The mechanisms of manual therapy in the treatment of musculoskeletal pain: A comprehensive model

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Abstract

Prior studies suggest manual therapy (MT) as effective in the treatment of musculoskeletal pain; however, the mechanisms through which MT exerts its effects are not established. In this paper we present a comprehensive model to direct future studies in MT. This model provides visualization of potential individual mechanisms of MT that the current literature suggests as pertinent and provides a framework for the consideration of the potential interaction between these individual mechanisms. Specifically, this model suggests that a mechanical force from MT initiates a cascade of neurophysiological responses from the peripheral and central nervous system which are then responsible for the clinical outcomes. This model provides clear direction so that future studies may provide appropriate methodology to account for multiple potential pertinent mechanisms.

1. Introduction

Available evidence suggests manual therapy (MT) as effective in the treatment of musculoskeletal disorders including low back pain (Licciardone et al., 2003; Childs et al., 2004), carpal tunnel syndrome (Rozmarin et al., 1998; Akalin et al., 2002), knee osteoarthritis (Deyle et al., 2000), and hip osteoarthritis (MacDonald et al., 2006). Moreover, recent studies have provided even stronger evidence when participants are classified into sub-groups (Childs et al., 2004; Cleland et al., 2006). Despite the literature supporting its effectiveness, the mechanisms of MT are not established leading to concern for chance associations rather than causation. Highlighting this concern, only one clinical prediction rule (Flynn et al., 2002) has, to our knowledge, been validated with a follow up study (Childs et al., 2004). An understanding of the mechanisms behind MT could assist in the identification of individuals likely to respond to MT by allowing a priori hypotheses as to pertinent predictive factors for future clinical prediction rules and a better understanding of the factors which are determined as predictive.

A second benefit of the identification of MT mechanisms is the potential for increased acceptance of these techniques by healthcare providers. Despite the literature supporting the effectiveness of MT in specific musculoskeletal conditions, healthcare practitioners at times provide or refer for MT at a lower than expected rate (Jette and Delitto, 1997; Li and Bomgardner, 2001; Bishop and Wing, 2003). The lack of an identifiable mechanism of action for MT may limit the acceptability of these techniques as they may be viewed as less scientific. Knowledge of mechanisms may promote more appropriate use of MT by healthcare providers.

The intention of this manuscript is to present a comprehensive model to guide future studies of MT mechanisms. For our purposes, MT includes a variety of techniques used in clinical practice for the treatment of musculoskeletal pain which target the skeletal system, soft tissue, and nervous system (Table 1).

2. Need for a comprehensive model

MT likely works through biomechanical and/or neurophysiological mechanisms. A limitation of the current literature is the...
failure to acknowledge the potential for a combined effect of these mechanisms. For example, prior studies have noted individual biomechanical (Gal et al., 1997; Coppieters and Butler, 2007) and neurophysiological effects (Vicenzino et al., 1998; Suter et al., 1999; Dishman and Bulbulian, 2000; DeVocht et al., 2005) associated with MT; however the potential interaction of these effects is frequently overlooked. Combined effects may be important to consider as the biomechanical parameters of a given MT may produce unique or dose dependent neurophysiological responses. For example, associated hypoalgesic response (McLean et al., 2002) and EMG response (Colloca et al., 2006) have an observed dependence on the force and force time profile of a given MT. Additionally, prior studies often focus on a single neurophysiological mechanism without consideration for competing explanations. For example neuromuscular changes such as decreased resting EMG activity (DeVocht et al., 2005) and decreased muscle inhibition (Suter et al., 1999; Suter and McMorland, 2002) have been associated with MT and theorized to occur due to stimulation of the mechanoreceptors or proprioceptors producing a spinal cord mediated effect (Suter et al., 2000; Suter and McMorland, 2002). While helpful in establishing the groundwork for the mechanistic study of MT, conclusions based on studies designed in this fashion may fail to consider other potentially pertinent mechanisms. Psychological factors have an observed association with muscular response in individuals with low back pain (Thomas et al., 2008) and MT has an observed effect on these psychological factors (Williams et al., 2007). Subsequently, outcomes reported in the prior studies (Suter et al., 1999; Suter and McMorland, 2002; DeVocht et al., 2005) could be explained by a descending supraspinal mediating effect due to changes in psychological factors such as fear. A consideration of the interaction between biomechanical and multiple potential neurophysiological effects necessitates a comprehensive model to synthesize the current literature and direct future research.

3. Proposed model

We propose the following model which provides a compilation of the existing mechanistic literature of MT as a framework for interpreting current and conducting future mechanistic research (Fig. 1). Briefly, this model suggests a mechanical stimulus initiates a number of potential neurophysiological effects which produce the clinical outcomes associated with MT in the treatment of musculoskeletal pain.

3.1. Mechanical stimulus

Biomechanical effects are associated with MT as motion has been quantified with joint biased MT (Gal et al., 1997; Colloca et al., 2006) and nerve biased MT (Coppieters and Alshami, 2007; Coppieters and Butler, 2007); however, the direct implication on clinical outcomes is questionable. First, only transient biomechanical effects are supported by studies which quantify motion (Gal et al., 1997; Colloca et al., 2006; Coppieters and Alshami, 2007; Coppieters and Butler, 2007) but not a lasting positional change (Tullberg et al., 1998; Hsieh et al., 2002). Second, biomechanical assessment is not reliable. Palpation for position and movement faults has demonstrated poor reliability (Troyanovich et al., 1998; Seffinger et al., 2004) suggesting an inability to accurately determine a specific area requiring MT. Third, MT techniques lack precision as nerve biased techniques are not specific to a single nerve (Kleinrensink et al., 2000) and joint biased technique forces are dissipated over a large area (Herzug et al., 2001; Ross et al., 2004). Additionally, different kinetic parameters are observed between clinicians in the performance of the same technique (Hessell et al., 1990; Ngan et al., 2005) and the choice of technique does not seem to matter as much as identifying an individual likely to respond (Kent et al., 2005; Cleland et al., 2006). Finally, studies have reported improvements in signs and symptoms away from the site of application such as treating cervical pain with MT directed to the thoracic spine (Cleland et al., 2005; Cleland et al., 2007) and lateral epicondylitis with MT directed to the cervical spine (Vicenzino et al., 1996). Collectively, the literature suggests a biomechanical effect of MT; however, lasting structural changes have not been identified, clinicians are unable to reliably identify areas requiring MT, the forces associated with MT are not specific to a given location and vary between clinicians, choice of technique does not seem to affect outcomes, and sign and symptom responses occur in areas separate

<table>
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<tr>
<th>MT technique</th>
<th>Definition</th>
<th>Desired outcomes</th>
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<td><strong>Joint biased</strong></td>
<td>• Manipulation: Passive movement of a joint beyond the normal range of motion</td>
<td>• Improved range of motion&lt;br&gt;• Decrease muscle spasm&lt;br&gt;• Decreased pain</td>
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<td></td>
<td>• Mobilization: Passive movement of a joint within its normal range of motion</td>
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<td><strong>Soft tissue biased</strong></td>
<td>• Swedish massage: Stroking and kneading of the skin and underlying soft tissue</td>
<td>• Improve circulation&lt;br&gt;• Decrease muscle spasm&lt;br&gt;• Relaxation</td>
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<td></td>
<td>• Deep tissue massage: Deep stroking and pressure across the muscles and soft tissue</td>
<td>• Re-align soft tissue&lt;br&gt;• Break adhesions&lt;br&gt;• Increase range of motion&lt;br&gt;• Release muscle spasm&lt;br&gt;• Remove cellular exudates&lt;br&gt;• Improve Circulation&lt;br&gt;• Decrease muscle spasm&lt;br&gt;• Relaxation</td>
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<td>• Trigger point massage: Deep pressure to areas of local tenderness</td>
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<td>• Shiatsu massage: Varying, rhythmic pressure from the fingers</td>
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<td><strong>Nerve biased</strong></td>
<td>• Neural dynamics: Passive, combined movement of the spine and extremities, within their normal range of motion, in ways to elongate or tension specific nerves.</td>
<td>• Improve range of motion&lt;br&gt;• Decrease pain</td>
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Classification of MT techniques referenced in manuscript along with specific examples of each. Proposed model is general and accounts for all techniques regardless of their theorized anatomical emphasis. Adapted from NCCAM website (http://nccam.nih.gov/, 2007).
from the region of application. The effectiveness of MT despite the inconsistencies associated with a purported biomechanical mechanism suggests that additional mechanisms may be pertinent. Subsequently, we suggest, that as illustrated by the model, a mechanical force is necessary to initiate a chain of neurophysiological responses which produce the outcomes associated with MT.

3.2. Neurophysiological mechanism

The proposed model accounts for the complex interactions of both the peripheral and central nervous system which comprise the pain experience. Current mechanistic studies of MT in humans are frequently unable to directly observe the central or peripheral nervous system. Subsequently, in the absence of direct observation, conclusions are drawn from associated neurophysiological responses which indirectly implicate specific mechanisms. Studies have measured associated responses of hypoalgesia and sympathetic activity following MT to suggest a mechanism of action mediated by the periaqueductal gray (Wright, 1995) and lessening of temporal summation following MT to suggest a mechanism mediated by the dorsal horn of the spinal cord (George et al., 2006). The model makes use of directly measurable associated responses to imply specific neurophysiological mechanisms when direct observations are not possible. The model categorizes neurophysiological mechanisms as those likely originating from a peripheral mechanism, spinal cord mechanisms, and/or supraspinal mechanisms.

3.3. Peripheral mechanism

Musculoskeletal injuries induce an inflammatory response in the periphery which initiates the healing process and influences pain processing. Inflammatory mediators and peripheral nociceptors interact in response to injury and MT may directly affect this process. For example, Teodorczyk-Injeyan et al. (2006) observed a significant reduction of blood and serum level cytokines in individuals receiving joint biased MT which was not observed in those receiving sham MT or in a control group. Additionally, changes of blood levels of β-endorphin, anandamide, N-palmitoylethanolamide, serotonin (Degenhardt et al., 2007) and endogenous cannabinoids (McPartland et al., 2005) have been observed following MT. Finally, soft tissue biased MT has been shown to alter acute inflammation in response to exercise (Smith et al., 1994) and substance P levels in individuals with fibromyalgia (Field et al., 2002). Collectively, these studies suggest a potential mechanism of action of MT on musculoskeletal pain mediated by the peripheral nervous system for which mechanistic studies may wish to account.

3.4. Spinal mechanisms

MT may exert an effect on the spinal cord. For example, MT has been suggested to act as a counter irritant to modulate pain (Boal and Gillette, 2004) and joint biased MT is speculated to “bombard the central nervous system with sensory input from the muscle proprioceptors (Pickar and Wheeler, 2001).” Subsequently, a spinal cord mediated mechanism of MT must be considered and is accounted for in the model. Direct evidence for such an effect comes from a study (Malisz et al., 2003b) in which joint biased MT was applied to the lower extremity of rats following capsaicin injection. A spinal cord response was quantified by functional MRI during light touch to the hind paw. A trend was noted towards decreased activation of the dorsal horn of the spinal cord following the MT. The model uses associated neuromuscular responses following MT to provide indirect evidence for a spinal cord
mediated mechanism. For example, MT is associated with hypo-
algnesia (Vicenzino et al., 2001; Mohammadian et al., 2004; George
et al., 2006), afferent discharge (Colloca et al., 2000; Colloca et al.,
2003), motoneuron pool activity (Bulbulian et al., 2002; Dishman
and Burke, 2003), and changes in muscle activity (Herzog et al.,
1999; Symons et al., 2000) all of which may indirectly implicate
a spinal cord mediated effect.

3.5. Supraspinal mechanisms

Finally, the pain literature suggests the influence of specific
supraspinal structures in response to pain. Structures such as the
anterior cingular cortex (ACC), amygdala, periaqueductal gray
(PAG), and rostral ventromedial medulla (RVM) are considered
instrumental in the pain experience (Hsieh et al., 1995; Vogt
et al., 1996; Derbyshire et al., 1997; Iadarola et al., 1998; Peyron
et al., 2000; Moulton et al., 2005; Guo et al., 2006; Bee and
Dickenson, 2007; Oshiro et al., 2007; Staud et al., 2007). Subse-
quently, the model considers potential supraspinal mechanisms
of MT. Direct support for a supraspinal mechanism of action of
MT comes from Malisz et al. (2003a) who applied joint biased
MT to the lower extremity of rats following capsaicin injection.
Functional MRI of the supraspinal region quantified the response
of the hind paw to light touch following the injection. A trend
was noted towards decreased activation of the supraspinal
regions responsible for central pain processing. The model
accounts for direct measures of supraspinal activity along with
associated responses such as autonomic responses (Vicenzino
et al., 1998; Sterling et al., 2001; Delaney et al., 2002; Moulson
and Watson, 2006; Zhang et al., 2006) and opioid responses
(Vernon et al., 1986; Kaada and Torsteinbo, 1989) to indirectly
imply a supraspinal mechanism. Additionally, variables such as
placebo, expectation, and psychosocial factors may be pertinent
in the mechanisms of MT (Ernst, 2000; Kaptchuk, 2002). For
example expectation for the effectiveness of MT is associated
with functional outcomes (Kalauokalani et al., 2001) and a recent
systematic review of the literature has noted that joint biased MT
is associated with improved psychological outcomes (Williams
et al., 2007). For this paper we categorize such factors as
neurophysiological effects related to supraspinal descending
inhibition due to associated changes in the opioid system (Sauro
and Greenberg, 2005), dopamine production (Fuentes-Fernandez
et al., 2006), and central nervous system (Petrovic et al., 2002;
Wager et al., 2004; Matre et al., 2006) which have been observed
in studies unrelated to MT.

4. Implementation of comprehensive model

The comprehensive model delineates potential mechanisms
associated with pain relief from MT allowing researchers to
identify domains of interest their studies are designed to
evaluate and potential mechanisms not adequately considered.
The model is intended to highlight differing possibilities when
conclusions are drawn which may be further explored in
subsequent studies. For example, studies have reported hypo-
lgesia following MT (Mohammadian et al., 2004; George et al.,
2006). George et al. (2006) suggested a spinal cord mediated
mechanism due to associated hypalgesia of temporal summa-
tion. The model indicates that while monitoring a spinal cord
mediating effect (temporal summation), the potential for a
peripheral or supraspinal mediating effects was not considered
(Fig. 2). A recent study attempted to replicate these prior findings
while accounting for potential supraspinal influence (Bialosky
et al., 2007). For this paper we categorize such factors as
neurophysiological effects related to supraspinal descending
inhibition due to associated changes in the opioid system (Sauro
and Greenberg, 2005), dopamine production (Fuentes-Fernandez
et al., 2006), and central nervous system (Petrovic et al., 2002;
Wager et al., 2004; Matre et al., 2006) which have been observed
in studies unrelated to MT.
5. Limitations of proposed model

The model is intended to be applicable to all forms of MT. While the biomechanical application of joint biased, soft tissue biased and nerve biased MT are different, the related neurophysiological responses are similar and adequately encompassed within the model given the current state of knowledge. The proposed model provides a platform to empirically test hypotheses related to different biomechanical and neurophysiological effects specific to types of MT, an area that is currently lacking in the literature. The proposed comprehensive model is intended to explain the mechanisms of MT on musculoskeletal pain. MT has a postulated role in the treatment of disorders of other body systems such as asthma (Balon and Mior, 2004) and high blood pressure (Plaugher and Bachman, 1993); however, those effects are beyond the scope of the current model. Finally, this model is strictly intended to guide research questions regarding the mechanisms of MT. A body of literature already exists suggesting the effectiveness of MT. The proposed model is intended to complement and provide underlying explanations to the existing body of literature suggesting the effectiveness of MT.

6. Future directions

A limitation in the current literature is the failure to account for the non-specific mechanisms associated with MT in the treatment of musculoskeletal pain. A number of neurophysiological responses associated with MT are also associated with non-specific effects such as placebo (Fig. 4). Current study designs have not adequately accounted for non-specific effects, and subsequently, their role in the clinical outcomes associated with MT is unknown. Future mechanistic studies in MT should consider determining the influence of non-specific effects. The model presents a guide to design future mechanistic studies so that all relevant possibilities are included.

The model is based primarily on associated responses as the current body of mechanistic literature is lacking in studies which directly observe regions of interest. As technology improves, the means to directly observe specific regions is becoming possible. More recent studies in the acupuncture literature have reported direct observation of the spinal cord (Wang et al., 2006; Chen et al., 2007) and supraspinal centers (Dougherty et al., 2008; Fang et al., 2008) in
response to treatment. Similar studies are possible in MT and will allow direct observation of the nervous system response to MT with a subsequent improved understanding of where the techniques exert their effect.

Interdisciplinary collaboration has been recommended in the study of the mechanisms of MT (Khalsa et al., 2006). The comprehensive model provides a framework for such efforts to study both specific sections of the model and their interaction. For example, a team of researchers could work together including a manual therapist to provide treatment, a biomechanist to monitor the biomechanical parameters of the studied MT, an endocrinologist to monitor potential spinal cord and supraspinal mechanisms, and a psychologist to monitor the influence of non-specific effects such as expectation, fear, and catastrophizing.

7. Conclusion

The mechanisms behind the clinical effectiveness of MT are not established. Limitations of prior mechanistic studies are the study of individual mechanisms without regard for others and a failure to adequately account for non-specific effects. We have proposed a comprehensive model to consolidate the current research and guide future research into the mechanisms of MT.

Acknowledgements

The project was supported by Grant Number R-21 AT002796-01 from the National Institutes of Health – National Center for Complementary and Alternative Medicine (SZG, MDB, MER, DDP). This manuscript was written while JEB received support from the National Institutes of Health T-32 Neural Plasticity Research Training Fellowship (T32HD043730).

References


Ernst E. Does spinal manipulation have specific treatment effects? Fam Pract 2009;26:539–49.


