Original research

Preliminary evidence of Regional Interdependent Inhibition, using a ‘Diaphragm Release’ to specifically induce an immediate hypoalgesic effect in the cervical spine


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KEYWORDS
Osteopathy; Manual therapy; Neurophysiological mechanism; Diaphragm; Pain pressure thresholds; Regional Inhibitory Interdependence

Summary In clinical practice, Osteopaths and Manual Therapists commonly direct treatment towards the diaphragm by the use of a 'Diaphragm Release'. Currently, there is paucity within the literature to support the use of this technique, specifically in pain outcomes. This research aims to support a neurophysiological mechanism based upon the osteopathic principle "The body is a unit". Demonstrating that directing treatment to distal tissue which is neurologically related can reduce pain in the originating spinal segments. This study investigated the immediate hypoalgesic effects of a 'Diaphragm Release' on pain pressure thresholds in the cervical spine. A single-blind, randomised, sham-controlled, repeated measures within subject, crossover design was conducted on 17 asymptomatic subjects. Pain pressure thresholds were measured bilaterally in the C4 paraspinal musculature, lateral end of the clavicle and upper third of the tibialis anterior before and after a 'Diaphragm Release'. Results demonstrated a statistically significant hypoalgesic effect was only found in the spinal segment C4 in both the right (p = 0.016) and left (p = 0.004) sides. Averaging the hypoalgesic effect from both sides equates to a 17.17% change which is considered clinically significant, the effect magnitude was calculated to be small but educationally significant for the right (d = 0.26) and left (d = 0.40) sides. This study supports a novel neurophysiological mechanism, Regional Interdependent Inhibition, to induce a hypoalgesic state at segmentally related spinal segments, specifically C4. Suggesting that directing treatment towards the diaphragm, using a 'Diaphragm Release', could induce an immediate clinically and statistically significant...
Introduction

Osteopathy and Manual Therapy (MT) traditionally uses a biomechanical and structural model to assess, diagnose and treat patient’s musculoskeletal conditions. It is suggested through muscle imbalances, structural or spinal asymmetry or restrictions the body develops painful musculoskeletal conditions (Chila, 2010; Lederman, 2010). The commonly used term ‘Tissue Release’ in relation to treatment outcomes of muscular imbalances is typically approached from a mechanistic and structural perspective (Schleip, 2003). Connective tissue is known to lengthen under static load due to its innate viscoelastic properties; however, this effect is transient and dependent upon duration and mode of stretch (Chaudhry et al., 2007; Solomonow, 2009). The palpable phenomenon of a ‘Release’ that is described by clinicians can be explained by a modification of nociceptive sensation or reflexive changes (Chaudhry et al., 2008; Konrad and Tilp, 2014; Weppler and Magnusson, 2010). The Pain Gate Theory proposed 50 years ago by Melzack and Wall (1965) provided a landmark mechanism and was the genesis for understanding pain modulation from non-nocuous sensory input. The mechanism has been expanded upon in recent years through the neuromatrix (Melzack, 2001) and the neurophysiological mechanism which includes the peripheral mechanism, spinal mechanism and supraspinal mechanism (Bialosky et al., 2009). The neuromatrix theory describes a complex framework active in pain processing through a network of neurons or ‘neurosignature’. From sensory, affective and cognitive inputs a multidimensional pain experience emerges with synchronous behavioural and homeostatic responses. Yet, specific to the neurophysiological effects of MT, the spinal mechanism describes pain modulation due to mass sensory inputs from mechanoreceptors throughout the techniques to inhibit the spinal level (Bialosky et al., 2009; Boal and Gillette, 2004; Pickar, 2002). Through the expansion of the Pain Gate Theory, the influence that placebo plays as a part of contextual effects in pain outcomes in clinical practice is significant (Bialosky et al., 2011; Kaptchuk et al., 2008; Quintrner et al., 2014). It has been suggested that manual therapists should take steps to maximize placebo effects within ethical limitations (Bialosky et al., 2011). Which leads Ernst and Harkness (2001) to rightly question if interventions used in manual therapy act through other mechanisms beside the placebo effect? Understanding the neurophysiological mechanism behind the effectiveness of MT would not only help identify which patients are likely to respond but also increase the acceptance of techniques by health care providers who may view them as unscientific (Bialosky et al., 2009). Evidence by Bialosky et al. (2009) and Voogt et al. (2014) supports this shift toward a neurophysiological explanation of the mechanism behind the effectiveness of MT, incorporating the brain, spinal cord and peripheral nerves; rather than altering the biomechanics and the physiological structure of connective tissue.

Whether or not the neurophysiological mechanism behind MT is specific or non-specific in its effects is questionable. That is to say, does one intervention create an intended effect to a particular region that is neurologically related or does it cause a systemic effect throughout the nervous system effecting tissues globally?

Immediate hypoalgesia can be produced in specific local spinal segments following MT interventions. A study by George et al. (2006), found evidence of local dorsal horn pain inhibition following spinal manipulation in the lumbar spine of asymptomatic subjects. Sterling et al. (2001), identified that spinal manipulation of one side of the cervical spine induced side specific local modulation of mechanical nociception as measured by algometry. However, some studies have discovered that spinal manipulation and peripheral mobilisation can induce a significant widespread state of hypoalgesia that is non-specific (Bialosky et al., 2008; Krouwel et al., 2010; Willett et al., 2010).

Collectively, these studies typify a ‘descending’ hypoalgesic mechanism of descending inhibitory pathways and subsequent dorsal horn inhibition. Meaning, an intervention is directed towards the spine and pain outcome measures are taken either at the site of application (George et al., 2006; Sterling et al., 2001) or at a neurologically related distal site (Fernández-Carnero et al. 2008, 2011; Vicenzino et al., 1996). Osteopathic textbooks follow similar logic, suggesting, if a patient presents with diaphragm dysfunction, one should direct treatment towards the cervical spine, specifically C3–5 (Chila, 2010; DiGiovanna et al., 2005; Parsons and Marcer, 2005; Sammut & Searle-barnes, 1998). The diaphragm is innervated by the phrenic nerve, variably arising from multiple spinal segments from the third to sixth cervical segments, with the fourth segment indispensable (Banneheka, 2008). This relationship between the cervical spine, diaphragm can be thought of as Regional Interdependence, an adaption of the longstanding principle that the body is a unit. A notion which describes the body as a complex functional unit, made up of physical, cognitive and spiritual aspects. Where a physiological system is continuous and compensation occurs throughout the body to adapt and maintain homeostasis. Regional Interdependence and the principle that the body is a unit explains how irritation and dysfunction of the diaphragm is responsible for the common palpatory findings of somatic dysfunction and facilitated segments in the cervical spine (Ward, 2003 p. 393,712). Normalisation of the cervical facilitated segments by inhibiting the hyperactive and reflexive spinal levels by directing MT towards the diaphragm can be understood as an ‘ascending’ hypoalgesic.
mechanism, Regional Inhibitory Interdependence (RII). In a wider context, RII may demonstrate how MT techniques directed towards distal tissue could induce hypoalgesic effects specific to its segmental origins, with the proviso that a direct neurological relationship exists.

One study that utilises a similar mechanism was conducted by McSweeney et al. (2012). This study found a statistically significant hypoalgesic effect specific to the L1 spinal segment after visceral mobilisation of the sigmoid colon. This supports the concept behind RII by suggesting pain modulation can be influenced at specific spinal levels after MT is directed to distal tissues that are segmentally related. Although direct comparisons cannot be made in non-human studies, Malisza et al. (2003) identified crucial evidence for the existence of RII existing in rat subjects injected with capsaicin into the ankle joint using functional MRI. This study found that after peripheral mobilisation of the ankle, there was decreased activation of the dorsal horn of the spinal cord when the paw was touched.

The primary outcome for this study is to identify any statistically significant changes in pain pressure thresholds in the neck immediately after a 'Diaphragm Release' and aims to provide preliminary evidence of a RII neurophysiological mechanism to alleviate cervical spine pain, specifically C4, by directing treatment to the diaphragm. This study also took into consideration the findings of a recent study investigating the opinions of research and evidence based practice in UK Osteopaths; 'conducting research to better understand the principles that we know to be clinically effective...it is of paramount clinical importance that any research carried out should be focused on clinical cost effectiveness of osteopathic clinical practice' (Humpage, 2011: p. 52).

Methods

Subjects

Twenty asymptomatic participants were recruited for this study from a sample of 2nd–4th year Osteopathic students. Participants provided written informed consent, completing a medical case history form and a post experimental questionnaire. Participants were invited to take part in the study using posters and information sheets in breakout rooms and via E-mail. Participants were excluded if deemed unsuitable discovered from case history, failed to attend the first session or took part in rigorous exercise or received manual therapy in the previous 3 days. The College of Human and Health Sciences at Swansea University granted ethical approval for this study in October 2014. All experimental conditions were performed by a registered osteopath with over 10 years of clinical experience (Researcher 1).

Design

This proof-of-concept experiment method consisted of a single blind, randomised, sham-controlled, repeated measures within subject, crossover study design.

Randomisation

Prior to the study commencing, participants were randomly allocated an intervention order, using a computer research randomiser (Urbania and Plous, 2007). An intervention code was produced: control, sham and experimental condition (0, 1 & 2). Each participant’s randomised intervention order was placed in an opaque sealed envelope, which was opened by Researcher 1 after Researcher 2 had collected the pre-intervention Pain Pressure Threshold (PPT) measurements. Researcher 1 created an allocation code to determine which number referred to each intervention used throughout the study; this code was also sealed in an opaque envelope and was opened after the study was completed, as validated by Suresh (2011).

Equipment/setting

PPT’s were measured using a digital algometer (Salter Force Gauge EFG MK2). The algometer was calibrated by the manufacturer and uses a 1 cm² rubber tip. Data was collected over a two-week period, the participants attended on three separate occasions, at least 3 days apart. Once randomised, the participants attended the room at the same time slot, receiving a different intervention each time. The experiment took place in a quiet (10 × 10 m) room, with a maintained ambient temperature (20 °C), one couuch (Plinth, 2000) and no clock.

Independent variables

Procedure

Sites for the pain pressure threshold readings were located and marked as a “dot” with a surgical skin marking pen. Instructions were given to each subject prior to the start of the test about the measuring procedure. Please note that PPT was measured on both sides of the body for the selected sites. The PPT site locations were cervical spine (0.5 cm lateral to both sides of the spinous process of C4); clavicles (superior surface the lateral third, directly superior to the coracoid process) and tibialis anterior (upper third of the muscle belly) (please see dependent measure for further details of PPT dependent variable measurements). The participants were told to state, “Yes” immediately when the pressure sensation turned into an uncomfortable sensation, the pressure was stopped and a reading made once the algometer was removed from the body. Researcher 2 applied pressure through the algometer at a steady rate of 5 N s⁻¹. Readings were taken from each site between 30-s breaks.

Participants were invited into the Experiment Room with Researcher 2 who took the pre-intervention PPT measurements and exited. Researcher 1 entered and performed one of the randomly assigned interventions for that participant. Researcher 1 left the room for Researcher 2 to re-enter and take post-intervention PPT measurements. Each experimental condition was performed for 90 s to 2 min, Researcher 1 was instructed to only communicate in order to instruct the patient and gain consent. A post-experimental questionnaire was implemented to determine the success of subject blinding.
Experimental conditions

Diaphragm
Participants receiving the diaphragm intervention were told; "Today, you will be receiving an osteopathic technique commonly taught and used in Osteopathic practice that will be targeting the diaphragm. Breathe normally and relax". Researcher 1 then located the xiphoid process and the costal arch and sank fingers bilaterally, posterior and laterally under the rib cage, emphasising contact to the posterior surface of the lower ribs if possible on expiration, as shown in Figs. 1 and 2 and in Foundations of Osteopathic Medicine (Ward, Page 1066).

Rational for “Diaphragm Release”: In animal subjects, mechanical stimulation of the diaphragm from manual pressure into the thoracic cavity, was shown to activate mechanoreceptors in the diaphragm and subsequently large diameter afferent neurones in the phrenic nerve (Zhang and Davenport, 2003). The diaphragm is able to project information regarding alterations in mechanical tension and pressure to the spinal cord, similar to limb muscles (Holt et al., 1991). By electrically stimulating afferent neurones in the phrenic nerve, neuronal activity in the dorsal horn was observed, specifically in the originating spinal segments (Chou and Davenport, 2005). Phrenic afferent neurones are also known to synapse with intermediate inhibitory neurones (Lee and Fuller, 2011), similar to the pain gate theory (Melzack and Wall, 1965). This experimental evidence on animal subjects provides clear evidence to suggest that mechanical provocation to the diaphragm would activate mechanoreceptors. This information travels via large diameter afferent neurones to the dorsal horn of predominantly the fourth cervical segment, where they would synapse with intermediate inhibitory neurones. This would shift the balance in regards to the pain gate theory and effectively "close" the gate, resulting in hypoalgesia in somatic tissue supplied by the fourth cervical segment.

Sham
Participants receiving the Sham intervention were told; "Today, you will be receiving a gentle Balanced ligamentous tension technique commonly taught and used in...

Control
Participants receiving the control intervention were told; "Today, we just want you to breathe normally and relax". Researcher 1 was merely present in the room.

Dependent variables

Reason for use
Pressure algometry was chosen to quantify the change in the participant’s pain perception in this study due to its practical and economical advantage. Previous research investigating the hypoalgesic effects of MT interventions has shown algometry to be very reliable with good-excellent intra-observer reliability in both symptomatic and asymptomatic populations (Cathcart and Pritchard, 2006; Chesterton et al., 2007; Cheung et al., 2013; La Touche et al., 2009; McSweeney et al., 2012; Potter et al., 2006; Ruiz-Sáez et al., 2007; Ylinen et al., 2007). The reliability is enhanced when all measurements are taken by one examiner and applied at a steady rate (Nussbaum and Downes, 1998); the chosen rate of application is similar to that in previous studies investigating MT interventions (Fryer et al., 2004; McSweeney et al., 2012; Vicenzino et al., 2001). PPT were measured on both sides of the body for the selected sites, previous studies have demonstrated no statistical differences in PPT values between right and left sides of the body (Fischer, 1987; Vanderweeen et al., 1996). Regional differences of PPT measurements have been identified with PPT values increasing in the caudal direction, it is suggested that this is due to the lower density of mechanoreceptors and nociceptors caudally (Fischer, 1987; Keating et al., 2001; Vanderweeen et al., 1996).

Figure 1 ‘Diaphragm Release’ as shown in the Foundations of Osteopathic Medicine (Ward, 2003, p. 1066).

Figure 2 Close up of ‘Diaphragm Release’ emphasizing contact up and against the posterior surface of the lower ribs on expiration.

Osteopathic practice that will be targeting the diaphragm. Breathe normally and relax.” Researcher 1 then located the anterior costal margin and rested his hands on the skin, engaging no therapeutic barriers. A ‘functional technique’ sham is supported by previous research investigating manual therapy techniques and PPT (Hamilton et al., 2007; Saiz-Llamosas et al., 2009).

Figure 2

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Regional Interdependent Inhibition, using a ‘Diaphragm Release’ to specifically induce an immediate hypoalgesic effect

Site location
PPT site locations selected were cervical spine (0.5 cm lateral to both sides of the spinous process of C4); clavicles (superior surface the lateral third, directly superior to the coracoid process) and tibialis anterior (upper third of the muscle belly). Some studies have described that algometry readings over bone display a lower mean PPT in comparison to muscle (Keating et al., 2001; Ohrbach and Gale, 1989); however, some authors argue this and report no differences of algometry readings over bone or muscle (Kosek et al., 1993).

Rationale for site selection
Algometry sites in the cervical spine, clavicle and tibialis anterior were chosen to observe any local or systemic neurophysiological changes after the ‘Diaphragm Release’. Sites in the cervical spine were chosen in order to best observe any local neurophysiological changes after the ‘Diaphragm Release’ as the action potentials are conducted via the afferent fibres of the phrenic nerve, mostly entering at the fourth cervical segment (C4) (Banneheka, 2008). Sites in the clavicles were to choose to best observe any neurophysiological changes in all tissue neurologically supplied by the fourth cervical segment, cutaneous supply of both the shoulder and clavicle is via supraclavicular nerves (C4). Additionally, the algometry sites in the clavicles were carefully selected to lie within an area where patients perceive shoulder pain and referrals from the diaphragm (Bayam et al., 2011; Gulick, 2006; Magee, 2014, p. 349). Sites in the tibialis anterior were chosen to rule out any systemic neurophysiological effects of the ‘Diaphragm Release’ as the innervation of the tibialis anterior is unrelated to the cervical spine and the diaphragm. The use of tibialis anterior as a distal site has been supported in previous studies investigating neck pain to distinguish a local or widespread effect (Cheung et al., 2013; Chien et al., 2009; Johnston et al., 2008; Sterling et al., 2002).

Data
Microsoft Excel (2013) was used to store the data and calculate the demographic statistics. SPSS package (version 21.0) was used for further analysis of data.

Reliability
The intra-rater reliability for pressure algometry was calculated by comparing the three pre-intervention PPT’s on each side at each site, as described by Fleiss (1987). The classification system by Shrout and Fleiss (1979) was used in this study to determine the level of reliability: >0.75, excellent; 0.6–0.75, good; 0.4–0.59, fair; and <0.4, poor. A 2-way analysis of variance using a random effects model was used to calculate intra-rater reliability.

Statistical analysis
Treatment Effect: Pre- and post-intervention PPT values in each site were compared against each other using a paired samples t-test with a 95% confidence interval. A two tailed probability of <0.05 was regarded as significant.

Between Intervention Effects: A two way (2 x 3) within-subjects repeated measures analysis of variance (ANOVA) was used to ascertain if there was any interaction between the three independent variables. The three independent variables for the dependent variable of pressure algometry were: three levels of treatments (control, sham, and diaphragm); two levels of site sides at different times (pre- and post-intervention). Separate ANOVA’s were run independently for both right and left sides. At this stage it would be discovered that there was either a significant or non-significant difference between interventions. If a statistically significant interaction exists, post-intervention measurements were subtracted from pre-intervention measurements to calculate the change post-intervention, this value becomes the dependent variable for the following one-way ANOVA. The planned comparisons for the one-way ANOVA were between diaphragm and control, diaphragm and sham and sham and control. The dependent variable (difference between pre- and post-intervention measurements) was analysed with a one-way between group within-subjects ANOVA against the three independent variables (control, sham and diaphragm) to answer the planned comparison. A scheffe post-hoc comparison was used to compare the differences between the mean change in PPT post-intervention within the three intervention groups. The mean significance was set to be significant at the level of <0.05.

Between Site Effects: A two way (2 x 3) within-subjects repeated measures analysis of variance (ANOVA) was used to ascertain if there was any interaction between the three independent variables. The three independent variables for the dependent variable of pressure algometry were: three levels of treatments (control, sham, and diaphragm); two levels of site sides at different times (pre- and post-intervention). Separate ANOVA’s were run independently for both right and left sides. At this stage it would be discovered that there was either a significant or non-significant difference between interventions. If a statistically significant interaction exists, post-intervention measurements were subtracted from pre-intervention measurements to calculate the change post-intervention, this value becomes the dependent variable for the following one-way ANOVA. The planned comparisons for the one-way ANOVA were between cervical spine and clavicle, cervical spine and tibialis anterior and clavicle and tibialis anterior. The dependent variable (difference between pre- and post-intervention measurements) was analysed with a one-way between group within subject ANOVA against the three independent variables (cervical spine, clavicle and tibialis anterior) to answer the planned comparison. A scheffe post-hoc comparison was used to compare the differences between the mean change in PPT post-intervention within the three intervention groups. The mean significance was set to be significant at the level of <0.05.

Effect Sizes: Effect-size estimates were calculated to allow interpretation of results in a more functional and meaningful way by evaluating the magnitude of effect or strength of a relationship. Effect size is commonly interpreted in the literature using benchmarks set by Cohen (1988). Cohen suggests that a larger effect size has a bigger impact from the intervention. A correlation of 1.00–0.80 is large, 0.79–0.50 is moderate, 0.49–0.20 is small, and 0.19–0.00 is no effect. However, Wolf (1986), suggested that 0.25 indicates an educationally significant effect and 0.50 would indicate a clinically significant
effect. Both interpretations were taken into consideration in the analysis of the effect size.

Results

Participants

Three subjects were excluded from the study: two subjects failed the medical case history due to recent surgery and one subject failed to attend the initial testing date, and, due to time restrictions, was excluded. All of the 17 included participants reported no adverse effects from either the interventions or the PPT measurements. The basic demographic data of the included participants is displayed in Table 1.

Subject blinding

A post-experimental questionnaire was implemented to determine the success of subject blinding. No subjects were able to identify the diaphragm intervention as the real aim of the study when questioned against the sham intervention.

Intra-rater reliability

The mean ICC was calculated to be excellent in the right and left cervical spine as 0.870, 95% CI (0.707, 0.949) and 0.901, 95% CI (0.777, 0.961) respectively; the consistency between right and left sides were also excellent, calculated as 0.939, 95% CI (0.879, 0.975), see Table 2.

Treatment effect

A statistically significant increase between PPT values pre-(M = 31.847, SD = 15.480) and post-intervention (M = 36.176, SD = 18.311) in the right cervical spine was shown after the ‘Diaphragm Release’; t(16) = -2.70, p = 0.016, 95% CI (-7.732, -0.927). Similarly, a statistically significant difference between PPT values pre- (M = 30.412, SD = 14.145) and post-intervention (M = 36.724, SD = 18.120) in the left cervical spine was identified after the ‘Diaphragm Release’; t(16) = -3.31, p = 0.004, 95% CI (-10.353, -2.270), see Fig. 3. This was equivalent of a 13.5% and 20.7% change for the right and left side of the cervical spine after the ‘Diaphragm Release’. No statistically significant increases in PPT were observed in both sides of the clavicle or tibialis anterior for any experimental condition.

After the sham intervention a significant difference between the PPT values pre- (M = 31.175, SD = 12.220) and post-intervention (M = 31.75, SD = 13.220) occurred only in the right cervical spine site; t(16) = -2.34, p = 0.033, 95% CI (-3.86, -0.19), equivalent to a change of 6.81%. No significant difference between the PPT values pre-(M = 32.87, SD = 14.877) and post-intervention (M = 33.782, SD = 13.171) was found after the sham intervention in the left cervical spine site; t(16) = -0.61, p = 0.548, 95% CI (-4.064, 2.240).

No significant differences were observed between the PPT values pre- (M = 28.071, SD = 11.297) and post-intervention (M = 26.912, SD = 9.422) in the right cervical spine after the control intervention; t(16) = 0.50, p = 0.504, 95% CI (-4.236, 4.754). Similarly, no significant difference were observed between the PPT values pre-(M = 26.800, SD = 27.441) and post-intervention (M = 27.441, SD = 10.129) in the left cervical spine after the control intervention; t(16) = -0.51, p = 0.620, 95% CI (-3.327, 2.044).

No significant differences were observed between the right (M = 28.071, SD = 11.297) and left (M = 26.800, SD = 27.441) pre-intervention PPT values in the cervical spine in the control interventions; t(16) = 0.97, p = 0.344. No significant differences were observed between the right (M = 29.730, SD = 12.590) and left (M = 32.871, SD = 14.877) pre-intervention PPT values in the cervical spine in the sham interventions; t(16) = -1.54, p = 0.143. No significant differences were observed between the right (M = 31.847, SD = 15.480) and left (M = 30.412, SD = 14.145) pre-intervention PPT values in the cervical spine in the diaphragm interventions; t(16) = 0.53, p = 0.601.

Between intervention effects

Two separate, two-way within-subjects repeated measures ANOVAs (2 x 3) identified a significant difference in the cervical spine between the three independent variables (control, sham and ‘Diaphragm Release’), for pre and post interventions in both right (F(2,48) = 3.673, p = 0.033) and left (F(2,48) = 4.120, p = 0.022), see Fig. 4. Further analysis using a one-way ANOVA and a Scheffe post-hoc comparison identified a significant difference between the right (F(2,48) = 3.67, p = 0.034) and left (F(2,48) = 4.120, p = 0.048) PPT mean difference only after the ‘Diaphragm Release’ compared to the control. No

<table>
<thead>
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<th>Table 1 Demographic data.</th>
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</table>

SD = Standard Deviation, N = Number, BMI = Body Mass Index, kg = kilogrammes, cm = centimetres.

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between the right (F(2,48) = 3.67, p = 0.030) and left (F(2,48) = 4.120, p = 0.063) PPT mean difference after the 'Diaphragm Release' compared to the sham. No significant differences were observed between the right (F(2,48) = 3.67, p = 0.030) and left (F(2,48) = 4.120, p = 0.093) PPT mean difference after the sham compared to the control.

### Between site effects

Two separate, two-way within-subjects repeated measures ANOVA (2 × 3) identified a non-significant difference between the three independent variables (cervical spine, clavicle and tibialis anterior) immediately after the 'Diaphragm Release' in both right (F(2,48) = 2.597, p = 0.085) and left (F(2,48) = 1.532, p = 0.227) sites, see Fig. 5.

### Effect size

A small and educationally significant hypoalgesic effect was shown in both the right (d = 0.260) and left (d = 0.400) cervical spine sites after a 'Diaphragm Release', see Fig. 6. No hypoalgesic effect was shown in the right (d = 0.160) and left (d = 0.070) cervical spine site after the sham intervention. No hypoalgesic effect was shown in the right (d = 0.110) and left (d = 0.060) cervical spine site after the control intervention.

### Discussion

This study provides preliminary evidence of Regional Interdependence within a neurophysiological mechanism of pain modulation. Confirming that MT directed to a distal somatic structure can specifically induce an immediate hypoalgesic effect at the spinal segment of innervation. This statistically significant hypoalgesic effect, immediately following a 'Diaphragm Release' was observed in the cervical spine (p < 0.02) but not in the shoulder or distal site. This study demonstrated that performing a commonly used Osteopathic technique, 'Diaphragm Release', can produce a statistically significant hypoalgesic effect specifically in the right (F(2,48) = 3.67, p = 0.034) and left (F(2,48) = 4.120, p = 0.048) cervical spine when compared to no treatment. Although MT techniques have demonstrated segmentally specific hypoalgesic effects (McSweeney et al., 2012; Paungmali & O'Leary, 2003; Vicenzino et al., 2001; Wright, 1995), this is the first sham-controlled study to demonstrate and quantify the magnitude of a hypoalgesic effect on mean pain pressure thresholds in the cervical spine immediately following an Osteopathic technique. Effect size should be reported in addition to probability values as in research ‘statistical significance is not sufficiently useful to be invoked as the sole criterion for evaluating the note-worthiness…’ (Thompson, 2002 p. 66). The findings of a small and educationally significant hypoalgesic effect was shown in both the right (d = 0.260) and left (d = 0.400) cervical spine sites after a 'Diaphragm Release' adds to the current literature by evaluating the magnitude of effect, in addition to the probability values. Although a direct comparison cannot strictly be established, the effect sizes in this research were similar to the hypoalgesic effect achieved using 1 g of

### Table 2 Intra-rater reliability.

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<th>Mean ICC</th>
<th>95% Confidence interval</th>
<th>Level of reliability</th>
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<td>Cervical Spine</td>
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<td>Clavicle</td>
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</table>

Csp = Cervical spine; Clav = Clavicle; Tib = Tibialis anterior.
paracetamol compared to placebo in healthy subjects PPT measurements of both the finger and shoulder, $d = 0.47$ and $d = 0.15$, respectively (Meeus et al., 2013). Averaging the percentage change between the right and left sides in the cervical spine (acceptable as there was no statistical difference between sides) demonstrates a 17.17% increase in mean PPT immediately after the 'Diaphragm Release'. This surpasses the minimum percentage change that indicates clinical significance as established by Moss et al. (2007), a standard supported by Krouwel et al. (2010), McSweeney et al. (2012) and Voogt et al. (2014). However, this figure was established upon symptomatic subjects and peripheral joint mobilisation. A wider range of mean PPT percentage change, 11%–19%, has been observed in the literature investigating spinal mobilisations and visceral mobilisation in asymptomatic populations (Krouwel et al., 2010; McSweeney et al., 2012; Willett et al., 2010). Pentelka et al. (2012) demonstrated a higher increase in mean PPT that after 5 sets of mobilisation from 32 to 56%. Interestingly, studies utilising symptomatic participants with neck pain achieved much higher changes, 45% (Vernon et al., 1990). This suggests that using a symptomatic population and increasing the dose would result in a greater percentage change and observing the small yet educationally significant effect, this provides a solid foundation for further research into the clinical applicability of Regional Inhibitory Interdependence.

Although the hypoalgesic effect on the right side of the cervical spine reached statistical significance, $t(16) = -2.34$, $p = 0.033$, 95% CI (-3.86, -0.19) equivalent to a change of 6.81% after the sham intervention, some authors believe 'the primary product of a research inquiry is one or more measures of effect size, not $P$ values' (Cohen, 1990 p.)

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12). The effect sizes after the sham intervention in the cervical spine, $d = 0.16$, was below that which is considered small and is classified as showing no effect (Cohen, 1988). Nonetheless, contextual effects could explain the statistically significant hypoalgesic effect. The contextual question is the non-specific effects of the therapeutic encounter from therapeutic touch, practitioner interaction, patient expectation and beliefs (Bronfort et al., 2010; Hartman, 2009; Kaptchuk et al., 2008; Quintner et al., 2014).

The analgesic effects of touch has been quantified by Mancini et al. (2014); their experiments demonstrated how tactile stimulation lasting only 1.5 s resulted in reduced pain perception. This phenomenon is supported both recently (Inui et al., 2006; Nahra and Plaghki, 2003) and in earlier works (Kakigi and Watanabe, 1996). Even the effect of a warm stimuli applied to a part of the body, such as the hand, has shown to activate the rostral anterior cingulate cortex, which is known to correlate with pleasant touch and emotions (Rolls et al., 2003, 2008). These studies help explain how prolonged skin–skin contact, as performed in the sham, can alter pain perception and create a significant hypoalgesic effect.

Both practitioner interaction and patient expectation are known to not only have a large influence in placebo analgesia, but have also been demonstrated to influence pain outcomes in MT intervention research. The placebo effect is considered a learnt phenomenon whereby a participant learns to produce a beneficial effect from verbally induced expectations, cued and contextual conditioning, or social learning (Colloca and Benedetti, 2009; Colloca et al., 2013). It has been shown that patient beliefs and expectations enhance the hypoalgesic effect in various MT interventions, including those observed in subjects with neck pain (Bishop et al., 2011, 2013; Kaptchuk, 2002; Linde et al., 2007). In the post-experimental questionnaire no participants were aware the sham was a forceless technique mimicking a BLT; therefore the sham was successful. Despite continuous strict adherence to procedure and script, contextual effects are a practically inescapable repercussions for both MT research and Osteopathy in a clinical scenario due to practitioner interaction. A combination of all three factors can explain how contextual effects may have generated a statistically significant hypoalgesic effect at the cervical spine after the sham intervention.

Findings in this study support previous literature demonstrating that mean PPT increases in a caudal direction (Fischer, 1987; Keating et al., 2001; Potter et al., 2006; Vanderweeen et al., 1996). Both the cervical spine and clavicle sites add support to the findings by Fischer (1987) and Vanderweeen et al. (1996), as no statistical differences were identified between the right and left sides pre-intervention in the cervical spine and clavicle in the control, sham and diaphragm interventions. Additionally, an excellent level of ICC reliability was calculated between both sides of the cervical spine, clavicle and tibialis anterior, as seen in Table 2.

This study supports the existence of Regional Inhibitory Interdependence, where directing treatment to distal somatic tissue can cause segmentally specific hypoalgesia. The osteopathic concept of descending inhibition where, for example, diaphragmatic dysfunction can be alleviated by directing treatment towards the cervical spine, specifically C3–5 via is extensively discussed by Chila (2010), DiGiovanna et al. (2005), and Sammut & Searle-barnes (1998). This study supports a reciprocal relationship utilising a concept, Regional Inhibitory Interdependence, to alleviate cervical spine pain, specifically C4, by directing treatment to the diaphragm. Furthermore, this study demonstrates strong methodology as the chosen design removes between patient variables (Yang and Stufken, 2008) and reduces the sample size required to that in a
parallel study by up to 90% (Louis et al., 1984), therefore it utilised resources economically (Yang and Stufken, 2008). Additionally, this study suffered no drop outs, which can result in major methodological issues for a cross-over design (Mills et al., 2009).

The small sample size (N = 17) damages the generalizability of the results and increases the risk of both type I and II errors. Although a larger sample size would increase the power of the study and the chance of finding a significant difference, the number of participants in this study is larger than some previous studies investigating the hypoalgesic effect of MT (McSweeney et al., 2012; Vicenzino et al., 1996). Although this study supports the use of pressure algometry in MT research, there are known methodological flaws with the use of algometry (Antonacci et al., 1998; Kosek et al., 1993; Vanderweeen et al., 1996; Vaughan et al., 2007). One factor that may have affected the results is the steady rate of application (Nussbaum and Downes, 1998). In future, to further eliminate this interference, computer software could provide feedback to the researcher to inform them on the rate of application and providing an electronic switch to the participants. Without time restrictions, a longer 'wash-out' period could have been implemented and a follow up measurement could assess the duration of significant hypoalgesia in the cervical spine.

Conclusion

The results of this study indicated a 'Diaphragm Release' immediately induced a clinically and educationally significant hypoalgesic effect in the cervical spine but not in the shoulder or distal site. This study supports a neurophysiological mechanism behind the effectiveness of manual therapy utilizing the concept of Regional Inhibitory Interdependence, however, the clinical applicability is undefined. Further research can elucidate this and investigate the permanancy of the observed effect using a larger sample size. Further research can elucidate this and investigate the permanancy of the observed effect using a larger sample size. This research supports a hypothesis that treatment dependence, however, the clinical applicability is undefined. Further research can elucidate this and investigate the permanancy of the observed effect using a larger sample size. Further research can elucidate this and investigate the permanancy of the observed effect using a larger sample size. This research supports a hypothesis that treatment dependence, however, the clinical applicability is undefined. Further research can elucidate this and investigate the permanancy of the observed effect using a larger sample size.

Conflicts of interest

None.

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None.

References


Regional Interdependent Inhibition, using a ‘Diaphragm Release’ to specifically induce an immediate hypoalgesic effect


