Effects of biomechanical parameters of spinal manipulation: A critical literature review

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Abstract

Spinal manipulation is a manual treatment technique that delivers a thrust using specific biomechanical parameters to exert its therapeutic effects. These parameters are shown to have a unique dose-response relationship with the physiological responses of the therapy. So far, however, there has not been a unified approach to standardize these biomechanical characteristics. In fact, it is still undetermined how they affect the observed clinical outcomes of spinal manipulation. The aim of this study was, therefore, to review the current body of literature to explore these dosage parameters and evaluate their significance with respect to physiological and clinical outcomes. From the experimental studies reviewed herein, it is evident that the modulation of manipulation's biomechanical parameters elicits transient physiological responses including changes in neuronal activity, electromyographic responses, spinal stiffness, muscle spindle responses, paraspinal muscle activity, vertebral displacement, and segmental and intersegmental acceleration responses. However, clinical trials conducted to date to determine the therapeutic relevance of these changes is still limited. In addition, there were some inherent limitations in both human and animal models due to the use of mechanical devices to apply the thrust. Future studies evaluating the effects of varying biomechanical parameters of spinal manipulation should include clinicians to deliver the therapy so as to explore the true clinical significance of the dose-response relationship.

Keywords: *spinal manipulation, biomechanical characteristics, biomechanical parameters, dosage, force-time profile*

1. Introduction

Spinal manipulation is a hands-on treatment technique for the management of spinal pain and musculoskeletal injuries. The therapy has proven to be nearly as effective as recommended therapies for spine related pain and other conditions. [1] However, it is not yet understood how spinal manipulation exerts its therapeutic effects. Both biomechanical and neurophysiological hypotheses have been proposed to explain how the therapy works, but evidences to support these theories are still limited [2-4]. Biomechanical hypotheses proposed to date have theoretical inconsistencies and lack plausible evidence supporting their explanation for the pain modulatory effects of spinal manipulation; hence, the relevance of these theories in relation to the observed therapeutic outcomes is uncertain [2-7].

For the above reason, there has been a shift towards the neurophysiological hypotheses of spinal manipulation in recent years. [2, 6, 7] It is now understood that the observed clinical effects of manipulation are primarily neurophysiological in origin, owing to its various neural responses observed in mechanistic studies. [2, 6-9] However, the therapeutic success of manipulation cannot be attributed to neurophysiological mechanisms alone; in effect, the underlying mechanisms are the likely sum of improved spinal biomechanics and neurochemical responses. [5, 6] Irrefutably, the biomechanical forces applied during the manipulative act triggers the neuromechanical responses responsible for therapeutic effects. [5-7]

Specific biomechanical (dosage) parameters (e.g., preload force, peak force, thrust duration, rate of force application, and application site) have been reported to influence the physiological outcomes elicited by spinal manipulation. [10-13] In fact, research has demonstrated a unique dose-response relationship between biomechanical parameters and physiological responses to manipulation. [14]

Recently, two scoping reviews by Lima et al. [15] and Pasquier et al. [16] conducted a comprehensive analysis of existing evidences and concluded that dosage parameters of spinal manipulation clearly have an effect on short-term physiological responses. These two reviews, however, were limited in several aspects. The review by Lima et al. was primarily specific to preclinical studies (i.e., non-cadaveric, animal studies), which makes the dosage effects difficult to interpret due to certain translational limitations. The review was also not exclusive to spinal manipulation alone. The authors assessed three different forms of manual therapy and mainly summarized the key findings evaluating a large body of literature. Pasquier et al., on the other hand, had a broader goal of succinctly summarizing the main findings of studies investigating the frequency and dosage effects of spinal manipulation. Their research question was mainly aimed at answering whether the frequency and dosages effects influence clinical and physiological outcomes. In brief, both reviews did not make an in-depth exploration on each of the dosage parameters (i.e., the significance of a typical parameter and its relationship with other parameters and how changes in an input parameter influences the clinical/physiological outcomes).

The purpose of this article is, therefore, to review the current body of literature, including those reviewed by Lima et al. and Pasquier et al., relating to different dosage parameters of spinal manipulation. Our aim is to explore various dosage parameters of manipulation and their significance with respect to clinical and physiological outcomes. We will also review the concept of delivery specificity during spinal manipulation and its clinical relevance with dosage parameters.

2. Discussion

Spinal manipulation typically includes three distinct phases: the prethrust (or preload) phase, the thrust (or high-velocity low-amplitude force) phase, and the resolution phase. [17, 18] Figure 1 depicts the typical force-time profile of spinal manipulation. In the first 2 phases, most of the force is delivered along the same line of action, perpendicular (at an angle of nearly 90°) to the articular surface. [19] The prethrust phase usually provides a consistent preload force for several seconds before the thrust is delivered. [17] The position attained at the end of this phase is known as the prethrust position. [18] The thrust phase involves delivering a controlled directional force to one or more target vertebra within the limits of anatomic joint motion. [17, 20] Box 1. highlights the dosage terms used in the current study for these phases.

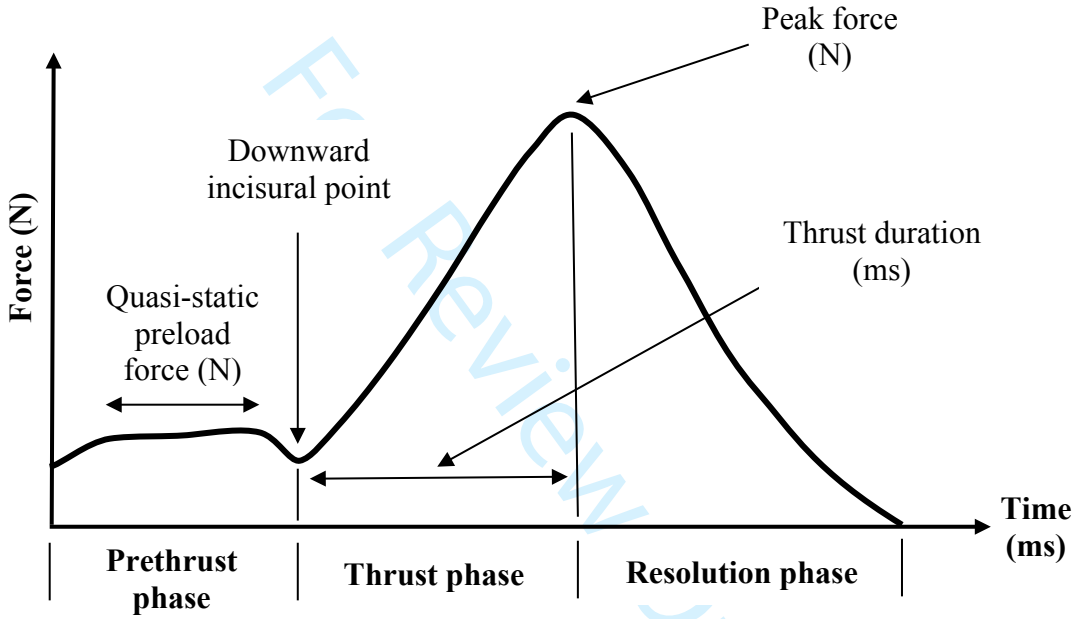

Figure 1. *Typical force-time profile of the perpendicular force applied during spinal manipulation. Adapted from Downie et al. [14] and Gorrell et al. [21]*

Box 1. Dosage terms used in this study to describe the biomechanical parameters of spinal manipulation

Dosage Terms [17-20]
Preload force – the constant force applied during the prethrust phase.
Preload duration – time of onset of the preload force to the end of prethrust phase.
Thrust force – the high-velocity, controlled force applied perpendicularly to the skin surface during the thrust phase.
Peak force – the highest force applied during the thrust phase.
Thrust duration – time between the onset of the thrust phase and the peak force occurrence.

Rate of force application – calculated using the formula: *peak force - preload force / thrust duration (or time to peak force)*.

2.1 Preload force

The preload force is the initial force gradually applied for several seconds before delivering the high-velocity, low-amplitude (HVLA) thrust. It precedes the delivery of the thrust impulse to remove slack from the intervertebral tissues and is assumed to prepare the disc to withstand forces of compression. [17, 18, 20] Preloading the joint brings the targeted spinal segment to its end range of motion, which prevents the dissipation of thrust force and energy to other areas during the thrust phase. [13, 22] This helps localize the thrust force to the targeted segment and improves patient comfort when the thrust is applied. The preload phase also guides the therapist during spinal manipulation. If the patient complains of pain or shows protective resistance while preloading a joint along the line of action, the therapist should not force the thrust. In such cases, the thrust can be performed only if it is intended at increasing joint mobility. [17]

The preload force has a linear relationship with the peak force induced during spinal manipulation. [23, 24] The application of preload force before the thrust impulse is reported to induce a complex significant interaction between thrust force, duration, and displacement amplitudes [25]. In fact, a preload force as low as 20 N can increase the activity of paraspinal muscles (the erector spinae) prior to thrust execution [26]. However, there is limited knowledge in the current literature regarding how preload force influences the segmental biomechanics. Although an instruction for preload force application just before the thrust can be found in the literature, to date little research has been conducted to investigate the effect of varying levels of preload.

In clinical efficacy studies of spinal manipulation, the gradual application of preload force is reported to increase the stiffness of the spinal unit (the bodies of two adjacent vertebrae with their intimately connected elements). [22, 27] Such increase in stiffness eventually helps the spinal unit to resist movement and minimize vertebral displacement when the thrust is applied. This was demonstrated in a recent experimental study by Nougarou et al.[13] where spinal manipulation yielded different vertebral displacements and local muscle activity responses depending on the dosage of preload force. During the preload phase, paraspinal muscle responses and vertebral segmental displacements were increased with increasing preload forces. In contrast, during and immediately after the HVLA thrust phase, the authors reported a significant decrease in electromyographic (EMG) responses and sagittal vertebral displacement with increasing preload forces.

In an animal model of 20 anesthetized cats, Reed et al.[27] demonstrated that the changes in preload magnitude and duration significantly increased mean instantaneous discharge frequencies (MIF) of paraspinal muscle spindle during the thrust. The greatest increase in

MIF, however, was noted when no preload force was applied. The authors also observed a significantly greater change in spindle discharge with smaller preload magnitude (18% of peak force) and longer preload duration (4 seconds) compared to larger preload magnitude (43% of peak force) and shorter preload duration (1 second). The authors attributed the increase in spindle discharge with longer preload duration to muscle history. However, the observed increases in spindle responsiveness with smaller preload magnitude was inconsistent with the thixotrophy phenomenon [28], which suggests that paraspinal muscle spindles would become more responsive if the muscle is further lengthened or kept in an elongated position following a lengthening history. Reed et al.[27] suggested that this effect might be due to the faster thrust rate that followed the lower preload force (i.e. the larger the preload magnitude, the slower the rate of force application). This assumption was supported in a previous study by Cao et al.[29], where the authors showed a rapid increase in muscle spindle discharge with slower thrust rate. In addition, the study by Nougarou et al.[13] also observed a linearly deceased EMG activity of paraspinal muscles with increasing preload forces.

Preload characteristics of spinal manipulation also include a third mechanical feature known as downward incisural point (DIP). [30, 31] Usually identified in force-time tracings, DIP is the brief diminution of preload force (about 5-6%) just before the thrust execution. This decrease or backing off is biomechanically undesirable as it may possibly reduce target specificity and increase slackening of tissue [14, 30]. This is because maintaining skin slack during the thrust helps maintain the original contact position. [32] The presence of DIP has also been thought to decrease muscle responsiveness during the manipulative thrust. However, this hypothesis was not supported in the study by Reed et al.[27], where the authors showed that preload DIP (around 9% of peak force) did not reduce muscle spindle discharge during HVLA manipulation.

In summary, preload characteristics are an important part of the force-time profile, which can alter vertebral displacement, EMG responses, and paraspinal muscle activity during spinal manipulation. The above data also suggest their possible influence on the neural responses evoked during the thrust. Preload duration appeared to be an important characteristic that may influence the sensory input during the manipulation. For preload force and DIP, however, the changes in neural responses may function through changes in the rate of force application. Therefore, further investigation in humans is needed to determine the specific effect of preload characteristics and their interactions with the rate of force application.

2.1.1 Preload parameters

Most studies on spinal manipulation do not report the specific parameters used to apply the preload force. [13] In general, preload parameters of a HVLA manipulation vary across patients, practitioners, and studies. This is largely due to the variations in manipulation techniques combined with the complex structural organization of the spinal units throughout

the spine. [14] Herzog et al.[22] suggested that the amount of force applied during preload can vary widely depending on the location at which the HVLA thrust is applied. For example, spinal units of the cervical spine are more vulnerable to trauma than relatively stiffer spinal segments of thoracic and lumbar spines; thus, it is highly like that substantially less force would be applied to treat cervical spine compared to thoracic or lumbar spine. [20, 23]

Herzog's lab showed that preload amplitude could be around 9–32% of the thrust force (ranging between 20 N and 180 N) and the preload duration could last between 0.5 to 5 s [22, 33, 34]. In experimental studies, preload forces used in the cervical spine for various manipulation techniques ranged from 1.9 to 39.5 N [33]. A wide range of preload forces has also been used for prone thoracic manipulations, ranging between 23.8 N and 310 N (mean value, 123.6 N) [13, 31, 35-37]. In the lumbar spine, no study on human subjects has so far reported any values for the preload forces. Two studies investigated biomechanical parameters for the sacroiliac joint manipulation and reported preload values ranging from 20 to 180 N, roughly comprising 25% of the thrust force, and lasting between 0.5 and 2.2s [31, 38].

2.2 Peak force, thrust duration and rate of force application

Thrust force magnitude and duration are perhaps the most widely studied biomechanical parameters of spinal manipulation. Over the past decade, both animal and human studies have been conducted to determine the effects of thrust parameters on various physiological outcomes of spinal manipulation [10, 11, 25, 26, 29, 39-52]. To date, however, only two human randomized clinical trials investigated the effects of varying thrust dosages on clinical outcomes [55, 56].

In human studies, physiological outcomes that were most commonly investigated during simulated spinal manipulation include pressure pain threshold (PPT), vertebral displacement and muscular amplitude response [see Table 1]. There is, however, currently no evidence that suggests modulation of force magnitude and duration during spinal manipulation may modify PPTs [39, 43, 45, 46]. The majority of studies on vertebral displacement and muscular response amplitude reported an increase in displacements and EMG responses with increasing thrust force [26, 39-42, 44]. Similar findings were reported in animal studies. Colloca et al.[11] utilized a custom mechanical actuator to assess the effects of varying force-time profiles on ovine lumbar spine. In this study, increased displacement responses and larger vertebral motions at the L3 spinous process were observed with greater force magnitude. Two subsequent studies by Colloca et al.[53, 54] also reported positive displacement and EMG responses with increasing force magnitude. Furthermore, evaluating acceleration response outcomes in sheep, Keller et al.[47, 48] also showed an increase in vertebral displacement and adjacent segment accelerations in three axes (axial, medio-lateral and posterior-anterior) with increasing thrust magnitude.

Although a wide range of thrust durations (10–250ms) have been reported in manual therapy literature, studies that evaluated physiological outcomes of varying levels of thrust durations are mostly conducted in anaesthetized animals [11, 25, 29, 49-52]. Investigation on human subjects to evaluate the effects of thrust duration is still limited. Recently, Page et al.[44] using a servo linear actuator device evaluated the effects of varying thrust durations (125ms, 175ms, 225ms, and 275ms) on thoracic paraspinal muscles of 22 healthy adults. The authors observed a linear increase in EMG response with decreasing thrust duration but no difference in vertebral displacement with varying duration. These results are consistent with the findings of Colloca et al.[11] where the authors observed increased EMG responses to thrust duration of 100 and 200ms. They also reported that a shorter thrust duration of 10ms produced greater movement in the adjacent vertebras compared to longer thrust durations. This was supported in an early study by Lee and colleague[57] which reported larger displacement and acceleration in the adjacent vertebral segment with shorter thrust duration.

On the other hand, studies conducted on muscle spindle activity in animals have consistently reported an increase in MIF during simulated spinal manipulation when either shorter thrust durations or higher thrust forces or sometimes both were applied [29, 49-52, 58]. This increase in spindle responses is characterized by a curvilinear increase in discharge frequency, and the steepest increase is reported to occur with decreasing thrust duration, specifically at 100ms or shorter. Larger changes in spindle discharge are also observed in an animal model study by Reed et al.[51], where the authors noted the presence of stable spindle responses under force control when a given threshold was reached, between thrust durations of 75 and 150ms.

Furthermore, in a recent study, Nougarou and colleagues[10] evaluated the effects of rate of force application on 25 healthy subjects. The authors found that under constant rate of force application, modulation of peak force did not increase neuromuscular responses but yielded changes in the vertebral displacement. These findings suggest that neuromuscular responses of spinal manipulation are largely influenced by the rate of force application while vertebral displacements are modulated by thrust force magnitude. The suggestions by Nougarou et al., however, are in line with the findings of previous animal model studies [27, 49-51], which reported increased MIF of muscle spindles with increasing rate of force application, specifically at rates larger than 300 N/s.

Finally, of the two clinical trials investigating the effects of thrust dosage, the first one was a pilot study on chronic neck pain patients and the latter one was on chronic thoracic pain population. The first trial[55] evaluated the effects of a traction force-based therapy. Three different traction force ranges were used in 48 participants with neck pain: low force, medium force, and high force. Participants in both medium and high traction force groups demonstrated significant improvement in pain and disability than those in the low force group. Although the findings of this study are promising, the scoping review by Pasquier et al.[16] identified this specific randomized trial to be at high risk of bias and thus refrained

from making any definitive conclusion regarding its clinical outcomes. The second trial[56] investigated the clinical and biomechanical outcomes of different spinal manipulation doses in 81 participants with chronic thoracic pain. The authors of this study, however, failed to demonstrate any significant outcome of spinal manipulation doses in chronic pain patients compared to those in the no intervention control group.

In light of the above evidence, it is clear that thrust parameters significantly influence short term physiological responses during spinal manipulation. Higher peak forces and shorter thrust durations were shown to elicit changes in vertebral displacement, muscle spindle activity, EMG responses, and neuronal activity. Collectively, these studies provide more evidence to the concept that therapeutic responses to spinal manipulation are force-time parameter specific. However, despite these positive findings, more research is still needed to establish any formal relationship between dosage parameters and clinical outcomes of spinal manipulation.

2.3 Effects of application site

The application site, or the location, at which spinal manipulation is applied may potentially influence clinical outcomes. Most authors researching on the application parameters of spinal manipulation have reached to a conclusion that the therapy is no different than other physical therapies and its effects may be modified by application site [59-62]. So far, however, little research has been done to elucidate the relation between the application site of spinal manipulation and the response of spinal tissues. Moreover, experimental studies conducted to date to investigate this relationship are mainly based on animal models. This limits the extrapolation of these results to living human spines due to the anatomical and biomechanical differences. Hence, it requires utmost caution to extrapolate the findings of these studies.

The available evidence suggests that the application of spinal manipulation at specific locations may influence muscle spindles sensory input, spinal stiffness and spinal tissue loading characteristics. Using an animal model of 16 anesthetized cats, Reed et al.[59] showed that the application site of a given thrust significantly affects the magnitude of sensory input arising from paraspinal muscle spindles. The authors noted a greater increase in muscle spindles sensory input when manipulation was applied to the target vertebra than an adjacent vertebra. However, when the authors tested three different application sites on the target vertebra, they found no significant difference in neural responses between these contact sites, which is suggestive of similar stretching of paraspinal muscles while activating their spindles. This finding is slightly in contrary to the findings of a biomechanical study by Edgecombe and colleagues[60] where significant changes in spinal stiffness were observed when the thrust was applied to the specific application site. Edgecombe et al. speculated that the transmission of thrust force to deeper connective tissues might change due to the differences in soft tissue thickness of the application site.

On the other hand, several studies have investigated the loads experienced by spinal tissues when the thrust is applied. It is possible that the application of spinal manipulation may load some tissues preferentially and to a much higher magnitude compared to others. This has been demonstrated in a porcine cadaveric study by Kawchuk et al.[63] where the authors observed that the intervertebral disc experienced the greatest load after spinal manipulation. Although these findings are promising, only a limited number of studies has been conducted to date to investigate whether the application of spinal manipulation at different locations influences the load distribution within spinal tissues. Using an animal model of 10 porcine cadavers, Funabashi and colleagues[61] reported that the application site of a given spinal manipulation significantly influences not only the spinal tissue loading characteristics but also the forces experienced by spinal structures. The same research group in a recent biomechanical robotic study on thirteen porcine cadavers demonstrated that application of spinal manipulation with a constant force at different locations of the lumber spine created different vertebral movements of the spinal segments and loaded spinal tissues in significantly different magnitudes [62]. The authors also reported that application of thrusts over the soft tissue between vertebra significantly reduced loads on the intact specimen.

Recently, a randomized clinical trial by McCarthy et al. [64] compared the effects of a clinician-defined, targeted thrust with a non-specific thrust applied through the whole lumbosacral region. The authors found no between-group differences in PPTs and pain scores for any of the muscles studied. Although a statistically significant difference was reported between the two groups in the surface EMG reflex response of the multifidus muscles, no significant difference was noted in pain scores across the three visits. They concluded that the non-specific spinal manipulation was as good as the targeted approach in reducing participants' pain scores over the course of three visits. They also discussed that their findings challenge the need for comprehensive training courses currently required for applying specific manipulation techniques. However, it needs to be noted that the trial had several limitations. The study was underpowered and single blind, which raise the chance of getting a false negative result and the risk of a selection bias. In addition, of the three outcome measures utilized in the trial, the reliability of two measures (PPT and self-reported pain assessment) is questionable. As discussed above, there is currently no evidence that thrust parameters of spinal manipulation modify PPTs. [39, 43, 45, 46] On the other hand, the pain scores did not reflect the true effect at the spinal level, as demonstrated in the surface EMG reflex responses. Therefore, the results of this trial need to be interpreted with caution.

Taken together, from the evidence presented herein, it remains inconclusive whether the contact site at which the thrust manipulation is delivered influences the therapeutic outcomes. Although the current evidence is mixed, Reed and Pickar [65], however, further challenged the appropriateness of delivering the thrust at a specific vertebra. The authors demonstrated that even if well-localized thrusts are delivered, mechanoreceptor responses do not occur at the specific vertebra or contact site where the thrust is applied; in fact, such responses occur several vertebral segments away. This demonstration makes the concept of delivery

specificity less important as mechanoreceptor responses may be elicited even with less precise thrust delivery. On the other hand, it is to be noted that manual therapy practitioners still have limited ability to accurately identify the application site. [66-68] Therefore, more mechanistic and clinical studies are needed to determine the relationship between the anatomical site at which the thrust is delivered and the responses arising from spinal tissue. If it can be demonstrated that the application of spinal manipulation at specific sites preferentially modifies spinal tissue response, the therapy could be provided to a specific location tailored to each patient's condition, potentially improving safety and efficacy of spinal manipulation.

2.4 Recommendation for future research

2.4. 1 Study design

In the current literature, most studies evaluating the effects of various biomechanical parameters of spinal manipulation are primarily based on animal models. Although these models have similarities in biomechanical characteristics with humans and usually attempt to reproduce the same range of forces typically delivered during spinal manipulation, they may not reflect the true physiological and clinical effects in humans. In addition, most of these studies were performed on anesthetized animals, which limits the extrapolation of data to human spine. On the other hand, while some human studies on biomechanical parameters utilized different manual manipulation techniques to apply the thrust, [69-71] a majority of human and animal studies primarily utilized a mechanical device to deliver the thrust. These devices, however, do not represent the real therapy applied by manual therapists in a given clinical setting. Collectively, the results of these studies need to be interpreted with caution.

Therefore, future studies investigating the clinical efficacy of various spinal manipulation dosage parameters should consider applying the therapy by clinicians to explore the true dose-response relationship. Such studies may utilize different force-sensing technology (e.g., strength gauges, manikin, and force-sensing tables) to quantify the force-time parameters of spinal manipulation.

2.4.2 Dosage parameter

Another major challenge encountered in most spinal manipulation studies is the operational definitions used for various dosage parameters. The definition for these parameters remains highly ambiguous and no formal attempt has been made to standardize them. [16] Indeed, quite a few studies differed with the definition and terms used in this review. This high variability in biomechanical characteristics can be attributed to the specific manipulation technique used, the contact site of the thrust, the underlying condition, the physical complaint, and the body-type of the patient and/or clinician. [15]

Recently, Groeneweg et al. [72] suggested a list of criteria for the reporting of mechanistic studies on spinal manipulation. In line with their recommendations, we would like to add that future studies should provide detailed information regarding the biomechanical parameters used in the investigation. If possible, the authors should describe such parameters using treatment characteristics resulting from the force-time profile.

3. Conclusion

In this study, we reviewed studies investigating the effects of various biomechanical parameters of spinal manipulation on physiological and clinical outcomes. It is clear that there exists a dose-response relationship between these parameters and physiological responses of spinal manipulation. The total amount of force (preload force + thrust force) applied in a given time appears to influence the physiological outcomes of spinal manipulation. However, these responses are largely transient in nature and do not reflect any meaningful change in clinical outcomes. Although these responses are thought to be clinically relevant with respect to the observed therapeutic outcomes of spinal manipulation, to date only little research has been conducted to evaluate the true clinical significance of biomechanical parameters. Therefore, it is still inconclusive whether the delivery of varying spinal manipulation dosages produces significant clinical outcomes.

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Table 1. Summary of studies evaluating the effects of spinal manipulation dosage parameters on physiological outcomes. (N=Newton)

Authors	Sample type (n)	Biomechanical parameters	Vertebral level	Outcomes measure	Major findings
Nougarou et al.[12]	Human participants (n = 23)	**Preload forces:** 5 N, 50 N, 95 N, 140 N **Preload duration:** 750 ms **Peak force:** 300 N **Thrust duration:** 125 ms	T6 to T8	Neuromuscular response amplitude	EMG responses increased with increasing preload forces during the preload phase
				Vertebral displacement	Decrease in sagittal vertebral displacement with increasing preload forces during and after the thrust phase
Nougarou et al.[16]	Human participants (n = 26)	**Preload force:** 20 N **Preload duration:** 1000 ms **Peak forces:** 80 N, 130 N, 180 N, 255 N **Thrust duration:** 250 ms	T6 and T8	Neuromuscular response amplitude	EMG responses increased linearly with increasing peak force
Nougarou et al.[9]	Human participants (n = 25)	**Preload force:** 25 N **Rate of force application:** 2200 (±8) N/s **Combination of thrust forces / thrust durations:** 57 ms/150 N, 80 ms/200 N, 102 ms/250 N, 125 ms/300 N	T6 and T8	Neuromuscular response amplitude	No differences in EMG responses with varying force-time profiles
			T6 to T8	Vertebral displacement	Increase in vertebral displacements with increasing peak forces
Page et al.[41]	Human participants (n = 20)	**Preload force:** 20 N **Peak force:** 255 N **Thrust durations:** 125 ms, 175 ms, 225 ms, 275 ms	T7, T8	Neuromuscular response amplitude	Increase in EMG responses with decreasing thrust durations
				Vertebral displacement	No differences in sagittal vertebral displacements across all impulse duration conditions

Page and Descarreaux[51]	Human participants (n = 81)	**Preload force:** 20 N **Preload duration:** 1s **Group 1** (thrust force: 135 N; thrust duration: 125 ms; rate of force application: 920 N/s) **Group 2** (thrust force: 250 N; thrust duration: 125 ms; rate of force application: 1840 N/s) **Group 3** (thrust force: 250 N; thrust duration: 250 ms; rate of force application: 920 N/s)	T6 to T8	Neuromuscular response amplitude	No differences across all four groups.
Keller and Colloca[39]	Human participants (n = 40)	• **Intervention group:** (preload force: approximately 25 N; peak force: 190 N; thrust duration: <5 ms) • **Sham group:** (preload force: approximately 25 N; peak force: 19.5 N)	Bilateral PSIS, sacrum, S1 and L5, L4, L2, T12 and T8	Neuromuscular response amplitude	Increase in EMG responses of the erector spinae muscle with higher peak force amplitude
Krouwel et al.[40]	Human participants (n = 30)	Large-amplitude = between 50 N and 200 N. Small amplitude = between 150 N and 200 N. Quasi static = 200 N sustained pressure. **Duration:** 3 sets of 1 min **Peak force:** 200 N at 1.5 Hz	L3	Pressure pain threshold	No statistically significant difference in pressure pain threshold changes between varying thrust amplitudes
Colloca et al.[36]	Human participants (n = 4)	**Thrust forces**: 30 N, 150 N	L4	Pressure pain threshold	No statistically significant difference in pressure pain threshold values
			L1 to L3	Neuromuscular response amplitude	Positive EMG responses with maximum thrust force setting
			L1 to L3	Vertebral displacement	Increase in vertebral motions with higher force

Page et al.[38]	Human participants (n = 51)	**Preload forces:** 20 N **Preload duration:** 750 ms **Thrust forces:** 75 N, 125 N, 175 N, 225 N **Thrust duration:** 125 ms **Rate of force application:** 440 N/s, 840 N/s, 1240 N/s, and 1640 N/s	L3	Neuromuscular response amplitude	EMG responses increased linearly with increasing thrust force
Pentelka et al. [42]	Human participants (n = 19)	**Thrust durations:** 30s, 60s	L4	Pressure pain threshold	No statistically significant difference in pressure pain threshold values
Willett et al. [43]	Human participants (n = 30)	**Duration:** 3 sets of 1 min **Force amplitude:** 100-200 N **Rate of application:** 1 Hz, 2 Hz or as a quasi-static pressure	L5	Pressure pain threshold	No differences
Colloca et al.[37]	Human participants (n = 9)	**Thrust forces:** 30 N, 88 N, 117 N, 150 N	L3 to S2	Vertebral displacement	Increase in vertebral displacement with higher force amplitudes
Colloca et al.[10]	Anesthetised merino sheep (n = 10)	**Force–time profiles** **(1)** Preload: 10 N; Thrust durations: 10 ms, 100 ms, 200 ms; Constant thrust force: 80 N **(2)** Preload: 10 N; Thrust force: 20 N, 40 N, 60 N; Constant thrust duration: 100 ms	L3, L4	Neuromuscular response amplitude	EMG responses increased linearly with increasing thrust force
			L3	Vertebral displacement	Fourfold linear increase in vertebral displacement with increasing force amplitude
			L1, L2	Segmental acceleration response	At constant force, increased segmental acceleration with the lowest thrust duration
Keller et al.[44]	Anesthetised merino sheep (n = 10)	**Thrust forces:** 133 N, 245 N, 380 N	L1, L2 and L1-L2	Segmental and intersegmental acceleration response	Increase in acceleration responses across 3 axes (axial, medio-lateral and posterior-anterior) with multiple thrust forces. The greatest increase in responses was with the low force setting.

Vaillant et al.[15]	Anesthetised cats (n = 22)	**Preload force:** 10% of body weight **Preload duration:** 4.31 s **Thrust forces:** 25%, 55% and 85% of body weight **Thrust displacements:** 1.0mm, 2.0mm, 3.0mm **Thrust durations:** 0, 25 ms, 50 ms, 75 ms, 100 ms, 150 ms, 200 ms, 250 ms	L6	Spinal stiffness	Under displacement control with and without a preload, amplitude and duration parameters of spinal manipulation affected spinal stiffness.
Reed et al.[17]	Anesthetised cats (n = 20)	**Preload magnitude:** 18% and 43% of thrust force **Preload durations:** 1 and 4s **DIP:** 5% of preload **Peak force:** 21.84 N **Thrust duration:** 75 ms	L6	Muscle spindle response	Increase in MIF with smaller preload magnitude and longer preload duration
Cao et al.[19]	Anesthetised cats (n = 112)	**Thrust forces:** 25, 55, 85% of body weight **Thrust displacements:** 1, 2, 3mm **Thrust durations:** 0, 25, 50, 75, 100, 150, 200, 250 ms	L6	Muscle spindle response	Sustained increases in resting MIF with the lowest amplitude thrust displacement (1mm)
Pickar et al.[47]	Anesthetised cats (n = 54)	**Thrust displacements:** 1 or 2 mm **Thrust durations:** 12.5, 25, 50, 100, 200, and 400 ms	L6	Muscle spindle response	• Short thrust duration increased MIF compared to longer thrust durations. • Spindle afferents were more sensitive to 1mm displacement amplitude compared to 2 mm.
Reed et al.[49]	Anesthetised cat (n = 1)	**Peak forces:** 78.2 to 121.8N **Thrust duration:** <5 ms	L7	Muscle spindle response	Greater change in MIF with extremely short thrust durations.

Reed et al.[53]	Anesthetised cats (n = 6)	**Thrust force:** 22 N, 44 N or 67 N	L6	Muscle spindle response	Decrease in muscle spindle discharge with short thrust duration; most afferents required an increased time (>6s) to return to baseline MF values.

MIF: Mean Instantaneous Discharge Frequency, MF: Mean Frequency, EMG: Electromyographic, PSIS: Posterior Superior Iliac Spine