Mechanisms of Action of Manipulative Therapy

Bill Vicenzino
Professor in Sports Physiotherapy
Head of Division of Physiotherapy
Chapter 5
A new proposed model of the mechanisms of action of Mobilisation with Movement

Bill Vicenzino, Toby Hall, Wayne Hing and Darren Rivett
Manipulation

1. **Low Velocity Techniques** ‘Passive Mob’
   - Under control of client
   - Passive ± active or functional components*
   - Includes soft tissue, joints, neural ...

2. **High Velocity Thrust Techniques**
   - Beyond control of client
   - Small amplitude (ie, HVLA)
What is the major difference between mobilisation and HVT?

Indicates successful manipulation!

Significance to mechanism of action?
Brodeur R 1995 The audible release associated with joint manipulation JMPT 18: 155-64

Audible release caused through cavitation mechanism that is responsible for:

Initiating reflex effects

Producing forces in target tissues without damaging muscle
Does it work?
Or
What is its clinical efficacy?

Figure 7. Forest plot of comparison: Cervical manipulation: manipulation versus mobilisation (pooled) - pain

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>1.4.1 Multiple sessions: Intermediate-term follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hurwitz 2002 (1)</td>
<td>2.66</td>
<td>2.72</td>
<td>35</td>
</tr>
<tr>
<td>Hurwitz 2002 (2)</td>
<td>1.73</td>
<td>2.15</td>
<td>30</td>
</tr>
<tr>
<td>Hurwitz 2002 (3)</td>
<td>1.82</td>
<td>1.82</td>
<td>34</td>
</tr>
<tr>
<td>Hurwitz 2002 (4)</td>
<td>2.85</td>
<td>2.41</td>
<td>34</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>133</td>
<td></td>
<td>136</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.10, Chi² = 7.94, df = 3 (P = 0.05); I² = 62%
Test for overall effect: Z = 0.37 (P = 0.71)

Total (95% CI) | 133 | 136 | 100.0% | -0.07 [-0.47, 0.32] |

Heterogeneity: Tau² = 0.10, Chi² = 7.94, df = 3 (P = 0.05); I² = 62%
Test for overall effect: Z = 0.37 (P = 0.71)

(1) Hurwitz 2002: manipulation v mobilisation; duration: NR; follow up: 6 month; instrument: NRS (0 to 10)
(2) Hurwitz 2002: manipulation and heat and EMS v mobilisation and heat and EMS; duration: NR; follow up: 6 month; instrument: NRS (0 to 10)
(3) Hurwitz 2002: manipulation and heat v mobilisation and heat; duration: NR; follow up: 6 month; instrument: NRS (0 to 10)
(4) Hurwitz 2002: manipulation and EMS v mobilisation and EMS; duration: NR; follow up: 6 month; instrument: NRS (0 to 10)

Authors’ conclusions

Cervical manipulation and mobilisation produced similar changes. Either may provide immediate- or short-term change; no long-term data are available. Thoracic manipulation may improve pain and function. Optimal techniques and dose are unresolved. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

FIGURE 5. Estimated marginal means (predicted means of each dependent variable across levels of each factor) for headache index preintervention (Pre), 4 weeks postintervention, and 12 months postintervention.

Spinal manual therapy appears efficacious...in short to mid term

- MWM versus Sham versus Control
- 11 male & 13 female
- mean age 46.1 ± SD 9.86 yrs
Interaction Plot ROM

ROM: ICC = 0.98 and SEM 1.33°

ROM (in degrees)

Pre Post

MWM
Sham
Control

9.9 (4.3 to 15.6)
11.4 (2.3 to 20.5)
PPT: ICC = 0.96 and SEM 10.7 kPa
Passive Anterior-Posterior Glide


- Acute ankle sprain (<72 hrs); n = 38
- Random assignment to control (RICE) or AP mobs (no pain) + RICE. All had home program.
- Treatment every 2 days for max. 2 weeks or D/C.
- D/C criterion = no difference in DF side to side
- Outcomes = number of treatments, pain free dorsiflexion (nonWB), 3 gait variables (stride speed, step length and single support time)

- 13/19 (68%) subjects discharged at 4th treatment in PA mob group compared to 3/19

- DF improved earlier in treatment group (11° compared to 6° from baseline to treatment 2)

- Gait variable improvements tended to favour the treatment group

• N = 14, grade II ankle sprain (40±24 days old)
• WB DF, PPT and TPT (heat and cold)
• Deficit only on:
  – WB DF = 42 mm
  – PPT (ATFL) = 58 kPa
• WB-MWM, Placebo, control

*(dorsiflexion: 12 mm; p<0.017)*
Initial effect of Mulligan MWM on ankle DF in normals: Weight bearing versus non-weight bearing techniques. Vicenzino B, Prangle I, Martin D

(SMA website)

[N=27 (18-27yr)]

- 16 traumatic & 16 non-traumatic subjects with > 10° of unilateral side flexion restriction
- Thrust manipulation applied to side of restriction
- Measurement of ROM @ 0.5, 4, 24 & 48 hrs
- 12° improvement @ 0.5 & 4 hours
- Improvement not evident at 48 hours
McCollam & Benson 1993 Effects of P-A mobilisation on lumbar extension and flexion, JM&MT 1: 134-141.

- PA mobilisation to L3, 4 & 5 spinous process for 9 minutes in 65 asymptomatic participants
- Compared to prone lying for 9 minutes
- 7.1% improvement in Ext for PA
- Not present @ 1 week post treatment
Spinal manual therapy is efficacious

Need for more peripheral manual therapy studies

Short term effects are shown for a number of joints
Does it work?

...yes!
How does it do it?
Manual Therapy

- Widespread clinical use
  - Treatment of pain (± dysfunction)
- Clinically efficacious
- Mechanisms of Action
  - Poorly understood
  - Complex
Complex multifaceted

Complex multifaceted

A proposed model for the mechanisms of action of manual therapy
Biomechanical

Boney luxations

Reversing luxations

• Straighten spine (Pare 1958)
• Unlocking locked joint (Twomey 1992)
• Shift an IVD fragment (Cyriax 1975)
• Reduce annular distortion (Farfan 1973)
• Stretching, tearing or rupturing adhesions that limit joint or nerve range (Zusman 1986, Chrisman et al 1964)
• Remove blockage or interference of blood flow (Still 1899), nerve compression (Palmer 1910), sympathetic chain (Kunert 1965), and cerebrospinal fluid circulation (DeJanette 1967)
• Correct abnormal somatovisceral reflexes and visceral organ dysfunction (Dhami & DeBoer 1992)
• Stretch contracted muscles, causing relaxation (Perl 1975)
• Remove ‘irritable’ spinal lesions (Korr 1976)
• Intense reflex effects (mainly musculature, Lewit 1985)
• Modulate peripheral nociceptors (Zusman 1987)
• Inhibition of reflex muscle contraction (Zusman 1987)
• Activates gating mechanism, neurotransmitters, opioide peptides (Dhami and DeBoer 1992)
Proposed mechanism:

- Neurophysiological
- Biomechanical

MT
Proposed mechanism:

Biomechanical

Neurophysiological

MT
Subluxations?

Biomechanical

MT
Subluxation hypothesis
Subluxation hypothesis

Chiropractic & Osteopathy

Debate

Subluxation: dogma or science?
Joseph C Keating Jr*1, Keith H Charlton2, Jaroslaw P Grod3, Stephen M Perle4, David Sikorski5 and James F Winterstein6

Address: 16135 North Central Avenue, Phoenix, AZ, 85012, USA, 2School of Medicine, Mayne Medical School, University of Queensland, Herston, Queensland 4006, Australia, 3Department of Graduate Education and Research, Canadian Memorial Chiropractic College, 6100 Leslie Street, Toronto ON, M2H 3J1, Canada, 4Department of Clinical Sciences, College of Chiropractic, University of Bridgeport, 225 Myrtle Ave., Bridgeport, CT 06604, USA, 5Department of Chiropractic Procedures, Southern California University of Health Sciences, 16200 E. Amber Valley Drive, Whittier, CA 90604, USA and 6President, National Univeristy of Health Sciences, 200 East Roosevelt Road, Lombard, IL 60148, USA

Email: Joseph C Keating* - JCKeating@aol.com; Keith H Charlton - khcharlton@bigpond.com; Jaroslaw P Grod - jgrod@cmcc.ca; Stephen M Perle - perle@bridgeport.edu; David Sikorski - DavidSikorski@scuhs.edu; James F Winterstein - jwinterstein@nuhs.edu

* Corresponding author

Published: 10 August 2005
Received: 25 May 2005
Accepted: 10 August 2005

This article is available from: http://www.chiroandosteo.com/content/13/1/17

© 2005 Keating et al; licensee BioMed Central Ltd.
Sub-acute ankle sprain (n =8)  
Non-injured (n =11)  

1.8mm (-0.81 to 4.39)


4.5 cm PVAS reduction following 1 treatment

7.4 units/day on Kaikkonen scale with treatment over 5 weeks compared to 1.4 units/day with natural resolution

...because there is a beneficial therapeutic effect, it does not follow that the proposed (speculated) mechanism underlying the treatment is supported!
Subluxations: may well occur but difficult to measure?

Unresolved: does the MT reverse bony luxation?
Effects of manipulations on bony position?

• Evaluated positional change after unilateral PA T-sp HVT in cadavers using 3D kinematic analysis and force mat

• Demonstrated that:
  – < 10 mm linear displacement of vertebra
  – Change in position was short lived - mostly for the duration of the technique
  – Restoration of baseline position within 10 minutes of the treatment application

R 1st MCP pain with F after hyperabduction injury

Positional fault on MRI: \(4^\circ\) pronation of R 1st MCP

Glide reversed positional fault on MRI

Post-3 weeks self treatment: pain and function improved but positional fault stayed same

Note: therapist was blind to this finding
Factors such as:
Direction, Force,
Velocity/Frequency,
Technique,
Localization, Audible

Specificity of application?

MT

Human studies

BIOMECHANICS

Transient change
in bone position
Direction of force:
Direction of force:

Specificity of direction: Manual therapy improves ROM

FIGURE 5. Comparison of external rotation at baseline and after each treatment by group (mean ± SEM).
Direction of force:


Unresolved issue:

What is the relevance of ROM improvement in ROM in pain (mm VAS) & function outcomes
Lateral glide with 0° or 5° posterior inclination

NOT 5° anterior to direct lateral

Concept of the joint plane: gross
Applied Force (N)

In the Treatment Plane  Out of the Treatment Plane

Glide Orientation / Direction
Concept of the joint plane: fine tune
Amount of force:

Maximum force applied by practitioner

Optimal change in outcome (66% of maximum force)

No change in outcome (50% of maximum force)

Negative change in outcome (33% of maximum force)

Force Levels (% maximum)
Direction & Amount of force:

• Are important
• Are related

...to produce better effects
Localization of spinal level:
Localization of spinal level:


- 140 patients with non-specific LBP
- Randomized to therapist selected level or random selected level
- Both groups showed improved pain
- Selected level did not seem to be superior to random
- Low lumbar spine mobilisation was superior to upper
Localization of spinal level:


- 126 patients with non-specific neck pain
- Randomized to therapist selected level or levels below (4’ pain relieving traction)
- Both groups showed improved pain
- Selected level did not seem superior

¿ was there mechanical/treatment overflow from 3 levels below?
Direction & Amount of force:

, but not the exact location in the spine

• Are important
• Are related

...to produce better effects
Spinal versus peripheral?: 

[Images of clinical examinations]
Audible (joint pop/crack sound):
Audible (joint pop/crack sound):

Herzog 1996 On sounds & reflexes JMPT 19(3):216-8

PA T-sp (n 26):
  high velocity versus low velocity -> both audible ‘pop’
  only high velocity produced muscle effects (EMG)
BIOMECHANICS
Human studies

Factors such as:
- Direction, Force,
- Velocity/Frequency,
- Technique,
- Localization,
- Audible

MT

Transient change in bone position & Increase ROM
Potential mechanisms:

- Descending Pain Inhibitory Systems (DPIS)
- Endogenous opioid mechanisms
- Neurotransmitters (5HT, NA, SP)
- Spinal mechanisms
- Gating Theory (Melzack and Wall)
- Peripheral receptors

NEUROPHYSIOLOGIC

Pain effects
human
animal

Associated systems & modeling

BIOMECHANICS

Human studies

MT

Transient change in bone position & Increase ROM

- Sustained or repetitive end range mobilisations
  -> reduction in firing rate (neural hysteresis)
  - Afferents fail following sustained intense loads, end range positions, repetitive movements in normal animal joints

- Clinically manual therapy is not applied to normal joints.

- Notably, inflamed joint afferents exhibit:
  - Spontaneous activity in neutral or rest and heightened responses and reduced excitation thresholds to midrange motion

- Indicating manual therapy may well provoke pain through this mechanism not alleviate it!
Gate control theory (Melzack and Wall 1965)

- Large diameter input modulating small diameter pain fibres (e.g., TENS)
- Problem with this model for manipulative therapy is that in an inflamed joint otherwise non-painful movements become pain provocative.
- However, some large diameter fibres are spared (i.e., not sensitised)
- Manual therapists may through their examination target these spared afferents?
Treatment effect > placebo & control


Initial manipulation induced hypoalgesia demonstrated in other studies:

- 45% increase in PPT post HVT of Csp (Vernon et al 1990)
- 140% increase in cutaneous pain tolerance following T-sp HVT (Terrett and Vernon 1984)
- 17 & 11% increase in VAS following HVT and mobilisation, respectively (Cassidy et al 1992)
- 50% increase in VAS following PT manual therapy (Zusman et al 1989)
What are the features?
• endogenous opioid
• neurotransmitters

NEUROPHYSIOLOGIC
Pain effects human

Manual therapy produces an initial hypoalgesia
Treatment effect > placebo/control procedures

Opioid mechanisms:

Naloxone blockade

Tolerance to repeated stimulation

Plasma levels?
Opioid mechanisms: *naloxone/tolerance*?


Opioid mechanisms: plasma levels?


Evidence of opioid mechanism:
What are the features?

Xendogenous opioid

• neurotransmitters

Manual therapy produces an initial hypoalgesia
Treatment effect > placebo/control procedures

What are the features?
Xendogenous opioid
• Neurotransmitters?

Manual therapy produces an initial hypoalgesia
Treatment effect > placebo/control procedures

MT

BIOMECHANICS
Human studies

NEUROPHYSIOLOGIC
Pain effects human Animal?

Transient change in bone position & Increase ROM

5-HT & Norad = DPIS

No local spinal circuitry & no opioid involvement
Heightened Flexor Withdrawal Response in Individuals With Knee Osteoarthritis Is Modulated by Joint Compression and Joint Mobilization

Carol A. Courtney, Paul O. Witte, Samuel J. Chmell, and T. George Hornby

University of Illinois at Chicago, Chicago, Illinois.

Abstract: Patients with chronic pain often present with hyperalgesia, possibly due to hyperexcitability of nociceptive pathways. The aim of the present study was to investigate alterations in flexor withdrawal reflex (FWR) excitability in individuals with knee osteoarthritis (OA) and the potential effect of specific physical inputs or therapeutic interventions (ie, joint compression and mobilization) on these behaviors. Ten subjects with and 10 without knee OA (age 45–75) were recruited. The FWR was examined utilizing suprathreshold, noxious electrocutaneous stimuli applied at the medial foot. Surface electromyographic (EMG) was recorded from the tibialis anterior (TA) and biceps femoris (BF), and peak joint torques recorded at the hip, knee, and ankle. FWR threshold was ascertained and responses at 2× threshold recorded after the following conditions: a maximal, volitional, joint-compression task, a sham hands-on intervention, and a Grade III oscillatory joint-mobilization intervention. A decreased threshold-to-flexor withdrawal response was found in the OA vs control group ($P < .01$). EMG and joint-torque FWR responses were further augmented in the OA group following the maximal joint-compression task ($P < .05$), yet remained unchanged or diminished in controls. Joint mobilization, but not sham intervention, reduced reflex responses significantly, although primarily by decreasing BF activity and knee torques ($P < .05$).

Perspective: Application of specific physical inputs to individuals with knee OA similar to those encountered during activity of daily living or during therapeutic interventions appear to modulate involuntary, nociceptive reflex responses. Routine weight-bearing activities such as walking may potentially enhance heightened FWR responses, while joint mobilization, a commonly used clinical intervention, may diminish reflex excitability.
Nociceptive flexion reflex (NFR) threshold
(Lim E, Sterling M, Stone A, Vicenzino B. 2011)
Initial non-opioid hypo-algesia: DPIS - PAG mediated?

NEUROPHYSIOLOGIC
Pain effects Human Animal

BIOMECHANICS
Human studies

MT

Transient change in bone position & Increase ROM
Are there any other features of manipulation induced hypoalgesia that may add to our understanding of the underlying mechanisms of action?


Sympathoexcitation is:

Treatment technique specific
- PA vs CLG vs Symp. Slump (magnitude)
- HVLA vs mobilisation

Frequency specific
- Not present at less than 1 Hz oscillation

Region specific
- Osteopathic HVT show differences
Are there any other features of manipulation induced hypoalgesia that may add to our understanding of the underlying mechanisms of action?

**NEUROPHYSIOLOGIC**

- Pain effects: human, animal
- Associated systems & modeling

Initial sympatho-excitation

Confirmatory Factor Model

Manipulation Induced Hypoalgesia

ULTT2b: 0.30*
PFG: 0.52*
PPT: 0.68*

Sympatho-excitation

HNDFLX: 0.03
HNDTMP: 0.57*
SKNCON: 0.58*
ELBFLX: 0.48*

* AUC effect; ML Method; Chi-square = 11.94; df = 8; p-value = 0.154; CFI = 0.922
Adapted from Lovick (1991) & Fanselow (1991)

Stimulus

Dorsal/Lateral PAG
- Analgesia (non-opioid)
  - Sympathoexcitation
  - Movement

Ventrolateral PAG
- Analgesia (opioid)
  - Sympathoinhibition
  - Immobility

Adapted from Lovick (1991) & Fanselow (1991)
preganglionic sympathetic outflow to:
- hindlimb
- kidney and adrenal medulla

(Carrive 1993)
Ventral medulla sympathetic premotor centres:

1. cutaneous vasoconstrictor*
2. muscle vasoconstrictor
3. visceral vasoconstrictor*
4. renal
5. sudomotor*
6. respiratory *
7. RVLM, SRF, PGL

VII facial nucleus
IO inferior olive
(McAllen et al 1995)
Confirmatory Factor Model*

Manipulation Induced Hypoalgesia

0.30* 0.52* 0.68*

Sympatho-excitation

0.03 0.57* 0.58* 0.48*

ULTT2b  PFG  PPT  HNDFLX  HNDTMP  SKNCON  ELBFLX

* AUC effect; ML Method; Chi-square = 11.94; df = 8; p-value = 0.154; CFI = 0.922
Adapted from Lovick (1991) & Fanselow (1991)

Stimulus

- Dorsal/Lateral PAG
  - Analgesia (non-opioid)
  - Sympathoexcitation
  - Movement

- Ventrolateral PAG
  - Analgesia (opioid)
  - Sympathoinhibition
  - Immobility

Descending Pain Inhibitory System:

Adapted from Lovick (1991) & Fanselow (1991)
**Stress response or pain induced DNIC?**


**Methods**
- Stress & pain levels before, during and after treatment
- Double blind, placebo-controlled, repeated measures (n = 24)

**Results**
- No stress or pain was perceived during treatment
- Stress was greatest at the first session regardless of treatment condition applied on that day, reducing on day 2 & 3.

**Conclusion**
- Stress and pain are not features of the lateral glide
**Stress response or pain induced DNIC?**


**Important to understand:**

All the techniques we have studied have been non-painful during their application.
NEUROPHYSIOLOGIC

Pain effects  human animal

Associated systems & modeling: motor?

Facilatory and inhibitory effects reported
¿unsure if this adds or detracts!
¿depend on deficit?

(e.g., Vicenzino et al 2010, Abbot et al 2001)

Are there any other features of manipulation induced hypoalgesia that may add to our understanding of the underlying mechanisms of action?
MT
Specificity of application

Initial non-opioid hypo-algesia: DPIS-PAG mediated?

NEUROPHYSIOLOGIC
Pain effects human animal
Associated systems & modeling

BIOMECHANICS
Human studies

Transient change in bone position & Increase ROM

Direction
Force level
Temporal (f, v)
Technique
Localization? Not the pop!
Manipulation as a physiological stimulus

- Skin, muscle and joint input (Souvlis et al 2004)
MT
Specificity of application

BIOMECHANICS
Human studies

NEUROPHYSIOLOGIC
Pain effects  human animal
Associated systems & modeling

Initial non-opioid hypo-algesia: DPIS -PAG mediated?

Direction
Force level
Temporal (f, v)
Technique
Localization? Not the pop!

Transient change in bone position & Increase ROM

Adequate stimulus?
Complex multifaceted

Psychological effects

Treatment application

Time

Wright (1995)
Pre-existing beliefs:
Injury & damage
Catastrophisation
Fear-avoidance
Expectations:
Placebo
Practitioner
Treatments

Chronic pain = conditioned (learned) phenomenon (Zusman 2004)

MWM = a re-conditioning of a pain-movement association -
[possibly through non-associative learning theory mechanism (Zusman 2004)]
Repetition seems to be critical in successful treatment!

Chronic pain = conditioned (learned) phenomenon (Zusman 2004)

MWM = a re-conditioning of a pain-movement association - 
[possibly through non-associative learning theory mechanism (Zusman 2004)]