)	0	0	0	0	0	0	0	↑	↑	↑	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vicenzino et al. (1994)	↑	↑	NS	0	NS	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vicenzino et al. (1998b)	↑	0	0	0	↑/↓	↑	↓	0	0	0	↑	0	0	↑	0	0	0	NS	↑	0	0	↑	0	0
Vicenzino et al. (1995)	↑	↑	↑	NS	↑	0	0	0	0	0	1	0	0	0	0	0	0	NS	0	0	0	0	0	0
Wright et al. (2007)	0	0	0	0	0	0	0	0	0	0	0	NS	0	0	0	0	0	0	0	NS	0	0	0	0
Total	↑	↑	NS	NS	NS	↑	↓	↑	↑	↑	↑	↑	↑	↑	↓	↓	↓	NS	↑	↑	NS	↑	NS	NS

Table 4
Population weighted mean differences between the intervention and control measurements

Outcome measures	Mean (SD)
SC	35.1 (16.5)
PPT	19.2 (10.8)
ULNT	19.5 (15.5)

In contrast to the above mentioned measures, there is conflicting evidence regarding the effect of passive accessory mobilisation on skin temperature (ST) (Petersen et al., 1993; Vicenzino et al., 1994, 1995, 1998b; Chiu and Wright, 1996, 1998; Sterling et al., 2001). In summary, passive accessory mobilisation techniques appear to produce changes in a range of measures which are considered to be indicators of sympathetic nervous system activation.

3.4. Motor function measures

There is evidence for improvement in PFG after cervical mobilisation (Vicenzino et al., 1996, 1998b). Furthermore, one study showed a decreased electromyographic (EMG) activity of the superficial neck flexor muscles after treatment, possibly indicating improved function of the deep cervical flexor muscles (Sterling et al., 2001). This finding could not be reproduced in healthy subjects (Wright et al., 2007). In another study no significant change in a VAS rating of arm function was reported (Vicenzino et al., 1996). There is therefore limited evidence to support an effect of passive accessory mobilisation on motor function.

We found moderate evidence that mobilisation had no effect on perceived stress (Vicenzino et al., 1999).

4. Discussion

This review has two main findings. We found compelling evidence that passive accessory cervical mobilisation triggers hypoalgesia and change in a range of measures that suggest activation of the sympathetic nervous system. These effects extend beyond the specific body segment receiving the treatment. There appears to be concurrent activation of pain modulatory and sympathetic nervous system effects suggesting the high likelihood that key brain regions must be involved in coordinating these responses. Based on these findings we suggest that current views in relation to the mechanism of action of manual techniques require some revision.

4.1. Pain modulation in the brain

It has been suggested that the set of phenomena observed in these trials are similar to those evoked by stimulation of the periaqueductal gray (PAG) region of the midbrain (Wright, 1995, 2002). However, a lack of consistent motor effects may question the potential role of PAG in coordinating the response to manual therapy treatment (Wright et al., 2007). Our review found four articles, which focused on the influence of passive accessory mobilisation on motor function, and their results were inconclusive. Vicenzino et al. (1996, 1998b) both found an improvement in PFG which, however, was accompanied by a hypoalgesic effect. Sterling et al. (2001) enrolled patients with cervical pain and found a reduction in superficial flexor muscle activation with a likely improvement of deep neck flexor activity and concurrent hypoalgesia. Cervical pain and cervicogenic headache patients typically present with a deficit of deep neck flexor muscle function (Watson and Trott, 1993; Jull et al., 1999). In the study by Sterling et al. (2001) as well as by Vicenzino et al. (1996, 1998b) improvement could have occurred either as a direct effect of the technique or by a reduction of pain inhibition. The only study (Wright et al., 2007) which was performed in healthy subjects could not replicate the motor activation phenomenon. We hypothesise that it might only be possible to produce an effect when motor function is impaired, or the change in motor function is secondary to the pain inhibitory effect of the treatment. There is little evidence to support any direct modulatory effect on motor function.

Current evidence from the reviewed studies suggests that passive accessory mobilisation techniques applied to the cervical spine produce mechanical but not thermal hypoalgesia that is extrasegmental in nature and lasts for a period of up to 24 h. The evidence also strongly supports the influence of these techniques on a range of other measures that are linked to sympathetic nervous system function. This appears to be a widespread extrasegmental effect.

Based on the available information it would appear that there is strong evidence to support the involvement of the central nervous system in mediating the response to manual therapy treatment. The range of responses involved suggests that supraspinal centres are likely to be important in controlling this effect, however, there is not sufficient evidence yet (particularly related to motor function) to suggest that the response might involve specific activation of the PAG region.

What are the limitations of this review? Most of the included studies in this review were carried out by the same group of authors, thus potentially influencing the evidence. Although we were particularly careful to retrieve all existing evidence, which included searches in different databases, checking of reference lists and author contacts, we cannot rule out, that publication bias led to an inflation of the agreement between studies. However, since some of the studies indeed also showed conflicting results we believe that the study sample assessed in this review provides a realistic review of the topic.

4.2. Implications for research

We believe that the evidence is compelling enough to suggest that contrary or in addition to existing paradigms, the central nervous system is involved in mediating the responses to passive cervical joint mobilisation.

Only the evidence for motor involvement is still scarce and conflicting findings are reported. Future studies should therefore focus on the influence of manual therapy on motor function. Moreover, future research should aim to identify brain areas and central nervous system pathways involved in mediating this effect. Preliminary research of this nature has suggested that spinal release of serotonin and noradrenaline from descending neurons may be important in mediating the pain modulatory effect of manual therapy (Skyba et al., 2003).

It is also important that randomised controlled trials investigating the efficacy of manual therapy should include outcome measures designed to evaluate the multisystem effects of treatment. We encourage authors to systematically include accurate and complete data in their papers in order to facilitate future meta-analysis and comparison of results.

4.3. Implications for practice

At this point, drawing conclusions for practice might be premature. However, we see potential to use the non-segmental nature of the hypoalgesia by applying treatment to a more proximal joint rather than the one that is specifically painful. This may be particularly useful if the target joint is inflamed or excessively painful. There might also be a potential to integrate manual therapy with strategies also known to influence central nervous system processing such as patient education, graded movement and pharmacological strategies.

5. Conclusion

In conclusion, this systematic review seems to suggest that passive accessory cervical mobilisation activates central nervous system mechanisms responsible for pain control and modulation of autonomic function. When confirmed in other studies these findings highlight the need for a revision of the current peripheralist models underlying the use of passive mobilisation and related physiotherapeutic interventions.

Acknowledgement

The assistance of Benjamin Soon Tze Chin is gratefully acknowledged.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.math.2007.12.007

References

Butler DS. The sensitive nervous system, 1st ed. Unley, S. Australia: Noigroup Publications; 2000.

Chiu T, 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. Manual Therapy 1996;l(4):198–203.

Chiu T, Wright A. Comparing the effects of two cervical mobilisation techniques on sympathetic outflow to the upper limb in normal subjects. Hong Kong Physiotherapy Journal 1998;16:13–8.

Coppieters MW, Stappaerts KH, Wouters LL, Janssens K. The immediate effects of a cervical lateral glide treatment technique in patients with neurogenic cervicobrachial pain. Journal of Orthopaedic and Sports Physical Therapy 2003a;33(7):369–78.

Coppieters 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. Journal of Manipulative and Physiological Therapeutics 2003b;26(2):99–106.

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials 1996;17(1):1–12.

Jull G, Barrett C, Magee R, Ho P. Further clinical clarification of the muscle dysfunction in cervical headache. Cephalalgia 1999;19(3): 179–85.

Maitland GD, Hengeveld E, Banks K, English K. Maitland's vertebral manipulation, 7th ed. London: Elsevier; 2005.

McGuiness J, Vicenzino B, Wright A. Influence of a cervical mobilization technique on respiratory and cardiovascular function. Manual Therapy 1997;2(4):216–20.

Melzack R, Wall P. Pain mechanisms: a new theory. Science 1965;150(699): 971.

Paris S. Mobilization of the spine. Physical Therapy 1979;59(8):988–95.

Petersen N, Vicenzino B, Wright A. The effects of a cervical mobilisation technique on sympathetic outflow to the upper limb in normal subjects. Physiotherapy Theory and Practice 1993;9(3): 149–56.

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(11):678—84.

Skyba DA, Radhakrishnan R, Rohlwing JJ, Wright A, Sluka KA. Joint manipulation reduces hyperalgesia by activation of monoamine receptors but not opioid or GABA receptors in the spinal cord. Pain 2003;106(l-2):159–68.

Sterling M, Jull G, Wright A. Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. Manual Therapy 2001;6(2):72–81.

van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the Cochrane collaboration back review group. Spine 2003;28(12):1290–9.

van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the Cochrane collaboration back review group for spinal disorders. Spine 1997;22(20):2323–30.

Verhagen AP, Peeters GG, de Bie RA, Oostendorp RA. Conservative treatment for whiplash. Cochrane Database of Systematic Reviews 2001(4):CD003338.

Vicenzino B, Cartwright T, Collins D, Wright A. Cardiovascular and respiratory changes produced by lateral glide mobilization of the cervical spine. Manual Therapy 1998a;3(2):67–71.

Vicenzino B, Cartwright T, Collins D, Wright A. An investigation of stress and pain perception during manual therapy in asymptomatic subjects. European Journal of Pain 1999;3(1):13–8.

Vicenzino B, Collins D, Benson H, Wright A. An investigation of the interrelationship between manipulative therapy-induced hypoalgesia and sympathoexcitation. Journal of Manipulative and Physiological Therapeutics 1998b;21(7):448–53.

Vicenzino B, Collins D, Wright A. Sudomotor changes induced by neural mobilisation techniques in asymptomatic subjects. The Journal of Manual and Manipulative Therapy 1994;2(2):66–74.

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.

Vicenzino B, Gutschlag F, Collins D, Wright A. An investigation of the effects of spinal manual therapy on forequarter pressure and thermal pain thresholds and sympathetic nervous system activity in asymptomatic subjects: a preliminary report. In: Shacklock M, editor. Moving in on pain. Australia: Butterworth-Heinemann; 1995. p. 185–93.

Watson DH, Trott PH. Cervical headache: an investigation of natural head posture and upper cervical flexor muscle performance. Cephalalgia 1993;13(4):272–84 [discussion 232].

Wright A. Hypoalgesia post-manipualtive therapy: a review of a potential neurophysiological mechanism. Manual Therapy 1995;1:11–6.

Wright A. Pain-relieving effects of cervical manual therapy. In: Physical therapy of the cervical and thoracic spine. USA: Churchill Livingstone; 2002. p. 217–38.

Wright A, Schmid A, Soon B, Fridriksson E, Gresslos E, Cheong P. The effect of cervical mobilisation on motor function and pain perception in pain free individuals. Unpublished data; 2007.

Wyke B. Articular neurology and manipulative therapy. In: Glasgow E, editor. Aspects of manipulative therapy. Edinburgh: Churchill Livingstone; 1985.

Zusman M. Spinal manipulative therapy. The Australian Journal of Physiotherapy 1986;32(2):89–99.