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The Popping Sound During High Velocity Low Amplitude Thrust Spinal Manipulation

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Preface

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"if you can see it here,

and you have the courage enough to speak it,

it will happen."

Abstract

Introduction

Spinal Manipulation is one of the most performed and debated manual therapy intervention for the treatment of the most common musculoskeletal disorders. However, there is still debate in the scientific literature on a clear and unanimous definition. The most fruitful attempt to define spinal manipulation has been made by the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT) that include the popping sound and a better description of the effects as part of the definition.

That is, neither the expectation of one single pop emanating from the target or dysfunctional facet joint nor the expected side during high velocity low amplitude (HVLA) thrust manipulation is consistent with the existing literature. In fact, both anecdotal evidence and the existing literature suggest that it is common for one HVLA thrust manipulation to produce 2 or more distinctive joint popping sounds.

In spite of the heterogeneity in definition, practice, application rationale, and theory behind spinal manipulation, current literature still recommends this conservative intervention into a multimodal package for the most prevalent musculoskeletal conditions of the spine, supporting the use of this intervention in clinical practice as a cost-effective treatment when used alone or in combination with other treatment approaches.

Thus, there is a need of an evidence-based framework in order to meet the request of a standardization in definition, rationale and application of this therapeutic intervention.

Objective and Hypothesis

Our aim was to determine from which side of the spine the popping sound (PS) was emanated during a cranio-cervical, cervicothoracic and lumbosacral junction using a time-frequency analysis. Secondary aims were to calculate the average number of PS, the duration of spinal thrust manipulation, and the duration of a single PS.

Methods

Skin mounted accelerometers were secured bilaterally in the vicinity of the zygapophyseal joints cranio-cervical, cervicothoracic and lumbosacral junction before a HVLA thrust manipulation delivery in healthy pain-free individuals**.** The accelerometers were connected to a data acquisition system (FOCUSRITE Scarlett 2i2, 96 KHz, 24-bit conversion) and a MacBook Pro laptop with AUDACITY software for audio acquisition with a sampling frequency set at 96,000 Hz. The AUDACITY software normalized automatically the audio energy to values ranging between -1 and +1 (no unit of measurement). For each manipulation, 2 audio signals were extracted and singularly processed via spectrogram calculation to obtain the release of energy over time on each side of the targeted area.

Because the absence of a comparative data of the novel analysis methodology using a time-frequency analysis on the topic the authors did not run a sample size calculation (i.e. descriptive analysis).

Results

Bilateral popping sounds were detected in 34 (91.9%) of 37 manipulations while unilateral popping sounds were detected in just 3 (8.1%) manipulations applied to the cranio-cervical junction; that is, popping sound was significantly (P < 0.001) more likely to occur bilaterally than unilaterally. Of the 132 total popping sounds, 72 occurred ipsilateral and 60 occurred contralateral to the targeted articulation, i.e., C1-C2. In other words, popping sound was no more likely to occur on the ipsilateral than the contralateral side (P = 0.294). The mean number of pops per C1-2 rotatory HVLA thrust manipulation was 3.57 (95%CI: 3.19, 3.94) and the mean number of pops per subject following both right and left C1-2 manipulations was 6.95 (95% CI: 6.11, 7.79). The mean duration of a single audible pop was 5.66ms (95% CI: 5.36, 5.96) and the mean duration of a single manipulation was 96.95ms (95% CI: 57.20, 136.71).

Unilateral popping sounds were detected in 53 (91.4%) of 58 cervicothoracic HVLA thrust manipulations and bilateral popping sounds were detected in just five (8.6%) of the 58 thrust manipulations; that is, popping sound was significantly (p<0.001) more likely to occur unilaterally than bilaterally. In addition, popping sound was significantly (p<0.0001) more likely to occur on the side contralateral to the clinician’s short-lever applicator. The mean number of popping sounds per thurst manipulation was 4.35 (95% CI 2.88, 5.76). The mean duration of a single manipulation was 60.77ms (95% CI 28.25, 97.42) and the mean duration of a single popping sound was 4.13ms (95% CI 0.82, 7.46). In addition to single-peak and multi-peak energy bursts, the spectrogram analysis also demonstrated high frequency sounds, low frequency sounds, and sounds of multiple frequencies for all 58 manipulations.

During 60 HVLA thrust manipulations applied to the lumbo-sacral junction, a total of 320 PSs were recorded. 176 occurred ipsilateral and 144 occurred contralateral to the targeted L5-S1 articulation; that is, PS was no more likely to occur on the upside than the downside facet following right or left rotatory L5-S1 HVLA thrust manipulation. Moreover, PSs occurring on both sides at the same time were detected very rarely (i.e., 2% of cases) of the lumbar HVLA thrust manipulations. The mean number of audible PSs per lumbosacral HVLA thrust manipulation was 5.27 (range 2-9). The mean duration of a single manipulation was 139.13ms (95% CI: 5.61, 493.79) and the mean duration of a single PS was 2.69ms (95% CI: 0.95, 4.59).

Conclusion

A single model may not be able to explain all of the audible sounds during HVLA thrust manipulation. Thus, the novel advance in knowledge on this topic with the presented studies may inform practitioners of spinal manipulative therapy in better selecting the appropriate HVLA thrust manipulation technique. Thus, a traditional approach based on the targeting of a single ipsilateral or contralateral facet joint in the spine may not be realistic. A deeper knowledge of the mechanisms of actions of spinal manipulation can have a clinical and research impact.

Resumen

Introducción

La manipulación vertebral es una de las intervenciones de terapia manual más usadas para el tratamiento de desórdenes musculo-esqueléticos. Sin embargo, aún existe controversia en la literatura científica en torno a una definición clara y unánime. El intento más provechoso para definir la manipulación vertebral fue llevado a cabo por la Federación Internacional de Fisioterapeutas Manipulativos Ortopédicos (en inglés IFOMPT) e incluye el sonido de la cavitación y una mejor descripción de los efectos como parte de la definición.

De hecho, ni la expectativa de un único sonido de cavitación procedente de la articulación diana o faceta articular en disfunción, ni el deslizamiento previsto durante la movilización de alta velocidad y baja amplitud (en inglés HVLA), son consistentes con la literatura. En realidad, tanto las pruebas anecdóticas como la literatura, sugieren que es frecuente que una manipulación produzca dos o más sonidos de cavitación articular característicos.

A pesar de la heterogeneidad en la definición, práctica y teorías que sustentan la manipulación vertebral, la literatura actual recomienda este abordaje conservador, dentro de un paquete multimodal, para las condiciones músculo-esqueléticas más prevalentes de la columna vertebral, apoyando el uso de esta intervención en la práctica clínica como un tratamiento efectivo, usado tanto de forma aislada como combinado con otras aproximaciones terapéuticas.

Por tanto, existe la necesidad de crear un marco basado en la evidencia de modo que se establezcan unos requerimientos estándares en la definición y aplicación racional de esta intervención terapéutica.

Objetivo e Hipótesis

Nuestro objetivo fue determinar de qué lado de la columna vertebral procedía el sonido de la cavitación producido durante una manipulación cráneo-cervical, una manipulación cérvico-torácica o manipulación lumbosacra, utilizando un análisis tiempo-frecuencia. Los objetivos secundarios fueron calcular la media de sonidos de cavitación, la duración de la manipulación, y la duración aislada del sonido de cavitación.

Métodos

Se colocaron bilateralmente acelerómetros de superficie en la proximidad de las articulaciones cigapofisarias a nivel cráneo-cervical, cérvico-torácico y de la unión lumbosacra, previamente a la realización de una movilización de alta velocidad y baja amplitud en individuos sanos sin dolor. Los acelerómetros se conectaron a un sistema de adquisición de datos (FOCUSRITE Scarlett 2i2, 96 KHz, 24-bit conversión) y a un ordenador portátil MacBook Pro con el software AUDACITY para la captura del sonido con una frecuencia de muestra fijada en 96,000 Hz. El software AUDACITY normalizaba automáticamente la energía acústica a valores entre -1 y +1 (sin unidad de medida). Por cada manipulación se extrajeron dos señales de audio que se procesaron independientemente mediante cálculo del espectrograma para obtener la liberación de energía en el tiempo en cada lado de la región manipulada.

Debido a la ausencia de datos con los que comparar esta novedosa metodología utilizando un análisis tiempo-frecuencia de la cavitación, los autores no llevaron a cabo un cálculo del tamaño de la muestra (análisis descriptivo).

Resultados

Se detectaron sonidos de cavitación de forma bilateral en 34 (91.9%) de las 37 manipulaciones mientras que el sonido fue unilateral en solo 3 (8.1%) de las manipulaciones aplicadas a la unión cráneo-cervical: el sonido de cavitación tenía una probabilidad significativamente mayor ($P < 0.001$) de ocurrir bilateralmente que de forma unilateral. De los 132 sonidos de cavitación totales, 72 tuvieron lugar en el mismo lado, y 60 en el lado contrario a la articulación diana, en este estudio, C1-C2. Dicho de otro modo, el sonido de cavitación no tenía mayor probabilidad de tener lugar en el mismo lado o lado contrario ($P > 0.294$). El número medio de cavitaciones por técnica manipulativa en rotación de C1-C2 fue de 3,57 (95%IC 3,19 - 3,94) y el número medio de cavitaciones por sujeto tras manipulaciones a ambos lados derecho e izquierdo C1-C2 fue 6,95 (95%IC 6,11 - 7,79). La duración media de una sola cavitación audible fue de 5,66 ms (95%IC 5,36 - 5,96) y la duración media de una manipulación fue de 96,95 ms (95%IC 57,20 - 136,71).

Se detectaron sonidos de cavitación de forma unilateral en 53 (91.4%) de las 58 manipulaciones cérvico-torácicas y sonidos de cavitación bilateral sólo 3 (8.6%) de las 58 manipulaciones: el sonido de cavitación tuvo una probabilidad mayor ($P < 0.001$) de producirse unilateralmente que bilateralmente. Además, el sonido de cavitación tenía una probabilidad significativamente mayor ($P < 0.001$) de ocurrir en el lado contralateral al de la aplicación de la palanca del terapeuta. El número medio de sonidos de cavitación por empuje manipulativo fue de 4,35 (95%CI 2,88 - 5,76). La duración media de una sola manipulación fue 60,77 ms (95%IC 28,25 - 97,42) y la duración media de un sonido aislado de cavitación fue 4,13 ms (95% IC 0,82 - 7.46). Además de las ráfagas de energía de un solo pico y de varios picos, el análisis del espectrograma también demostró sonidos de alta frecuencia, de baja frecuencia y frecuencias múltiples para cada una de las manipulaciones.

Durante la ejecución de las 60 manipulaciones aplicadas a la unión lumbosacra, se recogieron un total de 320 sonidos de cavitación, de los cuales 176 tuvieron lugar en el mismo lado y 144 en el lado contrario a la articulación diana (L5-S1). Es decir, la cavitación secundaria a la manipulación derecha o izquierda L5-S1 no tenía mayor probabilidad de producirse en la faceta articular de arriba que en la del lado de apoyo. Es más, sonidos de cavitación simultáneos en ambos lados se detectaron excepcionalmente (2% casos) durante las manipulaciones lumbares. La media de cavitaciones audibles por técnica manipulativa lumbosacra fue 5,27 (rango 2-9). La duración media de una manipulación aislada fue 139,13ms (95% IC 5,61 - 493,79) y la duración media de un sonido de cavitación aislado fue 2,69 ms (95%IC 0,95 - 4,59).

Conclusión

Un solo modelo podría no ser suficiente para explicar la totalidad de los sonidos audibles durante las técnicas manipulativas de alta velocidad y baja amplitud. Por tanto, el novedoso avance en el conocimiento de esta materia con los estudios presentados aporta información a los terapeutas que realizan terapia manipulativa vertebral para hacer una mejor selección de una técnica manipulativa concreta. La aproximación tradicional basada en dirigir la técnica a una faceta articular diana ipsilateral o contralateral no resultaría realista. Un conocimiento más profundo en torno a los mecanismos de acción de la manipulación vertebral puede tener un gran impacto en la aplicación clínica y en la investigación.

Índice

Introduction

Definition of Spinal Manipulation

Spinal manipulation is a therapeutic intervention, whose use began more than two thousand years ago, and it is still one of the most performed and debated manual therapy technique for the treatment of common musculoskeletal disorders [1]. Yet, different terms are used in the literature to refer to the same procedure: spinal adjustment, spinal manipulation, high velocity low amplitude (HVLA), thrust, joint manipulation, chiropractic adjustment, or osteopathic adjustment [2]. In fact, many of these terms are related to the professional applying the intervention and not the technique itself. This remarkable abundance of terms shows the lack of a clear, unambiguous and unanimous definition of the above-mentioned technique [2].

There should be relatively easy to find a suitable definition, were it not for the fact that the year of history and the more or less conscious delivery of this technique - which was even associated to magic halo more than science - has made this process extremely difficult to undertake. There are mostly two problems underlying this difficulty, i.e. the “fear” of the manipulation itself due to potential risks, along with the “communication” problems amongst clinicians involved in its performance (physical therapists, osteopaths, chiropractors, insurance companies, patients and physicians) [3].

A more complete definition, based on an accurate investigation of the scientific literature rather than a merely empirical approach, is undoubtedly required; this process has the potential to detect those unique characteristics of manipulation without including either further techniques or different therapeutic approaches.

The most fruitful attempt to define Spinal Manipulation has been lately provided by the International Federation of Orthopaedic Manipulative Physical Therapists (IFOMPT), a recognized group of the World Confederation for Physical Therapy (WCPT), in Cape Town, in March 2004. During the General Meeting, the IFOMPT did include characteristics and purposes in the definition of Spinal Manipulation, by stating that this eventually leads to:

"*A passive, high-velocity, low-amplitude impulse applied to a complex joint within its anatomical limit, with the intent to restore optimal motion, function, and/or to reduce pain.*"

Nevertheless, such a definition required further integrations, in order to match the subsequent publications upon this issue. Therefore, IFOMPT rephrased the definition, during the Teachers Meeting, in Glasgow, in July 2016, as follow:

"Spinal Manipulation is the application of rapid movement to vertebral segments producing joint surface separation, transient sensory afferent input, and reduction in perception of pain. Joint surface separation will commonly result in intra-articular cavitation, which in turn, is commonly accompanied with an audible pop. Post manipulation reductions in pain perception are influenced by supraspinal mechanisms including expectation of benefit"

(McCarthy, Bialosky, Rivett 2015: Grieve's Modern Musculoskeletal Therapy 4th Ed)

That is, the last definition included the popping sound (PS) and a better description of the effects were integrated as part of the definition of spinal manipulation.

Popping Sound during Manipulative Procedures

The PS or audible cracking consists of a high frequency vibration that should be expected as a desired effect of the delivery of a high velocity thrust (HVLA) applied by an external force that creates motion at a joint level [4, 5]. The PS is considered one of the main features in order to define a HVLA thrust manipulation [4] and to achieve an effective delivery of this technique [6–11]. Many clinicians and research teams still repeat the HVLA thrust manipulation if the PSs is not emanated [6, 10, 12]. However, the PS phenomenology is not fully understood yet.

Since the early 1900s, considerable attention has been paid both to the anatomical structures involved and the exact mechanisms behind the genesis of the PS [13]. More specifically, gas bubble collapse [14] into the joints driven by the "cavitation" physic phenomenon has been traditionally accepted as the main mechanism [1, 4, 7, 14–17].

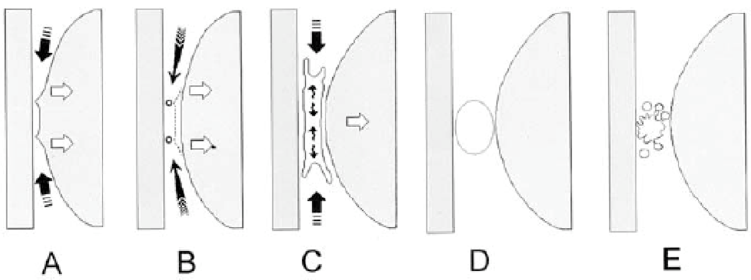

Fig 1. *Cavitation. Schematic representation of surface geometry and shapes of growing cavities at a high separation speed (v > > vc as is likely with HVLAT manipulation) where doughnut (toroidal)-shaped cavities form around, rather than at the center, of the contact zone.* ***A****, During separation, the outer regions of the circular contact zone become pointed. This deformation occurs because at this speed, the central region of the contact zone separates, whereas the outer region remains almost unmoved, creating a circular rim.* ***B****, Surfaces snap back at the circular rim where the cavity initially forms.* ***C****, Coalescence of toroid into single dendritic cavity that grows to reach a maximum bubble size.* ***D****, The newly formed spherical bubble reaches its maximum size.* ***E****, Because of its instability, the single bubble collapses to form a "cloud" of many smaller bubbles (demonstrable by radiography as a radiolucent region), which later shrink as the gas and vapor dissolve (see later). Adapted from Chen YL, Kuhl T, Israelachvili J. Mechanism of cavitation damage in thin liquid films: collapse damage vs. inception damage. Wear 1992;153:31-51. Reproduced with permission from Elsevier Science.*

Figure 1: Previous theories about popping sound (reprinted with permission by the author)

Roston and Haines [18],and more recently Kawchuk et al. [13] have observed that the joint PS is associated with a cavity inception within the meta-carpal-phalangeal (MCP) joint by using rapid cine magnetic resonance images. This is the first *in-vivo* macroscopic demonstration of the “tribonucleation” physic process as a new theoretical model of the mechanism of the PS phenomenon. Tribonucleation occurs when two opposed joint surfaces, separated by a film solution, are rapidly separated by a distractive force that overcomes the viscous attraction.

More recently, Chandran Suja and Barakat [19] used a complex mathematical model based on condenser microphones placed at a certain distance from the MCP joint. They have found that the PS was not related to the cavity inception (i.e. tribonucleation); on the contrary, it results from the intra-articular pressure drop leading to cavitation bubble release in the synovial fluid. In other words, the results of this study confirm the very first experimental observation that Unsworth et al. made in 1971. However, the persistence of a cavity after the sound production is congruent with the observation made by Kawchuk et al. [13].

These findings cannot be generalized, as they were observed only on MCPs joints in few number of subjects [13, 14, 18, 19]. Moreover, one must consider clear anatomical differences between the MCP and the zygapophyseal joints [ZJ] of the spine. Cascioli et al. [20] did find neither gas genesis into the cervical joint space nor an increased joint gapping (i.e. joint width) whilst using CT scans immediately after an HVLA thrust manipulation delivery to the cervical region. However, by using MRI in order to measure the central anterior-posterior joint space, Cramer et al. found a greater gapping of the lumbar ZJ following a single session of spinal manipulation in patients suffering of Low Back Pain (LBP) especially if compared to those who received side-posture positioning (i.e. no-thrust manipulation) [21]. Moreover, in a previous study, Cramer observed a direct relation between the popping sound and the gapping phenomena, although he could not determine the extent of the joint gap [22]. Notably, Kawchuk et al. [13] found a void within the joint, which persists after the sound production that could explain the ZJ gapping after HVLA thrust manipulation observed by Cramer et al. [21, 22].

During the last decade, our research group tried to analyze the PS phenomenon using sound wave signals processed by a time-frequency analysis [23, 24]. The authors observed that the sound was composed of single and multiple energy releases (*i.e.* single versus multi-peak sounds). Furthermore, we identified high, low and sounds of multiple frequencies. These multiple features findings of the PS suggest multiple mechanisms in addition to the tribonucleation and/or cavitation underlining the PS origin (these theories will be discussed later in this dissertation).

Sound recording (*i.e.* microphones and accelerometers) has been also extensively used as an indirect measure, in order to improve the comprehension of the PS phenomenon in previous studies. Woods and West compared the PS emanated from different spine regions (i.e. temporo-mandibular, cervical, thoracic and lumbar spine) [25]. The authors run a frequency analysis of the sound signals by using a *Fast Fourier Transformation* whilst they observed a multiple frequencies feature. Reggars, was the first author highlighting, in a critical review, the necessity of a discriminative spectrographic analysis, in order to delve deeper into both the PS at the ZJ level [25]; subsequently, this author validated the reliability and accuracy of multiple surface mounted microphones as an acquisition system to detect the PS of the third MCP joint [15].

Reggars and Pollard [26] took a decisive step towards the introduction of the spectrographic analysis of the recorded signal from skin mounted microphones during HVLA thrust manipulation of the cervical spine. This study pioneered the observation of both the side and the number of PSs emanated during a HVLA thrust manipulation delivery leading to questioning the expected real target specificity. The authors concluded that an explanation of this phenomenon based on a single mechanism was simply not possible because the observation of heterogeneous frequency peaks in the same recording suggested that a validated technology, along with further acquisition methodologies, should be required [26]. Herzog et al [7], were the first ones in using piezoelectric accelerometers for the vibrating signals founding that skin mounted accelerometers can accurately measure "bone vibration". Subsequently, accelerometers usage was found to be valid in accurately locate the source of PS after the application of manipulative interventions [6, 8]. In summary, whilst using accelerometers, the authors analyzed the sound signals by a spatial differentiation algorithm reporting multiple PSs (i.e. range 2-6) for each HVLA thrust manipulation with a 50% of accuracy on the target segment of the spine for both the thoracic and lumbar spine [8]. More recently, Cramer et al. using a complex system of 9 accelerometers red by an oscilloscope found multiple PSs from the same ZJ [6]. The authors found that most PSs (93.5%) were recordered on the upside ZJs with a 71% of target accuracy (i.e. with a range error of 3 adjacent segments) [6]. Further, neither the expectation of one single pop emanating from the target or dysfunctional facet joint nor the expected side during HVLA thrust manipulation is not consistent with the existing literature for the lower cervical [15, 26], thoracic [8] or lumbar [6, 8, 27] regions. Moreover, both anecdotal evidence and the existing literature suggest that it is common for one HVLA thrust manipulation to produce 2 or more distinctive joint PSs [8, 15, 26, 27].

However, in spite of the heterogeneity in definition, practice, application rationale, and theory behind spinal manipulation, the most recent literature still recommends this conservative intervention into a multimodal package for the most prevalent musculoskeletal conditions of the spine [28–31], supporting its use in clinical practice as a cost-effective treatment when used alone or in combination with other treatment approaches [32, 33].

Thus, there is a need of an evidence-based framework in order to meet the request of a standardization in definition, rationale and application of this therapeutic intervention.

Objectives

Time-frequency analysis is a widely adopted method in monitoring different fields like radar signals [34, 35], myoelectric signals [36, 37] and sound signals [38, 39]. Previous studies did not apply the time-frequency analysis, since they aimed at investigating the PS phenomenon only by sensing the presence/absence of sound signals (i.e. the actual sound releases) and then counting the number and location of reported PS [1, 6, 8, 15, 26, 27]. Otherwise, applying the time-frequency analysis will permit not only to observe with a higher precision previous mentioned features directly on the spectrograms, but also it will permit to calculate the duration of the PS phenomenon. To the best of the author's knowledge, this is the first research line experience trying to identify the side of joint PS during different spinal thrust manipulations and the first study using a time-frequency analysis with the goal of improving the methodology in studying the PS phenomenon.

Therefore, the objectives of this PhD thesis were:

1. To investigate the signal processing of the popping sound during spinal thrust manipulation by proposing the use of a time-frequency analysis.
2. To determine the side of spine, the location, the duration and the number of the popping sound emanated during spinal thrust manipulation.
3. To determine if there were differences between the side and the location of the popping sounds between cranio-cervical, cervico-thoracic, and lumbo-sacral junction thrust manipulation.

Methods

Participants

In these studies, asymptomatic participants, aged between 18 and 65 years, were recruited by convenience sampling from a private physical therapy outpatient clinic in Italy from 2012 to 2016. For subjects to be eligible, they had to have experienced no pain in any spine region over the past 3 months. Participants were excluded if they exhibited any of the following:

1, any potential red flag (*i.e.*, tumor, fracture, metabolic diseases, rheumatoid arthritis, osteoporosis, resting blood pressure > 140/90 mmHg, prolonged history of steroid use, etc.);

2, neurologic signs consistent with nerve root compression (i.e., muscle weakness, diminished deep tendon reflex, or altered sensation to pinprick in any dermatome);

3, any diagnosis of lumbar or cervical spine stenosis;

4, exhibited bilateral extremity symptoms;

5, any evidence of central nervous system disease (i.e., hyperreflexia, sensory disturbances in the hand, intrinsic muscle wasting of the hands, unsteadiness during walking, nystagmus, loss of visual acuity, impaired sensation of the face, altered taste, the presence of pathological reflexes); or,

6, either a history of recent trauma or any prior surgery to the cervical, thoracic or lumbar spine

The ethics committee at the Universidad Rey Juan Carlos, Madrid, Spain, approved this study as a part of a spinal manipulative therapy protocol developed at the Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine. All participants provided written informed consent before their participation in the study.

Risks of Upper Cervical Spine Manipulation

Considerable attention has been given to the potential risks associated with HVLA thrust manipulation procedures in the cervical region [40–45]. However, the safety around spinal manipulation is characterized by substantial disagreement about its actual rather than putative risks [3]. In addition, evidence about spinal manipulation safety is eclipsed by anecdotal beliefs emerging from interprofessional rivalries and sensationalized media coverage of rare, catastrophic events [3]. That is, low quality current evidence suggesting that spinal manipulation is associated with but not causally related to adverse events [46]. Whedon et al [47] observed that the likelihood to occur in adverse event following spinal manipulation was greater in that patient that was seeking care for relief pain of musculoskeletal-like symptoms underlining other severe medical conditions. Thus, the natural progression of the underline medical pathology (e.g. dissection already in process) appears to occur independent of the application of spinal manipulation [40, 46, 47]. Alternatively, the presence of an un-diagnosed medical condition mimicking musculoskeletal pain may be an absolute contra-indication to any manual therapy intervention [48, 49]. The most recent study by Cassidy et al [40] and Whedon at al [47] provide evidence for the risk of vertebrobasilar artery (VBA) stroke and cervical thrust manipulation. Contrary to traditionally held views [50, 51], Cassidy et al [40] found no greater risk of VBA stroke associated with cervical HVLA thrust manipulation than general, primary medical physician care. However, they found an increased association in cases in which the practitioner visit was for neck pain or headache from a non-ischemic clinical presentation of a VBA dissection that was already in process [40, 47, 52]. Recent systematic reviews [41, 53, 54] also concluded there is no strong evidence linking the occurrence of serious adverse events with the use of cervical manipulation or mobilization in adults with neck pain.

The two largest randomized controlled trials [55, 56] within the past 10 years comparing the effectiveness of cervical HVLA thrust manipulation with cervical non-thrust mobilization did not report the assessment of specific vertebral motion segment targeted with the cervical thrust manipulation procedure. Therefore, it is unknown whether patients with chronic neck pain in these studies received upper, middle or lower cervical HVLA thrust manipulation [55, 56]. Notably, there were no serious neurovascular adverse events reported by the participants in either of the trials [55, 56], and both trials reported no statistically significant difference in the incidence of minor adverse events between the cervical HVLA thrust manipulation and cervical non-thrust mobilization groups. Therefore, to date, there is no clear evidence supporting the notion that upper cervical thrust manipulation carries any greater risk of injury than middle or lower cervical thrust manipulation, or that non-thrust mobilization to any region of the cervical spine carries any less risk than thrust manipulation to the same region [40–42, 44].

Since there is controversy in relation to the safety of upper cervical spine thrust manipulation, the following examination was considered in our study. The literature suggests that pre-manipulative VBA insufficiency cervical testing is unable to identify subjects at risk of vascular complications from upper cervical manipulation and any symptoms detected during pre-manipulative testing may be unrelated to changes in blood flow in the vertebral artery [44]. That is, pre-manipulative VBA insufficiency tests showed a low reliability as screening tool because a very low sensibility and diagnostic accuracy, with a high risk to erroneously label “patient with adverse event low risk following manipulation” profile (i.e. high number of false negative) [57]. Hutting et al. [57] found a high value of specificity for these tests; however, the positive likelihood ratio is close to 0%. Therefore, a negative test neither predicts the absence of arterial pathology nor the propensity of the artery to be injured during upper cervical spine thrust manipulation, with testing neither sensitive or specific [58]. Notably, the pre-manipulative VBA insufficiency tests could be even dangerous as the end-range rotation and extension provide more strain forces on the vertebral artery compared to cervical spine manipulation [59].

Additionally, the role of upper cervical instability test in pre-treatment procedures has been questioned [60]. Although a rare event [61, 62], upper cervical instability (i.e. cervical fracture, cranio-cervical junction ligament rupture or congenital pathologies like the basilar impression) is a life-threatening condition and need to be carefully screened in patient presenting in direct access settings [63]. Notably, many of these conditions can be asymptomatic since adulthood and clinically presenting mimicking musculoskeletal disorders [63–65].

Traditionally, instability testing was anecdotally designed to manually detect abnormal accessory mobility in order to screen those patients at risk to develop adverse events after cervical spine manipulation [66]. However, the most recent evidences concluded that those screening tests cannot accurately used [60]. That is, the specificity of almost all the tests was sufficient, which means that the tests (i.e. the Sharp-Purse test, the Anterior Shear test, the alar ligament test, the atlanto-axial membrane test and the tectorial membrane test) can be used to rule in patients with upper cervical spine instability [60]. In other word, the upper cervical instability test must be clinically interpreted as provocative tests (i.e. able to modify neurologic signs and symptoms) and only be used after a screening process during the history taking of risk factors (i.e. cervical trauma, recent upper respiratory tract infection, inflammatory condition such as rheumatoid arthritis and ankylosing spondylitis, etc.) [64, 67–70], of preceding transient neurological symptoms (neck tongue syndrome, face sensibility changes, balance disturbance, dizziness, function changes of cranial nerves, etc.) [71, 72], the usage of validated clinical decision tool (e.g. the Canadian cervical spine rules, that seem informative even without following a rigid process) [64, 69, 70, 73, 74] and a neurological testing (i.e. Hoffman reflexes, Romberg test, Cranial Nerve testing, etc.) [63, 75, 76] when the therapist still have doubts on the differential diagnosis process to refer the patient to the proper medical professional.

In summary, there is a need of shifting the paradigm to a differential diagnosis one. The responsibility of the practitioner is not to attempt to identify the patient who is at risk of "post-manipulative severe adverse events", but to attempt to identify the individual who is having a medical pathology outside the scope of practice of physiotherapy so appropriate referral can be made [46].

Screening process and specific questions for cervical artery dysfunction and cranio-cervical instability were negative in individuals included in our study about upper cervical spinal manipulation, but pre-manipulative cervical artery and upper cervical instability testing was not used.

Therapist Delivering Spinal Manipulative Interventions

A single, U.S. licensed physical therapist performed all HVLA thrust manipulations. At the time of data collection, the physical therapist had completed a post-graduate Master of Science in Advanced Manipulative Therapy, had worked in clinical practice for 15 years, and routinely used HVLA thrust manipulation of the spine in daily practice.

Upper Cervical Spine Thrust Manipulative Technique

A single rotatory HVLA thrust manipulation directed to the upper cervical spine (C1-2) with the patient supine was performed **(Fig. 2)**. For this technique [77], the patient's right posterior arch of the atlas was contacted with the lateral aspect of the proximal phalanx of the therapist's right second finger using a "cradle hold". To localize the forces to the right C1-C2 articulation, secondary levels of extension, posterior-anterior translation, right (ipsilateral) lateral-flexion and left (contralateral) lateral translation were applied [77].

Whilst maintaining the secondary levels, the therapist performed a single HVLA thrust manipulation to the right atlanto-axial joint using the combined primary thrusting levers of left rotation in an arc toward the underside eye of the subject and translation toward the table [77]. This technique was repeated by using the same procedure, albeit directed to the left C1-C2 joint. Popping or cracking sounds were heard on all thrust manipulations; hence, any further second attempt was unnecessary.

Figure 2: High-velocity low-amplitude thrust manipulation directed to the left cranio-cervical (C1-C2) junction (image from the author)

Cervicothoracic Junction Thrust Manipulative Technique

A single “lateral break” thrust manipulation directed to the cervico-thoracic junction with the patient in the prone position was performed **(Fig. 3)**. The level T1-T2 was the targeted area since this segment is in the center of the three articulations (i.e., C7-T1, T1-T2, T2-3) that are considered to be primarily affected by manual forces during prone HVLA thrust manipulations to the cervico-thoracic junction [78–81]. In order to perform this technique, a short or lower lever was alternatively produced by means of a contact between the therapist’s proximal phalanx, metacarpal, web space and thumb of the right hand and the superomedial aspect of the patient’s right shoulder girdle. The therapist placed both the heel and palm of his left hand over the temporal region of the patient’s lateral cranium.

To localize the forces to the left T1-T2 articulation, secondary levers of extension, lateral flexion, translation and minimal rotation were used. Whilst maintaining the secondary levers, the therapist performed a single HVLA thrust manipulation using the simultaneous delivery of the thrusting primary levers of lateral flexion from the upper lever and lateral translation from the lower lever, i.e., a lateral break. The same procedure - albeit directed to the right T1-T2 articulation - was performed in order to repeat this technique. Popping/cracking noises were heard on all thrust manipulations; hence, no second attempt was requested.

Figure 3: High-velocity low-amplitude thrust manipulation directed to the articulation of the left cervicothoracic (T1-T2) junction (image from the author)

Lumbosacral Junction Thrust Manipulation Technique

A single “mamillary process body drop” HVLA thrust manipulation directed to the left lumbosacral junction (L5-S1) with the patient in the side-lying position was performed **(Fig. 4)**. In order to perform this technique, the short lever was produced by means of a contact between the therapist’s hypothenar eminence of the right (i.e. caudal) hand and the left sacral base just medial (i.e. 2 fingerbreadths lateral to midline) to the left posterior-superior iliac spinous (PSIS). As the patient is rolled forward, the long lever was engaged by having the therapist place his anterior thigh over the patient’s lateral thigh and lateral pelvis.

To localize the forces to the left L5-S1 joint, secondary levers of flexion and counter rotation to the thoracolumbar spine were used. Whilst maintaining the secondary levers, the therapist performed a single HVLA thrust manipulation using the simultaneous delivery of the thrusting primary levers of rotation to the sacrum from the short lever and a body drop from the long lever (*i.e.* from rapid descent of the therapist’s body weight on to the patient’s thigh and pelvis). Additionally, and as part of the thrust, the operator’s left (*i.e.* cephalad) hand provided a counter force to the patient’s anterolateral pectoral region by pushing down to the table with cephalad and posterior traction force. The same procedure - albeit directed to the right L5-S1 articulation - was performed in order to repeat this technique. Popping or cracking sounds were heard on all thrust manipulations; hence, no second attempt was requested.

Figure 4: High-velocity low-amplitude thrust manipulation directed to the left lumbosacral (L5-S1) junction (image from the author)

Target Side Randomization

Prior to data collection, the target side and the order of the thrust manipulations were randomized using a table of randomly assigned numbers for all subjects for avoiding accumulative effects of the results.

Accelerometer Placement and Sound Collection

Skin mounted accelerometers were secured bilaterally on the transverse process of C1 **(Fig. 5)**, 25 mm lateral to the midline of the T1-T2 interspace **(Fig. 6)**, and 25 mm lateral to the midline of the L5-S1 interspace **(Fig. 7)** before the HVLA thrust manipulation delivery, for the cranio-cervical, cervico-thoracic, and lumbo-sacral junction, respectively. The accelerometers were connected to a data acquisition system (FOCUSRITE Scarlett 2i2, 96 KHz, 24-bit conversion) and a MacBook Pro laptop with the AUDACITY software for audio acquisition [23, 24] with a sampling frequency set at 96,000 Hz. The AUDACITY software normalized automatically the audio energy to values ranging between -1 and +1 (no unit of measurement). Subsequently, all subjects received randomly a HVLA thrust manipulations on both sides. The sound wave signals and resultant PSs were recorded for data extraction and analysis.

Figure 5: Placement and securing of skin mounted microphone over the lateral aspect of the transverse process of the atlas (image from the author)

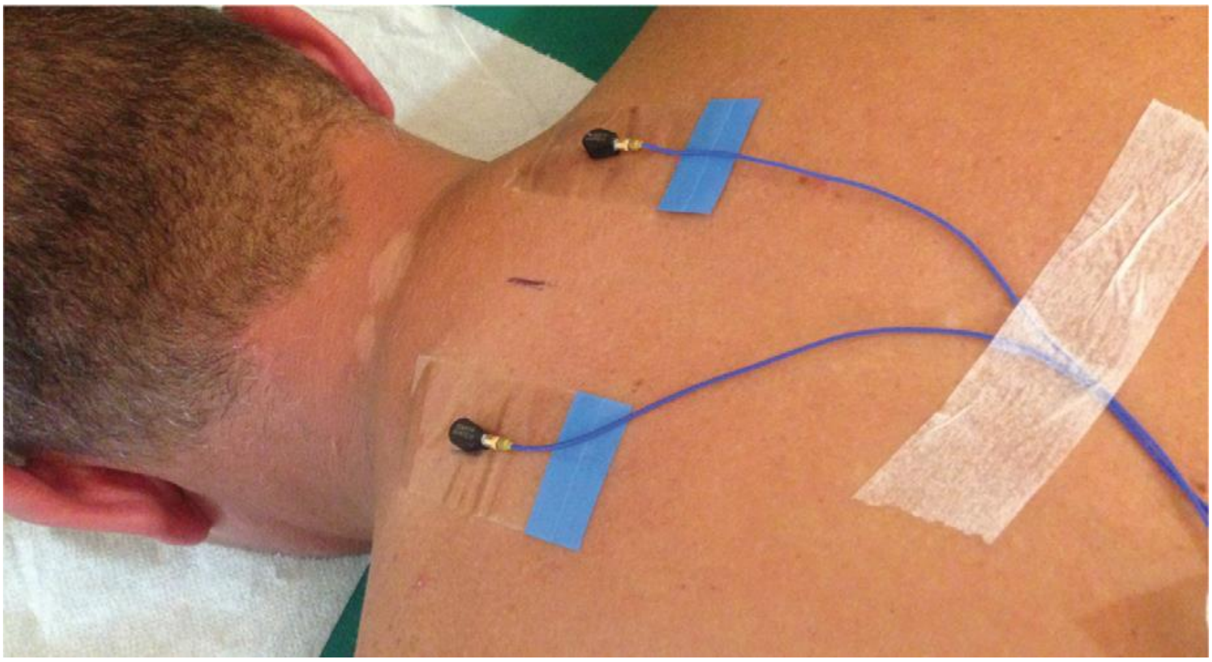

Figure 6: Bilateral placement and securing of skin-mounted accelerometers 25 mm lateral to the midline of the T1-2 interspace (image from the author)

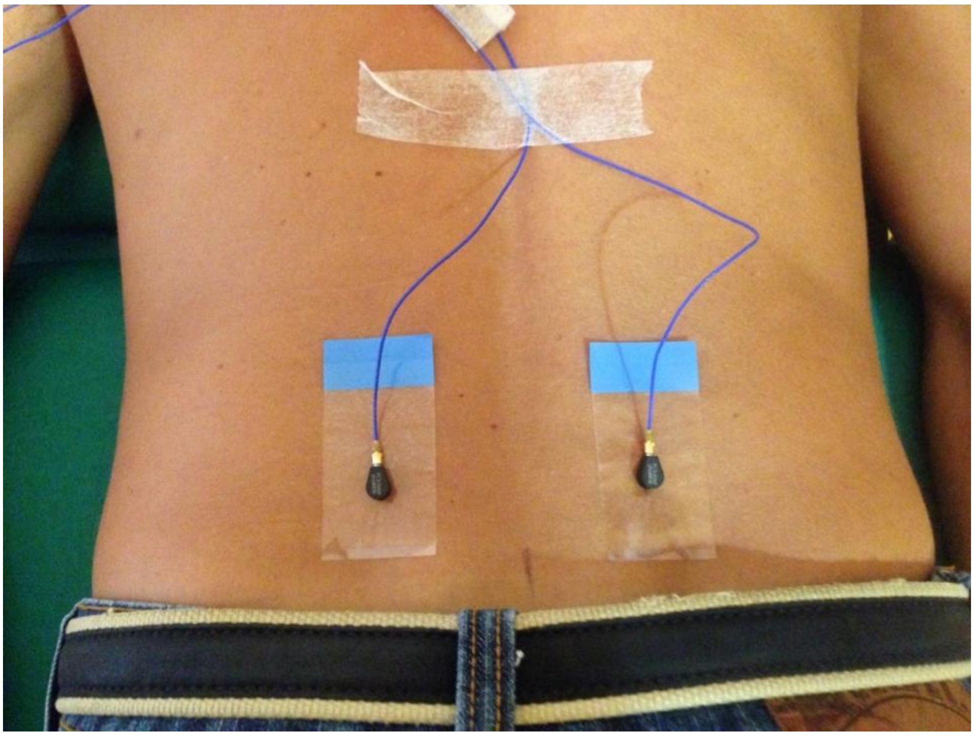

Figure 7: Bilateral placement and securing of skin-mounted accelerometers 25 mm lateral to the midline of the L5-S1 interspace (image from the author)

Sample Size

Because the absence of a comparative data of the analysis methodology (i.e. time-frequency analysis) and based on previous studies [1, 6, 8, 15, 26, 27] on the topic the authors did not run a sample size calculation (i.e. descriptive analysis).

Data Extraction

The sound signals were processed by Short-Time Fourier Transformation (STFT) in order to obtain the spectrograms of each thrust manipulation. A spectrogram provides a representation of the energy of a signal as a function of time and frequency. A color map was used to express the energy of the sound represented with time on the x-axis and frequency on the y-axis **(Figs. 8-10)**. Under those circumstances, the spectrograms were analyzed in order to evaluate the frequency content of both signals over time. The epoch length was set to 0.78ms (i.e. 75 times the sampling rate) with a 0.1% overlap between adjacent epochs, resulting in a frequency resolution of 94 Hz. The frequency scale was set between 10 Hz and 23 kHz, since this is the audible spectrum for a human being (including a small margin of error).

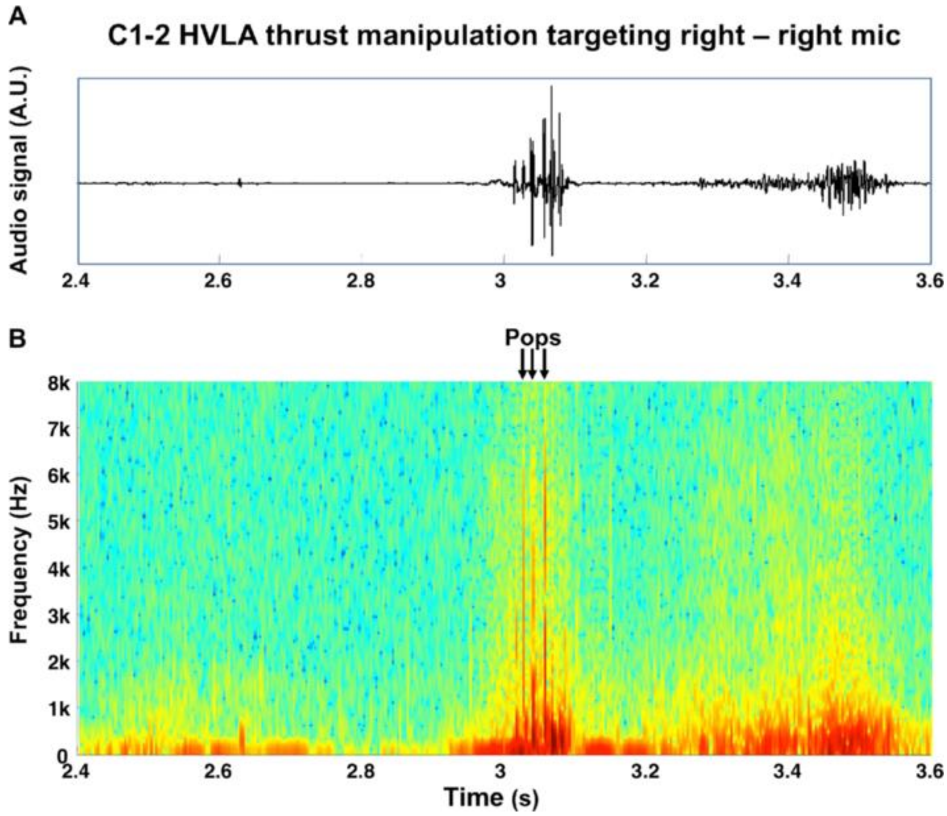

Figure 8: Raw audio signal (above) detected during a C1-C2 thrust manipulation and the corresponding spectrogram (below) (image from the author).

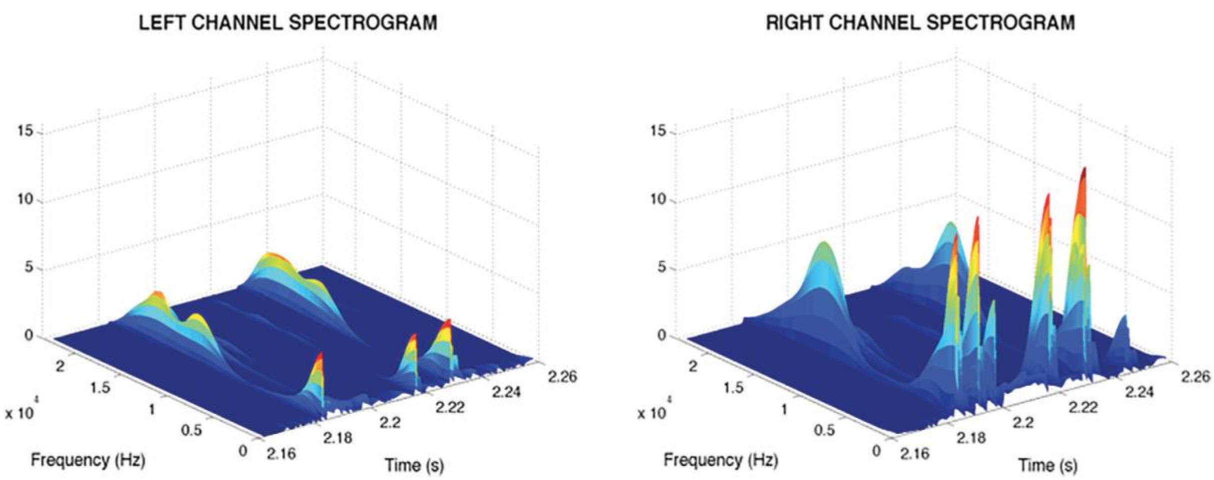

Figure 9: Spectrograms for the left and right audio channels during cervicothoracic HVLA thrust manipulation. Vertical energy peaks represent individual pops (image from the author).

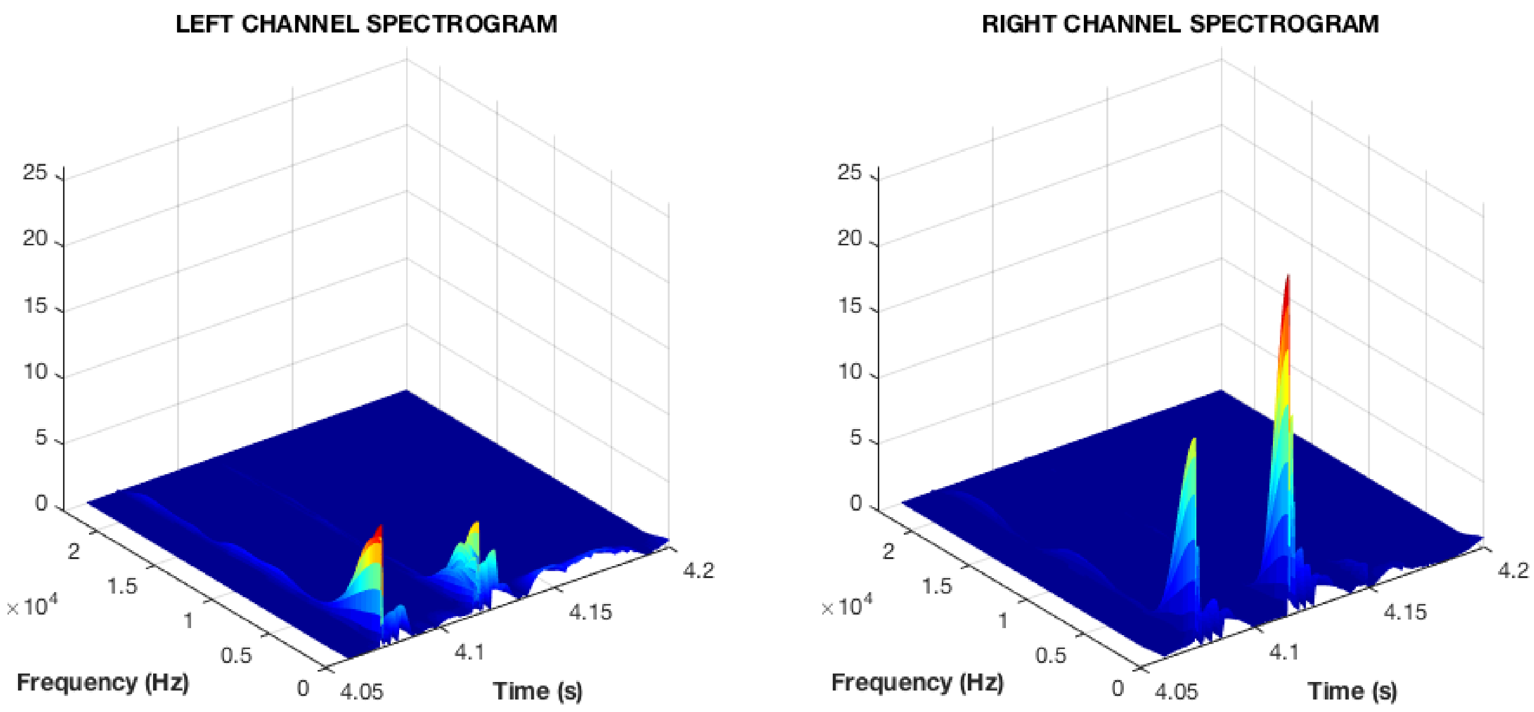

Figure 10: Spectrograms for the left and right audio channels during lumbosacral HVLA thrust manipulation. Vertical energy peaks represent individual pops (image from the author).

Data Processing

The sound in every audio track was modelled as a digital signal with the energy varying discretely as a function of time. The left and the right channels, representing, respectively, the two recordings of the left and right accelerometers during a single HVLA thrust manipulation, was analyzed separately. What is more, a left and a right graph representing the variation of the sound energy over time was plotted. However, for each person and for each manipulation, we did jointly inspect them to determine whether the popping phenomenon was an ipsilateral or contralateral event and whether it occurred on one side or on both at the same time. The graphs also enabled us to sum precisely the total number of pops during a single manipulation.

In order to isolate the time interval in which the manipulation took place, we first listened to the audio tracks of the left and right channels (relative to a single manipulation) using a stereophonic system. The peculiar sound emitted, together with the visual inspection of the right and left graphs of the digital audio signal, allowed for easy recognition of such an interval**.** The correct time interval featuring the manipulation event was then confirmed and adjusted by decelerating the audio speed by a factor 0.01 and listening to the track again. This allowed us to identify the beginning and the end of the thrust manipulations, and also to identify how many PSs were present. More specifically, this operation permitted us to increase the temporal resolution of the human ear by 100-fold, allowing us to discriminate and sum the total number of PSs.

The spectrograms show the “location” of the energy of the audio signals over time and over frequency jointly. Since we were interested to any PS occurring during the manipulation, independently on its different frequency contributions, the spectrograms were finally integrated over frequency, in order to obtain 2 curves (one per channel) with the time on the x-axes and the globally released sound energy on the y-axes. Such curves constitute the graphic representation used to analyse the PS phenomena.

Process for Counting the Number of Popping Sounds

The curves that represent the amount of released energy over time in both the left and right accelerometer channels were visually inspected in order to identify instantaneous bursts corresponding to PSs **(Figs. 11-12)**. The total number of PSs per manipulation was the sum of the number of energy bursts identified. In case of multiple consecutive (*i.e.* overlap) energy burst we discriminate the single PS by measuring the interval between the end of the descending phase of an energy burst and the beginning of the ascent of the subsequent burst. If this exceeds two epochs, then we consider the bursts as different PS. Otherwise, we consider them as a part of the same PS. We choose two epochs as the threshold interval to distinguish between the two events in order to increase the margin of safety of one epoch to the minimum interval necessary for 2 different peaks to be discriminated against each other, which coincides with the resolution of the spectrogram and is equal to one epoch. Notably, as no previous studies have used a time-frequency analysis to investigate the PS, it has not been possible to compare the used procedure with other ones or with a gold standard in terms of reliability or accuracy.

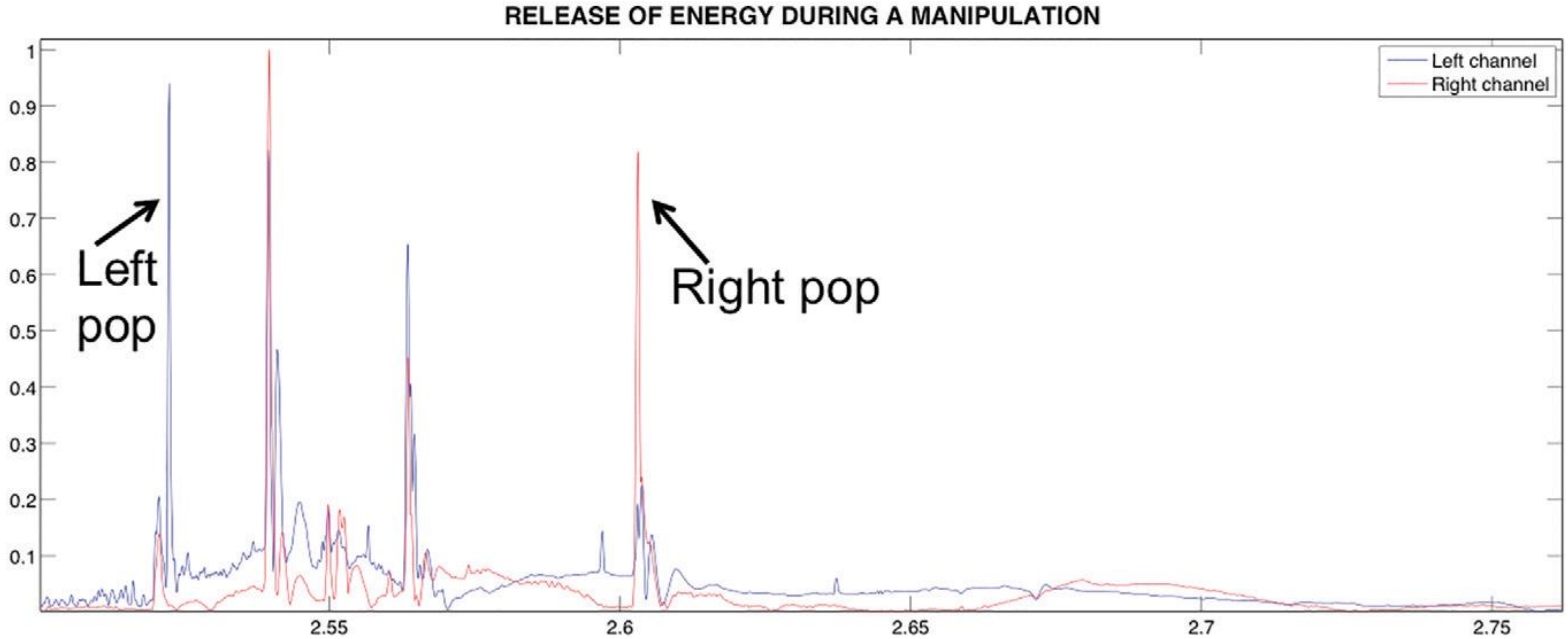

Figure 11: Amount of energy released over time for the right and left accelerometry channels during cervicothoracic thrust manipulation (image from the author).

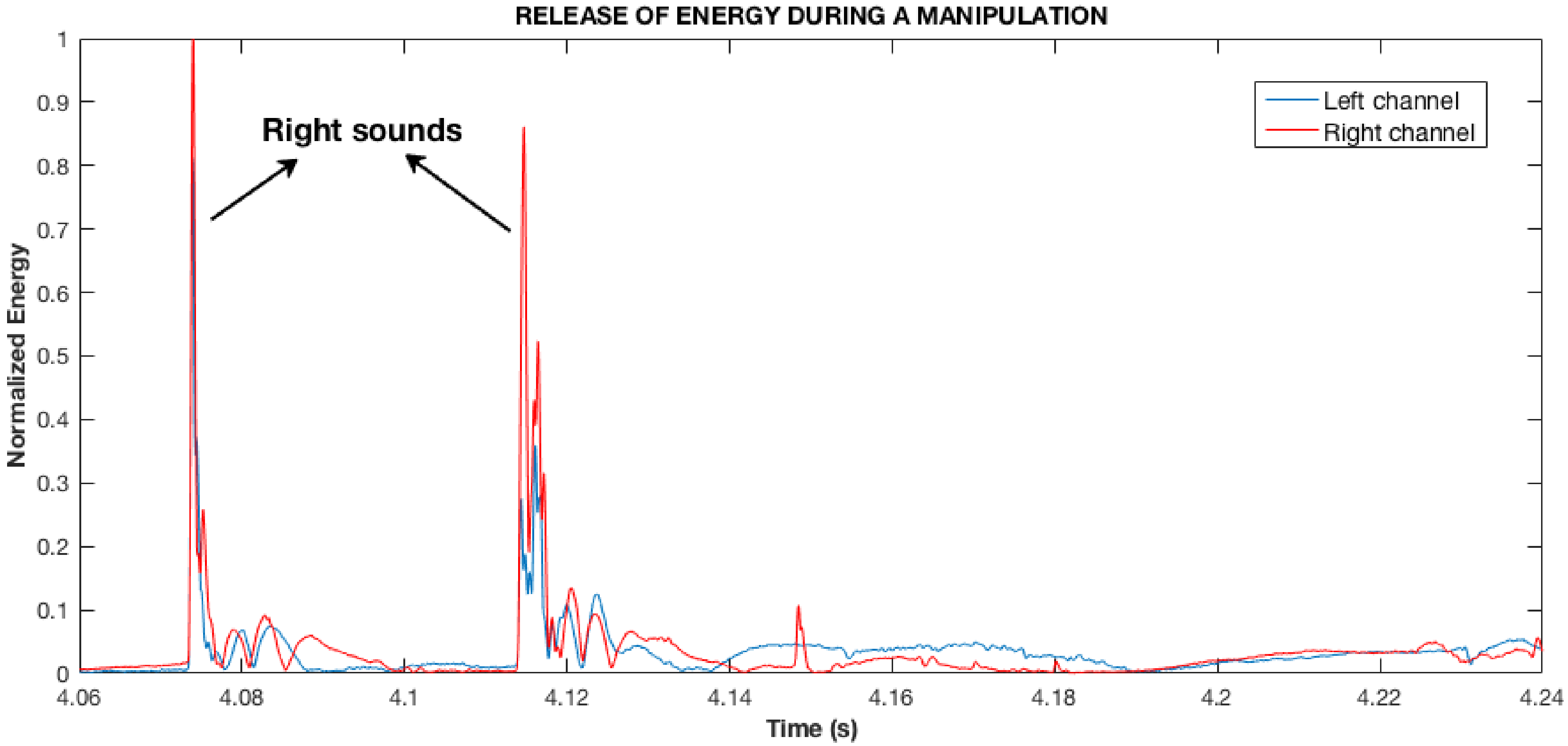

Figure 12: Amount of energy released over time for the right and left accelerometry channels during lumbosacral HVLA thrust manipulation (image from the author).

Process for Determining the Side of Popping Sound

The side of PS was determined by inspecting each of the energy bursts for the right and left spectrograms. Since we computed graphs and quantified the amount of energy at each epoch separately for the 2 channels, the side of PS could be immediately determined. As previously described [24], in an event of simultaneous bursts on both the right and the left channels, we considered the PS as occurred on that side where the burst that began earlier and had the higher energy value was reported. To put it bluntly, this means that the sound wave generated by the PS reached the accelerometer placed on this side before than the one placed on the other side and suffered less dispersion (i.e. PS was physically nearer this side than the other). The burst sensed on the latter was discarded and not considered in the calculation of the average number and duration of a PS.

Process for Calculating the Duration of a Single Pop

For each of the PS detected during the thrust manipulations, the time interval between the beginning of the ascent of the first energy burst and the end of the descent of the last energy burst of a PS event was considered as the duration of a single pop (**Figs. 13-14**).

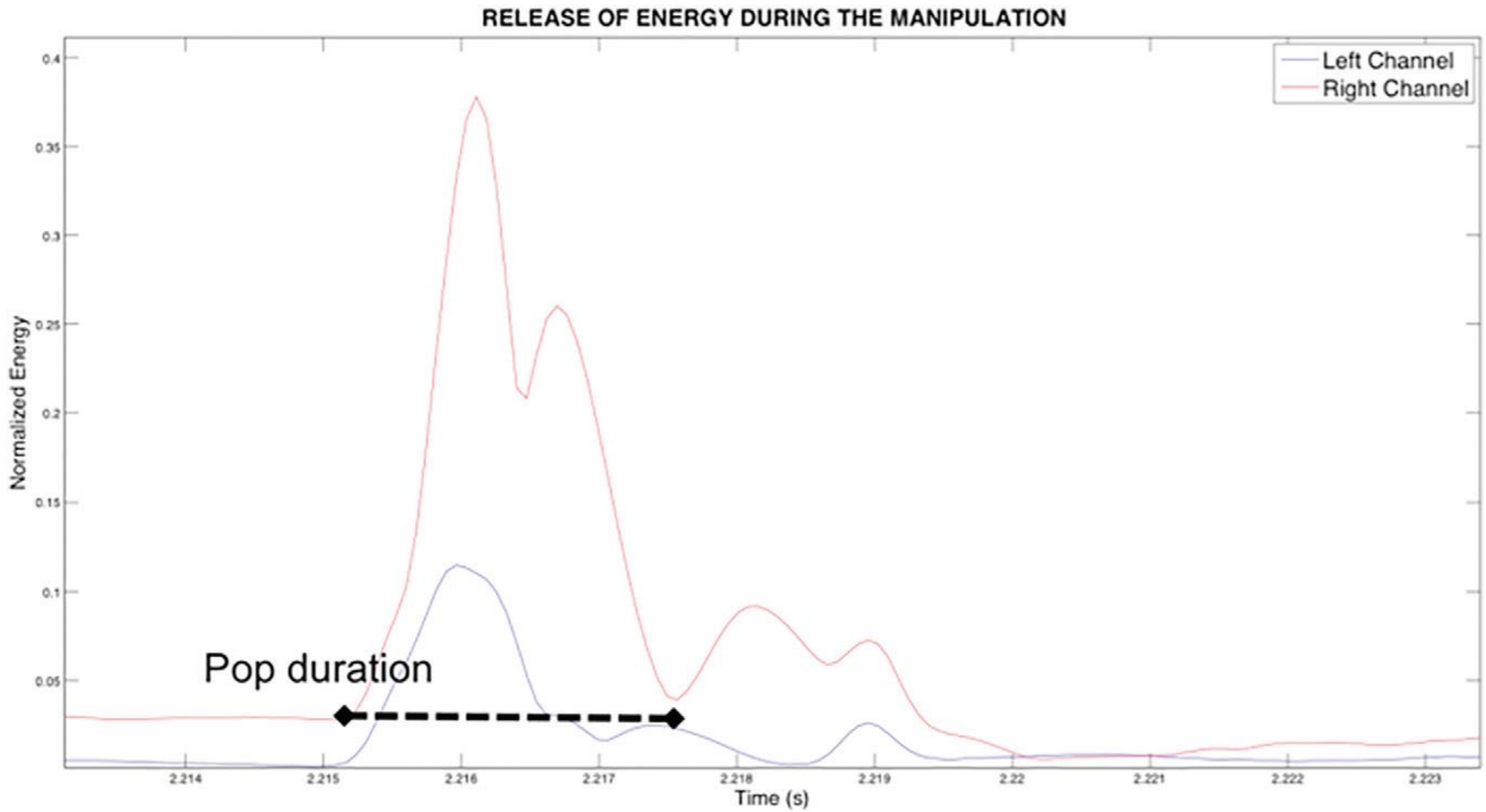

Figure 13: The time interval used to calculate the duration of a single pop during cervicothoracic HVLA thrust manipulation

(image from the author).

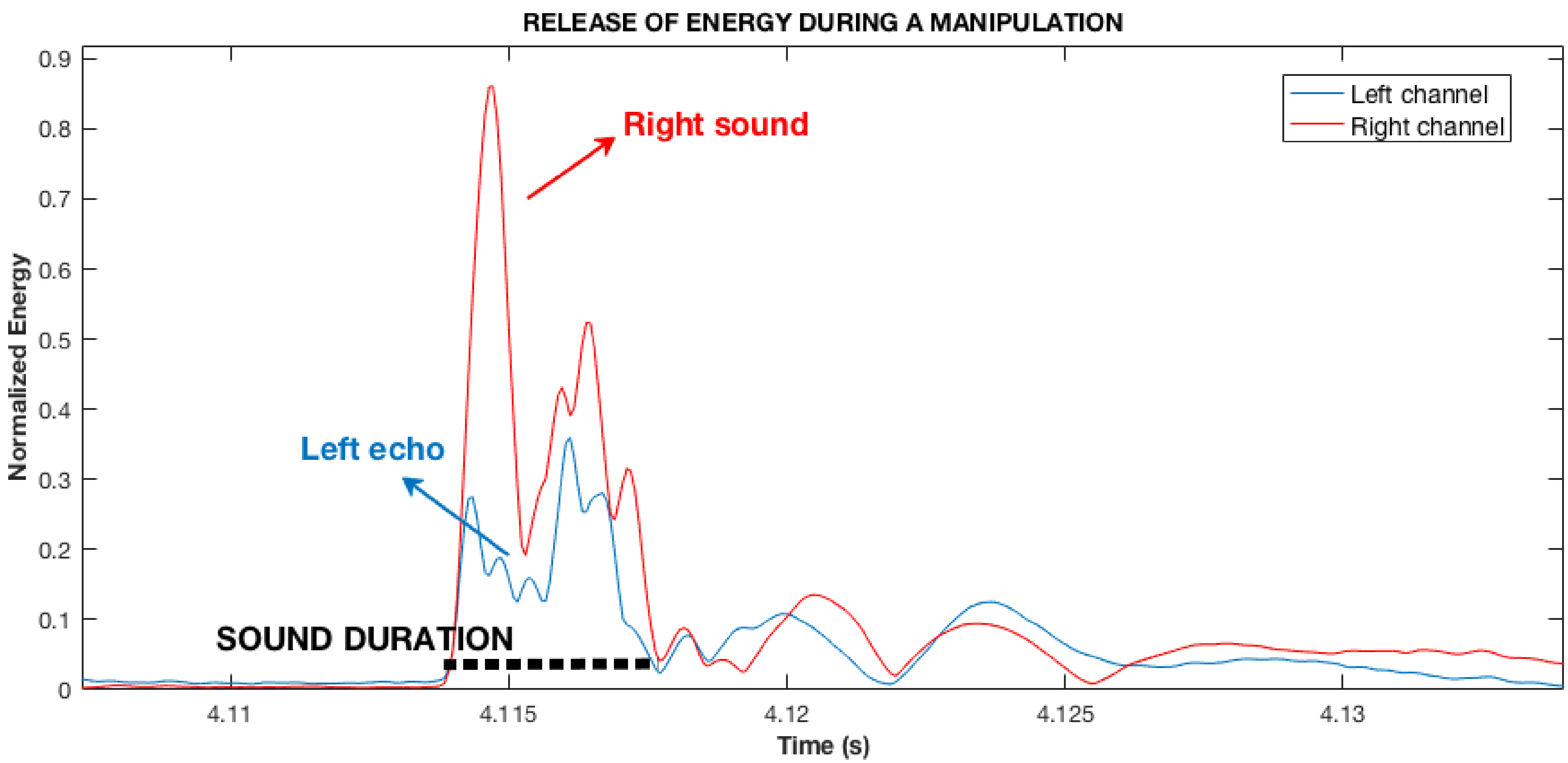

Figure 14: The time interval used to calculate the duration of a single pop during lumbosacral thrust manipulation (image from the author).

Process for Calculating the Duration of the Thrust Manipulation

As described in previous studies [23, 24] the duration of the thrusting procedure was considered as the time interval between the beginning of first pop and the end of the last pop **(Figs. 15-16).**

Data Presentation

Sound waves resulting from the HVLA thrust manipulations were displayed in graphical format**.** Each subject had one right and left graph, describing each thrust procedure (*i.e*., 2 channels per 2 graphs, namely four graphs in total for each subject). Means and standard deviations of the data were calculated to summarize the average number of pops, along with the duration of thrust manipulations, and the duration of a single PS. We compared the percentage of PSs occurring on each side during the HVLA thrust manipulation.

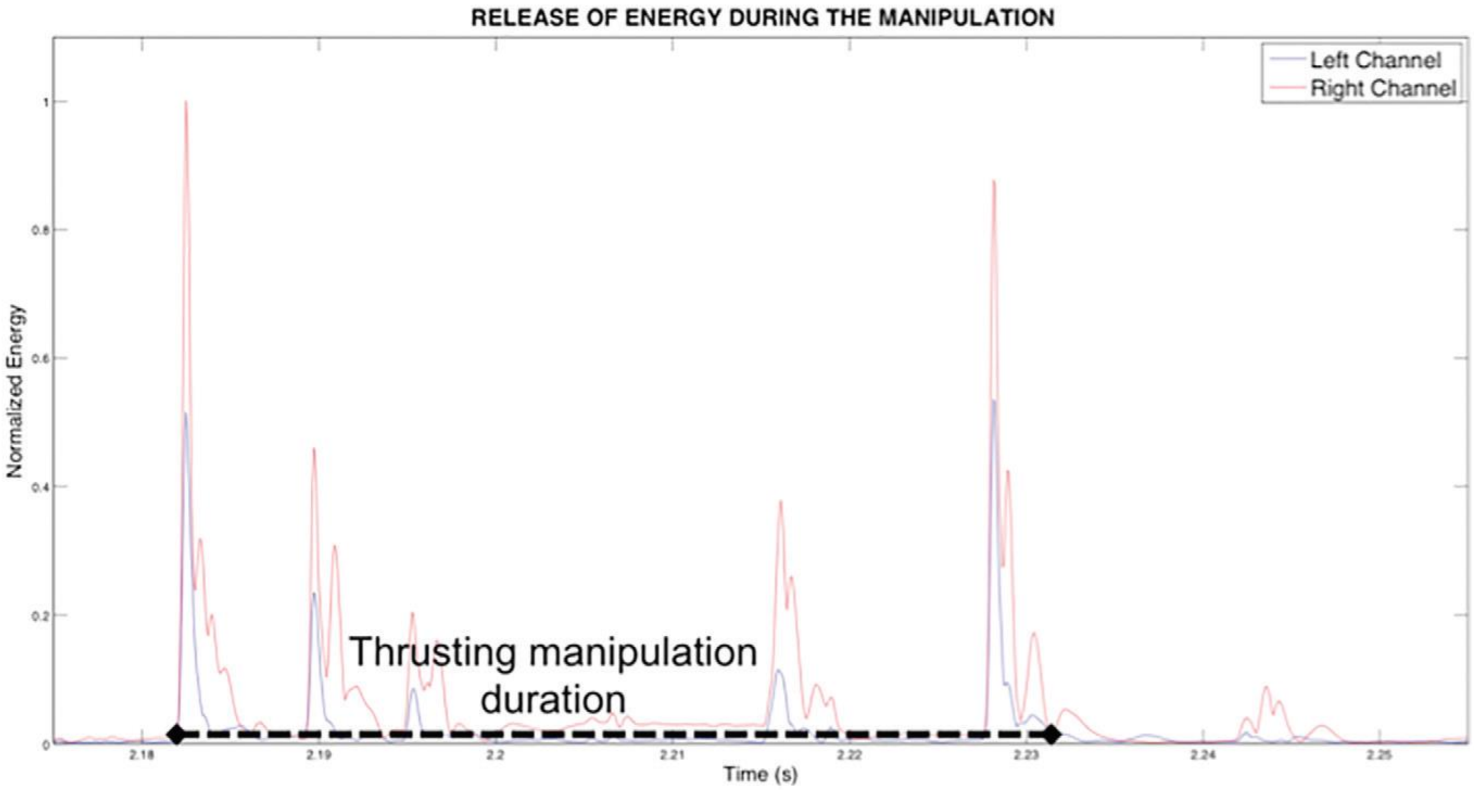

Figure 15: The time interval used to calculate the duration of cervicothoracic HVLA thrust manipulation (image from the author).

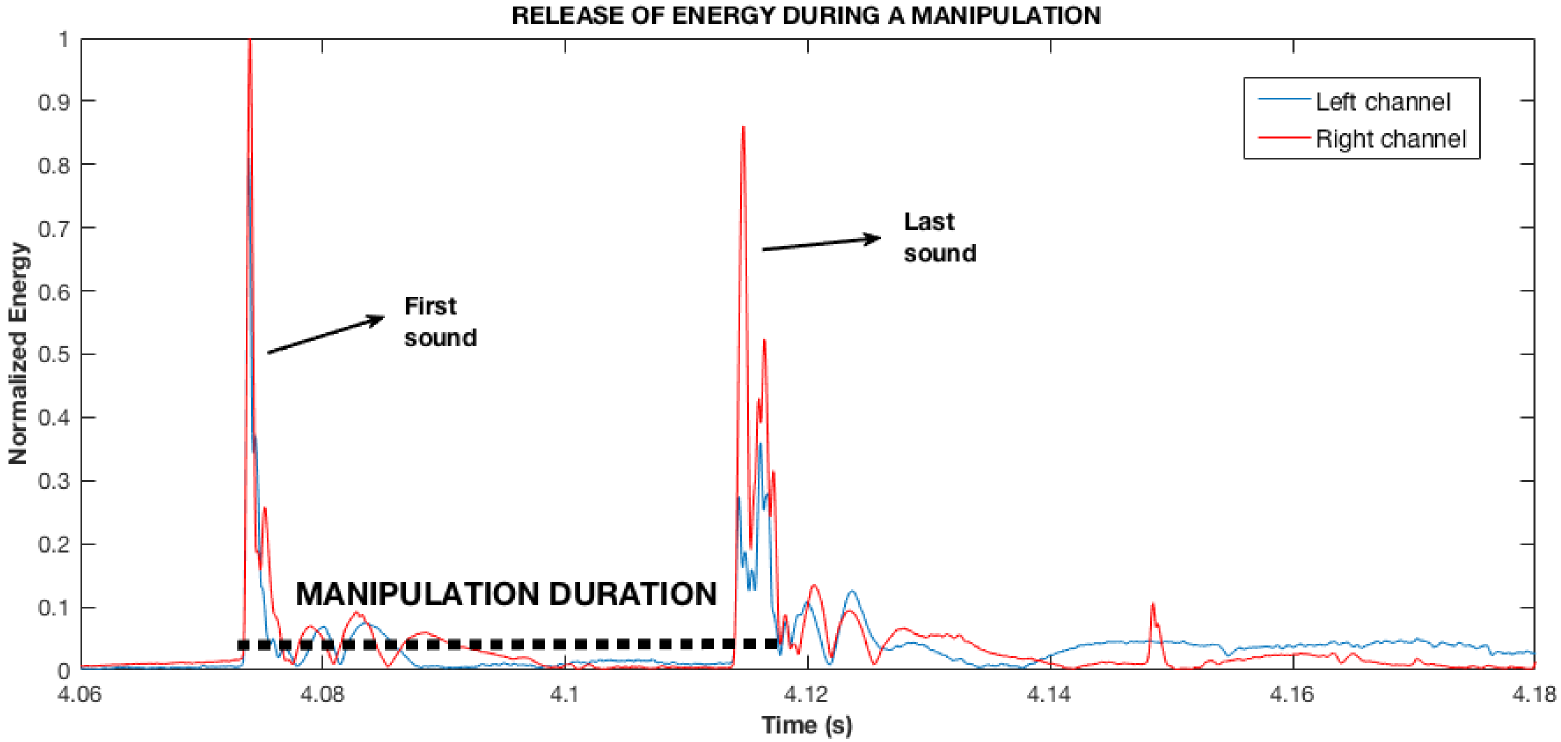

Figure 16: The time interval used to calculate the duration of lumbosacral HVLA thrust manipulation (image from the author).

Results

Upper Cervical Spine (C1-C2) Thrust Manipulation

For this study, 19 asymptomatic subjects (10 females and 9 males) were recruited from a private physical therapy outpatient clinic in Brescia, Italy. Their ages ranged between 18 and 52 years with a mean (SD) of 26.4 (8.6) years. Height ranged between 161 and 183 cm with a mean (SD) of 172.0 (7.3) cm. Weight was 46.0 kg to 110.0 kg with a mean (SD) of 68.3 (15.6) kg.

Of the 132 total PSs obtained during the upper cervical spine manipulation, 72 occurred ipsilateral and 60 occurred contralateral to the targeted C1-C2 joint; that is, cavitation was no more likely to occur on the ipsilateral than the contralateral side (P=0.294) following right or left rotatory C1-2 thrust manipulation **(Fig. 17-18)**. More specifically, when targeting the left C1-C2 joint, bilateral PSs were detected in 17 (94.4%) of the 18 upper cervical rotatory HVLA thrust manipulations, whereas unilateral PSs were detected in just 1 (5.6%) of the thrust manipulations. Likewise, when targeting the right C1-C2 joint, bilateral PSs were detected in 17 (89.5%) of the 19 upper cervical rotatory HVLA thrust manipulations, whereas unilateral PSs were detected in just 2 (10.5%) of the 19 thrust manipulations. Bilateral PSs were detected in 34 (91.9%) of the 37 upper cervical rotatory HVLA thrust manipulations and unilateral PSs were detected in just 3 (8.1%) of the 37 thrust manipulations: PS was significantly ($P < 0.001$) more likely to occur bilaterally than just unilaterally **(Figs. 17-18)**. Moreover, during upper cervical rotatory HVLA thrust manipulation targeting the right or left C1-C2 joint, the resulting popping sounds were 11.3 times more likely to occur bilaterally than just unilaterally.

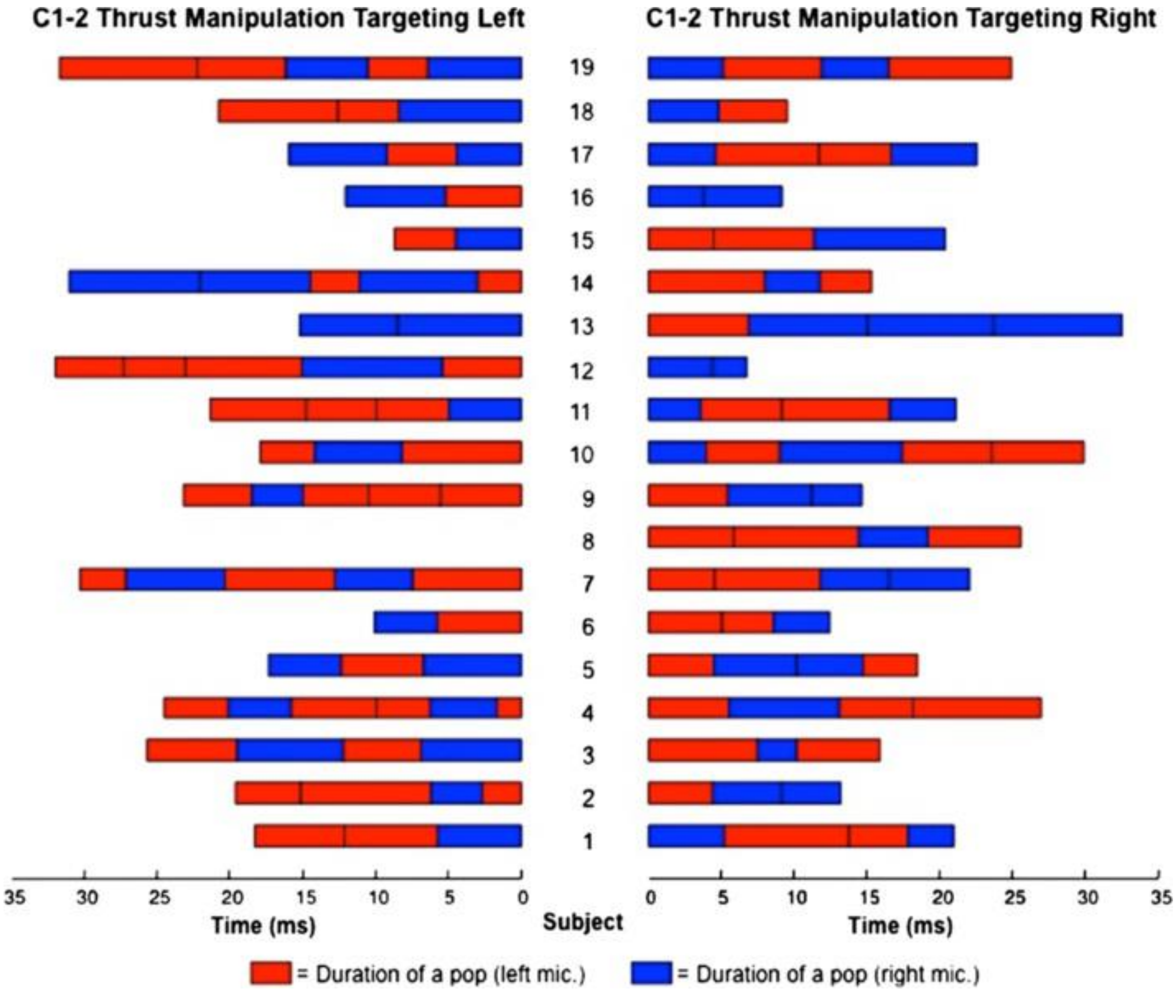

Figure 17: For each of the 19 subjects, the side and the duration in milliseconds for each of the 132 popping sounds during 37 separate HVLA thrust manipulations targeting the right or eft C1-C2 joint (image from the author).

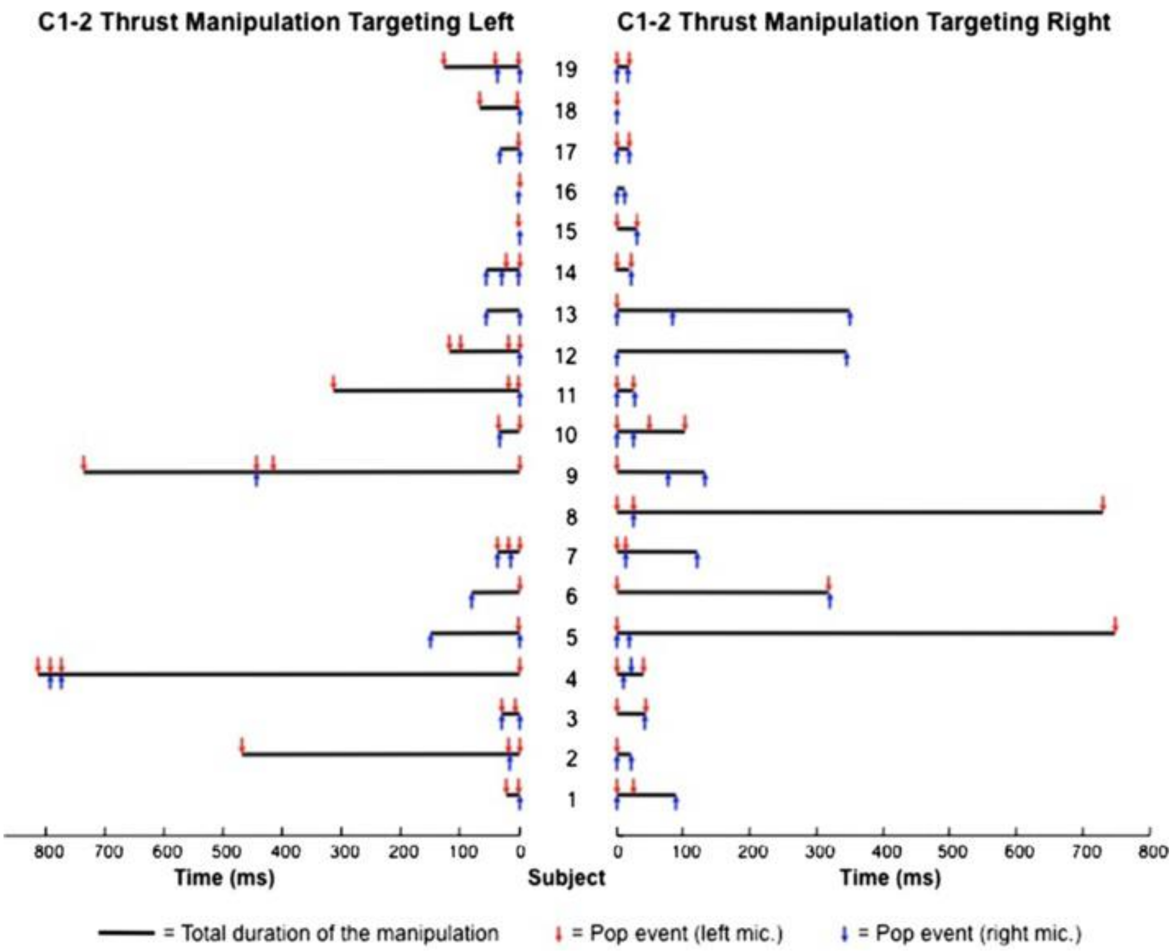

Figure 18: For each of the 19 subjects, the side and time point of occurrence in milliseconds for 132 popping sounds (red and blue arrows) and the total duration in milliseconds for 37 C1-C2 rotatory HVLA thrust manipulations (black horizontal bars) following spectrogram analysis are depicted (image from the author).

All 37-upper cervical HVLA thrust manipulations resulted in two or more audible joint PSs. One hundred thirty-two (n=132) PSs were detected following 37 upper cervical thrust manipulations giving a mean of 3.57 (95% CI: 3.19, 3.94) distinct pops per C1-C2 thrust manipulation procedure. Two distinct PSs were produced in 7 (18.9%) of the manipulations, whereas 11 (29.7%), 12 (32.4%), 5 (13.5%), and 2 (5.4%) manipulations produced 3, 4, 5, and 6 distinct PSs, respectively. Nineteen subjects received 37 manipulations (two each, with the exception of one subject whose data was not retrievable after one of the manipulations); therefore, the mean number of pops per subject after right and left C1-C2 thrust manipulation (two separate thrust procedures) was 6.95 (95% CI: 6.11, 7.79) with a range of 3 to 10 pops.

The mean duration of a single pop was 5.66ms (95% CI: 5.36, 5.96) and the mean duration of a single upper cervical rotatory HVLA thrust manipulation was 96.95 ms (95% CI: 57.20, 136.71).

Cervico-Thoracic (C7-T1) Junction Thrust Manipulation

Thirty-two individuals (20 females and 12 males) were recruited from a private physical therapy outpatient clinic in Florence, Italy. Their ages ranged between 23 and 69 years with a mean (SD) of 39.1 (10.7) years. Height ranged between 152 and 182 cm with a mean (SD) of 170.1 (8.5) cm. Weight was 50.0 kg to 96.0 kg with a mean (SD) of 67.7 (12.6) kg.

Of the 252 total PSs during 58 HVLA thrust manipulations, 22 occurred ipsilateral and 230 occurred contralateral to the targeted T1-T2 articulation; that is, the PS was significantly more likely to occur on the side contralateral to the short-lever applicator of the manipulative physiotherapist ($P < 0.001$) following right or left thrust manipulation to the CTJ. Moreover, during T1-T2 HVLA thrust manipulation targeting the right or left CTJ, the resulting PS were 10.5 times more likely to occur on the contralateral side than the ipsilateral side.

All 58 cervicothoracic HVLA thrust manipulations resulted in one or more audible PS. Two hundred fifty-two (n=252) PSs were detected following 58 cervicothoracic thrust manipulations giving a mean of 4.35 (95%CI 2.88, 5.76) distinct PSs (i.e. pops or cracks) per cervicothoracic HVLA thrust manipulative procedure. More specifically and on average, for each cervicothoracic HVLA thrust manipulation procedure, 3.97 (SD 1.65) of the 4.35 PSs (i.e. 91.3%) occurred on the contra-lateral side to the short-lever applicator of the physiotherapist, whereas, 0.38 (SD 0.75) of the 4.35 PSs occurred ipsilateral (i.e. 8.7%). Unilateral PSs were detected in 53 (91.4%) of the 58 cervicothoracic lateral break HVLA thrust manipulations and bilateral PSs were detected in just 5 (8.6%) of the 58 thrust manipulations; that is, PS was significantly ($P < 0.001$) more likely to occur unilaterally than bilaterally. One distinct PS (i.e. a single popping noise) was produced in 4 (6.9%) of the manipulations, whereas 2 (3.5%), 12 (20.7%), 10 (17.2%), 15 (25.9%), 13 (22.4%), 1 (1.7%) and 1 (1.7%) manipulations produced 2, 3, 4, 5, 6, 7 and 8 distinct PSs, respectively. The mean duration of a single PS was 4.13ms (95%CI: 0.82, 7.46) and the mean duration of a single CTJ HVLA thrust manipulation was 60.77ms (95%CI 28.25, 97.42).

Lumbosacral (L5-S1) Junction Thrust Manipulation

Thirty-four asymptomatic participants, (17 females and 17 males) aged between 18 and 65 years were recruited by convenience sampling from a private physical therapy outpatient clinic in Florence, Italy.

Of the 320 total PSs during 60 HVLA thrust manipulations, 176 occurred ipsilateral and 144 occurred contralateral to the targeted L5-S1 articulation; that is, PS was no more likely to occur on the ipsilateral than the contralateral side following right or left rotatory L5-S1 HVLA thrust manipulation ($P = 0.073$). Moreover, distinct PSs occurred 98% of the time on the ipsilateral (upside) or the contralateral (downside) facet articulations, but very rarely (i.e., 2% of cases) occurred at the same time on both side during a single lumbosacral HVLA thrust manipulation.

All 60 lumbosacral HVLA thrust manipulations resulted in two or more audible joint PSs (range, 2-9) with a mean of 5.33 (95% CI: 4.82, 5.85) distinct pops per lumbosacral thrust manipulation procedure. More specifically and on average, for each lumbosacral HVLA thrust manipulation procedure, 2.93 (SD 2.16) of the 5.33 pops (i.e., 54.97%) occurred on the side ipsilateral to the short-lever applicator of the physiotherapist (i.e., the ceiling side), whereas, 2.40 (SD 2.08) of the 5.33 pops occurred contra-lateral (i.e., 45.03%).

Generally, bilateral PSs (i.e. both side occurrence but not necessarily at the same time) were detected in 36 (60.0%) of the 60 lumbosacral thrust manipulations and unilateral (i.e. single side occurrence but not necessarily at the same time) PSs were detected in 24 (40.0%) of the 60 thrust manipulations; that is, PS was not more likely to occur bilaterally than unilaterally ($P = 0.1213$). Nevertheless, during lumbosacral thrust manipulation targeting the right or left L5-S1 joint, the resulting PSs were 1.5 times more likely to occur bilaterally than just unilaterally during a single thrust manipulation delivery.

Two distinct PSs were produced in six (10.0%) of the manipulations, whereas 7 (11.7%), 8 (13.3%), 9 (15.0%), 11 (18.3%), 13 (21.7%), 1 (1.7%) and 5 (8.3%) manipulations produced 3, 4, 5, 6, 7, 8 and 9 distinct PSs, respectively. Thirty-four (n=34) subjects received 60 manipulations (i.e. 2 on each subject); however, data was not retrievable for 12 procedures, thus data for 60 manipulations in 34 subjects was analyzed. The mean duration of a single pop was 2.69ms (95% CI: 0.95, 4.59) and the mean duration of a single lumbosacral junction HVLA thrust manipulation was 139.13ms (95% CI: 5.61, 493.79).

Discussion

The current study found that a single spinal thrust manipulation applied to the upper cervical (C0-C1), cervico-thoracic (T1-T2) or lumbo-sacral (L5-S1) junction produces more than one single popping sound, located ipsi- or contra-lateral in the same proportion and with a duration ranging from 2.69mm (lumbo-sacral junction) to 5.66ms (cranio-cervical junction). The mean duration of the spinal manipulative procedure ranged from 60.77ms (cervico-thoracic junction) to 139.13ms (lumbo-sacral junction). Slightly differences in the duration and the location of the popping sound were also observed depending on the targeted area.

Side of the Popping Sounds

It is difficult to directly compare the results of our studies with previous ones on this topic [1, 6, 8, 15, 26, 27] because our studies are the first one investigating cranio-cervical junction, cervico-thoracic junction and lumbo-sacral junction thrust manipulation and to use a time-frequency analysis. Two previous studies [1, 26] investigating the side of PS associated with cervical spine manipulation reported that the popping was significantly more likely to occur on the contralateral side to the applicator contact during “ lateral to medial and rotatory” [26] or “rotatory” [1] manipulations targeting C3-C4 articulation. This finding was the contrary than our study; in addition, the upper cervical thrust technique used in our study cannot be considered synonymous with the mid-cervical thrust technique used in these two studies. Moreover, we mounted microphones directly over the target vertebra (i.e. the lateral aspect of the transverse process of C1), while both Bolton et al. [1] and Reggars and Pollard [26] mounted microphones over the articular pillar and the transverse process, respectively, of the C2 vertebra when the target was the C3-C4 joint. Our result indicate that PSs were significantly more likely to be a bilateral “event” than just a unilateral “event” in general.

No previous studies investigated the side of the PSs; however, Ross et al. [8] found most thoracic and lumbar thrust manipulations produced 2 to 6 audible cavitation sounds with an average error from the target joint of 3.5cm or 5.29cm, respectively. The results of our studies indicate that cavitation was significantly more likely to occur on the contralateral side to the short-lever applicator of the manipulative therapist following cervico-thoracic junction thrust manipulation.

Beffa and Mathews [27] reported that lumbar and sacroiliac thrust manipulations had low specificity and poor accuracy for the target joint. The authors identified in this study that 8.7% of the PSs occurred ipsilateral and 91.3% of the PSs occurred contralateral to the short-lever applicator of the manipulative therapist. In contrast with previous result, Cramer et al. [6] reported 93.5% of the PSs occurred on the upside facet articulations (i.e. ipsilateral to the short-lever applicator). However, Cramer et al. only looked at the number of sound releases (i.e. not the side) during the HVLA lumbar thrust manipulation [6]. We found that PS during lumbosacral thrust manipulation targeting L5-S1 joint resulted that PSs were 1.5 times more likely to occur bilaterally (i.e. both side occurrence but not necessarily at the same time) than just unilaterally during a single HVLA thrust manipulation delivery.

Number of Popping Sounds

We identified an average of 3.57 distinct pops and a range of 1 to 7 PSs per C1-C2 thrust manipulation. Similarly, Reggars [15] reported a mean of 2.46 pops and a range of 1 to 5 PSs per C3-4 thrust manipulation. Reggars [15] found the majority of subjects (64%) produced 2-3 distinct popping sounds, whereas our study found that the majority of subjects produced 3-4 popping sounds.

Similarly, Reggars and Pollard [26] reported a mean of 2.32 PSs on 64% of the subjects per manipulation and a range of 1to 5 pops following a thrust manipulation targeting C3-4. It seems that cervical spine thrust manipulation induces more than a single popping sound.

We identified in 91.3% of time an average of 4.35 distinct PSs and a range of 1 to 8 PSs per C7-T1 thrust manipulation. Similarly, although in a different thoracic and lumbar spine region, Ross et al*.* [8] found a range of 1 to 6 audible PSs per thoracic or lumbar thrust manipulation. Additionally, Cramer et al. [6] further found 2 or more popping sounds per lumbar thrust manipulation. Again, in the lumbosacral junction we identified an average of 5.33 distinct pops (i.e., 54.97% of the time) and a range of 2 to 9 PSs per thrust manipulation.

Whether the multiple PSs found in our studies emanated from the same joint, from the contralateral facet or adjacent ipsilateral (i.e. uncovertebral joints), or even extra-articular soft-tissues remains to be elucidated. Furthermore, we observed PSs composed of single energy releases as well as sounds composed of multiple energy releases - *i.e.* single vs. multi-peak sounds. We identified high frequency sounds, low frequency sounds, and sounds of multiple frequencies [23, 24]. Therefore, as opposed to a single model being able to explain all of the audible sounds during thrust manipulation, the possibility that several phenomena may be occurring simultaneously must not be ruled out. Notably, Shekelle [82] suggested that thrust manipulation may affect the following: (1) “release of entrapped synovial folds”, (2) “disruption of intra- or periarticular adhesions”, (3) “unbuckling of motion segments that have undergone disproportionate displacements”, or (4) “sudden stretching of hypertonic muscle”.

Although no study has clearly explain the clinical significance (i.e. its relationship to pain and disability) of the PSs up to now, the traditional expectation of achieving just one single pop per just one thrust manipulation in the cervical, thoracic, or lumbopelvic regions is not supported by the literature [1, 6, 8, 15, 23, 24, 26, 27]. Therefore, "one pop" should no longer be taught as the "goal" or "expectation" in conventional manual therapy training programs. Consequently, it is impossible to recognise beyond doubt the specific joints undergoing the PS process during a thrust manipulation [83, 84].

Duration of an Individual Popping Sound

Meal and Scott [17] first measured the duration of a single pop. The authors found in their studies that the duration of a single audible PS to be 25-75ms. However, they investigated thrust manipulation to the MCP joints, not the spine as we did. In addition, Herzog et al. [7] reported triphasic "cavitation signals" of a mean duration of 20ms. Notably, it is unclear whether this value represents a single PS or multiple PSs.

We found the mean duration of a single pop to be 5.66ms (95%CI 5.36, 5.96) after C1-C2 thrust manipulation which is consistent with the 4ms duration reported by Reggars and Pollard [26]. Additionally, the observed mean duration of a single PS during cervicothoracic thrust manipulation was 4.13ms (95%CI 0.82, 7.46) and 2.69ms (95%CI 5.61, 493.79) for a single lumbosacral HVLA thrust manipulation. Unlike previous studies [7, 8, 26], the gap between the beginning of the ascent of the first energy burst and the end of the descent of the last energy burst of a PS event was calculated and used for the duration of a single pop in this study.

Duration of the Spinal Manipulative Procedure

Unlike previous studies [7, 9, 85], we used the interval between the first and last PS of each manipulative procedure in order to represent the duration of the actual thrusting procedure from onset to arrest. In fact, our studies are the first to report a duration for the thrusting procedure targeting the cranio-cervical, cervico-thoracic and lumbo-sacral junctions. Triano [9] analyzed the force-time history graphs during a C2-C3 lateral break manipulation to measure the duration of the thrust; whereas, Ngan et al [85] used a four camera motion analysis system to measure head on trunk angular movements (and indirectly manipulation duration) during lower cervical rotational manipulations in eight asymptomatic subjects. In addition, Herzog et al [7] used an "instantaneous acceleration signals" from a mechanical accelerometer during T4 posterior to anterior manipulation in 28 subjects with thoracic pain in order to measure the thrust duration. Considering the different techniques and the instrumentation/analytical methods (*i.e.* respectively force-time history graphs analysis, camera motion analysis and "instantaneous acceleration signals" from a mechanical accelerometer) on each of these previous studies [7, 9, 85], there does not appear to be a consistent reference standard for measuring thrust duration and a comparison with data obtained in our study is not possible.

We found a mean duration of a single upper cervical rotatory thrust manipulation of 96.95ms (95%CI 57.20, 136.71), a value that is consistent with Triano [9] (135 ms), Herzog et al. [7] (80-100ms) and Ngan et al. [85] (158ms). Additionally, we found the mean duration of a single cervicothoracic thrust manipulation was found to be 60.77ms (95%CI 28.25, 97.42). Moreover, we found the mean duration of a single lumbosacral thrust manipulation to be 139.13ms (95%CI 5.61, 493.79), a value that is consistent with the 150ms reported by Herzog et al. [7, 86] for a lumbar spine thrust manipulation.

Biomechanics and Kinematics

Identifying normative values for kinematic and biomechanics of spinal manipulative procedures for different spinal regions may help facilitate a better understanding of the physical parameters (e.g. velocity, acceleration) [7, 9, 23, 24, 85] and the specific skills required by practitioners to efficiently perform this intervention [79, 80, 85].

Notably, spinal manipulation is defined as a High Velocity Low Amplitude (HVLA) procedure. That is, this is one of the few definitions in manual therapy that includes all its main kinematic and biomechanics characteristics. The most relevant feature of this technique is the delivery of speed and amplitude **-** *i.e.* the application of an external force **-** on a body segment, which is performed by a physiotherapist. Such characteristics have been extensively explored by many research groups, with the objective of uniform spinal manipulation procedures for clinical, educational and research purposes. According to Herzog et al. [86] this technique is composed by three phases: 1) Preload phase; 2) Thrust phase; 3) Resolution phase **(Fig. 19)**. The *preload phase* starts with the application of a force, whose intensity remains almost constant. It lasts several seconds before the beginning of the *thrust phase*, during which it is possible to observe, within a short time, a relevant increase of both the force and the acceleration applied by the physiotherapist, until it reaches a force-velocity peak. This phase starts engaging the so-called ‘barrier’ (i.e. the physiotherapist perception of the tension focusing during the Preload phase). The subsequent *resolution phase* is featured by a rapid decrease of both the applied force and speed. These three phases must be intended as a continuum.

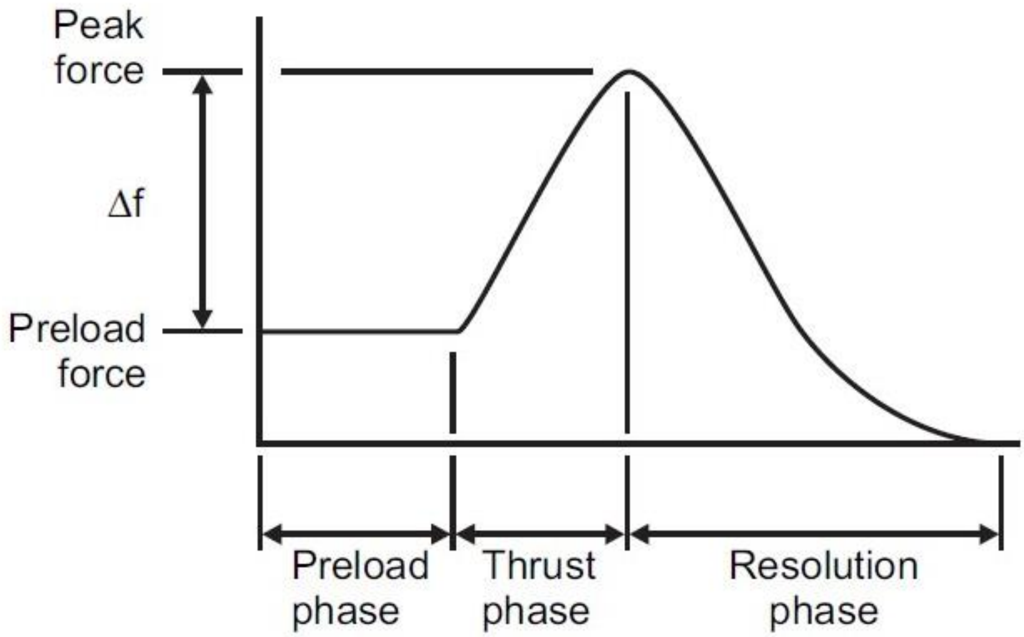

Figure 19: Definitions of the 3 phases of spinal manipulation (reprinted with permission by the author)

According to Ngan et al. [85], Klein et al. [87] and Triano & Schulz [88] the angular displacement to be added during the preload phase in order to build the barrier should not exceed the physiological active range of motion (i.e. mid-range barrier). Notably, Buzzatti et al. [89], using ultrasound-based motion tracking system on fresh human cervical specimens found that displacement induced with the present technique seems not to be able to endanger vital structure on the spinal cord and the vertebral artery. Moreover, no significant differences were registered on the mean displacements in different spinal level (e.g. C3 and C5) meaning that the components of the barrier are carried at the applicator contact level without any specific locking procedures [87]. This phase requires 7 seconds before the thrust phase (i.e. optimal setting of the barrier) and a mean de-rotation displacement of 4.8º needed to get the proper acceleration for the thrust (i.e. momentum technique) [80, 85].

An amplitude displacement ranging from 11.4º to 13.0º were recordered during the thrust phase underlining the small amplitude performed during the thrust [85, 88]. That is, this amplitude must be obtained within short duration and high velocity with an average peak manipulative velocity of 127º per second and a mean peak acceleration of 2183º per second square [85]. These features are significantly related to the de-rotation displacement and the subsequent acceleration. The axial rotation and the lateral bending displacement are correlated, and their peak occur simultaneously during the thrust (i.e. multidirectional thrust) [87]. Notably, the ratio between velocity and the force is inversely proportional [90], that is, the total forces from pre-load to peak force during the thrust increased by a factor of 10 (e.g. from 24 Newton to 238 Newton during a cervical spine manipulation) [91]. However, the applied forces can vary depending on the analyzed phase and anatomical region [86].

Clinical Relevance of the Popping Sound

Spinal manipulation represents a complex therapeutic intervention, characterised by specific and contextual elements tied to the interventions itself, along with the patient, the physical therapist and the setting where the treatment is administered. Their interaction enables the variation of the outcomes [92]. Spinal manipulation is commonly recommended and administered in physical therapy clinical practice in order to reduce pain and disability [93] in various musculoskeletal disorders, such as low back pain [30, 31] and neck pain [28, 29].

Evans and Lucas [4] found that audible PSs within the affected joint is one of the five empirically-derived features necessary for a valid thrust manipulation. In other words, the audible popping that “occurs within a joint” should be present to satisfy the proposed manipulation criteria [4]. However, few authors in the past suggested that PS after a lumbar thrust manipulation delivery was not necessary to determine clinical outcomes changes [94–97]. Nevertheless, the PS is considered a technical indicator for a successful HVLA thrust manipulation delivery in clinical practice [6, 7, 9–11]. There is anecdotal evidence suggesting an association between clinical outcomes and PS during a manipulative procedure. As a matter of fact, many clinicians and researches still repeat the manipulative procedure if the PSs were not emanated [10–12, 50, 51, 98, 99].

The phenomenology of the PS is still unknown and under debate. Moreover, the traditional expectation of achieving just one single pop from the target joint per thrust manipulation in the lumbopelvic, cervicothoracic and upper cervical regions is not supported by the current literature [1, 6, 8, 15, 23, 24, 26, 27].

Notably, Smith and Bolton [100] in a systematic review underscore the absence of reliable and valid diagnostic protocols to determine the need (*i.e.* when and where) of spinal manipulation in patients suffering of spinal pain. In addition, these findings show a lack of valid diagnostic criteria; therefore, the quality of previous randomized clinical trials concerning manual therapy and the traditional rationale of how to determine which joint target during thrust delivery should be considered with caution [100]. In fact, it is widely accepted that the majority of spinal palpatory diagnostic procedures are unreliable [101]. However, the pain provocation tests or the use of subjective symptoms are the most clinically relevant findings - especially in comparison with the perception of the clinician - making these finding the only reliable clinical tool during the treatment decision process [101]. Additionally, another questionable aspect is what really happens to a vertebral segment during the intervention delivery. That is, the displacement induced during the delivery of manipulative procedure is unintentional, unpredictable and not reproducible [89]. Despite the self-evident uncertainty of the rationale and the more effective and reliable administration modality, the impact of spinal manipulation is relevant, as it is a largely used, recommended tool in clinical practice [29, 30]. Nonetheless, the underline mechanisms of its efficacy and underlying mechanisms have not been clearly defined yet [102] and they represent a topic of debate [103–107].

Historically, spinal manipulation has been supposed to operate by involving both biomechanical and neurophysiological mechanisms. However, their combined interaction has been frequently neglected: on the one hand, this could explain the reason of its effectiveness, in spite of the heterogeneity of the administration modalities; on the other hand, it might clarify the above-mentioned criticality (*i.e.* non-specificity in PS, unreliable and unreproducible palpation tests, etc.) [108].

The interpretative approach offered by Joel Bialosky et al in 2009 [109] – which has been integrated in 2018 [92] - represents the most exhaustive and updated proposal currently available in the literature. According to the authors, the external force induced by spinal manipulation and transmitted across the biological tissues of the patients can trigger a cascade of responses with either a limited impact in terms of biomechanics but a more relevant neurophysiological effects on both the central nervous system and the peripheral nervous system. In fact, due to the inconsistency of the biomechanical model, the scientific community has dismissed this part of the above-mentioned interpretative approach by replacing it with rather more defined neurophysiological effects [92].

Spinal Manipulation Mechanisms

Biomechanical effect

The literature suggests that biomechanical effects of spinal manipulation seem to be able to increase the range of motion, along with a decrease in muscle spasm and a modification in the intradiscal pressure [83, 110–112]. Nonetheless, some critical issues may emerge and undermine this construction: the lack of long-term structural changes; physical therapists may not be able to detect the target spinal levels that require to be manipulated (*e.g.* low levels of inter- and intra-reliability) [101]; the heterogeneity between physiotherapists in applying the same forces on specific vertebral levels (*e.g.* PS is not predictable); a lack of difference of clinical outcomes by using specific techniques (*e.g.* different rationale in technique application); therapeutic responses far from the manipulated area (*e.g.* lumbar spine manipulation with modification of the lower limb symptoms) [109]. Therefore, the inconsistency of the biomechanical model has driven the scientific community to replace this specific part with a more defined neurophysiological effects [92].

Peripheral Neurophysiological Effect

Spinal manipulation has been shown to modify the concentrations of inflammatory mediators and peripheral nociceptors [109]. In fact, spinal manipulation compared to *sham manipulation* (*i.e*. a spinal manipulation without impulse) and to a control group has been shown to decrease cytokine levels in both blood and serum [113]. Further, a decrease of β-endorphins, as well as in the levels of AEA (Anandamide), N-palmitoylethanolamide, serotonin and endogenous opioids in the hematic levels [114, 115] has been also observed.

Spinal Neurophysiological Effect

The activity of the spinal cord has been also found to be influenced by spinal manipulation; hence, it determines a decrease in the activity of the dorsal horn of the spinal cord and influences neuromuscular activities [109]. Hypoalgesia has been also observed after spinal manipulation due to temporal summation changes and selective blockage of neurotransmitters [116–125]. Further parameters, such as afferent discharge [126–129], motoneuron pool activity [130] and muscular activity [131–133], have also shown significant changes this procedure.

Supra-spinal Neurophysiological Effect

The current literature suggests a neurophysiological supra-spinal effect that should influence the activity of the brain areas involved in the descending pain modulation (i.e. anterior cingulate cortex, amygdala, periaqueductal gray matter and rostral ventromedial medulla) [109, 134, 135]. Additionally, even the activity of other areas - *i.e.* sensorimotor cortex S1 and S2, cerebellum, insular cortex - seem to be also influenced by spinal manipulation [136].

A decrease in the combined activity of the cortex and brain areas assigned to sensory and affective discrimination (i.e. primary somatosensory cortex and the posterior insular cortex) and an increased activity between affective brain regions of the descending pain modulation (*i.e.* insular cortex, periaqueductal gray matter) [137] has been also observed after the application of a manipulative procedure. Supra-spinal neurophysiological responses also can change the somatosensory evoked potentials suggesting that the central nervous system is also involved after spinal manipulation [138–140]. Moreover, spinal manipulation has been shown to determine an opioid response [141], as well as autonomic responses, which have been observed as changes in skin temperature and conductance, peripheral blood flow, cortisol levels and heart rate [116, 142, 143].

Placebo Effect

Spinal manipulation has been shown to be influenced by psychosocial variables, patient's expectations, placebo mechanisms [144] and by the therapist features (e.g. specific intervention preferences). That is, although some neurophysiological effects - including mechanisms of pain modulation - following spinal manipulation seem to be not influenced by *placebo effect* [144], a number of contextual factors (*i.e*. expectation and therapeutic alliance) have been proved to be effective in the elicitation of *placebo effects* and they play a decisive role in the influence of specific clinical outcomes, *i.e.* pain, function and disability [145–147]. In order to obtain the best favourable outcomes, modern and informed therapist instead considering the *placebo effect* as a justification for ineffective intervention in itself (e.g. manual therapy technique) have to accept the *placebo effect* as part of the treatment itself. The placebo effects must be considered as an active (i.e. that can be managed by the therapist) component that can activate a modulation of endogenous pain [144].

Benefits of Spinal Manipulation

Cervical Spine Manipulation

The qualitative synthesis of the most recent Guidelines concluded that the use of spinal manipulation is weakly/moderately recommended in patients suffering of both recent and persistent neck pain and associated symptoms in the absence of objective physical signs and neck pain and associated symptoms in the presence of objective physical signs and without evidence of neurological involvement as a single intervention or combined with other treatments (i.e. exercise, counseling, education, etc.) [29, 148, 149]. That results are consistent with the Clinical Neck Pain Revised Guidelines recently updated by the American Physical Therapy Association (APTA) [150]. More specifically, spinal thrust manipulation seems to provide temporary fast pain relief compared to other intervention (i.e. mobilization) [29].

Moreover, the results emerging form this qualitative review show that spinal thrust manipulation delivery to the cervical spine is: moderately recommended for patient with persistent non-specific neck pain with mobility impairment and/or associated with headache; weakly/moderately recommended for those presenting with recent non-specific neck pain; and weakly recommended for non-specific neck-pain with radiating pain. It is also recommended to combine cervical thrust manipulation with other techniques (e.g. exercise, traction, dry needling, etc.) and/or apply the thrust manipulation to other spinal regions like the thoracic spine in order to achieve the best clinical outcome improvements in terms of pain and disability reduction with recent or persistent non-specific neck pain associated or not with headache and/or radiated pain to the upper extremity [28, 29, 149, 150].

Physiotherapist must choose the appropriate technique based on the patient's clinical presentation, patient's expectation, and clinical expertise. As the efficacy of spinal manipulation resulted to be similar to other therapeutic interventions, it is recommended to include this intervention in a multimodal approach, given the high cost-effectiveness ratio and the limited side effects [28, 29, 149, 150].

Thoracic Spine Manipulation

Thoracic pain is defined by the International Association for the Study of Pain (IASP) as pain perceived in the body region delimited at the top by a transversal line that crosses the spinous process of T1, inferiorly by a transversal line that crosses T12, and laterally by two vertical line that passes tangentially to the lateral edge of the erector spinae muscle [151].

There is a lack of specific guideline for the management of thoracic pain; however, the Australian Guideline on the management of acute spinal pain [152, 153] and a recent systematic review classify that disorder in four subgroups: recent non-specific mechanical thoracic pain; persistent non-specific mechanical thoracic pain; recent non-visceral chest pain; persistent non-visceral chest pain. Another subgroup to consider is the scoliosis group. Based on the qualitative analysis, the evidences recommend that thrust manipulation must be integrated in a multimodal program in association with other conservative interventions [152–156]. Although thoracic thrust manipulation is widely used for the treatment of neck disorders, there is no significant improvement in pain, pressure pain thresholds (PPT) and in patient satisfaction compared to placebo or other treatments in short and long term [152–156].

Moreover, there is a weak recommendation of spinal thrust manipulation in patient reporting recent non-specific mechanical thoracic pain. However, the authors underline the low-quality of the trials; that is, the studies included in the systematic review published by Southerst et al. [153] presents limitations and bias. Adequate and rigorous quality evidences are needed in order to report reliable results on this topic.

Lumbar Spine Manipulation

The most recent Cochrane Reviews on the effectiveness of spinal manipulation for the management of recent and persistent low back pain, with or without radiated pain to lower limb concluded that spinal manipulation is effective as much other conservative interventions (exercise, physiotherapy and medical usual care) [157, 158]. Notably, the randomized controlled trials included in this review included both non-thrust mobilization and thrust manipulation indistinctively. A recent systematic review with meta-analysis [49] that included only randomized controlled trials with spinal manipulation as the intervention (i.e. clearly declared not to be non-thrust mobilization) offered alone or in a multimodal regimen for the management of recent low back pain concluded that there are moderate quality evidences that lumbar spine thrust manipulation has a statistically significant association with pain reduction and function improvement up to six weeks from the treatment, despite the heterogeneity of the included trials (i.e. professional who applied the treatment, type of technique). Notably, no randomized controlled trial reported any serious adverse events. Only minor transient adverse events such as increased pain, muscle stiffness, and headache were reported 50% to 67% of the time in large case series of patients treated with spinal thrust manipulation.

Moreover, Coulter et al. [159] found that thrust manipulation significantly reduced pain and disability, compared to other active comparators including exercise and physical therapy following a subgroup analyses of the data. On the other hand, non-thrust mobilization interventions, as compared to other active comparators including exercise regimens, significantly reduced pain but not related-disability. The authors concluded that there is moderate-quality evidence that manipulative and mobilizative procedures are likely to reduce pain and improve function for patients with chronic low back pain; however, thrust manipulation appears to produce a larger effect compared to non-thrust mobilization.

Additionally, two recent systematic reviews [32, 33] support the use of spinal thrust manipulation in clinical practice as a cost-effective treatment when used alone or in combination with other treatments.

However, because the heterogeneity of the studies, there are still no answers to the question how the best treatment posology is, which health care professional (i.e. the rational of application) is more efficient and what type of patient will benefit more from lumbar spinal thrust manipulation treatment.

Limitations of the Study

The results of this study may not be generalizable to the middle and lower cervical, thoracic, upper and middle lumbar spine because of differences in the morphology and arthrokinematics of the zygapophyseal joints in these regions and the upper cervical spine, cervico-thoracic and lumbosacral junction. Furthermore, the results of our study cannot be generalized to other manual techniques that use different combinations of primary and secondary, physiologic or accessory component levers. One further limitation of this study is that only one practitioner administered all of the spinal manipulations; hence, it cannot be assumed that the individual and subtle nuances to technique delivery adopted with time and experience would be identical in other practitioners administering the same procedure. Future research should determine the vertebral level (or levels) at which the popping sounds are emanating from and investigate the clinical relevance of cavitation phenomenon following spinal manipulation in patients with spinal pain and associated disorders. In addition, future trials should investigate whether a relationship exists between the number of cavitation sounds and the degree of change in the clinical outcomes of pain and disability in these subgroups of patients.

Conclusions

The results of the current PhD thesis include the following conclusions:

1. The signal processing of recording the popping sound during spinal thrust manipulation by using a time-frequency analysis is a useful procedure that could assist in future studies.
2. A single spinal thrust manipulation applied to the cranio-cervical (C1-C2), cervico-thoracic (C7-T1) or lumbo-sacral (L5-S1) junction produces more than one single popping sound which is located ipsi- or contra-lateral to the targeted side in the same proportion, with a duration ranging from 2.69mm (lumbo-sacral junction) to 5.66ms (cranio-cervical junction).
3. The duration of the spinal manipulative procedure ranged from 60.77ms (cervico-thoracic junction) to 139.13ms (lumbo-sacral junction).
4. There were slightly differences in the duration and the location of popping sounds depending on the targeted area.

Understanding whether the PSs phenomenon during a spinal thrust manipulation is an ipsilateral, contralateral or bilateral event can help practitioners in selecting the appropriate technique that will most effectively target the symptomatic (*i.e.* not the dysfunctional for the limited reliability of the manual tests) joint with the ultimate aim of reducing pain and disability.

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