THE ROLE OF SUBLUXATION IN CHIROPRACTIC



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Anthony L. Rosner, Ph.D., LL.D.[Hon.]

FORWARD

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The concept of subluxation is a uniquely chiropractic contribution to healthcare. I am not referring to the general medical definition of "less than a luxation" but to the complex and complicated entity at the heart of chiropractic practice. In preparing this forward for this text I thought to go back in time and relate a personal story. It encapsulates where our profession was and where it has gone since.

I entered chiropractic college- at the then National College of Chiropractic- in 1976. Unlike many of my classmates, I had no exposure to chiropractic before I was accepted at NCC, and as it happens I fell into the profession. I had a conversation with my father, who was developing a radio promotion for a local chiropractor in Pontiac, MI. My dad gave me the materials the chiropractor had provided him- a catalogue from NCC among them. I read over the book, saw all the medical terms therein, and decided to apply along with my other applications to dental school, master's degree programs and so on. Several weeks later I received my acceptance letter.

Not knowing anything about the profession, I went to our local library in Oak Park, MI. I found one book- In the Public Interest: The Case Against Chiropractic. I did not know it was piece of anti-chiropractic propaganda, but the stories it told were appalling. What had I gotten myself into?

One of the charges against the profession, as brought up in that book, related to subluxation, for which the argument was made that chiropractors were looking for a nonexistent entity and even if that entity did exist, it could not lead to the effects claimed for it.

This was notwithstanding the fact that good research already did exist. Research published by our profession in, as one example, the Annals of the Swiss Chiropractic Society had already been published, and early pioneers such as Henri Gillet had begun to investigate the effects of subluxation. This was developed further by other early researchers and practitioners, including L. John Faye and Akio Sato. Thus, we had research that looked at the mechanical impact of subluxation (Gillet and Faye) as well as its neurological impact (Sato, who focused on the effects of subluxation on viscerosomatic and somatovisceral reflex traffic). And the creation of our own journals, such as the Journal of Manipulative and Physiological Therapeutics, which I was privileged to edit for nearly two decades, provided us vehicles for publishing this work.

When I look at the contents of this text, I am reminded of all the hard work that was done behind the scenes of what you read here. What you read in the text represents thousands of person-hours of elegant research. We had our early researchers- chiropractors who went and earned academic doctorates in addition to their clinical degrees. I think of Reed Phillips, John Triano and Cheryl Hawk. We had our polymaths, with three academic degrees- Scott Haldeman and Rand Swenson and Paul Bishop. All of them were, and are, working to better define subluxation, by examining how it affects mechanoreceptors, impacts the spinal cord and brainstem, and so much more.

From those heady days in the early 1980s, we have seen a growing number of chiropractors earn academic doctorates and continue researching the effects of subluxation. As a result, subluxation has continually evolved and our understanding of it has expanded. Heidi Haavik has studied neuroplasticity related to subluxation. Steven Injeyan has looked at cytokine activation. We have our current research leaders- Dr. Christine Goertz, Dr. Cindy Long, Dr. Katie Pohlman, all of whom have demonstrated leadership at the national/political level, in the larger biomedical research world and in understanding the nature of adverse events professionally and globally. Clinical trials exist not only for low back pain and neck pain, but for conditions such as asthma and hypertension. Basic science has looked at how neurons process and regulate mechanical input; see the work of Joel Pickar.

I can easily name many more, but there is a point here. It is that the dedicated work of our colleagues, done at great expense and over long periods of time, have led us to where we can capture all the intricacies and nuances related to how our profession views subluxation.

That is the purpose of this book. It is deeply informative and deeply researched. And it is testament to our profession to see how deep that understanding goes.

THE ROLE OF SUBLUXATION IN CHIROPRACTIC, v.2.0 Anthony L. Rosner, Ph.D., LL.D. [Hon.] Version 9: ROSNER'S FINAL REVIEW + PERMISSIONS + ACKNOWLEDGEMENTS

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GLOSSARY

101	
ACA	American Chiropractic Association, Australian Chiropractic Association
ACC	Association of Chiropractic Colleges
AK	Applied kinesiology
APB	Abductor pollicis brevis
ARCS	Academy for Research in the Chiropractic Sciences
ASMT	Activator spinal manipulative thrust
BS	Bachelor of Science
CBI	Cerebellar inhibition
CCA	Canadian Chiropractic Association
CCD	Chronic compression of dorsal root ganglia
CCE	Council on Chiropractic Education
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CMS	Centers for Medicare & Medicaid Services
CNS	Central nervous system
CRP	C-reactive protein
CSC	Chiropractic subluxation complex
CSMC	Central segmental motor control
CTS	Carpal tunnel syndrome
CST	Craniosacral therapy
CVS	Congenital vertebral synostosis
DAC	Distinguished Advisory Council
DC	Doctor of Chiropractic
DRG	Dorsal root ganglia
ECU	European Chiropractic Union
EEG	Electroencephalography
FCLB	Federation of Chiropractic Licensing Boards
fMRI	Functional magnetic resonance imaging
FN	Functional neurology
FVS	Foundation for Vertebral Subluxation
GABA	
GABA	Gamma amino butyric acid
	General Chiropractic Council Hoffman reflex
H-reflex	
HPA	Hypothalamic-pituitary-adrenal
HVLAT	High-velocity low-amplitude thrust
IAF	Institute for Alternative Futures
ICA	International Chiropractors Association
ICEC	International Chiropractic Education Collaboration
ICL	Index to Chiropractic Literature
IFCO	International Federation of Chiropractors & Organizations
IL-10	Interleukin-10
IL-1β	Interleukin-1-beta
IL-6	Interleukin-6
LBP	Low back pain
MANTIS	Manual Alternative and Natural Therapy Index System
MAP	Mean arterial blood pressure
MCRP	Movement related cortical potential
MEP	Motor evoked potential
MRI	Magnetic resonance imaging
mRS	Modified Rankin Scale
MS	Master of Science
MVC	Maximum voluntary contraction
NBCE	National Board of Chiropractic Examiners
NBF	Nerve blood flow

NET	Neuro Emotional Technique
NMDA	N-methyl D-aspartate
NZA	New Zealand Chiropractic Association
PEDro	Physiotherapy Evidence Database
РКСу	Protein kinase y
PLI	Phase lag index
PNI	Psychoneuroimmunology
sEMG	Surface electromyography
SEP	Somatosensory evoked potential
SHM	Sham manipulation
SMT	Spinal manipulative treatment
SCNP	Subclinical neck pain
SST	Sit-to-Stand Test
ТА	Tibialis anterior brevis
TENS	Transcutaneous electrical nerve stimulation
TUG	Time Up and Go
TMS	Transcranial magnetic stimulation
TNF-a	Tumor necrosis factor alpha
VC	Venepuncture
VSC	Vertebral subluxation complex
WFC	World Federation of Chiropractic
WHO	World Health Organization

Mobilization: Movement applied singularly or repetitively or at the physiologic range of joint motion, without imparting a thrust or impulse, with the goal of restoring joint mobility.¹

Manipulation: Manual procedure that involves a directed thrust to move a joint past the physiologic range of motion, without exceeding the anatomic limit.¹

Adjustment: Any chiropractic procedure that utilizes controlled force, leverage, direction, amplitude, and velocity and which is directed at specific joints or anatomic regions. Chiropractors commonly use such procedures to influence joint and neurophysiological function.¹

A cohort participating in a workshop at the National Institutes of Health in February 1975 discovered that the term "subluxation" lacked the same meaning for all ascribed functions, opening the door to misunderstandings, debate, and rancor—even among chiropractors. This finding made it evident that there existed a paucity of chiropractic research.² Although there have been multiple attempts at using synonyms and substitutions to redefine the subluxation to improve communications, acceptance of the chiropractic concept of the subluxation has required more consistency and clarity.

Gatterman identified over 100 synonyms for subluxation.¹ Researchers and historians have noted that the term has become "overburdened with clinical, political, and philosophical meaning and significance for chiropractors, that the concept that once helped to hold a young, besieged profession together"³ now became a point of contention.¹ Rome has gone a step further, identifying just under 300 alternatives to subluxation cited in the literature, ranging from "Aberrant Motion" to "Zygapophyseal Pathophysiology."⁴ The diversity of historical perspectives is further amplified in Peters' historical perspective.⁵

"Extraordinary claims require extraordinary evidence" is a phrase popularized by the astronomer Carl Sagan.⁶ This would apply to the chiropractic subluxation. Through its evolving conceptualizations for over a century, the subluxation remains a matter of dispute and division within the ranks of all healthcare providers, including chiropractors. **This monograph aims to review the literature that has defined the chiropractic subluxation and to place it in a perspective than can be accepted by a broader collection of healthcare providers, government agencies, payers, and the public. This will be accomplished with documentation as to how the subluxation is manifested with the presentation of credible biomechanical, physiological, and clinical evidence. More significantly, these experimental findings will suggest a remarkable consistency with D.D. Palmer's original use of the term "tone," which was grounded in physiology with such attributes as "neural tension," "sub-clinical symptoms," "a cause-and-effect model for chiropractic," and "a moral ethic for improving public health" during chiropractic's 128-year history.**

Yet a recent definitive review of Palmer's teachings and its interpretation indicates that the importance of "tone as the founding principle of health in chiropractic began to wane from around 1903, and by 1961—the end point of this investigation— was of limited interest to chiropractic [italics mine]." ⁷ Thus, this monograph's emphasis upon neurological manifestations and their reversal by interventions within the scope of chiropractic brings this entire discussion back to what may be considered the epicenter of chiropractic which had been apparently diminished through the passage of time. A major part of this epicenter is the subluxation, at this time not assigned a definitive anatomical location but rather a disruption that lies at one end of the spectrum of neural derangements that may or may not be expressed in patient complaints.

1.0 THE SUBLUXATION HISTORY

1.1. General and Medical History

In Greek, the roots of the term subluxation sub and lux describe "less than a dislocation." The first naming of subluxation and luxation originated circa 400 years BC, appearing in part 61 of Peri Arthron in the Corpus Hippocrateum:⁸

In a word, luxations and subluxations take place in different degrees, being sometimes greater and sometimes less, and those cases in which the bone has slipped or been displaced to a much greater extent, are in general more difficult to rectify than otherwise, and if not reduced, such cases have greater and more striking impairment and lesions of bones, fleshy parts, and attitudes, but when the bone has slipped, or been displaced to a less extent, it is easier to reduce such cases than the other.

During the Renaissance in 1582, a prominent surgeon Ambroise Pare devoted a chapter on vertebral dislocation based on Hippocrates' approach.⁹ By 1746, it was Hieronymus who wrote:¹⁰

Subluxation of joints is recognized by lessened motion of the joints, by slight change in position of the articulating bones and pain.

This definition partially agrees with the medical terminology, which describes subluxation as a location where a connecting bone is partially out of the joint. A luxation, on the other hand, is understood to be a complete dislocation.¹¹ (However, this is only a static component to this definition, whereas chiropractors describe both static and dynamic components to the subluxation.) Indeed, Harrison in 1821 was a visionary when he added the concept of a series of aberrant nerve signals originating from a subluxation:¹²

When any of the vertebrae become displaced or too prominent, the patient experiences inconvenience from a local derangement in the nerves of the part. He, in consequence, is tormented with a train of nervous systems, which are as obscure in their origin as they are stubborn in their nature.

He went on in 1824 to agree with Hieronymus that there was aberrant motion at the site of a subluxation:¹³

The articular motions are imperfectly performed, because the surface of the bones do not fully correspond.

Specifically relating to vertebral subluxations, a fellow at the Royal College of Surgeons in England described how subluxated vertebral segments cause aberrant nerve conduction at the foramen which can impact the organs and muscles throughout the body.¹⁴

Every organ and muscle in the body is dependent, more or less upon nerves...one or two of the vertebrae may be pressing injuriously upon either the anterior or the posterior root of some nerve. When one vertebra forms a slight exception in the regularity of the spinal line, either by height or distance from its fellows, a serious train of nervous symptoms may supervene...if any organ is deficiently supplied with nervous energy or blood, is immediately, and sooner or later its structure becomes deranged...various branches that arise from the sixth, seventh, and eighth dorsal ganglia...become irritated by contact, or sympathy with disease, in the notches through which the nerves pass out of the vertebrae.

1.2. Chiropractic History

Although subluxation refers to any displaced anatomic body part in most medical applications, D.D. Palmer echoed Edward Harrison and J. Evans Riadore by emphasizing the nervous system (which the medical definition omits) and focusing exclusively on subluxations of the spine and the implications on pain and end-organ function. In 1903, over half a century later, while teaching and practicing in Santa Barbara, California, D.D. Palmer taught that misaligned (subluxated) vertebral segments could compress the nerve roots exiting through the vertebral foramina,¹⁵ replicating Riadore's treatise.¹⁴ Palmer hypothesized that any pressure on the nerves would produce excessive neural impulses reaching the end-organs, causing them to become inflamed. Interestingly, this inflammation hypothesis was a revisiting of Palmer's original concept in 1902¹⁶ that the

displacement or altered position of vertebrae and associated arteries, veins, nerves, muscles, and ligaments was the source of the end-organ inflammation.

These sequelae are where Palmer departed from the original medical definition; the vertebral subluxation was now considered capable of generating many disease states.¹⁷ D.D. Palmer's son, B.J., broadcast this notion in antiquated and inaccurate terms as the "foot-on-the-hose" theory,¹⁸ falsely assuming intervertebral foraminal encroachment in all vertebral subluxations. He also avoided mention of D.D. Palmer's concept of tone.⁷

The term chiropractic originates from the word "chiro" to describe the hand and the Greek "praktikos" to describe practical). D.D. Palmer taught that the "practical hands"¹⁹ could find the aberrant motions in the spine from vertebral subluxations and adjust them to their proper position, thus relieving end-organ inflammation.

The writings of Willard Carver paralleled Palmer's thinking that "dis-ease"[sic] meant abnormal function. Thus, removing the cause of nervous system irritation would allow normal physiological processes to resume.²⁰

After reiterations in 1927 by Ralph W. Stephenson,^{21, 22} B.J. Palmer further circumscribed the subluxation definition in 1934 by stating: ²³

The hour has arrived when a distinction must be made between a misalignment that IS a subluxation, and a misalignment which is ONLY a misalignment; between a SUBLUXATION which IS occluding the foramen, producing pressure upon nerves, and does interfere with local as well as a multiplicity of transmissions having various exits below itself and some vertebra which is out of alignment in a relationship with ones above and below, but does not and is not occluding a foramen, producing pressures upon nerves, and is not the source of interference with transmission because thereof.

Up to this point, critical characteristics of the vertebral subluxation as illustrated in Figure 1 include one or more of the following: (i) vertebral displacement, (ii) nerve impingement, and (iii) disc collapse or displacement.

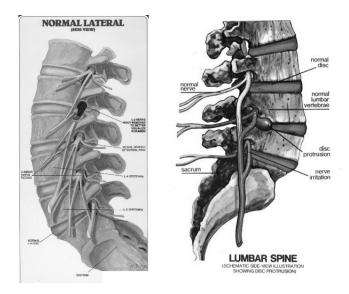


FIGURE 1: Characteristics of the vertebral subluxation. Left: Normal; Right: With subluxations.

Fred Illi, a prominent chiropractic researcher in the first half of the 20th century, emphasized that the transformation to an erect posture in humans produced immense stresses upon the highly circumscribed mobility of the sacroiliac joints²⁴ Ili opined that this produced a subluxation when the articular surfaces of either sacroiliac joint became misaligned.²⁵

Janse (1947) further refined the concept by adding that the critical aspect of a subluxation was that the vertebra became relatively fixed in an abnormal position, no longer participating in the normal movement of the spine. Vertebrae that possess normal mobility, on the other hand, were not regarded as subluxated.²⁶ Consequently, curing diseases thought to be caused by the presence of vertebral subluxations converted rigid segments into moveable ones.²⁵

The concept of hypomobility, introduced in 1906,27 was invigorated in 1952 by Henry Gillet of Belgium. Gillet determined that the term "fixation" was more accurate than "subluxation" to describe the clinical phenomenon addressed by chiropractors. For the same reason, Gillet did not consider fixation an entirely accurate term, since vertebrae are generally not fixed or ankylosed to each other. Instead, Gillet described a mobility reduction produced by varying degrees of dysfunction of the articular soft tissue.²⁸

In 1976, osteopath Irwin Korr expanded the subluxation concept. His model included neural or reflex aberrations resulting from vertebral segment deep tissue derangements. He suggested that both somatic and visceral spinal reflexes were plastic, continually changing, and subject to continual modulation and adjustment in force, velocity, amplitude, trajectory, and final configuration. He noted that neuronal recruitment depends on the activity and destination of a nerve, regardless of the intervertebral foramen. Clinically facilitated spinal segments have neuronal excitation and conduction disturbances in afferent input. Causes of nerve conduction disturbances can be physical or chemical. Nerve compression or stretching are physical alterations, whereas chemical changes may involve the presence of inflammatory cytokines or alternations in neurotransmitters. Korr's insight includes the possibility of central excitatory sensitization in the presence of vertebral subluxations. Central sensitization goes beyond the earlier, more straightforward concept of nerve compression.²⁹

Sandoz (1989) pointed out that the term subluxation was gathering more and more all-encompassing connotations. The word became applicable to any derangement of the spine's primary functions (static, dynamic and nervous system protection).^{30, 31}

In a prescient observation in 1962, A.E. Homewood declared that:³²

Toxaemia has the less dramatic effect of making the patient more pain sensitive than usual. Pottenger has illustrated the increased susceptibility of the patient with lung or intestinal disease to viscerosensory reflexes, or referred pain, in the presence of toxaemia. The same may be said for the patient with a somatic disturbance, such as arthritis, sprains or subluxations. Considering the latter, it may be appreciated that many people have subluxations of vertebral segments without conscious awareness of the structural problem until toxaemia, or other modifying influences, reduce the synaptic resistance of the neural pathways to that degree necessary for the transmission of neural impulses from the locus of distortion to the higher brain centre, the postcentral gyrus of the cerebral cortex, where the stream of impulses are interpreted as pain or discomfort...

Ronald Gitelman offered a strikingly forward-looking outlook in 1974. He described the psychosocial elements involved in the pain experience and when a "subluxation" if present.³³

Pain is not merely the stimulation of receptors...that stimulus enters a nervous system that is already a total of past experience, trauma, anxiety, cultural factors, etc. These higher processes, these past experiences, and the state of the nervous system at the time of stimulus participate in the selection, abstraction and synthesis of information from the total sensory input.

While much of the preceding historical perspective has been presented in comprehensive reviews by Peters⁵ and Senzon,³⁴⁻³⁸ subluxations also became known through an additional lens known as the subluxation complex.

1.3. The Subluxation Complex

Given the increasing layers of detail piled onto the definitions of the chiropractic subluxation through the years, it seemed almost inevitable that numerous concepts would be advanced that involved additional tissues, giving rise to the term subluxation complex.

Introduced in 1980 by Ralph Gregory, the term "vertebral subluxation complex" (VSC) acknowledged the connective tissues associated with the misaligned joint.39, 40 It was Leonard Faye, however, who first described the VSC in 1981 as a complex with five distinct components which married the biomechanical, neurobiological, pathological, musculoskeletal, inflammatory, and stress responses into a single model.⁴¹

What was significant in Faye's model is that it recognized that such muscle changes as spasms, hypertrophy,

atrophy, and degeneration as well as inflammatory responses could be based on stress syndromes as articulated by Selye.⁴² There was not a simple relationship between a spinal nerve and the organ, but far more indirect routes involving physical, mental, and chemical causes, producing the numerous and previously unexplained effects of stress. This model provided a rational explanation for both clinicians and patients which instilled new confidence and hope for clinical improvement.⁴²

Adding to Faye's model was what Robert Dishman termed the CSC—the chiropractic subluxation complex. It emphasized the neuropathophysiological component, combining descriptions of the osteopathic lesion and chiropractic subluxation as representative of a "facilitated segment of the spine maintained by endogenous impulses entering the corresponding dorsal root." This concept suggests that the spinal cord was hyperexcitable at the CSC level and could become more excitable through the numerous reflex systems. Clinical interventions, therefore, needed to take into account lowered excitatory thresholds in the presence of a CSC.⁴³ Charles "Skip" Lantz, who earned a Ph.D. in pharmacology, emphasized biochemical changes related to biomechanical and functional properties of the connective tissues related to every component of joint degeneration associated with reduced joint mobility. Lantz noted that over time, the effects of inflammation and connective tissues changes became more apparent as the degeneration progressed. He also began identifying neurological involvement associated with facet degeneration, which led to a better understanding and description of the concept of the VSC. Indeed, this is precisely the evidence that emerged in the years to follow and which will be described in detail below. This theory was also the essence of the VSC as envisioned by Lantz.⁴⁴

Subsequently in 1989, Lantz proposed an 8-component model to supersede the 5-part VSC model, including such functional components as the inflammatory response, vascular abnormalities, and tissue-level disruptions.⁴⁵ It was evident that the complexity of subluxation models was increasing exponentially. This complexity was considered unruly by some, resulting in calls for consensus and research. Accordingly, each of the latter two topics are discussed in Sections 1.5 and 4.0 below.

1.4. The Osteopathic Equivalent

Osteopathic medicine bears numerous similarities to chiropractic, so it is not surprising that the Glossary of Osteopathic Terminology (2017) has provided a definition of somatic dysfunction that could be interpreted as a variation of the vertebral subluxation complex:⁴⁶

Somatic dysfunction: Impaired or altered function of related components of the body framework system: skeletal arthrodial and myofascial structures, and their related vascular, lymphatic and neural elements. It is characterized by positional asymmetry, restricted range of motion, tissue texture abnormalities, and/or tenderness. The positional and motion aspects of somatic dysfunction are generally described by: (1) The position of the body part as determined by palpation and referenced to its defined adjacent structure, (2) The directions in which motion is freer, and (3) The direction on which motion is restricted. Somatic dysfunction is treatable using osteopathic manipulative treatment.

In its infancy, the osteopathic lesion as conceived by Still emphasized how disorders of the vital body fluids (blood, lymph, cerebrospinal fluid) could occur. Therefore, diseases were considered to result from anatomical abnormalities that led to physiologic impairments. Obstructions of the body fluids or disruptions of their neural control centers, called lesions, would lead to flow disturbances. Osteopathic manipulative treatments rather than pharmaceutical drugs could correct these lesions.⁴⁷ The parallels to the chiropractic concept of the subluxation are evident.

1.5. Consensus Processes

In the effort to develop more unified conceptions of the subluxation, consensus processes began to appear in the 1960s and 1970s. By 1984, a research symposium of chiropractic scholars convened in St. Louis⁴⁸ and given the charge by Moderator John Stiga to "[seek] a common, universal language, one that we can share with engineers, orthopedic surgeons, and so on so as to open lines of communication." [Historically, this has been the primary challenge: to arrive at an evidence-based, yet transparent definition of subluxation.] The Distinguished Advisory Council (DAC) of the Academy for Research in the Chiropractic Sciences (ARCS) representing several techniques and philosophies concluded with a unique definition that was not to be heard from again:⁴⁸

A subluxation is any relative malposition of a joint that produces consistent misalignment of its articular surfaces...A subluxation's physical definition is the distance a vertebral unit or units are displaced from their zero or optimum position or origin, multiplied by the amount of resistance that holds it displaced."

A 3-year consensus process organized by Meridel Gatterman and sponsored by the Consortium for Chiropractic Research convened an international panel of 60 representative educators and researchers. The consensus produced over 80% agreement on every one of the ten terms,⁴⁹ as shown in Table 1:

Table 1: Agreement and Definitions of 10 Terms Proposed at the 1991 Conference on Research and Education³⁴

Delphi Panel Agreement	Definition
88%	Motion segment: A functional unit made up of the two adjacent articulating surfaces and the connecting tissues binding them together.
83%	Spinal motion segment: Two adjacent vertebrae and the connecting tissues binding them to each other.
84%	Subluxation: A motion segment, in which alignment, movement integrity and/or physiological function are altered although contact between joint surfaces remains intact.
81 %	Manipulable subluxation: A subluxation in which altered alignment, movement and/or function can be improved by manual thrust procedures.
82 %	Subluxation complex: A theoretical model of motion segment dysfunction (subluxation) which incorporates the complex interaction of pathological changes in nerve, muscle, ligamentous, vascular, and connective tissues.
83%	Subluxation syndrome: An aggregate of signs and symptoms that relate to pathophysiology or dysfunction of spinal and pelvic motion segments or to peripheral joints.
91 %	Manual therapy: Procedures by which the hands directly contract the body to treat the articulations and/or soft tissue.
91 %	Manipulation: A manual procedure that involves a directed thrust to move a joint past the physiological range of motion, without exceeding the anatomical limit.
88%	Mobilization: Movement applied singularly or repetitively within or at the physiological range of joint motion, without imparting a thrust or impulse with the goal of restoring joint mobility.
87%	Adjustment: Any chiropractic therapeutic procedure that utilizes controlled force, leverage, direction, amplitude, and velocity which is directed at specific joints or anatomical regions. Chiropractors commonly use such procedures to influence joint and neurophysiological function.

By no means did this panel put an end to discussions as to what chiropractic subluxation could mean. Leach, for example, pointed out that the definition lacked the tenet originally conceived by Palmer that the subluxation could affect organ function and general health.⁵⁰ Nor was the radiographic question resolved, since some believed that even if a misalignment was visible on a plain film radiograph, there could be excessive motion in the compromised joint, such that manipulation was contraindicated. At the other pole of this dilemma was the fact that subluxation might not be visible by conventional radiography. Accordingly, as of January 1, 2000, Medicare stopped requiring an x-ray to demonstrate a subluxation so long as there was documentation of two of the four criteria of (i) pain/tenderness, (ii) asymmetry/misalignment, (iii) range of motion abnormality, and (iv) tissue tone, texture, and temperature abnormality.

Although Medicare still allowed practitioners to use radiography to document a subluxation, these services were not reimbursable.⁵¹ This stipulation was surprising because radiographic visualization of a subluxation had been the initial requirement for treatment by chiropractors under the United States Medicare and Medicaid Acts, yet the procedure itself was not initially reimbursable.¹

Further consensus processes attempted to resolve diverging opinions and divisions within the chiropractic profession, to say nothing of attempting to convey a unified message to the world outside of chiropractic. One such example was a definition of the subluxation conceived by the Association of Chiropractic Colleges in July 1996 that collapsed earlier models into a simple statement that provided legal and legislative "wiggle room" but lacked the detail and precision needed to inform rigorous research:⁵²

Chiropractic is concerned with the preservations and restoration of health, and focuses particular attention on the subluxation. A subluxation is a complex of functional and/or structural and/or pathological changes that compromise neural integrity and may influence organ system's function and general health. A subluxation is evaluated, diagnosed, and managed through the use of chiropractic procedures based on the best available rational and empirical evidence.

The emergence of research in the structural, neurological, and biochemical fields created an impression that concentrating the discussion exclusively on the spine could be a liability. In contrast, the neurological implications emerging from research data demanded amplification. The result was the Fourth Edition of the Clinical Practice Guidelines issued by the Council on Chiropractic Practice in 2013:⁵³

Subluxation is a neurological imbalance or distortion in the body associated with adverse physiological responses and/or structural changes, which may become persistent or progressive. The most frequent site for the chiropractic correction of the subluxation is via the vertebral column.

2. IMPEDIMENTS TO COMMON CHIROPRACTIC DEFINITIONS

Like many entities with public exposure, subluxation has been interpreted widely by varying chiropractic institutions and associations to the point of crossing the boundary between the scientific and political/legal realms. It has even been touted as a marketing tool. Other institutions have abandoned the term entirely, not mentioning subluxation in their curricula (ex., Southern California University of Health Sciences, Canadian Memorial Chiropractic College, National University of Health Sciences),⁵⁴ resorting to politically neutral terms such as "articular lesion.⁵²" The inconsistent use has led to confusion and division within the chiropractic community, such that the message becomes blurred and even contentious. According to the chiropractor Craig Nelson, "there have been several efforts and projects devoted to redefining subluxations...this movement has not brought clarity and consensus to the subluxation debate but rather obfuscation and confusion." Nelson raises questions that speak to the importance of establishing a viable nexus between the basic science and the subluxation:"⁵⁵

1. How does the anatomy of the spine relate to subluxations?

2. What specific neurologic changes characterize subluxations?

This monograph would add:

3. What biochemical changes are characteristic of subluxations?

What makes the problem even more compounding is the development of scores of chiropractic techniques over the years. The list compiled by Bergmann (2005) revealed that there was no indication of displacement of techniques in favor of newer ones.⁵⁶ Rather, the terms "patient-centered care" and "precision medicine" have come into vogue. By recognizing the individual under treatment, Cooperstein and Glaberzon have argued that the list of definitions of subluxation should grow as well. They argued that "any meaningful usages should derive from the real world of chiropractic clinical practice." Accordingly, they suggested that a Linnaean taxonomy of subluxation-equivalents should be established by identifying the primary characteristics of patient presentation and technique into which more specialized concepts of the subluxation might be assigned, removing ideological elements in favor of the context of actual practice.⁵⁷

To bring these speculations to a head, it is imperative to assess the current evidence from the basic and clinical sciences to arrive at a contemporary conception of the subluxation. It will become evident that there will be a shift in how the subluxation is viewed. To proceed, it is necessary first to review some aspects of inflammation, shown herein to be a central component of the vertebral subluxation.

3.0 INFLAMMATION

3.1. Purpose and Mechanism

Inflammation has become more and more associated with the effects of subluxation. As discussed below, several reports identify the abatement of inflammation, its associated pain, and its markers as an indication of correcting the subluxation. And the relief of pain, often resulting from an underlying inflammatory condition, is the most common reason patients seek chiropractic care.⁵⁸

The inflammatory response is the innate characteristic of the immune system's reaction to harmful stimuli, such as pathogens, toxic compounds, irradiation, or damaged cells.⁵⁹ The inflammatory response removes injurious stimuli and initiates the healing process,⁶⁰ thus considered a vital defense mechanism.⁶¹ The mitigation process is designed to restore tissue homeostasis and resolution of the acute stage of inflammation. However, uncontrolled acute inflammation may worsen, contributing to a variety of chronic inflammatory diseases.⁶² While bacteria, viruses, and other microorganisms are known as infectious factors triggering inflammation, a wide variety of non-infectious factors shown in Table 2 are responsible and play a significant role in enlarging the discussion of what might be involved in a subluxation.

Classification	Specific Factors
Physical	 Burn Frostbite Physical injury Foreign bodies Ionizing radiation
Chemical	 Glucose Fatty acids Toxins Alcohol Chemical irritants (e.g. fluoride, nickel, other trace elements).
Biological	Damaged cells
Psychological	• Excitement (stress)

To summarize, common mechanisms of the inflammatory response involve (i) the recognition of detrimental stimuli by cell surface receptors, (ii) the activation of inflammatory pathways, (iii) the release of inflammatory markers, and (iv) the recruitment of inflammatory cells. Briefly, inflammatory stimuli activate intracellular signaling pathways that subsequently activate the production of inflammatory mediators. Primary inflammatory stimuli include the cytokines interleukin-1 β (IL- β), interleukin-6 (IL-6), and tumor necrosis factor α (TNF- α).

3.2. The Cytokines

Discussions of inflammation and pain invariably involve the cytokines. These are proteins which generate an inflammatory process that can be both beneficial (driving protective immunity) or detrimental (such as the induction of immunopathology). They were first identified in 1957^{64} and number more than 90. The cytokine tumor necrosis factor alpha (TNF- α) is a crucial modulator of systemic inflammation and a key regulator of the cytokine network.⁶⁵ TNF- α is also prominent in activating prostaglandins and other agents producing neuroexcitation and pain perception.⁶⁶ Indeed, TNF- α has been recognized as a primary mediator of pain.⁶⁷ Interleukin-1 beta (IL-1 β) as another cytokine is a crucial mediator of the inflammatory response, capable of

exacerbating damage during chronic disease and acute tissue injury. Overproduction of IL-1 β is implicated in the pathophysiological changes that occur during a variety of disease states.⁶⁸⁻⁷⁰

One additional cytokine, interleukin-6, lies at the top of the inflammatory chain and is a central mediator of the immune system. Specific autoimmune responses linked to IL-6 include experimental autoimmune encephalomyelitis,⁷¹ collagen-induced arthritis,^{72, 73} and experimental autoimmune myocarditis..⁷⁴ The inflammatory capability of IL-6 has been closely linked to colitis,^{75, 76} Crohn's disease,^{75, 77} rheumatoid arthritis,⁷⁸ psoriasis,⁷⁹ and several forms of cancer.⁸⁰ Serum IL-6 levels have been correlated with the clinical course of adults with hematologic malignancies.⁸¹

Interleukin-10 (IL-10), on the other hand, is a potent anti-inflammatory immunosuppressive cytokine with a broad range of effects both directly and indirectly on innate and adaptive immunity.⁸² It inhibits proinflammatory cytokine responses⁸³ by activated macrophages.⁸⁴ Accordingly, responses of these four cytokines to spinal manipulation become a matter of interest in controlling pain and may shed light upon defining the subluxation.

4.0. THE EVIDENCE

4.1. The Basic Sciences: Animal Models

Animal models are advantageous for inducing subluxation-like conditions and demonstrate biomechanical and physiological conditions that might approach what could occur in humans. There are both mechanical and chemical means by which a subluxation can be initiated. The outcomes help to arrive at a more precise concept of what the subluxation might be.

4.1.1. Mechanical intervention, structural/anatomical outcomes

The mechanical approach would produce a fixation between adjacent vertebral joints in an animal model. In the rat model, one elegant strategy was to immobilize three contiguous lumbar segments L4-L6 with a specially engineered vertebral fixation device. The rat has six lumbar vertebrae. The fixation links were maintained for 1, 4, or 8 weeks compared to unlinked controls. The vertebral fixation devices were implanted in a neutral, flexed, or rotated configuration (Figure 2). Subgroups of animals were examined for mechanical (stiffness)⁸⁵, physical (arthritic degeneration)^{86, 87} and neurological (cord synapse morphology)⁸⁸ effects 1, 2, 4, 6 or 12 weeks after the links were removed in each of the three fixation link periods. The physical effects assessed were (i) degenerative changes in the vertebral bodies and intervertebral discs, (ii) formation of osteophytes in the zygapophyseal joints, and (iii) degeneration of the articular surfaces of the zygapophyseal joints, and (iv) changes in spinal cord synapse density and morphology.



FIGURE 2: Link configurations: $A = \text{control rat: implanted but unlinked; } B = \text{linked in neutral configuration; } C = \text{linked in rotation: initially linked as in neutral configuration (B) and then middle L5 stem (arrow) was forced into rotation relative to the two outer stems. This figure was reprinted with permission from JMPT.$

As expected, more extended link periods (1, 4, or 8 weeks) were associated with incrementally greater stiffness, joint degeneration, and synapse morphology changes. However, most interesting, these changes continued to progress after the fixation devices were unlinked, with more significant changes occurring with more extended unlinked periods (up to 17 weeks, the most prolonged unlinked period evaluated). This suggests that intervertebral hypomobility induces progressive, chronic changes in spine stiffness, joint degeneration, and spinal cord synapse morphology.^{88, 89}

The spinal cord synapse changes are consistent with increased synaptic activity in the superficial dorsal horn with lumbar spine hypomobility, supporting the long-held chiropractic theory that vertebral subluxations produce chronic neurological changes.^{90, 91}

These observations proved a mimic as to what traditional spinal subluxation models provided, in that both fixation and misalignment of spinal segments in this animal model produced residual degenerative changes on spinal articular surfaces, osteophyte formation, and residual spinal stiffness and misalignment—even after the fixation links were removed. The progressive effects after link removal provided a model by which acute effects could become chronic. Overall, this model gives an important glimpse into how both earlier concepts of subluxation (hypomobility and misalignment) could produce degenerative changes over time.⁸⁵ It is understood that human studies are needed to examine the subluxation model further, as will be discussed below.

4.1.2. Mechanical intervention, neurophysiological outcomes

Sympathetic nervous system responses to mechanical stress of the spinal column in rats were documented as early as 1984, when Sato and Swenson applied forces from 0.5 to 3.0 kg to the spinal segments T10 to T13 and L4 to L7. Stimulation of the thoracic or lumbar region produced significant decreases in blood pressure and a slight reduction in the heart rate. In addition, significant and immediate decreases were found in renal nerve activity. The responses generally outlasted the stimulus. Cutting dorsal sensory roots T10 to L2 abolished the response to lower lumbar stimulation. The authors concluded that the observed responses were not due to spinal cord compression but were due to afferent fiber mediated reflexes.⁹²

Beyond the spine, Sato and his colleagues extensively elucidated the effects of noxious or non-noxious mechanical stimulation of various cutaneous areas on cerebral blood flow in the hippocampus in anesthetized rats. Noxious (pinching) stimulation increased local and systemic blood flow, while non-noxious stimulation (brushing) had no such effect. If the spinal cord was transected at T1, a forepaw pinch caused no change in blood pressure but still increased hippocampal blood flow.⁹³ Sato extensively demonstrated somato-gastrointestinal, somato-vesical, somato-cardiac, somato-adrenal medullary, and somato-immune reflexes in a rat model elsewhere.⁹⁴

In a medical textbook, Sato spelled out the connection of spinal manipulation to findings that could be used as indirect probes to the properties of the chiropractic subluxation:⁹⁵

The elucidation of the neural mechanisms of somatically induced autonomic reflex responses, usually called somato-autonomic reflexes, is, however, essential to developing a truly scientific understanding of the mechanisms underlying most forms of physical therapy, including spinal manipulation and traditional as well as more modern forms of acupuncture and moxibustion.

These data suggest that aberrant stimulation of spinal or paraspinal structures may lead to segmentally organized reflex responses of the autonomic nervous system, which in turn may affect visceral function.^{96, 97} What stands out in this finding is the need to more thoroughly understand neural mechanisms lying at the heart of most forms of physical medicine, including spinal manipulation, if an appreciation of what is regarded as the subluxation is ever to be achieved.

4.1.3. Chemical intervention: neurophysiological outcomes from noxious activation

Another investigation with rats found that injection of 0.9% saline or capsaicin into the left (ipsilateral) L4/5 facet joint produced small but significant decreases in the mean arterial blood pressure (MAP) and left sciatic nerve blood flow (NBF). However, injections applied to the L4/5 interspinous ligament led to a significant and sustained increase of MAP and NBF, recorded exclusively with the capsaicin from 20-120 seconds post-injection. The authors concluded that spinally mediated somatoautonomic reflexes displayed a strong segmental tendency, drawing attention to a spinal locus capable of eliciting systemic neurological effects.⁹⁸

Elsewhere, Budgell supported a neurophysiologic rationale for the concept that aberrant stimulation of spinal or paraspinal structures, such as could be achieved by a subluxation, could lead to segmentally organized reflex responses of the autonomic nervous system. This, neurophysiologic response, in turn, was deemed capable of altering visceral function.⁹⁶ By directing attention to the spine and a locus as the area of disruption , these observations are consistent with more traditional concepts of the subluxation.

4.1.4. Mechanical intervention, behavioral and neurophysiological outcomes

Physical attempts to replicate the subluxation have been carried out at the Yale University Medical Center with anesthetized rats with stainless steel rods inserted into the foramen at L4 and L5, producing a chronic compression of the dorsal root ganglia (CCD). Instead of diminishing cutaneous sensitivity with nerve compression, the researchers observed the opposite. Increased foot withdrawals from a heated floor indicated elevated thermal hyperalgesia. In addition, reflex withdrawals upon stroking the foot with a cotton wisp indicated increased mechanical allodynia. No such effects were observed with a sham operation with no rod insertions. In addition, chronically compressed dorsal root ganglions (DRGs) generated spontaneous ectopic discharges. These discharges were proposed to contribute to the observed hyperalgesia and allodynia.⁹⁹ The excitable DRGs were suspected of contributing to low back pain and sciatica in humans.

Interestingly, intrathecal administration of the NMDA receptor antagonists D-2-amino-5-phosphonovaleric acid (APV) and dizocilpine maleate (MK-801) inhibited the thermal hyperalgesia observed in CCD animals.100 This observation directed attention to the role of the neuron receptor in regulating neural transmission. This raises questions as to the role the neural receptor may play in defining the subluxation, a subject of future research.

A greatly expanded assessment of the effects of both CCD of the DRG and decompression (de-CCD) and responses to repeated instrumental (Activator) spinal adjustments at L5 and L6 in male Sprague-Dawley rats (Figure 3) was afforded by Song and his colleagues at Parker University. These investigators found that the following indicators of neural activity and plasticity were all suppressed by the repetitive application of Activator thrusts to specific spinal segments:

- a. Behavioral pain determined by increased thermal and mechanical hypersensitivity of the affected hindpaw (Figure 4);
- b. Inflammation as measured by the inflammatory intermediates TNF- α and IL-1 β in the DRG, (Figure 5);
- c. Neuron hyperexcitability (Figure 6);
- d. Neuron inflammation revealed by hematoxylin and eosin staining under the dissecting microscope (Figure 7); and
- e. Induction of c-Fos protein and PKCy (Figure 8).
- f. Repeated Activator thrusts also increased the anti-inflammatory IL-10 in the spinal cord (Figure 9).¹⁰¹

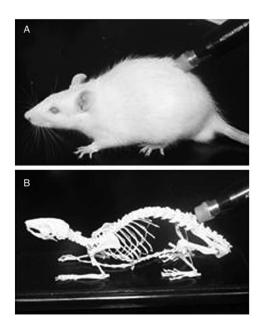


FIGURE 3: Activator spinal manipulative treatment (ASMT) to the L5 and L6 segments in the rat.¹⁰² This figure was reprinted with permission from JMPT.

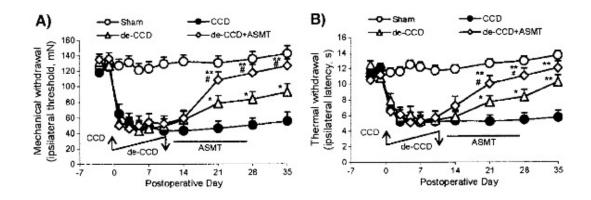


FIGURE 4: Effects of repetitive ASMT on thermal hyperalgesia and mechanical allodynia after CCD and de-CCD, respectively. Time courses of effects before, during, and after ASMT. A: Thermal hyperalgesia; B: Mechanical allodynia. *p < .05; **p < .01 (vs Sham); #p < .05 (vs CCD).¹⁰¹ This figure was reprinted with permission from JMPT.

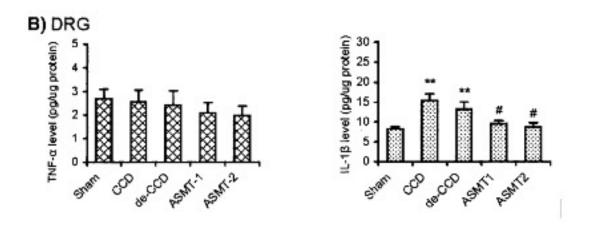


FIGURE 5: Effects of repetitive ASMT on the expression of cytokines TNF- α and IL-1 β in DRG. **p < 0.01 (vs Sham); #p < 0.05 (vs CCD).101 This figure was reprinted with permission from JMPT.

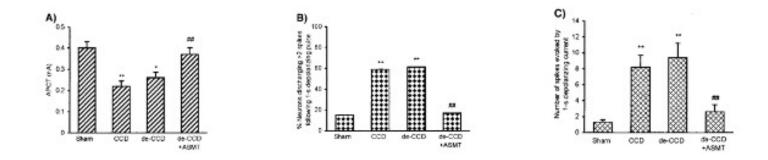


FIGURE 6: Effects of repetitive ASMT on the DRG neural hyperexcitability after CCD and de-CCD, respectively. A: Action potential current threshold; B: Number of neurons discharged > 2 spikes following a depolarizing current; C: Number of repetitive discharges evoked by a depolarizing current. *p < 0.05, **p < 0.01 (vs Sham); ##p < 0.01 (vs CCD)101 This figure was reprinted with permission from JMPT.

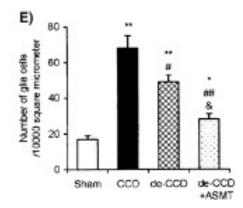


FIGURE 7: Effects of de-CCD and ASMT on the CCD and de-CCD DRG neurons characterized by changes in the number of neuroglia cells. p < 0.05, p < 0.01 (vs Sham); p < 0.05, p < 0.01 (vs CCD); p < 0.05 (vs de-CCD).101 This figure was reprinted with permission from JMPT.

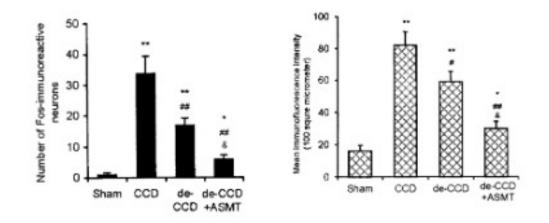


FIGURE 8: Effects of repetitive ASMT on expressions in the dorsal horn after Sham, CCD, de-CCD, and de-CCD with ASMT, respectively. A: c-Fos; B: PKC γ . *p < 0.05, **p < 0.01 (vs Sham); #p < 0.05, ##p < 0.01 (vs CCD); &p < 0.05 (vs de-CCD) ¹⁰¹ This figure was reprinted with permission from JMPT.

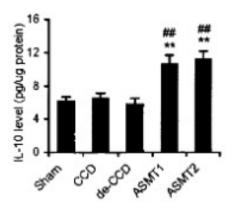


FIGURE 9: Effects of repetitive ASMT on expression of cytokine IL-10 in the spinal cord after Sham, CCD, and de-CCD with ASMT, respectively.**p < 0.01 (vs Sham); ##p < 0.01 (vs. CCD) 101 This figure was reprinted with permission from JMPT.

What was evident in these findings was that HVLA thrusts in the prevention of inflammation were also preventing maladaptive plastic changes of thermal and mechanical hyperalgesia. This spoke to the linkage of the immune and nervous systems responding to a spinal aberration and its reversal by ASMT, pointing to what

is deemed to be the subluxation.

4.1.5 Chemical intervention, behavioral, neurophysiological, and histochemical outcomes

But what if chemical means induced inflammation specifically at the L5 foramen by chemical means? To reverse the inflammatory effects, would manipulation need to be explicitly administered at the L5-S1 lumbosacral junction? The Song investigative group sought to answer these questions using a rat model. The researchers injected an inflammatory cocktail of bradykinin-5-hydroxytroptophan, histamine, and prostaglandin at the L5 foramen. The inflammatory chemicals led to changes in the L5 dermatome and myotome. Inflammatory changes manifested as thermal hyperalgesia and mechanical allodynia. These changes were observed by reduced latencies of hind foot withdrawals to heat and a von Frey filament, respectively. Other observations included DRG hyperexcitability shown by electrophysiological recordings. Pathological studies revealed vascularization and satellitosis (an abnormal clustering of glial cells around damaged neurons). All were reduced by thrusts with the percussive Activator Adjusting instrument at the L5 and L6, but not the L4 segments. Control animals were administered the surgical procedure required for the injection but without the needle stick, with or without the Activator spinal manipulative treatment (ASMT).¹⁰²

These effects were replicated elsewhere using the same experimental design, except that a topical ibuprofen cream was applied to the skin over the L5 inflamed area instead of ASMT. Thus, it was apparent that the effects of a localized area of mechanical derangement involving the IVF of the spine could also be reduced by a site-localized application of an anti-inflammatory compound (ibuprofen). The anti-inflammatory cream reduced hyperexcitability at both the behavioral and neuronal levels.¹⁰³ Yet an additional investigation demonstrated that intraperitoneal injection of vitamins B1, B6, and B12 singly or in combination would reduce thermal, but not mechanical hyperexcitability in the same rat model of neuropathic pain (spinal ganglia compression or loose ligation of the sciatic nerve).¹⁰⁴

The significance of this finding is that vitamin supplements may be capable of mimicking at least some of the beneficial effects obtained with ASMT or site-specific application of an anti-inflammatory compound. The mechanism by which at least vitamins B6 and B12 may reduce inflammation is suggested by studies demonstrating reduced levels of homocysteine,¹⁰⁵⁻¹⁰⁷ an inflammatory marker that is a known risk factor for life-threatening inflammatory diseases¹⁰⁸ and significantly associated with inflammatory immune factors.¹⁰⁹ These findings suggest that identification of the subluxation which initiated the inflammation may not depend upon spinal manipulation in every instance.

4.2. The Clinical Sciences: Humans

To pinpoint the locus of dysfunctions characterizing the subluxation, four pathways in which the subluxation is proposed to be manifested are the following. These are intended to be tracers to what is ultimately a subluxation:

- 1. Mechanical derangement, described as the subluxation syndrome (the aggregate of signs and symptoms, primarily pain and disability, produced by mechanical disturbance of the various spinal and pelvic motion segments);¹
- 2. Biochemical, identified as inflammatory intermediates;
- 3. Neurophysiological, found in the muscles and nerves; and
- 4. Psychosocial alterations.

Each of these tracers are described below:

4.2.1. MECHANICAL: The subluxation syndrome

Known as the clinical manifestations of subluxation, those most closely identified with the spine according to Gatterman include (i) cervicogenic headache, (ii) whiplash injuries, (iii) cervicogenic dorsalgia, (iv) first rib subluxation, (v) thoracic subluxation syndrome, (vi) costovertebral subluxation syndrome, (vii) posterior

joint (facet) syndrome, (viii) intervertebral disc syndrome, (ix) sacroiliac joint syndrome, and (x) coccygeal subluxation syndrome.¹

Conditions beyond back pain, headache, and neck pain have been reported to respond to spinal manipulation with varying levels of evidence. These include colic,¹¹⁰ dysmenorrhea,¹¹¹ hypertension, ¹¹² asthma,¹¹³ otitis media,¹¹⁴ dizziness, balance disorders, and osteoarthritis.¹¹⁵ However, concerns have been raised regarding conflicting evidence as well as the quality of the studies mentioned above, leading some to conclude that there is currently insufficient evidence to support claims of non-musculoskeletal benefits from SMT.¹¹⁶

These considerations understandably lead to massive debates about the quality and true meaning of clinical evidence, beyond the scope of this discussion but which has been reviewed elsewhere.¹¹⁷ Accordingly, a critical review of the subjective outcomes (category #1 above, the subluxation syndrome) will be deferred to another occasion, and the remainder of this treatise will focus on objective outcomes #,2, #3, and #4.

4.2.2. BIOCHEMICAL: appearance and suppression of inflammatory intermediates

4.2.2.1. Cytokine modulation by spinal manipulation

SMT associated suppression of inflammatory intermediates has been documented by Stephen Injeyan and Julita Teodorczyk-Injeyan at Canadian Memorial Chiropractic College. In one trial, 64 asymptomatic subjects with restrictions in the segmental motion of the upper thoracic spine (T1-T6) were randomized to one of three groups: spinal manipulative therapy (SMT), a sham manipulation (SHM), and a venipuncture control (VC). The SMT was a single bilateral hypothenar (Carver-Bridge)-type adjustment, evaluated by audible cavitation. The SHM used a similar force with positioning and line of drive that did not produce cavitation. VC subjects were treated in every way like the SMT and SHM groups except for the thrust. Whole blood cultures obtained from subjects showed that cultures from SMT subjects revealed a gradual decrease of the cytokines TNF- α and IL-1 β , while the other two groups showed the opposite: progressive increases in the production of the two cytokines.¹¹⁸ Using a similar experimental design, Injeyan demonstrated that spinal manipulative therapy was specifically capable of increasing the production of the anti-inflammatory cytokine IL-10.¹¹⁹

Recently,¹²⁰ researchers demonstrated that the cytokine IL-6 as well as TNF- α and IL-1 β were significantly elevated in low back pain patients compared to asymptomatic controls, with increases in the chronic population more significant than those in the acute cohort. In a non-randomized controlled clinical trial, six spinal manipulative treatments delivered to the lumbosacral region over two-weeks significantly depressed the levels of all three cytokines at the end of the intervention period, as shown in Figure 10. The anti-inflammatory IL-10 levels were reduced in acute LBP patients, while SMT did not affect those levels, suggesting that the declines in TNF- α and IL-1 β following SMT were not related to IL-10.¹²¹

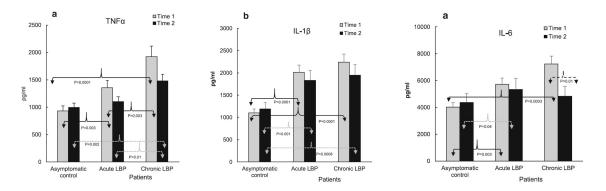


FIGURE 10: Production of the cytokines TNF- α , IL-1 β , and IL-6 in whole blood cultures from asymptomatic subjects (control) and patients with acute and chronic LBP determine at baseline (Time 1) and after two weeks during which LBP patients received 6 SMT treatments (Time 2). For IL-6, production was measured in lipopolysaccharide-stimulated whole blood preparations. This figure was reprinted with permission from Chiropractic & Manual Therapies.

4.2.2.2. Cytokine modulation by spinal manipulation plus psychosocial intervention:

The role of stress in triggering a cascade of physiological changes, including inflammation and other lifechanging events, cannot be overemphasized.¹²²⁻¹²⁶ Thus it is not surprising that a psychosocial overlay was recently found to enhance the effects of spinal manipulation in not only suppressing pain and disability markers, but also in reducing the levels of a broad spectrum of inflammatory markers. In other words, if SMT is considered a gateway to identifying the subluxation by suppressing its manifestations, then the relief of stress may be a key as well. What follows is an investigation that suggests that SMT and the relief of stress may exhibit a synergistic effect in relieving low back pain.

The psychosocial treatment, called the neuro-emotional technique (NET), is based on the principle that the stressor effects of dormant /or current unresolved issues or trauma can determine one's bodily responses. These responses are relatively personalized to the individual's conditioned, experiential, and emotional reality.¹²⁷ Compared to spinal manipulation alone, NET produced clinically and statistically significant declines (p < 0.001) in the Oswestry Disability Index, Quadruple Visual Analogue Scale, and the psychoneuroimmunology markers of blood serum levels of C-reactive protein, tumor necrosis factor α , and the interleukins 1,6, and 10 – as well as ten dimensions of the Short Form Health Survey.¹²⁸

The cytokine reductions are shown in Figure 11. These data underscored the significance of emotion as an exacerbator of subluxation effects.¹²⁹ However, future large-scale studies with follow-up for more than six months are warranted.

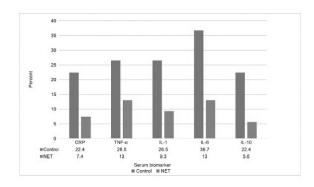


FIGURE 11: Blood serum levels of inflammatory markers outside of normal ranges. NET = neuro-emotional technique; CRP = C-reactive protein; TNF- α = tumor necrosis factor α ; IL = interleukin.¹²⁹ This figure was reprinted with permission from the JIM.

4.2.3. NEUROPHYSIOLOGICAL

4.2.3.1. Reflexes

In assessing surface electromyographic (sEMG) recordings, Murphy and Dawson found that the averaged amplitude of the Hoffman (H) reflex decreased by 12.9% in the ipsilateral leg following a sacroiliac joint manipulation. At the same time, there was no significant alteration in reflex excitability following the sham intervention. After sacroiliac joint manipulation, the contralateral leg showed no significant alteration in reflex excitability. The decreased H reflex in the ipsilateral leg was an early indication that joint manipulation exerted physiological effects on the central nervous system, probably at the segmental level.¹³⁰

Surface EMG recordings were also able to document reflex responses occurring within 50-200 msec when spinal manipulations were applied to the cervical, thoracic, and lumbar regions and the sacroiliac joint. These reflex responses were evident in most neck and back muscles, including the gluteal muscles.¹³¹ Manipulation of the sacroiliac joint also altered muscle inhibition in the involved and contralateral legs in unilateral or bilateral knee pain patients.¹³² The plantar flexors, also, were affected by spinal manipulation. Specifically, spinal manipulation led to a reduction of what is known as the Hoffman-reflex threshold, which was accompanied by

an increase in maximum voluntary contraction (MVC) force. The improvement in the MVC was likely the result of increased descending drive or modulation in afferents, In sum, spinal manipulation appeared to alter the net excitability of the low-threshold motor units, increase cortical drive, and prevent fatigue.¹³³

4.2.3.2. Neuroplasticity

Models in structural pathology fail to adequately account for several clinical and experimental findings in individuals with chronic musculoskeletal disorders¹³⁴ And treatments guided by these models fall short in managing many chronic disorders.¹³⁵ Neuroplastic changes in the central nervous system may be a missing link in our understanding of chronic musculoskeletal disorders¹³⁶ and, for that matter – chiropractic subluxations.¹³⁷ Neuroplasticity is not limited to neural injury and recovery. It includes dendritic remodeling, synapse turnover, long-term potentiation, and neurogenesis. It encompasses brain development, learning skills, formation and loss of memory, and self-repair from neural injuries.¹³⁸

Indeed, as the neuroscience researcher Heidi Haavik has offered:¹³⁹

The old theories of a bone out of place, squashing the nerve exiting the spine are becoming historical concepts, and only relevant to someone who has frank spinal cord or nerve root lesions, such as major disc herniations or spinal stenosis. The contemporary view of the chiropractic subluxation and the mechanisms of adjustments takes into account the new understanding within neuroscience about the incredible adaptability of the CNS. It is a neurobioplasticity model.

Interestingly, this assessment resonates strongly with a declaration of D.D. Palmer, the essence of which may have been overshadowed by the structural models until just recently. Palmer wrote:17, ¹⁴⁰

Life is the expression of tone. In that sentence is the basic principle of chiropractic. Tone is the normal degree of nerve tension. Tone is the expression of function by normal elasticity, activity, strength, and excitability of the various organs as observed in a state of health. Consequently, the cause of disease is any variation of tone—nerves too tense or static.

Essentially, these descriptions of tone and neuroplasticity necessarily involve neural disruptions, which open the door to a contemporary review of subluxation. In other words subluxation could conveniently be regarded as a model for the origin of some of the changes that occur in the nervous system that, if left unattended, emerge as symptoms and ultimately as pathologies. As will become apparent, the subluxation is largely—but not exclusively---a property of the spine domain with emphasis upon the nervous system, lending itself to an assortment of tests designed to pinpoint the area of neural dysfunction and helping to identify the optimal approach to treat that area.

Neuroplasticity is a fundamental principle in functional neurology, which posits that nerve connections in the brain may be modified or shaped by a variety of afferents, including those arising from sensory, cognitive, emotional, or motor experiences – and thus amenable to rehabilitation.¹³⁶ This contrasts with previous held scientific tenets that brain development is limited to a critical period in early childhood, remaining relatively unchanged thereafter.¹⁴¹ We now appreciate that the central nervous system is undergoing continuous adaptations to an ever-changing environment, including the noninvasive treatments provided by holistic health practitioners – including chiropractors.

4.2.3.3 Neuroplastic changes in response to pain

According to a new mechanism of pain development proposed by the International Association for the Study of Pain, nociplastic pain arises due to plastic changes in the neural circuits that carry nociceptive information.¹⁴² This is to be distinguished from nociceptive pain (resulting from tissue damage or the threat of tissue damage) and neuropathic pain (resulting from damage to the peripheral nervous system (PNS) or central nervous system (CNS). Symptoms may occur as a combination of these mechanisms.¹⁴² A peripheral injury may occur to the extent that it alters the somatosensory information processing system, often leading to evoked pain sensation from normally non-noxious stimuli. The alteration in this pain perception is often induced by structural and functional neuroplasticity of the spinal dorsal horn due to the closely related anatomical structures of each

of its laminae. Pain evoked by non-noxious stimuli is known as allodynia, a characteristic of neuropathic and nociplastic pain.¹⁴³ Pain circuits that are related to neuropathic and nociplastic pain include such mediators as the gamma isoform of protein kinase C (PKC γ), neurotensin, cholecystokinin (CCK), gamma aminobutyric acid (GABA), N-methyl-D-aspartate (NMDA), and 5-hydroxytrypamine receptor 2A (5-HT2A).¹⁴³ A more detailed description of these molecular regulatory intermediates is beyond the scope of this discussion. However, it is important to realize that specific neurochemicals (neurotransmitters) are involved in multiple pathways and synaptic changes that constitute the neuroplastic changes under discussion.

Neuropathic pain, in particular, is the expression of maladaptive plasticity within the nociceptive system, representing a series of changes that form a neural disease state. The multiplicity of alterations that are widely distributed across the nervous system contribute to complex pain phenotypes. Among the alterations are the ectopic generation of action potentials, facilitation and disinhibition of synaptic transmission, loss of synaptic connectivity, formation of new synaptic circuits, and neuroimmune interactions.¹⁴⁴

Synaptic modifications in the dorsal horn of the spinal cord may alter the balance of excitatory and inhibitory synaptic transmission in the lamina 1 projection neurons to the brain and one mechanism producing allodynia. Axonal sprouting and functional circuit reorganization of sacral spinal nerves involve both intracortical neurons and projection neurons, at least partially responsible for enabling allodynia.

Numerous studies have shown a network of brain areas that are activated with acute thermal, mechanical, and chemical painful stimuli, labeled as a "pain matrix."¹⁴⁵ The fact that neuroplastic changes occur in the brain to allow interaction is shown, for example, by the finding that negative emotions negatively impact the affective component of pain and decrease pain tolerance¹⁴⁶ while positive emotion increases pain tolerance.¹⁴⁷ This has led some to propose that pain is a specific form of what is known as interoception—the perception of the internal state of the body.¹⁴⁸

One example of neural plasticity within the brain (altered cortical processing in clinical conditions) has been demonstrated by somatosensory evoked potentials (SEP). These are electrical potentials elicited by either physiologic or electric stimulation of somatosensory receptors or their axons. For example, patients experiencing carpal tunnel syndrome compressing the median nerve have demonstrated significant increases in both cortical and brainstem SEP following stimulation of the affected compared to the unaffected ulnar nerve, demonstrating that a chronic pathological modification of peripheral sensorimotor inputs was associated with changes in the neural activity at multiple sites of the somatosensory system. Changes in the synaptic strength were proposed to explain the mechanism underlying ulnar nerve SEP changes.¹⁴⁹ This harkens back to the previously discussed synaptic changes in rat dorsal ganglia subjected to a spinal cord fixation described as a subluxation mimic by Bakkum.⁸⁸

A subcategory of neck pain has been defined as subclinical neck pain (SCNP), a condition in which individuals experience recurrent flare-ups of neck pain but have not yet sought regular treatment.¹⁵⁰⁻¹⁵² When presented with visual and multisensory (simultaneous audiovisual) tasks, 12 participants with SCNP had slower visual and multisensory response times than asymptomatic individuals (Figure 12). In the absence of treatment, these differences persisted over four weeks.¹⁵³

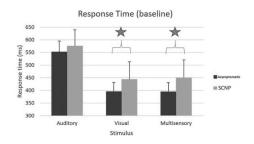


FIGURE 12: The baseline mean response time for all stimulus conditions presented with a comparison for each group alongside each stimulus. Single standard deviation caps are shown for each stimulus condition and group, with starts indicating a significant difference. SNCP = subclinical neck pain. Stars indicate a significant

difference.¹⁵³ This figure was reprinted with permission from JMPT.

Further details to this scenario occurred when SCNP subjects completed a more complex motor learning task. Specifically, selective changes in motor learning and retention correlated with differential changes in SEP peak amplitudes compared to SCNP and asymptomatic groups of participants. Only the SCNP group showed a lack of retention during the acquisition stage of learning. According to previous reports, this may have been influenced by compromised upper limb performance caused by altered afferent input to the SCNP group.^{150-152,} ¹⁵⁴ The impairments thus displayed were seen by changes in two SEP peaks (N18 and N24) related to cerebellar pathways.¹⁵⁵⁻¹⁵⁸ The authors concluded that the presence of SCNP altered how the CNS learns an upper limb motor task. In addition, the cerebellum may have been particularly affected by SCNP as shown by the changes in the N18 and N24 SEP peak amplitudes that matched differences in motor learning outcomes. Essentially, SEP may have served as a tool to identify maladaptive responses to motor skill acquisition in patients with early neck pain problems, a common target of chiropractic management and a possible manifestation of the subluxation.¹⁵⁹ This suggestion would be meaningless if it were not shown that both neck pain and the SEP profiles respond to chiropractic spinal manipulation, such that the pathways that led to pain and its relief from SMT might be clarified. The result would assist in more closely identifying objective, physiological aspects that in turn would characterize the subluxation.

Several trials that identify several neurobiological characteristics of pain and responses to SMT are described below.

4.2.3.4. Neuroplastic changes responding to spinal manipulation

4.2.3.4.1. Altered sensorimotor processing following spinal manipulation in the presence of pain: Involvement of prefrontal cortex

That spinal manipulation could lead to transient cortical plastic changes was demonstrated by Haavik and her colleagues in 2007 in a trial of 12 subjects with a history of recurring stiffness or neck pain. The investigative team focused upon somatosensory evoked potentials (SEPs), electrical potentials elicited by either physiologic or electric stimulation of somatosensory receptors and their axons. Compared to a passive head movement as a control procedure, a single session of spinal manipulation of dysfunctional joints resulted in attenuated cortical (parietal N20 and frontal N30) SEP responses to median nerve stimulation. The parietal N20 changes persisted for at least 30 minutes following the manipulation. The authors suggested that no prior study had shown persistent changes in either somatosensory processing or sensorimotor integration of afferent signals following spinal manipulation. A representative recording of the N30 peak changes is shown in Figure 13.¹⁶⁰

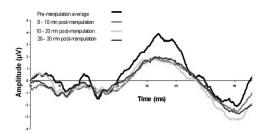


FIGURE 13: Changes to the N30 SEP component of a single subject recorded immediately before and after a session of cervical spine manipulation.¹⁶⁰ This figure was reprinted with permission from the author.

A sequel to this study was achieved when the same investigative team turned their attention to what is known as the dual SEP technique. The SEP technique is a measure of the ability of the CNS to appropriately suppress the response to simultaneous input from two peripheral nerves as compared to the arithmetic sum of nerve inputs. The technique mimicked a process known as "surround inhibition," a mechanism by which the CNS focuses on neuronal activity from one area by inhibiting input from adjacent (surrounding) areas. This suppression was evident for the frontal P22-N30 SEP wave component.¹⁶¹ The fact that patients with dystonia¹⁶² and Huntington's disease¹⁶³ are known to have increased dual SEP ratios suggests that these individuals may be

receiving excessive (not spatially filtered) afferent input from their affected limbs, which could potentially cause their motor system to transform these afferent inputs to abnormal motor outputs.

However, did this reflect a natural process during skill training or a maladaptive process that could lead to a degradation of the highly segregated sensorimotor cortical maps over time? The presence of spinal dysfunction could have been one such factor that induced those maladaptive central plastic changes. Therefore, the same researchers sought to determine whether spinal manipulation could change how the CNS responded to skill training, in this instance a typing task. Subjects had a history of neck pain but could not be experiencing pain at the time of the study. When subjects conducted a 20-minute typing task, there was an increase in the dual peripheral nerve stimulation SEP ratio. This finding was not present when the motor training task followed spinal manipulation. Instead, the SEP ratio decreased for the cortical P22-N30 SEP component. The results suggested that cervical spine manipulation altered the cortical integration of dual somatosensory input and changed how the CNS responded to subsequent motor training tasks. The authors suggested that these findings might clarify the mechanisms responsible for the effective relief of pain and restoration of functional ability documented after SMT.¹⁶⁴

4.2.3.4.2. Altered sensorimotor processing following spinal manipulation in the presence of subclinical neck pain: Involvement of both prefrontal cortex and cerebellum

To better understand how subluxation may be an underlying cause of pain and other clinical presentations, the Haavik research team selected a group of patients with subclinical neck pain (SCNP) for which participants had not yet sought treatment. Individuals in this group enabled the exploration of neurophysiologic dysfunction without the interactive effect of current pain, which has been described as a confounding factor altering the measurements of sensorimotor integration and motor control.¹⁶⁵⁻¹⁶⁷ A more intensive analysis of the N30 peak and brain source modelling indicated that only the prefrontal source showed reduced activity following SMT. This was identified as the locus of somatosensory processing at the cortical level.¹⁶⁸ Given the premise that neurological dysfunction is the ultimate indicator of subluxation, Haavik's focus upon the N30 peak as a specimen of the nervous system, its reduction following spinal manipulation concomitant with the reduction of pain compared to a sham control--and the demonstration that it resides within the pre-central motor cortex provides useful data upon proposed properties of the subluxation.

If a learning task is included in this protocol, the cerebellum appears to become involved. The Haavik research team chose to investigate whether there was a modulation in cerebellar output to the motor cortex in SCNP patients compared to healthy controls – and whether spinal manipulation and motor sequence learning affected sensorimotor integration concerning to both the cerebellum and motor cortex. Graded cerebellar stimulation on corticomotor output in a motor training task (operating a numeric keypad) showed that the cerebellum could inhibit cortical motor output in a modulated fashion in asymptomatic (control) patients. No such modulation was present in the SCNP group; however, the modulation resembled the pattern seen in healthy controls when a single session of chiropractic manipulation was provided before the training task. Motor training in the absence of prior manipulation was not performed, however. Even so, improving the subclinical neck dysfunction may have improved upper limb performance and execution. The overall suggestion was that spinal manipulation prior to the motor sequence learning might have restored the baseline functional relationship between the cerebellum and motor cortex,¹⁶⁹ extending the field effect of the subluxation.

The same outcomes were shown with subjects with recurrent mild neck pain and muscle tension but minimal acute pain at the testing time (for all intents and purposes, classified as SCNP). After typing randomized 8-letter sequences as quickly and accurately as possible, SCNP and entirely asymptomatic participants were subjected to twin coil transcranial magnetic stimulation (TMS) of the cerebellum and motor cortex as a baseline measure of cerebellar inhibition (CBI). Healthy participants were administered a sham control which involved light palpation applied to the neck with the head gently moved into lateral flexion and rotation similar to the actual neck manipulation. SCNP participants underwent spinal manipulation or the sham procedure as mentioned, after which all performed the same typing task with a final TMS to evaluate possible differences in CBI. At follow-up, the SCNP controls remained inhibited (58 + 33% of test motor-evoked potentials [MEPs]), compared to healthy controls who were disinhibited (98 + 95% of test MEP, p < 0.001). The spinal manipulated group

was facilitated (146 + 95% of test MEP, p < 0.001). The more significant inhibition in the neck pain sham vs healthy control groups suggested that neck pain may change cerebellar-motor cortex interaction. In contrast, the change to facilitation suggested that spinal manipulation may reverse the inhibitory effects of neck pain.¹⁷⁰ The fact that the manipulated group displayed a greater MEP than healthy controls remains a curiosity, possibly explained by an as yet unidentified inhibitory effect by the sham intervention that was omitted in the manipulated group, or that SMT reversed an occult CBI that might have been present in the healthy cohort.

4.2.3.4.3. Proprioceptive sensibility and spinal manipulation

In studies by Palmgren et al, patients with chronic cervical pain subjected to high-velocity and low-amplitude spinal manipulation were compared to a control group with the same disorder.¹⁷¹⁻¹⁷³ Both groups were given equal time with the treating chiropractor. Patients undergoing the manipulation after five weeks displayed an improved ability of the neuroarticulomuscular system to reposition the head in a neutral posture after active movements in different planes. This was accompanied by reductions in pain intensity as shown on the Visual Analog Scale in the manipulated group only. The outcomes suggested that the augmented head relocation accuracy produced by manipulation was an indicator of improved proprioception and motor response.

4.2.3.4.4. Altered cortical drive following spinal manipulation in the absence of pain

Another investigation found that the effects of spinal manipulation (SMT) could be found on transcranial magnetic stimulation input-out (TMS) curves. Specifically, spinal manipulation produced elevations of the maximum motor evoked potential (MEPmax) in both the abductor pollicus brevis (APB) and tibialis anterior brevis (TA) muscles. Movement related cortical potential (MCRP) amplitudes increased only with the manipulated group. The authors concluded that the SMT applied led to changes in cortical excitability. No changes in spinal measures (F wave amplitudes or persistence) were found, in either the experimental or control groups. Consequently, these investigators concluded that the changes were due to descending cortical drive rather than changes at the level of the spinal cord, and spinal manipulations were indicated for patients who had lost tonus of their muscles and/or were recovering from muscle degrading dysfunctions, such as stroke or after orthopedic operations.¹⁷⁴

An extension of this research found a single session of spinal manipulation compared to a control in its ability to increase the strength and cortical drive in the soleus (lower limb) muscle of elite Tae Kwon Do athletes.¹⁷⁵ In a randomized controlled crossover design, spinal manipulation compared to a passive movement control increased maximal voluntary contraction (MVC) force of the planter flexors and V-waves over time as indicators of increased muscle strength and corticospinal excitability. Specifically, MVC force measurements revealed a striking and statistically significant difference between the spinal manipulation and control interventions at 0- and 30-minutes post-intervention (p < 0.05) with significance just missed at 60 minutes post-intervention (p = 0.07). In the control intervention, muscle strength decreased. V-wave activity, a measure of supraspinal input or cortical drive, also increased specifically and lasted up to 60 minutes post-intervention with the manipulated group.

4.2.3.4.5.Viscerosomatic response interacting with nicotine

Spinal manipulation affected viscerosomatic function in a trial of 12 non-smoking adults and six smokers. The participants received a controlled unilateral pre-loaded impulse of high-velocity low amplitude thrust [HVLAT] delivered to the lumbosacral junction. Laser Doppler flowmetry measured relative changes in cutaneous blood flow over the L5 dermatome before the intervention, 5 minutes before delivery of a sham procedure followed by the thrust, and 5 minutes after the spinal adjustment. The non-smoking subjects showed a significant increase in blood flow perfusion while the smokers displayed a significant reduction in blood flow perfusion after the intervention. All subjects showed a slight decrease in blood perfusion after the sham procedure. Results are shown in Figure 14.¹⁷⁶

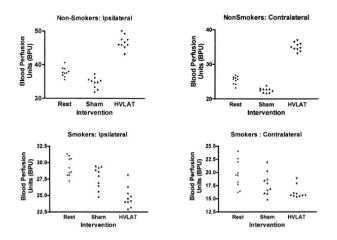


FIGURE 14: Average blood perfusion in nonsmokers and smokers plotted as the means of 10 subjects. This figure was reprinted with permission from JMPT.

These findings suggested that spinal manipulation may stimulate visceral function via a neurovascular route.¹⁷⁷ Differing physiological responses between the sham and HVLAT were prominent. The decreased vascular dynamics reported for smokers^{178, 179} may have appeared as an effect of nicotine on the sympathetic nervous system, essentially shutting down the stimulatory pathway resulting from the HVLAT. Inhibitions of this nature commonly appear in the scientific literature to establish the existence of a metabolic pathway.¹⁸⁰ Results such as these draw further attention to a neural pathway responding specifically to spinal manipulation. As mentioned in the conclusion of Section 4.2.3.4.2.above, the HVLAT may have overcome an asymptomatic, occult subluxation. Regardless, these findings call into prominence a neurological effect of a procedure that in other instances appears to counteract the effects of a subluxation via a neurological pathway.

4.2.4. PSYCHOSOCIAL

Involvement of the nervous system in discussions of the subluxation warrant a consideration of a biopsychosocial component, for years considered to be an essential component for understanding back pain,^{181.} ¹⁸² and considered a characteristic of the nervous system. By extension, the biopsychosocial component would pertain to the subluxation as well. Mind-body interrelationships, have become more widely recognized as a key to understanding health.¹⁸³ A transparent approach to describing the proposed psychological manifestations of the subluxation is to consider the role of stress. Essentially, stress is the body's reaction to any stimuli that disturbs homeostasis, the body's ability to maintain equilibrium. Thus, there appears to be a parallel to subluxation, which likewise disturbs the body's homeostasis.

One could surmise that stress is therefore everywhere, although as a model for living experience stress was virtually absent from narratives prior to the 1930s.¹⁸⁴ Yet its presence was considered to be sufficiently omnipresent that Hans Selye, the first to use the term in a biological context, considered stress to be "in addition to being itself, was also the cause of itself, and the result of itself." His definition of stress was "the non-specific response of the body to any demand placed upon it.¹⁸⁵

It is thus unlikely that anyone has escaped stress in his or her lifetime. The same is true for virtually every body system, the heart and blood vessels, immune system, endocrine system, digestive system, lungs, sensory organs and brain being the most likely targets to meet the perceived danger that constitutes stress.^{186, 187} It is an adaptive response that may in some instances be considered to be beneficial but more likely over time becomes a substantial risk factor.

If stressors are experienced repeatedly or over a prolonged period, stress becomes chronic. Typical stressors include ongoing work pressures, relationship problems, financial worries, or loneliness leading to a situation in which an individual may fail to see a way out. Eventually, chronic stress feeds upon itself by becoming self-perpetuating, and the person experiencing it may even fail to recognize that it is present.

As a state of prolonged tension, chronic stress will by definition exacerbate all the effects upon the body described above. Classic studies demonstrate that individuals engaged in relationship conflicts of one month or greater show a greater risk for developing illnesses and have slower wound healing. Weaker immune responses are found in students taking exams and reporting stressful events on a daily basis.¹⁸⁸ In terms of early life experience, it has been shown that stressful events very early in life have the capacity to alter the responsiveness of both the nervous and the immune system, and that either prenatal or early life stress may increase the likelihood of maladaptive immune responses to stress later in life.¹⁸⁹ These are properties that have been historically ascribed to the subluxation as well.^{1, 17} To complete the circle of chiropractic management and its relationship to the subluxation, the American Chiropractic Association recommends as one of the five elements that physicians and patients should question is item #4: "Do not provide long-term pain management without a psychosocial screening or assessment."¹⁹⁰

As mentioned earlier, the role of stress in triggering a cascade of physiological changes, including inflammation and other life-changing events, cannot be overemphasized.¹²²⁻¹²⁶ The enhancement of the positive pain, disability, inflammatory marker, and qualify of life responses achieved by spinal manipulation with the addition of a psychological approach via the Neuro Emotional Technique was described earlier (Section 4.2.2.2.).

The commonality of previously described disorders points to a neurological disorder. This disorder lies on a spectrum, the working model of which this monograph suggests is the subluxation.

The purpose of the foregoing review of evidence has been to track down the objective indicators as biomarkers that could lead to frank symptoms. As indicated earlier, they could be mechanical (syndrome), biochemical, neurophysiological, or psychological. It is the closer examination of these markers and demonstrating that they can be attenuated by such approaches as spinal manipulation, for example, that encourages one to identify a common launching point called the subluxation. It is no different from, for example, finding an elevated LDL cholesterol level and prescribing statins reduce them before frank cardiovascular problems arise. As in elucidating the subluxation, the process of identifying physiological pathways allows one to work backwards toward identifying the causative agent of downstream symptoms and health problems. The key in this exercise is to maintain focus on the objective markers and their relation to the nervous system.

5.0. IDENTIFYING THE SUBLUXATION

From a clinical standpoint, the challenge remains to describe and diagnose a chiropractic subluxation. In more concrete terms, the first three elements that evolved with the definition described in Section I are added to a fourth, as follows:

- 1. Misalignments.
- 2. Aberrations of movement integrity, referring to either deficient or excessive motion; and
- 3. Physiologic dysfunction, present with or without pain.
- 4. Aching, tenderness, and tenderness with pressure.

5.1. Plain Film Radiography

Evaluating a subluxation by radiography can be viewed through two lenses. One is static, in which chiropractors may have viewed subluxation as a mainly fixed phenomenon specifying vertebral misalignment. More recently, a growing number of practitioners have begun to view the subluxation in more dynamic terms, emphasizing abnormalities of articular motion and giving rise to the practice of functional radiography.

In terms of static radiography, there are questions as to whether full spine over segmental radiography is advisable. Taylor¹⁹¹ has outlined the following conditions in which full spine radiography might be indicated: (i) cases in which clinical examination discloses the need for radiography of several spine sections; (ii) cases in which severe postural distortion is evident; (iii) for scoliosis evaluation after a clinical assessment; (iv) cases in which a mechanical problem in one spinal area adversely affects other spinal regions; and (v) to specifically evaluate complex biomechanical or postural disorders of the spine and pelvis under weight-bearing conditions.¹⁹²⁻¹⁹⁵

Functional radiography, on the other hand, would typically be used to establish the presence of (i) segmental or global hypomobility or fixation, (ii) segmental or global hypermobility, (iii) segmental instability, (iv) aberrant segmental or global motion, (v) paradoxical motion, or (vi) postsurgical arthrodesis evaluation. In this regard, a valuable contribution was the attempt to quantify types of aberrant segmental dysfunction of the lumbar spine with the use of lateral flexion stress radiographs. The typing of motion patterns developed in the lumbar spine was reported by Grice,¹⁹⁶ Cassidy,¹⁹⁷ and Gitelman.¹⁹⁸ One example has been quantitative fluoroscopy as a mean for measuring intervertebral motion patterns for investigating back pain and degenerative disc disease with documented accuracy and repeatability.^{199, 200}

There is little doubt that the use of radiography in terms of radiation exposure and expense remains controversial. There is a growing consensus that contemporary chiropractic best practices should discourage routine use of spinal X-rays unless patients meet current imaging guidelines. A recent review of the current evidence suggests that:²⁰¹

- 1. Spinal X-rays should be used only to diagnose trauma and spondyloarthropathy and to assess severe pathologies, such as adolescent idiopathic scoliosis.
- 2. MRI is indicated to diagnose severe pathologies, such as cancer or infection and to assess the need for surgical management in radiculopathy and spinal stenosis.
- 3. Strong evidence has demonstrated the risks of imagining, such as excessive radiation exposure, overdiagnosis, sequent low-value investigation and treatment procedures, and increased costs.
- 4. In most cases the potential benefits from routine imaging, including spinal X-rays, do not outweigh the potential harms.
- 5. Spinal X-rays should not be routinely performed in chiropractic practice and should be guided by clinical guidelines and clinician judgment.

The American Chiropractic Association specifically provides the following warnings:¹⁹⁰

1. Avoid routine spinal imaging in the absence of clear clinical indicators for patients with acute low back

pain of less than six (6) weeks duration.

2. Do not perform repeat imaging to monitor patients' progress.

A Canadian study involving 1003 consecutively presenting patients with spinal symptoms revealed that, in the absence of red flags, there was a very low risk of missing any serious cases of spinal pain by omitting advanced imaging, The ACA recommendations were generally supported by these results.²⁰²

And yet, because the thresholds for developing cancer have been argued to be 100 to 1000-fold greater than the radiation received in x-rays, critics have attacked the ACA guidelines as unnecessarily restrictive.²⁰³ The Georgia Council of Chiropractic concurred in its rejection of the ACA guidelines, voting to support what they argued was evidence-based science for the appropriate radiologic evaluations of patients seeking chiropractic care developed by the International Chiropractors Association Practicing Chiropractor's Committee on Radiology Protocols (PCCRP).²⁰⁴

5.2. Motion Palpation

As opposed to static palpation, motion palpation is a means of assessing joint play within the vertebral column and complementing static palpation's determination of points of pain, tenderness, or palpable misalignments. A variety of studies showed interexaminer reliability to be poor, with concordance not much above chance levels.²⁰⁵⁻²⁰⁸ Explanations for the poor interexaminer reliability of motion palpation have included (i) variation in procedure,²⁰⁹ (ii) deficient interexaminer spinal level localization leading to possible misreported discrepancies,^{210, 211} (iii) incorrect spinal landmarks,²¹²⁻²¹⁴ and (iv) variations in the anatomy of the patient.²¹⁵ But many of these studies have been described as flawed since they have depended upon the intraclass coefficient, inappropriate since it is only effective if there were an equal chance of the subluxation occurring at all levels of the spine. What actually occurs is that there are "hot spots,"—transitional areas such as the upper cervical spine, cervicothoracic levels, thoracolumbar levels, and lower lumbar and sacroiliac joints that are commonly identified as subluxated.¹³⁹

More current studies have circumvented these design flaws by using what has been called a continuous measures approach, taking examiner confidence into account, and using a statistic that is not negatively impacted by its being applied to an entity that lacks variability.²¹⁶⁻²¹⁹ The continuous measure approach was to achieve close rather than exact agreement on a compromised vertebral level, identifying a region rather than a precise joint.²¹⁹ Good interexaminer reliability could be achieved, particularly when examiners were confident of their findings.²¹⁶⁻²¹⁹ The upshot of these determinations is that when central segmental motor control areas exist, there can be intersegmental movement problems that can be reliably detected by healthcare practitioners trained in chiropractic.

5.3. Leg Length Inequality

Discrepancies in leg lengths have been used to identify chiropractic subluxations. That said, what has to be understood is that leg length discrepancies may be either true (indicating an actual bony asymmetry between the head of the femur and mortise of the ankle) or functional (a physiological response to altered mechanics along the kinetic chain anywhere from the foot to the lumbar spine).²²⁰ Furthermore, the incidence of leg length discrepancies in the normal adult population has been suggested to be as high as 60-70%.²²¹ Nevertheless, leg length checks were deemed to be reliable for determining manipulable sites under certain conditions.^{222, 223,224}

Specifically, an additional analysis found that interexaminer agreement pooled across all spinal joints and at the L5/S1 level indicated fair agreement, only slight agreement at the L4/L5 and sacroiliac joints.²²⁵ A structured search of the literature in Medline, PubMed, CINAHL, and ICL supported by hand searches indicated that reliability appeared to be method-dependent for assessing the pelvis, while validity for the relationship to symptoms was not demonstrated.²²³ In particular, reliability of determining the side of the short leg with knees extended was good but fair for determining the amount of leg length difference and poor with what was known as a head rotation testing procedure.²²⁶ Yet another trial comparing an experienced with an inexperienced chiropractic student found substantial interexaminer reliability in both leg positions with substantial agreement

when straight and flexed knee results were combined for each participant.²²² An overall recommendation has been that leg length testing is "favorable with limitations for assessing the pelvis, based on high quality studies. Validity for relationship to symptoms has not been demonstrated. Reliability appears method-dependent.

But to determine whether the leg length discrepancies reflect an anatomical or physiological manifestation of subluxation, a reliable demonstration that the discrepancies are abolished or even diminished after a chiropractic adjustment is applied needs to be conducted. Furthermore, demonstrations of the validity of leg length checks to suggest the presence of subluxation in areas other than the pelvis (e.g. upper cervical spine) have yet to be performed.

5.4. Manual Muscle Testing

A specialized form of manual muscle testing that remains controversial has been suggested as a means of locating an aberrant neurological function that could be considered to be a subluxation. The response of a particular muscle to resistance applied by a trained professional examiner was first proposed by George Goodheart to be a summation of all the excitatory and inhibitory inputs of the anterior horn motoneurons, such that a failure of the muscle in the test could be linked to a dysfunction of the nervous system.²²⁷⁻²²⁹ This approach became known as Applied Kinesiology (AK). Muscle changes evaluated by the manual muscle test were suggested to be reflective of a change in the peripheral or central nervous system. Treatment was considered effective only if directed at the correct neural disruption.²²⁷ Distinct from the methods described above for locating a subluxation, the neural disruption disclosed by muscle testing has been proposed to be brought on by disturbances in joint function, lymphatic drainage, the vascular supply to a muscle or related organ, a nutritional deficiency or excess, imbalances in the meridian system, aberrations in the stomatognathic system, or psychosocial stressors.²³⁰ Some of these elements may be recognized as ones that were described above as proposed triggers of the subluxation. Earlier assessments of interexaminer reliability were poor;²³¹ however, more recent determinations have found good²³² to excellent²³³ reliability. One review suggested that AK following the International College of Applied Kinesiology guidelines demonstrated good construct, content, convergent, discriminant, and concurrent validity²²⁹ as long as experienced muscle testers were at hand.²³⁴ Research supporting the validity of AK has been criticized in the literature;²³⁵ however, these critiques have been refuted as well.²³⁶ Further confirmations of both reliability and validity are needed to secure this as a standard assessment tool. It is also incumbent upon manual muscle testing to establish bona fide precursors of frank symptomatology, such as headache.

6.0. EXTRASPINAL SUBLUXATION

The term "subluxation" has generally been referred to the spine by chiropractors. However, many chiropractors have maintained that non-spinal joints can be subluxated with associated neurological effects. Specifically, clinical experience has suggested that chiropractic adjustments can produce clinical improvement in the absence of demonstrable encroachment within the intervertebral foramen. Instead, an alteration of somatic afferent input has been suggested.⁹⁰ Therefore, our attention turns to manipulations directed at the extremities, for which a body of literature exists. The situation becomes even more complex when such multimodal applications as transcutaneous electrical nerve stimulation (TENS), interferential current, hot and cold packs, trigger point therapy, ultrasound, or vitamins and minerals are utilized. Even if this discussion is limited to use of the hands in manipulation, we are still faced with studies of varying rigor that have appeared in the treatment of a variety of conditions in a variety of locations. There still remains in these cases a common element of neurological dysfunction that this monograph suggests is the hallmark of subluxation.

6.1. Carpal Tunnel Syndrome and Repetitive Stress

The most direct manner of carpal tunnel syndrome (CTS) treatment has been to relieve pressure on the median nerve. With decompression and massage conducted directly on the symptomatic arm, manipulation of the carpal bones may release pressure on the median nerve, alleviating the pain and inflammation. Double crush syndrome, for example, is characterized by mechanical compression anywhere along a nerve (e.g. nerve roots, radiculopathy) making the peripheral nerve hypersensitive and hyperresponsive to more distal compression. The result is that nerve entrapment syndromes involving the extremities can still be considered in discussions of subluxation beyond the spine.²³⁷⁻²⁴⁰

Siu has described a variety of manipulations, including wrist extension, wrist flexion, transverse carpal extension, thenar radial abduction/extension, radial deviation, ulnar deviation, supination and pronation as osteopathic maneuvers designed to relieve pressure on the median nerve.²⁴¹ A single-blinded pilot trial of CTS patients found that after six weeks of osteopathic manipulations of the spine and one upper limb produced statistically significant improvements in systems and function along with patient assessments. However, changes in the electrophysiologic function of the median nerve were not observed.²⁴²

In a randomized controlled trial, Davis applied manipulations of the bony joints and soft tissues of the wrist and spine combined with ultrasound and wrist supports compared to a medical group that used wrist supports and ibuprofen. There was a significant improvement in perceived comfort and function, nerve conduction, and finger sensation overall, but no significant differences between groups in the efficacy of either treatment. Chiropractic management represented an alternative conservative treatment for CTS, particularly for a patient unable to tolerate ibuprofen.²⁴³

6.2. Shoulder and Upper Limbs

A total of 150 participants with shoulder complaints recruited into a pragmatic randomized controlled trial in a primary care setting revealed that a group receiving chiropractic care in addition to usual medical treatment displayed significant improvements. Specifically, manipulations (high-velocity low-amplitude thrusts) and mobilization (passive low-velocity movements within the range of motion) to the upper ribs, cervical spine, and upper thoracic spine over 12 weeks diminished the severity of shoulder and neck pain while improving shoulder and neck mobility after 26 weeks.^{244, 245}

Concerning upper extremities overall (shoulder, elbow, and wrist), a systematic review including case reports and clinical studies of chiropractic treatment including direct manipulations of the affected areas concluded that there was a "small and growing amount of research to support the management of upper limb syndromes by specific chiropractic management protocols."²⁴⁶ A broader systematic review of chiropractic, osteopathic, orthopedic, and physical therapy approaches that encompassed upper extremity problems including the elbow, wrist, hand, finger, and temporomandibular joint concluded that there was a fair level of evidence supporting

manual muscle therapy to specific joints and the full kinetic chain. In particular, soft tissue and/or myofascial treatment, advice, education, and temporomandibular joint multimodal therapies were described.²⁴⁷

6.3. Knee and Lower Extremities

With previous therapies involving multimodal approaches appearing to be effective, a research team at Macquarie University in Australia sought to determine whether a manual therapy technique directly applied to the knee could alter the self-reported pain experienced by a group of chronic knee osteoarthritis sufferers in a randomized controlled trial. The knee protocol involved two sections: a myofascial mobilization technique and a myofascial manipulation, examples of which are shown in Figures 15A and 15B:



FIGURE 15: Portions of myofascial manipulation technique: A: Finger wrap around the knee to the distal end of the popliteal space. An impulse type of thrust is delivered directed in the caudal direction to mobilize the joint in a near full extension position. B: Alternatively, the initial contact is taken with a bias toward the medial or lateral rotation of the tibio-femoral joint. This position is held through the subsequent traction and impulse thrust. This figure was reprinted with permission from the JCCA.

A control group experienced non-forceful manual contact to the knee followed by interferential therapy set to zero. After receiving three treatments per week for two consecutive weeks, the groups reported the following responses on an 11-question instrument utilizing the Visual Analog Scale (Table 3):

Table 3: Change in 11 Post Study Questions Utilizing Visual Analog Scale²⁴⁸

Visual Analog Scale	Control Mean	Treatment Mean	Difference	P value
1. How would you rate your pain?	3.1	1.9	1.1 (0.1,2.2)	0.042*
2. Do you feel the treatment has helped you?	4.1	7.0	-2.9 (-4.8, -1.1)	0.002*
3. Has the pain/discomfort improved?	3.5	6.7	-3.1 (-4.9,-1.4)	0.001*
4. Has the mobility of your knee improved?	3.9	6.4	-2.5 (-4.2,-0.7)	0.007*
5. The treatment was painful to receive	0.5	0.6	-0.1 (-1.2,1.0)	0.874
6. I feel this treatment to be effective#	4.2	7.4	-3.2 (-5.1,-1.2)	0.002*
7. I can perform general activities than before	3.8	6.5	-2.7 (-4.8,-0.6)	0.013*
8. The clicking and grinding sensations improved	3.4	6.0	-2.6 (-4.7,-0.5)	0.017*
9. Knee changes changed mobility in my hip	2.5	2.8	-0.2 (-2.3, 1.8)	0.815
10. I believe this type of treatment should be used	4.1	1.8	2.3 (0.8,3.8)	0.004*
11. How would you rate this program overall?##	4.7	7.8	-3.1 (-5.0,-1.3)	0.002*

#Compared with other treatment (analgesic/anti-inflammatory medication) ##In terms of effectiveness on decreased pain and increased function *Indicates statistical significance at the level shown Because a requirement for the study was for the knee pain to have been in a chronic stable condition, it is unlikely that the results for the intervention group could be explained in terms of spontaneous remission or natural resolution. Instead, it appeared that the direct intervention at the site of the knee offered a substantial improvement following the 2-week experimental period. Further research is clearly indicated to assess effects over the longer term.²⁴⁸

A review of the literature drawn from the CINAHL, MEDLINE, MANTIS, and Science Direct databases from inception to December 15, 2005 drew 76 relevant citations relating to the foot, ankle, knee, and hip. Of these, 29 citations included spinal treatment, 47 were peripheral, and two were spinal. It was evident from these data that manipulations and mobilizations were being directed beyond the spine.²⁴⁹

This was echoed by another systematic review of literature from December 2006 to February 2008 drawn from the CINAHL, PubMed, MANTIS, Science Direct, and Index to Chiropractic Literature which assigned a:

- a. B (fair) level of evidence for manipulative therapy of the knee or entire kinetic chain, and of ankle or foot, combined with multimodal or exercise therapy for knee osteoarthritis, patellofemoral pain syndrome, and ankle inversion sprain.
- b. C (limited) level of evidence for manipulative therapy of the ankle or foot combined with multimodal or exercise therapy for plantar fasciitis, metatarsalgia, and hallux limitus/rigidus.
- c. I (insufficient) level of evidence for manipulative therapy of the ankle or foot combined with multimodal or exercise therapy for hallux abducto valgus.²⁵⁰

An update published just three years later added 399 new citations that were accessed with 48 assessed for quality. Medline, MANTIS, Science Direct, Index to Chiropractic Literature, and 42 from the PEDro database were originally consulted. Levels of evidence were assigned as follows:

- a. B (fair) for short-term and C (limited) for long-term treatment of hip osteoarthritis.
- b. B (fair) for short-term and C (limited) for long-term treatment of knee osteoarthritis, patellofemoral pain syndrome, and ankle inversion sprain.
- c. B (fair) for short-term treatment of plantar fasciitis.
- d. C (limited) for short-term treatment of metatarsalgia and hallux limitus/rigidus and for loss proprioception and balance of the foot or ankle.
- e. I (insufficient) for treatment of hallux abductus valgus.²⁵¹

6.4. Craniosacral Therapy

Craniosacral therapy (CST) has been described as a derivative of osteopathic manipulative treatment consisting of a mindful, non-invasive fascial palpation technique applied between the cranium and sacrum.^{252, 253} In addition to releasing myofascial structures, CST has been proposed to normalize the sympathetic nerve activity increased in chronic pain patients by modifying craniosacral body rhythms.^{254, 255}

Once deemed not to possess sufficient valid scientific evidence to provide benefit to patients,²⁵⁶ CST in a recent systematic review of patients with neck and back pain, migraine, headache, fibromyalgia, epicondylitis, and pelvic girdle pain was shown to produce more significant post intervention effects on pain intensity and disability compared to usual treatment, manual/non-manual sham, and active manual treatments. Secondary outcomes showed significantly greater improvement in CST patients versus sham than in other groups except for the 6-month mental quality of life benchmark. Forest plots, graphical displays of estimated results from a number of scientific studies addressing the same question along with the overall results, are shown in Figures 16A and 16B. They demonstrate the robustness of the improvements in pain and disability produced by CST. While the precise mechanism of this intervention is unknown, CST serves as yet another example of the effectiveness of manipulations beyond the spine.²⁵⁷

	8	CST	Control					Std. Mean Difference	Std. Mean Difference	
Comparison	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% C	
1. Treatment as usual										
1.2. Post intervention									2007	
Elden 2013 [40]	41.5	23.5	63	49.6	22.5	60	69.6%	-0.35 [-0.71, 0.01]		
Hanten 1999 [42]	21.6	18.1	20	26.4	20.3	40	30.4%	-0.24 [-0.78, 0.30]		
Subtotal (95% CI)			83			100	100.0%	0.32 [-0.61, -0.02]	•	
Heterogeneity: Tau ² = 0.00: Chi	² = 0.1	1. df =	1 (P =	= 0.74);	$ ^2 = 0\%$					
Test for overall effect: Z = 2.09	(P = 0.0	04)								
2. Sham										
2.1. Post intervention										
Haller 2016 [41]	31.7	20.7	27	53.5	20.3	27	21.8%	-1.05 [-1.62, -0.48]		
Mann 2012 [35]		0.68		1.01		33	30.9%			
Mataran-Penarrocha 2011 [43]				78	13.07	41	37.6%			
Nourbakhsh 2008 [44]		1.8		4.1	3.1	12	9.7%			
Subtotal (95% Cl)			117			113	100.0%	-0.63 [-0.90, -0.37]	•	
Heterogeneity: Tau ² = 0.00; Chi	i ² = 3.0	1. df =	3 (P =	= 0.39);	$ ^2 = 0\%$					
Test for overall effect: Z = 4.66										
2.2. Follow-up										
Haller 2016 [41]	31.6	19	27	47.8	19.3	27	40.6%	-0.83 [-1.39, -0.28]		
Mataran Penarrocha 2011 [43]					13.22	41	59.4%	0.42 [-0.85, 0.01]		
Subtotal (95% Cl)			70	10.00	10.00	68	100.0%			
Heterogeneity: Tau ² = 0.02; Chi	$^{2} = 1.33$	df =	1 (P =	0 25)	$ ^2 = 25$	%				
Test for overall effect: Z = 2.88			. (.	0.20),						
3. Active manual treatment										
3.1. Post intervention										
Bialoszewski 2014 [37]	0.7	0.4	27	0.9	0.4	28	46.4%	-0.49 [-1.03, 0.04]		
Castro-Sánchez 2016 [39]	2.5	2.14	32	3.53	1.45	32	53.6%			
Subtotal (95% Cl)			59			60	100.0%		•	
									2	
Heterogeneity: Tau ² = 0.00; Chi	² = 0.03	3, df =	1 (P =	= 0.86);	$ ^2 = 0\%$					

FIGURE 16A: Forest plot of pain intensity. This figure was reprinted with permission from BMC Musculoskeleltal Disorders.

	CST Control							Std. Mean Difference	Std. Mean Difference	
Comparison	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
1. Treatment as usual 1.1. Post intervention										
Arnadottir 2013 [36]	55	8.2	10	57	10.1	10	14.5%	-0.21 [-1.09, 0.67]		
Elden 2013 [40]	37.81	2.83		45.35	16.44	60		-0.64 [-1.01, -0.28]		
Subtotal (95% CI)			73			70	100.0%	-0.58 [-0.92, -0.24]	•	
Heterogeneity: Tau ² = 0.00; Chi ² Test for overall effect: Z = 3.39 (1 (P =	0.37); I	° = 0%				6.000	
2. Sham 2.1. Post intervention										
Haller 2016 [41]	17.6	11.6	27	24.8	10.8	27	23.4%	-0.63 [-1.18, -0.09]		
Mann 2012 [35]		16.8	36	25.7	31.5	33	31.1%	0.25 [0.73, 0.22]		
Mataran-Penarrocha 2011 [43]	45.9		43	50.53	9.12	41	36.5%	-0.60 [-1.04, -0.16]		
Nourbakhsh 2008 [44]		1.1	11	-6	2.9	12	8.9%	-1.08 [-1.97, -0.19]		
Subtotal (95% CI)			117			113	100.0%	-0.54 [-0.81, -0.28]	•	
Heterogeneity: Tau ² = 0.00; Chi ² Test for overall effect: Z = 4.02 (3 (P =	0.39); I	² = 0%					
2.2. Follow-up										
Haller 2016 [41]		7.5	27	23.9	8.7	27	38.4%	-0.66 [-1.20, -0.11]		
Mataran-Penarrocha 2011 [43]	46.05	4.61		49.05	8.03	41		-0.46 [-0.89, -0.02]		
Subtotal (95% CI)			70			68	100.0%	-0.53 [-0.87, -0.19]	•	
Heterogeneity: Tau ² = 0.00; Chi ² Test for overall effect: Z = 3.07 (1 (P =	0.58); I	² = 0%					
3. Active manual treatment 3.1. Post intervention										
Bialoszewski 2014 [37]	0.3	0.5	27	0.5	0.5	28	47.5%	-0.39 [-0.93, 0.14]		
Castro Sánchez 2016 [39] Subtotal (95% CI)	3.12	2.22	32 59	5.12	3.03	32 60	52.5% 100.0%	-0.74 [-1.25, -0.24] -0.58 [-0.95, -0.21]	•	
Heterogeneity: Tau ² = 0.00; Chi ² Test for overall effect: Z = 3.08 (1 (P =	0.35); I	° = 0%					

FIGURE 16B: Forest plot of disability. This figure was reprinted with permission from BMC Musculoskeleltal Disorders.

The purpose of the foregoing discussion is not only to suggest that neither the interventions to relieve pain and disability nor their targeted subluxations may not necessarily be restricted to the spine, but also to demonstrate that conservative manual interventions other than high-velocity, low-amplitude thrusts may be effective in the same capacity under certain conditions.

7.0. RUBICON GROUP CONCEPT OF THE SUBLUXATION

From the considerations above considering the neurologically-centered concept of the subluxation and the evidence indicating that manipulations beyond as well as targeting the spine produce clinical benefits, a consortium of chiropractic educational institutions have spoken out. They have presented a model of the subluxation that embraces these concepts wedded to both the traditional principles of chiropractic and a philosophy rooted in vitalism. The consortium saw its beginnings as an informal gathering of persons and institutions sharing similar perspectives on chiropractic philosophy and education and the future of the profession. Calling itself the Rubicon Group, the consortium first convened in September of 2002 on the campus of Life University and has since held conferences in Geneva, Melbourne, Atlanta, and Paris. It includes as its members the Barcelona College of Chiropractic, the Chiropractic Academy at Dresden International University, Life Chiropractic College West, the New Zealand College of Chiropractic, and McTimoney College of Chiropractic in addition to Life University.

The Rubicon model embraces not only the elements of neural dysfunction and inflammation as discussed earlier, but also the effectiveness of holistic interventions well beyond high-velocity, low-amplitude thrusts directed exclusively at the spine. Rather, it cites vertebral motion segments as an example rather than an exclusive domain. Its concept of the subluxation developed in May 2017 is as follows:²⁵⁸

We currently define a chiropractic subluxation as a self-perpetuating, central segmental motor control problem that involves a joint, such as a vertebral motion segment, that is not moving appropriately, thereby yielding ongoing maladaptive neural plastic changes that interfere with the central nervous system's ability to self-regulate, self-organize, adapt, repair, and heal.

8.0. FUNCTIONAL NEUROLOGY

8.1. The Field Effect of the Subluxation

Given the updated and ever-evolving concept of the subluxation, it may be useful to refer to it in the context of functional neurology. The term embraces that entity which performs as the origin of changes in health which, if left unattended, emerge as symptoms and ultimately as pathologies. The entity in question is the nervous system, lending itself to an assortment of noninvasive tests designed to pinpoint the area(s) of neural dysfunction and helping to identify the optimal agent to target that area—ideally before more substantial disorders appear. Among those presumably noninvasive tests are the interventions provided by the chiropractor, including the high-velocity, low-amplitude thrusts to the spine known as adjustments—but also such hands-on interventions as mobilization, myofascial release, flexion-distraction, pelvic blocking, and trigger point therapy. Other interventions, such as nutritional counseling and supplements as well as certain classes of medications, have been considered but are beyond the scope of this discussion.

Functional neurology (FN) offers a conceptualization of the nervous system as an integrated network which controls the homeostasis of the body through balanced signalling. It is founded on the principle of neuroplasticity, in that nerve connections in the brain may be modified or shaped by a variety of afferents, including sensory, cognitive, emotional, or motor experiences--and thus amenable to rehabilitation. It stands in contrast to previous scientific tenets that brain development is limited to a critical period in early childhood, remaining relatively unchanged thereafter.¹⁴¹ Instead, FN encompasses a broader spectrum of conditions.

The origin of FN has been attributed to the chiropractic profession²⁵⁹ but has since expanded to a broad cross-section of health professions. It has been identified with the investigations and founding of an institute with multiple instructional programs by Frederick Carrick Dr. Carrick emphasizes that FN is not confined to chiropractic but is practiced by a variety of health professions. Similarly, the nervous system is "not specific to a chiropractic neurologist, a medical neurologist, or a dentist."²⁶⁰ From the foregoing, it is clear that it should encompass the interest, research, and practice of a broad spectrum of qualified and licensed healthcare practitioners trained in neuroscience. A detailed criticism ("unraveling") of FN has appeared in the literature;²⁶¹ however, substantial flaws in these critiques have been reported.²⁶²

In practice, FN involves the detection, evaluation, and management of functional aberrations of the neuroaxis. Functional neurology mechanisms are proposed for an ever-growing assortment of incompletely understood symptoms in the medical field, ranging for example from movement²⁶³ or musculoskeletal²⁶⁴ disorders to psychiatric issues and balance disorders.²⁶⁴ and beyond.

The promising therapeutic aspect of FN is that a reorganization of nerve cells is possible to restore or bypass the connections that have become disrupted or damaged, a perfect example being exercises to recover from stroke. The negative consequential aspect, however, is that if a neuronal pathway is not fired, synaptic connections may become inactive with the loss or inactivation of neurotransmitters and receptors, as exemplified by the cognitive decline in the elderly which requires an abundance of mental exercise to forestall its occurrence.²⁶⁵, ²⁶⁶ The reorganization of nerve cells described in Section 4.2.3. provides a mechanistic explanation for morbid consequences of subluxation and the therapeutic mechanisms underlying manual interventions performed by chiropractors.

Through its invitation of vigorous dialogues between the health professions, FN encompasses the broadest spectrum of elements that could affect an individual's health and well-being. That would range anywhere from stress and the emotions to the endocrine and immune systems to such neurotransmitters as acetylcholine, gamma amino butyric acid (GABA), N-methyl D-aspartate (NMDA), dopamine, and serotonin; individual neurons, and their receptors. In short, FN can be thought of as the field effect of the subluxation. It is the entity which could be thought of as embracing the subluxation and the downstream results of both its effects and its correction. It is expressed in terms that are the most amenable to 21st century research ranging from behavioral to molecular levels.

8.2. Psychoneuroimmunology and the Mind-Body Connection

If one is to consider that the subluxation is integral to the central as well as the peripheral nervous system while addressing broader networks, one should also recognize the integration of the neural, endocrine, and immune systems as a demonstration that mind and body are intimately connected. An example of the body's own integrated networks was the demonstration in the early 1980s by Candace Pert and Michael Ruff that the neuropeptides secreted by the brain modulating our moods and behavior were signaling cancer cells to metastasize to different parts of the body. Specifically, mutated lung cancer cells responding to the brain's bombesin secretion became bound to antibodies secreted by B cells, establishing a connection between cancer, the immune system, and toxicity in the body caused by such environmental factors as cigarette smoke.¹⁸³ Such was to indicate that the endocrine, immune, and nervous systems were engaged in cross-talk, confirming a suspicion by Ishigami back in 1919 that the integration of these body systems could be called a psychoneuroendocrine network, creating a field of study known as psychoneuroimmunology (PNI)²⁶⁷ and recognizing that mind and body are firmly connected.

These mind-body interactions have become recognized as the basis for maintaining homeostasis, involving the brain and central nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, and the immune system.²⁶⁸ An even deeper understanding of PNI is achieved by observing the reaction of the immune system to stress as well as to various psychological states²⁶⁹ ranging from ecstasy to depression and anxiety. It is then possible to regard the PNI network of interconnections as shown in FIGURE 17.

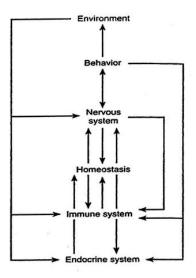


FIGURE 17: The multiple feedback loops and connections of body systems and components involved in homeostasis as envisioned by PNI.²⁷⁰ This figure was reprinted with permission from JMPT.

8.3. Summing Up: A Composite Concept of the Subluxation

In light of the foregoing discussion and recent research, the overarching principle of the subluxation is that it is deemed to represent *irregularities that exist in somatoautonomic reflexed functioning of the autonomic nervous system*. Such is not to discount the somatic nervous system in controlling muscle movement and relaying information from the skin, eyes, and ears to the central nervous system. With such neural dysfunctions postulated to indicate underlying clinical conditions, multiple elements need to be identified as the causes of these aberrations. They include:

- 1. Structural derangements (fixations and abnormal mobility).
- 2. Inflammations.
- 3. Nutritional problems.
- 4. Hormonal imbalances.
- 5. Emotional stress.

Therefore, although the bulk of these may be traced to the spine and a joint dysfunction or dislocation as envisioned by the more traditional definitions of the subluxation, the evolving concept appears to embrace the five entities listed above as existing problems that can be traced beyond the spine, requiring more diverse or even systemic noninvasive interventions. Indeed, as Joseph Brimhall, President of the Council of Chiropractic Education and Director of the Council of Chiropractic Education International explained, there was no wording in the accreditation standards of the Council of Chiropractic Education (US), the model standards of Council of Chiropractic Education International, or other jurisdictions that restricted the chiropractic profession to the spine.²⁷¹ Even D.D. Palmer wrote in 1910 that "The determining cause of disease are traumatism, poison, and auto-suggestion" tied to physical, emotional, and metal levels and deemed to be essential elements if chiropractic is to take a leadership role in wellness. He indicated that:²⁷²

In the study of pathology we should look to the etiological factors which, by their exciting or debilitating effects, retard or liberate stored up energy, resulting in abnormal functioning and morbid structure (italics mine)

This search for those etiological factors is precisely what D.D. Palmer recommended, using the experimental evidence in this monograph to frame a working, conceptual model that we call subluxation. Rather than stating that a subluxation is treated as such, this discussion suggests that subluxation remains a proposed causative factor within the nervous system that is manifested by the neuromusculoskeletal problems that chiropractors address. Its physical characteristics, while defined in the past with discrete structural properties primarily in the spine, are more appropriately extended to the nervous system at large for two reasons: (i) to accommodate more of the elements that can be addressed by chiropractic interventions that extend beyond spinal manipulation, and (ii) providing a less cliquish and opaque approach to treatment, allowing chiropractors to collaborate more successfully with other health practitioners. This in effect is the emergence of integrative medicine. The subluxation, meanwhile, remains a documented model whose work is in progress by which chiropractors address neuromusculoskeletal irregularities, largely but not exclusively within the spine.

9.0. RECOGNITION OF THE SUBLUXATION

Recognition of the chiropractic subluxation around the world has ranged from enthusiastic support to outright rejection. A sampling of responses of both organizations and teaching curricula reveals a complete spectrum of positive and negative outlook. Endorsement or rejection of these views is not to be construed in this presentation:

9.1. Organizations

9.1.1. International Federation of Chiropractors & Organizations (IFCO):²⁷³

The International Federation of Chiropractors and Organizations maintains and upholds that the objective of the chiropractor is separate and distinct from other health care professionals and disciplines and that it is focused on the location, analysis, and correction of vertebral subluxations.

Chiropractic colleges, the federal government, and international and state chiropractic associations define the unique and non-duplicative role and responsibility of chiropractic as focusing particular attention on the vertebral subluxation and its resulting neurological interference.

The use of vertebral subluxation as a rationale for care is supported by protocols that are safe, efficacious and valid. The literature is sufficiently supportive of its usefulness of these protocols in regard to chiropractic examination, analysis and correction. Additionally, vertebral subluxation as a primary and singular finding is consistent with the practice objective followed by thousands of doctors of chiropractic as explained in their Terms of Acceptance.

The chiropractor may use a variety of procedures to assess the vertebral subluxation to determine its presence and arrive at an impression, character, type, and chronicity. The correction of vertebral subluxation is appropriate for anyone determining the safety and appropriateness of chiropractic care. The chiropractor has a duty to disclose any unusual findings discovered in the course of examination.

9.1.2. Foundation for Vertebral Subluxation (FVS):274

STRATEGIC PLAN/MISSION: To advocate for and advance the founding principles and tenets of the chiropractic profession in the area of vertebral subluxation:

- Protect the right of all doctors of chiropractic to provide subluxation correction and of all people to choose to receive such care.
- Advance and promote traditional chiropractic to all people, including the public, the media, legislators and all those directly or indirectly associated with the chiropractic profession.
- Provide important clarification of the role of subluxation-centered chiropractic in health care.
- Support evidence-based practice guidelines and related research which protect the rights of patients to receive chiropractic care for the analysis and correction of vertebral subluxations.

9.1.3. International Chiropractors Association (ICA)²⁷⁵

The ICA holds that it is a basic responsibility of the doctor of chiropractic to employ such diagnostic processes as are necessary in his or her professional judgment to determine the need for care and, in particular, to detect the presence, location, and nature of chiropractic lesions (subluxation and attendant biomechanical, biochemical, structural, and neurophysiological problems, etc.) and prepare and administer an appropriate course of care within the realm of chiropractic specialty. In addition, Doctors of Chiropractic use diagnostic procedures for the purpose of:

A. Determining appropriate case management:

...2. To assess any subluxation complexes discovered in the patient along with related biomechanical, biochemical and neurophysiological presentations.

The Policy Handbook and Code of Ethics describes the subluxation as causing "interference with nerve transmission and expression, due to pressure, strain or tension, upon the spinal cord, spinal nerves, or peripheral nerves as a result of a displacement of the spinal segments or other skeletal structures."²⁷⁶

9.1.4. American Chiropractic Association (ACA)²⁷⁷

Doctors of chiropractic are experts in the treatment of neuromusculoskeletal conditions, subluxation complex, biomechanical dysfunction, and disease.

WHEREAS ACA's current policies and scope of practice, nutritional counseling, subluxation and wellness define chiropractic physicians as primary care providers.

9.1.5. Canadian Chiropractic Association (CCA)²⁷⁸

Subluxation is a term used to describe a problem with a spinal joint. The World Health Organization defines a "subluxation" as a functional problem related to a joint and the structures associated with the joint such as the muscles, tendons and nerves. Dysfunction can present itself in various ways such as pain, inflammation and restricted movement of the joint. Some types of dysfunction, such as a sprain, will not necessarily appear on x-ray. Chiropractors are trained to identify dysfunction that does not appear on imaging through the use of manual examination and non-imaging diagnostic tests.

Subluxation: A lesion or dysfunction in a joint or motion segment in which alignment, movement integrity and/ or physiological function are altered, although contact between joint surfaces remains.

Subluxation complex (vertebral): A theoretical model and description of the motion segment dysfunction, which incorporates the interaction of pathological changes in nerve, muscle, ligamentous, vascular and connective tissue.

9.1.6. Australian Chiropractic Association (ACA)^{279, 280}

We recognise that the practice of chiropractic focuses on the relationship between structure (primarily the spine) and function (as coordinated by the nervous system) and how that relationship affects the preservation and restoration of health.

We recognise that subluxations compromise the expression of innate intelligence, and that prevention and removal of subluxations will facilitate the expression of optimal health.

However, the Australian Chiropractic Association has recently adopted the World Health Organization's definition of the subluxation.²⁸¹

A lesion or dysfunction in a joint or motion segment in which alignment, movement integrity and/or physiological function are altered, although contact between the joint surfaces remains intact. It is essentially a functional entity, which influences biomechanical and/or neural integrity.

9.1.7. New Zealand Chiropractic Association (NZA)²⁸²

The Vertebral Subluxation Complex

In a nutshell, a vertebral subluxation is the impairment of optimal expression of your nervous system caused by physical, biochemical, or psychological dis-stress (see Causes section below).

The terms vertebral subluxation, vertebral subluxation complex (VSC) or simply subluxation are at the core of chiropractic care. Many other terms have been used to describe aspects of this condition such as spinal misalignment or dysfunction, fixation, facet syndrome, or manipulable lesion, however these synonyms are overly mechanical and fall short of describing the true nature, complexity and global health implications of the vertebral subluxation.

Essentially, a vertebral subluxation occurs when the joints of the spine fail to move properly and/or the spinal bones become misaligned causing interference with the nerve messages from the brain to the body and/or from the body to the brain. This can affect movement patterns, muscle balance and even the function of organs and the chemicals and hormones they produce. Most subluxations do not cause pain (as the majority of nerves are not nociceptive or pain-sensing).

Studies continue to elucidate and characterize the numerous and varied devastating effects that subluxations can have on overall health and function. The World Health Organization (WHO) now accepts it as a listing in the latest international classification of disease and related health problems, referred to as M 99.1 Subluxation complex (vertebral).

Chiropractors are highly trained health care professionals specializing in the analysis and correction of vertebral subluxations. Other manual care providers may use similar techniques to chiropractors to also help assist the body in functioning better but do not generally receive training in the specifics of the subluxation complex.

What are the Causes of Vertebral Subluxation?

Subluxations (spinal and nervous system dysfunction) can be caused by stressors (or forces) that your body cannot adapt to including:

- Physical (both macro and micro-traumas) such as the birth process, learning to walk, car accidents, accidents at work or home, poor posture (school, work, home), sports injuries, lifting children, prolonged sitting or standing, repetitive activities etc.
- Chemical factors including neurotoxins, excessive alcohol, tobacco, sugar, artificial sweeteners, food coloring, caffeine, MSG, biochemical constituents of foods (e.g., grain-fed red meat, hydrogenated fats), environmental toxins (e.g., mercury and other heavy metals), lack of proper nutrients (such as essential fatty acids, vitamins, minerals, protein), endocrine changes (for example increased relaxin and estrogen levels in pregnancy).
- Emotional tensions like chronic stress, family conflict, grief, anxiety, depression etc. These tensions subconsciously influence our posture and neurological tone.

One or a combination of these factors can result in alterations to joint function and neurological integration. Physical causes are the most obvious, but not necessarily the most common.

What are the Effects of Vertebral Subluxation?

Distorted nerve communications (Vertebral Subluxations) can be a cause of many other health problems beyond just headaches and back pain. Some symptoms arising from nervous system interference may seem totally unrelated to the spine, for example digestive or respiratory problems, infertility, incontinence, poor concentration and memory, mood swings, and broken sleep patterns.

This is not to say that all conditions or dysfunction is a result of subluxation alone. Disease can occur with, because of, or despite subluxations. However, subluxations always reduce the body's innate ability to express life and function. Our lifestyle, environment, nutrition, toxins, genetic makeup, and even attitude also influence our health and well-being.

The chiropractor's primary role is not to treat conditions or symptoms but to improve your nervous system function thus allowing your whole body to perform as well as possible. A growing number of athletes use

chiropractic care as a regular part of their training for injury recovery, prevention, and optimum performance. In fact many people who are not obviously unwell or suffering are surprised to feel even better after chiropractic adjustments.

The effects of the Vertebral Subluxation Complex on the nervous system can be categorized into segmental and global alterations, including:

- Compressive Lesions spinal vertebrae pinch or choke nerve tissue, diminishing signals to and/or from organs or tissues.
- Facilitative Lesions If spinal vertebrae chafe, stretch, or irritate nerve tissue then signals going from or to the affected organ or tissue can be over-excited.
- Dysafferentation (altered input) If spinal joints no longer move through their normal range of motion this reduces mechano-receptive input and increases nociceptive signals to the brain (the cerebellum in particular). This alteration to homeostatic integration has been shown to have wide ranging effects on posture, co-ordination and balance, along with mood and emotion, memory and other cognitive functions, elevated stress hormone levels and increased susceptibility to disease and degeneration (through spinocerebellar-cortical loops).

9.1.8. Association of Chiropractic Colleges (ACC)²⁸³

Chiropractic is concerned with the preservation and restoration of health, and focuses particular attention on the subluxation. A subluxation is a complex of functional and/or structural and/or pathological changes that compromise neural integrity and may Influence organ system function and general health. A subluxation is evaluated, diagnosed, and managed through the use of chiropractic procedures based on the most available rational and empirical evidence.

9.1.9. Council on Chiropractic Education (CCE)^{54, 284, 285}

The 2007 CCE Accreditation Standards mentioned subluxation 2 times.⁵⁴

The 2013 CCE Accreditation Standards cited subluxation 2 times as well:²⁸⁵

DCP education trains its graduates to...Assess and document a patient's health status, needs, concerns and conditions with special consideration of axial and appendicular structures, including subluxation/ neurobiomechanical dysfunction.

Performing case-appropriate physical examinations that include evaluation of body regions and organ systems, including the spine and any subluxation/neuro-biomechanical dysfunction that assist the clinician in developing the clinical diagnosis.

And the 2018 CCE Accreditation Standards mentions subluxation 2 times as well:²⁸⁴

- 1. Meta-Competency 1, page 22: Performs case-appropriate examinations that include evaluations of body regions and organ systems, including the spine and any subluxation/segmental dysfunction that assist the clinician In developing the diagnosis/es.
- 2. Outcomes, page 27: Students will be able to...identify subluxations/ segmental dysfunction of the spine and/or other articulations.

9.1.10. National Board of Chiropractic Examiners/Federation of Chiropractic Licensing Boards (NBCE/ FCLB)²⁸⁶

The specific focus of chiropractic practice is known as the chiropractic subluxation or joint dysfunction. A subluxation is a health concern that manifests in the skeletal joints, and through complex anatomical and

physiological relationships, affects the nervous system and may lead to reduced function, disability or illness. Typically, symptoms of subluxation include one or more of the following:

- pain and tenderness
- symmetry of posture, movement, or alignment
- asymmetry of posture, movement, or alignment
- range of motion abnormalities
- tone, texture and/or temperature abnormalities of adjacent soft tissues A doctor of chiropractic may detect subluxations through standard physical examination procedures, specific chiropractic assessments or special tests.

RESOLUTION 3-21 Adopted by the Delegate Body, May 1, 2021:287

Recognizing Subluxation

Whereas, the sciences make use of an appropriate subject-related vocabulary, and,

- *Whereas*, the term subluxation has been utilized since the time of Hippocrates and the first English definition of the term was in 1688, and,
- *Whereas*, there are several hundred modifications and alternative expressions utilized by chiropractic, medical and other professions to describe subluxation, and,
- *Whereas*, chiropractic definitions of subluxation include a neurological aberration and a mechanical disturbance, and,
- *Whereas*, the Association of Chiropractic Colleges (ACC) definition of subluxation is representative of these inclusions: "A subluxation is a complex of functional and/or structural and/or pathological articular changes that compromise neural integrity and may influence organ system function and general health." and,
- *Whereas,* research of subluxation correction had been conducted by Dr. B. J. Palmer from 1935-1961 with documented patient improvements in blood values, urological values, audiometric measures, electrocardiographic improvements, and basal metabolic improvements, and,
- *Whereas*, subluxation research by Dr. Sharpless in 1975, revealed that (as little as) 10 mm Hg pressure on spinal nerve roots reduced action potential from 100% down to 60% in 15 minutes, and,
- *Whereas,* subluxation is recognized by the U.S. Government's Medicare program, by the World Health Organization (WHO) ICD-11 classification of vertebral subluxation complex – ME93.Y and by the National Board of Chiropractic Examiners (NBCE), therefore, be it
- *Resolved,* that the Federation of Chiropractic Licensing Boards, in concert with public protection acknowledges and recognizes the Chiropractic Subluxation as a known entity and as a diagnosis germane to Chiropractic.

9.1.11. General Chiropractic Council (GCC)²⁸⁸

- 1. The chiropractic vertebral subluxation complex is an historical concept, but it remains a theoretical model.
- 2. It is not supported by any clinical research evidence that would allow claims to be made that it is the cause of disease.²⁸⁸

9.1.12. European Chiropractic Union (ECU)²⁸⁹

In 2012, the President of the European Chiropractic Union Oystein Ogre claimed:

- 1. The subluxation has never been scientifically defined, tested, or validated.
- 2. There is no valid or reliable test to determine the presence or absence of a subluxation.
- 3. There is no valid test how to find a subluxation.
- 4. Chiropractors have never agreed upon a testable definition of what a subluxation is.
- 5. Other healthcare personnel don't understand what it is, and the public don't really care.
- 6. No one knows, except chiropractors, what a subluxation is.

9.1.13. World Federation of Chiropractic (WFC)²⁹⁰

The subluxation is a complex of functional and/or structural and/or pathological articular changes that compromise neural integrity and may influence organ system function and general health.

However, in the 2019 20 Principles issues by the World Federation of Chiropractic, subluxation is not mentioned.²⁹¹

9.1.14. Centers for Medicare & Medicaid Services (CMS)⁵¹

- **3. Physical Exam:** If you demonstrate a subluxation you based on physical examination, two of the following four criteria (one of which must by asymmetry misalignment or range of motion abnormality) are required and you need to document the criteria:
 - **P Pain/tenderness:** The perception of pain and tenderness is evaluated in terms of location, quality, and intensity. Most primary neuromusculoskeletal disorders manifest with a painful response. Pain and tenderness findings may be identified through one or more of the following: observation, percussion, palpation, provocation, and so forth. Furthermore, pain intensity may be assessed using one or more of the following; visual analog scales, algometers, pain questionnaires, and so forth.
 - **A Asymmetry/misalignment:** Asymmetry/misalignment may be identified on a sectional or segmental level through one or more of the following: observation (such as posture and heat analysis), static palpation for misalignment of vertebral segments, and/or diagnostic imaging.
 - **R Range of motion abnormality:** Changes in active, passive, and accessory joint movements may result in an increase or a decrease of sectional or segmental mobility. Range of motion abnormalities may be identified through one or more of the following: motion palpation, observation, stress diagnostic imaging, range of motion, and/or other measurement(s).
 - **T** -**Tissue tone, texture, and temperature abnormality:** Changes in the characteristics of contiguous and associated soft tissue including skin, fascia, muscle, and ligament may be identified through one or more of the following procedures: observation, palpation, use of instrumentation, and/or test of length and/or strength
- **4. Diagnosis:** The primary diagnosis must be subluxation, including the level of subluxation, either so stated or identified by a term descriptive of subluxation. Such terms may refer either to the condition of the spinal joint involved or to the direction of position assumed by the bone named. The precise level of the subluxation must be specified by the doctor of chiropractic to substantiate a claim for manipulation of the spine.

9.1.15. World Health Organization (WHO)²⁸¹

Subluxation: A lesion or dysfunction in a joint or motion segment in which alignment, movement integrity and/or physiological function are altered, although contact between joint surfaces remains intact. It is essentially a functional entity, which may influence biomechanical and neural integrity.

Subluxation complex (theoretical): A theoretical model and description of the motion segment dysfunction, which incorporate the interaction of pathological changes in nerve, muscle, ligamentous, vascular and connective tissue.

9.1.16. International Chiropractic Education Collaboration (ICEC)²⁹²

Whereas the welfare of the patient is paramount and,

- *Whereas* chiropractic education should be of the highest quality and be founded on the principles of evidence based care, and
- *Whereas* curricula should be responsive to changing patient, societal and community needs and expectations within a modern health care system;

we, the undersigned chiropractic educational institutions, state as follows:

5. The teaching of vertebral subluxation complex as a vitalistic construct that claims that it is the cause of disease is unsupported by evidence. Its inclusion in a modern chiropractic curriculum is anything other than an historical context is therefore inappropriate and unnecessary.

Institutions that signed this declaration are identified below in Section 9.2.

9.1.17. National Board of Chiropractic Examiners NBCE)²⁹³

The specific focus of chiropractic practice is known as the chiropractic subluxation or joint dysfunction. A subluxation is a health concern that manifests in the skeletal joints, and, through complex anatomical and physiological relationships, affects the nervous system and may lead to reduced function, disability, or illness. Typically, the clinical evidence of a subluxation includes one or more of the following: pain and tenderness, asymmetry of posture, movement, or alignment, range of motion abnormalities, or tone; texture and/or temperature abnormalities of the adjacent soft tissues. A doctor of chiropractic may detect subluxations through standard physical examination procedures, specific chiropractic assessments, or special tests. The process is much more complex than stated; this simplification is presented so that those not familiar with the chiropractic profession will have a basic understanding and awareness of what is meant by chiropractic subluxation.

9.1.18 The Rubicon Group:²⁵⁸

The Rubicon Group, described in detail earlier in Section 7.0, has defined the subluxation as follows:

We currently define a chiropractic subluxation as a self-perpetuating, central segmental motor control problem that involves a joint, such as a vertebral motion segment, that is not moving appropriately, thereby yielding ongoing maladaptive neural plastic changes that interfere with the central nervous system's ability to self-regulate, self-organize, adapt, repair, and heal.

9.1.19. Institute for Alternative Futures (IAF)²⁹⁴

The Institute for Alternative Futures, closed since the end of 2019, was a nonprofit organization that created "sets of scenarios that considered differing paths in future space." Specifically, it developed envisioned expectable, challenging, and visionary alternatives."²⁹⁵

Scenario 1: Marginal Gains, Marginalized Field: Focused-scope oriented colleges recognized that quantum biology seemed to offer an explanation for healing that was consistent with subluxation, and joined leading academic medical centers in exploiting this new biological paradigm...Focused-scope chiropractors believe that he new understanding of healing and health form a deeper understanding of biology will lead patients back to adjustments for subluxation.

Scenario 2: Hard Times & Civil War; Another round of Medicare cuts in fee-for-service payments and the growth of low-cost subluxation-only chiropractic franchises with \$30 adjustments made it harder to make a living...Medicare continued to pay chiropractors only for subluxation adjustments—and with periodic fee cuts—but not for other clinical services like nutrition and tobacco counselling.

Scenario 4: Vitalism & Value: Chiropractic colleges also recognized that quantum biology offered an explanation for healing that was consistent with subluxation and joined healing and academic centers in exploring this new biological paradigm while also investigating threads of vitalism research into their work in establishing chiropractic outcomes...Given the availability of low-cost personal and biomonitoring tools to measure body energy flows, key biomarkers, and vital signs, subluxation was getting more clearly defined in terms and models accessible to research scientists. This research also clearly defined the role of the spine and nervous system in the body's internal and intracellular communication systems, energy transfer, and molecular operation.

9.2. Chiropractic Teaching Institutions

It should be apparent that the aforementioned diverging viewpoints as to the legitimacy of the subluxation have downstream effects. Thus, it is reflected by the diverse teaching curricula of the various chiropractic institutions—both within the United States and abroad.

Thus, Funk and his colleagues assessed course listings of chiropractic teaching institutions both domestically and abroad from 2015-2016 or 2016-2017 with multiple campuses listed as separate entities.²⁹⁶ A list of 46 chiropractic degree granting institutions was generated, including diploma, Bachelor of Science (BS), Master of Science (MS), and Doctor of Chiropractic (DC) programs. A total of 36 full course descriptions and 10 course title-only listings were retrieved either through Adobe Acrobat portable document format or through the college's web-based platform.

From the pool of 18 American chiropractic teaching institutions tabulated, the greatest number of mentions of the term subluxation in courses and course titles were from Life University (25), Sherman College of Chiropractic (17), and the Palmer College of Chiropractic, Florida (16). At the other end of the spectrum in which subluxation was not mentioned at all were the National University of Health Sciences and the Southern California University of Health Sciences. Parker University and Life College of Chiropractic West lay in the middle of the spectrum with ten mentions each.

A total of 28 non-US educational institutions were assessed, 18 of which are shown in Table 6B. Data were not available or incomplete from 10 institutions: Universidad Central de Chile (Chile), Tokyo College of Chiropractic (Japan), International Medical University (Malaysia), Universidad Estatal de Valle de Toluca (Mexico), Universidad Estatal de Valle de Ecatepec (Mexico), New Zealand College of Chiropractic (New Zealand), University of Johannesburg (South Africa), Skandinaviska Kiropraktorhogskolan (Sweden), University of Zurich (Switzerland), and McTimoney College of Chiropractic (United Kingdom). The term subluxation was mentioned rarely, within the range of 0-4 times. One would have expected the term to have appeared even in beginning courses mentioning the history of chiropractic, but such was not the case.

The problem with this study was that it only mined the word "subluxation" without delving into what actually was stated in the courses. It is entirely possible that several of the descriptions could have been critical of subluxation rather than supporting it. Indeed, the New Zealand Chiropractic College does not include "subluxation" in its course titles but does in the descriptions under Philosophy and Technique in the first year.²⁹⁷

The coolness toward subluxation is even more dramatically reflected by 13 teaching institutions that signed the declaration of the International Chiropractic Education Collaboration:²⁹⁸

- 1. Anglo-European College, Bournemouth
- 2. The Welsh Institute of Chiropractic, University of South Wales
- 3. The Education of Clinical Biomechanics, University of Southern Denmark
- 4. Chiropractic Medicine, University of Zurich
- 5. Institut Franco-Europeen de Chiropraxie
- 6. Department of Chiropractic, University of Johannesburg
- 7. Department of Chiropractic and Somatology, Durban University of Technology
- 8. Department of Chiropractic, Macquarie University
- 9. Discipline of Chiropractic, Murdoch University
- 10. Chiropractic Division, School of Health Sciences, Malaysia
- 11. University of Bridgeport, College of Health Sciences, School of Chiropractic
- 12. RCU Escorial Maria Cristina, Madrid College of Chiropractic
- 13. Canadian Memorial Chiropractic College

Item #5 in the Position Statement stated that:²⁹⁹

The teaching of vertebral subluxation complex as a vitalistic construct that claims that it is the cause of disease is unsupported by evidence. Its inclusion in a modern chiropractic curriculum in anything other than an historical context is therefore inappropriate and unnecessary.

The abundance of negative assessments of the subluxation requires a detailed analysis, the subject of the next section.

10.0. COMMENTARY: ANALYSIS OF THE NEGATIVE ASSESSMENTS OF THE SUBLUXATION

Adding to the lack of mention of subluxation by two American chiropractic teaching institutions, most non-American schools, and the anti-subluxation declaration by 13 colleges shown above has been an abundance of critical publications, most prominently represented by Keating (2005), Perle (2005), Mirtz (2011), Homola (2013), and Nelson (1997).3, 54, 55, 279, 300 The most vitriolic attack came from Keating and his colleagues, stating that:²⁷⁹

The dogma of subluxation is perhaps the greatest single barrier to professional development for chiropractors. It skews the practice of the art in directions that bring ridicule from the scientific community and uncertainty among the public. failure to challenge subluxation dogma perpetuates a marketing tradition that inevitably prompts charges of quackery. Subluxation dogma leads to legal and political strategies that may amount to a house of cards and warp the profession's sense of self and of mission. Commitment to this dogma undermines the motivation for scientific investigation of subluxation and hypothesis, and so perpetuates the cycle.

An effective response must begin with reframing the subluxation in terms that encompass not only the volume of evidence presented earlier, but are both understandable and of interest to other healthcare professions and the public alike. It seems evident from the preceding evidence that the subluxation possesses several characteristics:

- 1. It may lie beyond the spine as well as within it.
- 2. It is manifested by a cascade of aberrations in neurological transmission that interact with the brain.
- 3. It is also manifested by an inflammatory cascade that carries the risk of leading to an abundance of chronic diseases that may even be a mortality risk.
- 4. It also may be manifested by distinct signs and symptoms, such as pain and possibly cognitive impairment.
- 5. In several instances, it continues to be represented by misalignments and/or alterations of mobility of adjacent vertebral joints.
- 6. In several instances, it is relieved by high-velocity, low-amplitude thrusts adjustments) to vertebral joints exhibiting the properties indicated above in #4.
- 7. Its identification is traditionally achieved by the detection of provoked pain at a specific spinal segmental level or region. High-quality evidence with limitations has also been found for measures of static and motion palpation as well as measures of leg length inequality. Mixed quality evidence with limitations also has included postural evaluation. ²²³
- 8. Its detection with further research may be achieved by muscle testing, sensorimotor processing, or even blood chemistry determinations.

With these properties in mind, it is useful to list the primary arguments raised against the subluxation together with responses to them:

1. There is a lack of scientific evidence, claimed by some to be not enough even to reach a theoretical construct:

The collection of biomechanical, biochemical, neurophysiological, and behavioral evidence presented above in vitro, in animal models, and in humans more than satisfies a body of supporting robust evidence which, parenthetically, was recently found to exist in high quality in only 9.9% of reviews of medical treatments.³⁰¹ Regarding theoretical constructs, at least 50 of these have been listed in a comprehensive text on subluxation.¹

2. The subluxation lacks epidemiological evidence, failing to meet the criteria for causation:

The traditional pillars of causation, called "aspects of association," were introduced by Hill in 1965 (strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment,

and analogy).³⁰² But at the time of their unveiling, the mechanistic connections between exposure and disease were not well understood, in fact unknown and therefore omitted. Over the past 50 years, however, advances in molecular toxicology, genomics, statistics and analytical methods have provided researchers with a much more complex understanding of how diseases initiate and progress, opening what had been the "black box" of exposure to disease paradigm. As a result, new and more diverse criteria need to be considered when establishing causality. For example, statistical significance has replaced strength of association as one of the causality criteria. And instead of straight repetitive findings, triangulation among different types of observation suffices to satisfy the consistency criterion. Finally, occupational or residential exposure which was deemed to fulfil the criterion of specificity, has now been superseded by the actual dose of a chemical, physical, or biological agent.³⁰³ It is difficult not to observe that the elements of the updated consideration of the subluxation described in this monograph are much closer to the criteria mentioned above and are continuing to evolve towards an even closer union

3. The subluxation does not apply to general practice:

Increasing emphasis on prevention and wellness, partly to corral the prohibitive healthcare costs of an aging population beset with chronic disease, has demanded increased attention to the basic sciences and such causative factors as stress and inflammation as drivers of chronic conditions. The preceding evidence has attempted to demonstrate how more progressive concepts of the subluxation lie at the very epicenter of this effort to focus on the early stages of dysfunction which give birth to pathological conditions. Furthermore, these new concepts are couched in terms that are no longer cryptic or opaque but in common usage within the medical community.

4. The subluxation is a prime example of over-aggressive and over-diagnostic efforts to elucidate a nondisease state. It may even be a distraction from true patient benefit, which should be the prime mover of a healthcare profession:

This has been referred to as the Ulysses syndrome, an excessive treatment to correct something that may not be relevant.^{304, 305} Should these pursuits become excessively time-consuming in light of the patient's discomfort and risk, there is merit to this argument. At the same time, however, experimentation can never be discouraged in order to register advances in treatment and perhaps achieve prevention. The argument has been made, for instance, that without experimentation polio victims would still be treated in iron lungs.

5. For the anti-subluxation proponents, Hitchens' variation of Occam's Razor comes into play: "What can be asserted without evidence can be dismissed without evidence."

The riposte to this statement so commonly quoted at scientific conferences is, "Absence of evidence is not evidence of absence." And yet, the evidence in support of, and framing, the more progressive concepts of the subluxation cloaked in terms of physiological responses is in abundance.

6. Clinical studies of the effectiveness of spinal manipulation are conducted and reported without reference to the presence or absence or even the existence of subluxations.

Researchers have reported hundreds of studies on spinal manipulation without ever referring to subluxations, including Craig Nelson who has presented this argument.⁵⁵ Given the large number of institutions, organizations, and individuals who have omitted and even attacked subluxations, Nelson's assertion is no surprise. It does, however, beg the question. At the same time, one could point to countless medical papers that describe, for example, rehabilitation of polio patients without mentioning the pathogen that caused the disease. Such is not to obviate the need elsewhere to have sought the causative agent; otherwise, polio might never have been brought to nearly vanishing levels in many parts of the world.

7. Today there is no scientific gold standard for detecting subluxations as reputedly ubiquitous and presumably significant clinical entities. There is a lack of basic science data to illuminate this phenomenon.

Basic sciences and other forms of inquiry have regrettably been undervalued in traditional pyramids of rigor in evidence-based medicine. However, that inequity is currently being challenged with new and more inclusive models of evidence-based medicine with the recognition of real-world evidence.¹¹⁷ A gold standard may be a moot point in light of the facts that (i) multiple means of detecting the newer concepts of subluxation are at hand ,as discussed earlier, and (ii) triangulation among different observations is currently being accepted as a criterion of causation, also discussed above.³⁰³

Anecdotal evidence of clinical outcomes must be also recognized. Observations of this nature through the ages have fueled future research and should not be ignored.^{117, 306-309}

8. The best available rational and empirical evidence to detect and correct subluxations is a pseudoscience since the Association of Chiropractic Colleges (ACC) does not offer any evidence for the assertions made.

No single party—the ACC included—can be the arbiter of final evidence. Actually, the ACC has sponsored annual research conferences for over 20 years in which different forms of evidence in support of the subluxation have actually been presented as posters, platform and plenary sessions, and published papers. The purpose would be to gather and strengthen the evidence that describes and presumably supports the subluxation. This would nullify the above argument.

9. The available literature does not point to any preferred method of subluxation detection and correction.

A structured search on four databases (Medline, PubMed, CINAHL, and ICL) and hand searches retrieved ²⁰¹ qualifying articles that found that the most convincing favourable evidence was for methods which confirmed or provoked pain and tenderness at a specific spinal segmental level or region. High qualify evidence also supported the use, with limitations, of static and motion palpation as well as measures of leg length inquality.²²³

10. The literature does not offer any clinically practical method of quantifying compromised neural integrity.

Studies cited earlier in this discussion offer encouraging refutation that this particular argument will not endure. They offer promising evidence that indicators of compromised neural integrity could be measured and correlate with the presence and absence of pain and dysfunction. Specifically:

- a. Biochemical measurements of multiple cytokines as inflammatory intermediates decline in parallel with the chiropractic treatment and resolution of chronic back pain.^{121, 129} Inflammation has been shown to be an integral component of the subluxation, and cytokine production is thought to be launched by neural imbalances.
- b. The electrophysiological measurement of somatosensory evoked potentials (SEP) has been shown to decline with the chiropractic treatment and resolution of chronic neck pain.^{161, 310}
- c. The electrophysiological measurements of muscle strength (maximum voluntary contraction [MVC]) and cortical drive (V-wave/Mmax) were shown to increase with a chiropractic intervention compared to a sham control treatment in stroke patients,³¹¹

11. The literature does not offer any health benefit likely to result from subluxation correction.

In addition to identifying compromised neural integrity, the examples provided above in #10 provide encouraging evidence that correction of what is postulated to be the subluxation results in health benefits. The multiple musculoskeletal and visceral disorders that have been addressed and relieved by chiropractic intervention and linked to the subluxation have been addressed elsewhere.^{1, 312}

12. Subluxation has been presented as a "principle."

"Principle" has been defined as either:³¹³

- 1. A fundamental truth or proposition that serves as the foundation for a system of belief or behavior or for a chain of reasoning.
- 2. A general scientific theorem or law that has numerous special applications across a wide field.

Given the vast array of theories of subluxations that have been referenced in this discussion, there is little doubt that the second definition has prevailed through the ages. However, given the broadening awareness of what the subluxation can be defined as, it is a promising prospect that continuing research—much of which has already been accomplished as outlined in this discussion—will eventually allow the subluxation to become a foundation upon which general health may rest.

13. Orthopedic subluxation is not the same as what has been called the subluxation syndrome

As defined by Gatterman, subluxation syndromes are the aggregate of signs and symptoms produced by subluxation of the various spinal and pelvic motion segments.¹ In other words, the subluxation syndrome could be considered to be a downstream manifestation of what has been considered to be the subluxation—orthopedic or otherwise. Which is to say that the subluxation syndrome is the derivative of the orthopaedic species, such that the above argument is a moot point.

14. If subluxation research fails to live up to expectations, erosion of reimbursement for chiropractic services will ensue.

So goes the rule for such medical applications as the hygiene hypothesis, iron lung, or bloodletting—there is no disagreement with terms and practices that have outlived their usefulness in the face of contradictory evidence. However, one could argue that the subluxation has the potential to move in the opposite, positive direction. Specifically, as suggested in this monograph, a robust body of research addressing the subluxation has recently emerged and shows promise of growing even further. A key provision of this prognosis is the acceptance of progressive definitions of the subluxation beyond the hidebound limits of what has plagued this term in the past. Acceptance would necessarily admit the term into usage by the other healthcare professions and eventually into public discourse.

15. Homola has suggested that the subluxation, if it exists, has a temporary effect like a cold shower.³¹⁴ There is no evidence that it has a significant effect on general health.

The correlations of the electrophysiological and inflammatory manifestations of the subluxation with the respective appearances and resolution of back pain,^{121, 129} neck pain,^{161, 310} and stroke³¹¹ as discussed above in #10 offer ample evidence that the subluxation and its resolution produce substantially more than the temporary effects of a cold shower. Rather, as shown in this discussion, the subluxation may have a significant effect on general health. Furthermore, the ongoing research with cognition and motor processing^{159, 169, 170, 174, 175, 315-319} discussed earlier has provided further evidence that the subluxation and general health are closely linked. Finally, the adoption by medicine and its recognition of the term for the condition of cervicogenic headache hints of a subluxation concept thereby mitigating against Homola's notion.

16. According to Homola,³⁰⁰ Mirtz and Perle,⁵⁴ the CCE did not mention subluxation even once in their 2012 accreditation standards.

However, as indicated above, subluxation was clearly mentioned more recently in both the 2013²⁸⁵ and 2018²⁸⁴ versions.

11.0. POSTSCRIPT: ACCEPTING THE SUBLUXATION

Learning to accept the subluxation, which for all intents and purposes is invisible to the naked eye except for surrogate measures, is indeed a challenge. It may be much like what is so commonly observed in the basic sciences; for example postulating the existence of subatomic particles based upon their tracks found in a bubble chamber. Such is the case with the subluxation, in which experimentation such as that described in this report may enable it to emerge into the sunlight of broader acceptance.

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13.0 REFERENCES

- 1. Gatterman M. Foundations of Chiropractic: Subluxation, 2nd Edition. St. Louis, MO: Elsevier Mosby; 2005.
- 2. Goldstein M (editor). The Research Status of Spinal Manipulative Therapy. NINCDS Monograph No.15. Bethesda, MD; 1975.
- 3. Keating J. Science and politics and the subluxation. Amer J Chiropr Med. 1988;1:107-10.
- 4. Rome P. Usage of chiropractic terminology in the literature: 296 ways to say "subluxation": complex issues of the vertebral subluxation. Chiropr Tech. 1996;8:49-60.
- 5. Peters RE. The subluxation-historical perspectives. Chiropractic Journal of Australia. 2009;39:143-50.
- 6. Sagan C. Broca's Brain: Reflections on the Romance of Science. New York, NY: Random House; 1979.
- 7. McDowall DA. Daniel David Palmer's Heritage and His Legacy of Tone to Chiropractic. Canberra, Australia: Southern Cross University; 2021.
- 8. Corpus Hippocrateum, Peri Arthron.
- 9. Paris A. Opera, Liber XV, Cap. XVI; 1582; p. 440-441.
- 10. Hieronymous JH. Do luxationibus et sublucationibus. Jena, Germany; 1746.
- 11. Shiland BJ. Terminology & Anatomy for ICD-10 Coding, 2nd Edition: Elsevier Health Sciences; 2014; p. 107.
- 12. Harrison E. Observations respecting the nature and origin of the common species of disorder of the spine: With critical remarks on the opinions of former writers on this disease. The London Medical and Physical Journal. 1821;45:103.
- 13. Harrison E. Observations on the pathology and treatment of spinal diseases. The London Medical and Physical Journal. 1824;51:351.
- 14. Riadore JE. Treatise on Irritation of the Spinal Nerves as the Source of Nervousness, Indigestion, Functional and Organical Derangements of the Principal Organs of the Body, and on the Modifying Influence of Temperment and Habits of Man Over Diseases and Their Importance as Regards Conducting Successfully the Treatment of the Latter and on the Therapeutic Use of Water. London: J. Churchill; 1843.
- 15. Keating JC. "Heat by nerves and not by blood": The first major reduction in chiropractic theory, 1903. Chiropractic History: The Archives and Journal of the Association for the History of Chiropractic. 1995;15:71-7.
- 16. Smith O. Advertisment: Clarinda Herald. The Chiropractor's Protégé: The Untold Story of Oakley G. Smith's Journal with D.D. Palmer in Chiropractic's Founding Years. Rock Island, IL: Association for the History of Chiropractic; 2017.
- 17. Palmer DD. The Chiropractor's Adjuster: The Text-Book of the Science, Art and Philosophy of Chiropractic. Portland, OR: Portland Printing House; 1910.
- 18. Keating J, Cleveland CS, Menke M. Chiropractic History: A Primer. PracticeMakers_504474 .
- 19. McAllister P. Done by Hand. Pract Neurol. 2019:24-6.
- 20. Carver W. Carver's chiropractic analysis. Oklahoma City: Carver Chiropractic College; 1909.
- 21. Stephenson RW. Chiropractic Text Book. Davenport, IA: Stephenson; 1927.
- 22. Stephenson RW. The Art of Chiropractic. Davenport, IA: Stephenson; 1927.
- 23. Palmer BJ. The Subluxation Specific: The Adjustment Specific and Exposition of the Cause of all Disease. Davenport, IA: Palmer School of Chiropractic; 1934.
- 24. Illi F. The Vertebral Column--Lifeline of the Body. Chicago, IL: National College of Chiropractic; 1951.
- 25. Waagen B, Strang V. Origin and Development of Traditional Chiropractic Philosophy. Norwalk, CT: Appleton & Lange; 1992.
- 26. Janse J, House RH, Wells B. Chiropractic Principles and Technic: For Use by Students and Practitioners: National College of Chiropractic; 1947.
- 27. Palmer DD, Palmer BJ. The Science of Chiropractic: Principles and Adjustments, First Edition. Davenport IA: Palmer School of Chiropractic; 1906.
- 28. Gillet H. Chiropractic Research. Brussels, Belgium; 1952; p. 441 in Reference #25.
- 29. Korr IM. The spinal cord as organizer of disease processes: Some preliminary perspectives. J Am Osteopath Assoc. 1976;76:35-45.
- 30. Sandoz R. The natural history of spinal degenerative lesions. Ann Swiss Chiropr Assoc. 1989;9:149-92
- 31. Leach R. The chiropractic theories: Discussion of some important considerations. ACA J Chiropr. 1981;15.
- 32. Homewood AE. The Neurodynamics of the Vertebral Subluxation, 3rd Edition. St. Petersburg, FL: Valkyrie Press, Inc.; 1977.
- 33. Kane RL, Olsen D, Leymaster C, Woolley FR, Fisher FD. Manipulating the patient. A comparison of the effectiveness of physician and chiropractor care. Lancet. 1974;1:1333-6.
- 34. Senzon SA. The chiropractic vertebral subluxation Part 9: Complexes, models, and consensus from 1979 to 1995. J Chiropr Humanit. 2018;25:130-45.
- 35. Senzon SA. The chiropractic vertebral subluxation Part 1: Introduction. J Chiropr Humanit. 2018;25:10-21.

- 36. Senzon SA. The chiropractic vertebral subluxation Part 2: The earliest subluxation theories from 1902 to 1907. J Chiropr Humanit. 2018;25:22-35.
- 37. Senzon SA. The chiropractic vertebral subluxation Part 10: Integrative and critical literature from 1996 and 1997. J Chiropr Humanit. 2018;25:146-68.
- 38. Smallie DD. Static and dynamic components of the chiropractic subluxation complex: A literature review. J Manipulative Physiol Ther. 1989;12:152.
- 39. Moon D. The flight from the subluxation. Upper Cervical Monogr. 1980;2:1-2.
- 40. Gregory RR. A chiropractic dialogue. 1980;2:10-1.
- 41. Faye LJ. Course lecture notes. Huntington Beach, CA: Motion Palpation Institute; 1981.
- 42. Faye LJ. The subluxation complex. Journal of Chiropractic Humanities. 1999;9:28-31.
- 43. Dishman R. Review of the literature supporting a scientific basis for the chiropractic subluxation complex. J Manipulative Physiol Ther. 1985;8:163-74.
- 44. Lantz CA. Immobilization degeneration and the fixation hypothesis of chiropractic subluxation. Chiropr Res J. 1988;1:21-46.
- 45. Lantz C. The vertebral subluxation complex part 1: An introduction to the model and kinesiological component. Chiropractic Research Journal. 1989;1:23.
- 46. Giusti R. Glossary of Osteopathic Terminology, 3rd Edition. Chevy Chase, MD: American Association of Colleges of Osteopathic Medicine; 2017.
- 47. Liem T. A.T. Still's Osteopathic lesion theory and evidence-based models supporting the emerged concept of somatic dysfunction. J Am Osteopath Assoc. 2016;116:654-61.
- 48. Cooperstein R. The Leading Edge Research Symposium of 1984: Early attempt to achieve consensus on subluxation. Chiropractic History.34:32-54.
- 49. Gatterman MI, Hansen DT. Development of chiropractic nomenclature through consensus. J Manipulative Physiol Ther. 1994;17:302-9.
- 50. Leach R. The Chiropractic Theories, 4th Edition. Baltimore, MD: Williams & Wilkins; 2003.
- Centers for Medicare and Medicaid Services. Medicare Coverage for Chiropractic Services Medical Record Documentation Requirement for Initial and Subsequent Visits. MIN Matters. Washington, DC: Centers for Medicare & Medicaid Services Department of Health and Human Services; 2019.
- 52. Association of Chiropractic Colleges Chiropractic Paradigm / Scope & Practice. 40 The Subluxation. Bethesda, MD: Association of Chiropractic Colleges; 2022.
- 53. Council on Chiropractic Practice. Clinical Practice Guidelines, 4th Edition; 2013.
- 54. Mirtz TA, Perle SM. The prevalence of the term subluxation in North American English-Language Doctor of chiropractic programs. Chiropr Man Therap. 2011;19:14.
- 55. Nelson C. The subluxation question. Journal of Chiropractic Humanities. 1997;7:46-55.
- 56. Bergmann TF, Peterson D, Lawrence D. Chiropractic technique. In Foundations of Chiropractic: Subluxation 2nd Edition, St Louis (Mo): Elsevier Mosby. 2005:133-67.
- 57. Cooperstein R, Gleberzon BJ. Toward a taxonomy of subluxation-equivalents. Topics in Clinical Chiropractic. 2001;8:49-61.
- 58. Beliveau PJH, Wong JJ, Sutton DA, Simon NB, Bussieres AE, Mior SA, et al. The chiropractic profession: A scoping review of utilization rates, reasons for seeking care, patient profiles, and care provided. Chiropr Man Therap. 2017;25:35.
- 59. Medzhitov R. Inflammation 2010: New adventures of an old flame. Cell. 2010;140:771-6.
- 60. Ferrero-Miliani L, Nielsen OH, Andersen PS, Girardin SE. Chronic inflammation: importance of NOD2 and NALP3 in interleukin-1beta generation. Clin Exp Immunol. 2007;147:227-35.
- 61. Nathan C, Ding A. Nonresolving inflammation. Cell. 2010;140:871-82.
- 62. Zhou Y, Hong Y, Huang H. Triptolide attenuates inflammatory response in membranous glomerulo-nephritis rat via downregulation of NF-kappaB signaling pathway. Kidney Blood Press Res. 2016;41:901-10.
- 63. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, et al. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018;9:7204-18.
- 64. Isaacs A, Lindenmann J. Virus interference. I. The interferon. Proc R Soc Lond B Biol Sci. 1957;147:258-67.
- 65. Zhao X, Fan W, Xu Z, Chen H, He Y, Yang G, et al. Inhibiting tumor necrosis factor-alpha diminishes desmoplasia and inflammation to overcome chemoresistance in pancreatic ductal adenocarcinoma. Oncotarget. 2016;7:81110-22.
- 66. Watkins LR, Maier SF. Beyond neurons: Evidence that immune and glial cells contribute to pathological pain states. Physiol Rev. 2002;82:981-1011.
- 67. Mika J, Zychowska M, Popiolek-Barczyk K, Rojewska E, Przewlocka B. Importance of glial activation in neuropathic pain. Eur J Pharmacol. 2013;716:106-19.
- 68. Dinarello CA. Biologic basis for interleukin-1 in disease. Blood. 1996;87:2095-147.
- 69. Braddock M, Quinn A. Targeting IL-1 in inflammatory disease: new opportunities for therapeutic intervention. Nat Rev Drug Discov. 2004;3:330-9.
- 70. Dinarello CA. Therapeutic strategies to reduce IL-1 activity in treating local and systemic inflammation. Curr Opin

Pharmacol. 2004;4:378-85.

- 71. Samoilova EB, Horton JL, Hilliard B, Liu TS, Chen Y. IL-6-deficient mice are resistant to experimental autoimmune encephalomyelitis: Roles of IL-6 in the activation and differentiation of autoreactive T cells. J Immunol. 1998;161:6480-6.
- 72. Ohshima S, Saeki Y, Mima T, Sasai M, Nishioka K, Nomura S, et al. Interleukin 6 plays a key role in the development of antigen-induced arthritis. Proc Natl Acad Sci U S A. 1998;95:8222-6.
- 73. Alonzi T, Fattori E, Lazzaro D, Costa P, Probert L, Kollias G, et al. Interleukin 6 is required for the development of collagen-induced arthritis. J Exp Med. 1998;187:461-8.
- 74. Eriksson U, Kurrer MO, Schmitz N, Marsch SC, Fontana A, Eugster HP, et al. Interleukin-6-deficient mice resist development of autoimmune myocarditis associated with impaired upregulation of complement C3. Circulation. 2003;107:320-5.
- 75. Atreya R, Mudter J, Finotto S, Mullberg J, Jostock T, Wirtz S, et al. Blockade of interleukin 6 trans signaling suppresses T-cell resistance against apoptosis in chronic intestinal inflammation: evidence in crohn disease and experimental colitis in vivo. Nat Med. 2000;6:583-8.
- 76. Yamamoto M, Yoshizaki K, Kishimoto T, Ito H. IL-6 is required for the development of Th1 cell-mediated murine colitis. J Immunol. 2000;164:4878-82.
- 77. Gross V, Andus T, Caesar I, Roth M, Scholmerich J. Evidence for continuous stimulation of interleukin-6 production in Crohn's disease. Gastroenterology. 1992;102:514-9.
- 78. Hirano T, Matsuda T, Turner M, Miyasaka N, Buchan G, Tang B, et al. Excessive production of interleukin 6/B cell stimulatory factor-2 in rheumatoid arthritis. Eur J Immunol. 1988;18:1797-801.
- 79. Grossman RM, Krueger J, Yourish D, Granelli-Piperno A, Murphy DP, May LT, et al. Interleukin 6 is expressed in high levels in psoriatic skin and stimulates proliferation of cultured human keratinocytes. Proc Natl Acad Sci U S A. 1989;86:6367-71.
- 80. Trikha M, Corringham R, Klein B, Rossi JF. Targeted anti-interleukin-6 monoclonal antibody therapy for cancer: A review of the rationale and clinical evidence. Clin Cancer Res. 2003;9:4653-65.
- 81. Steinmetz HT, Herbertz A, Bertram M, Diehl V. Increase in interleukin-6 serum level preceding fever in granulocytopenia and correlation with death from sepsis. J Infect Dis. 1995;171:225-8.
- 82. 82. Moore KW, de Waal Malefyt R, Coffman RL, O'Garra A. Interleukin-10 and the interleukin-10 receptor. Annu Rev Immunol. 2001;19:683-765.
- 83. Kessler B, Rinchai D, Kewcharoenwong C, Nithichanon A, Biggart R, Hawrylowicz CM, et al. Interleukin 10 inhibits pro-inflammatory cytokine responses and killing of Burkholderia pseudomallei. Sci Rep. 2017;7:42791.
- 84. Fiorentino DF, Zlotnik A, Mosmann TR, Howard M, O'Garra A. IL-10 inhibits cytokine production by activated macrophages. J Immunol. 1991;147:3815-22.
- 85. Henderson CN, Cramer GD, Zhang Q, DeVocht JW, Fournier JT. Introducing the external link model for studying spine fixation and misalignment: part 2, Biomechanical features. J Manipulative Physiol Ther. 2007;30:279-94.
- 86. Cramer GD, Henderson CN, Little JW, Daley C, Grieve TJ. Zygapophyseal joint adhesions after induced hypomobility. J Manipulative Physiol Ther. 2010;33:508-18.
- 87. Homb NM, Henderson CN. Spinous process hypertrophy associated with implanted devices in the external link model. J Manipulative Physiol Ther. 2012;35:367-71.
- 88. Bakkum BW, Henderson CN, Hong SP, Cramer GD. Preliminary morphological evidence that vertebral hypomobility induces synaptic plasticity in the spinal cord. J Manipulative Physiol Ther. 2007;30:336-42.
- 89. Cramer GD, Fournier JT, Henderson CNR, Wolcott CC. Degenerative changes following spinal fixation in a small animal model. J Manipulative Physiol Ther. 2004;27:141-54.
- 90. Henderson CNR.Three neurophysiologic theories on the chiropractic subluxation. In: Gatterman MI, editor. Foundations of Chiropractic Subluxation. St. Louis, MO: Elsevier Mosby; 2005; p. 296-303.
- 91. Henderson CN. The basis for spinal manipulation: chiropractic perspective of indications and theory. J Electromyogr Kinesiol. 2012;22:632-42.
- 92. Sato A, Swenson RS. Sympathetic nervous system response to mechanical stress of the spinal column in rats. J Manipulative Physiol Ther. 1984;7:141-7.
- 93. Cao WH, Sato A, Sato Y, Zhou W. Somatosensory regulation of regional hippocampal blood flow in anesthetized rats. Jpn J Physiol. 1992;42:731-40.
- 94. Sato A. Neural mechanisms of somatic sensory regulation of catecholamine secretion from the adrenal gland. Adv Biophys. 1987;23:39-80.
- 95. Sato A, Sato Y, Schmidt RF. The impact of somatosensory input on autonomic functions. Rev Physiol Biochem Pharmacol. 1997;130:1-328.
- 96. Budgell BS. Reflex effects of subluxation: the autonomic nervous system. J Manipulative Physiol Ther. 2000;23:104-6.
- 97. Rome P, Waterhouse J. Neurodynamics of vertebrogenic somatosensory activation and Autonomic Reflexes-a review: Part 2: Autonomic nervous system and somatic reflexes. Asia-Pacific Chiropr J. 2021;1.
- 98. Budgell B, Holtz H, Sato A. Spinovisceral reflexes evoked by noxious and innocuous stimulation of the lumbar

spine. Journal of the Neuromusculoskeletal System. 1995;3:122-31.

- 99. Song XJ, Hu SJ, Greenquist KW, Zhang JM, LaMotte RH. Mechanical and thermal hyperalgesia and ectopic neuronal discharge after chronic compression of dorsal root ganglia. J Neurophysiol. 1999;82:3347-58.
- 100. Song XJ, Vizcarra C, Xu DS, Rupert RL, Wong ZN. Hyperalgesia and neural excitability following injuries to central and peripheral branches of axons and somata of dorsal root ganglion neurons. J Neurophysiol. 2003;89:2185-93.
- 101. Song XJ, Huang ZJ, Song WB, Song XS, Fuhr AF, Rosner AL, et al. Attenuation effect of spinal manipulation on neuropathic and postoperative pain through activating endogenous anti-inflammatory cytokine interleukin 10 in rat spinal cord. J Manipulative Physiol Ther. 2016;39:42-53.
- 102. Song X, Gan Q, Cao J-L, Wang Z-B, Rupert RL. Spinal manipulation reduces pain and hyperalgesia after lumbar intervertebral foramen inflammation in the rat. J Manipulative Physiol Ther. 2006;29:5-13.
- 103. Huang ZJ, Hsu E, Li HC, Rosner AL, Rupert RL, Song XJ. Topical application of compound Ibuprofen suppresses pain by inhibiting sensory neuron hyperexcitability and neuroinflammation in a rat model of intervertebral foramen inflammation. J Pain. 2011;12:141-52.
- 104. Wang ZB, Gan Q, Rupert RL, Zeng YM, Song XJ. Thiamine, pyridoxine, cyanocobalamin and their combination inhibit thermal, but not mechanical hyperalgesia in rats with primary sensory neuron injury. Pain. 2005;114:266-77.
- 105. Kataria N, Yadav P, Kumar R, Kumar N, Singh M, Kant R, et al. Effect of vitamin B6, B9, and B12 supplementation on homocysteine level and cardiovascular outcomes in stroke patients: A meta-analysis of randomized controlled trials. Cureus. 2021;13:e14958.
- 106. den Heijer M, Brouwer IA, Bos GM, Blom HJ, van der Put NM, Spaans AP, et al. Vitamin supplementation reduces blood homocysteine levels: A controlled trial in patients with venous thrombosis and healthy volunteers. Arterioscler Thromb Vasc Biol. 1998;18:356-61.
- 107. McKinley MC, McNulty H, McPartlin J, Strain JJ, Pentieva K, Ward M, et al. Low-dose vitamin B-6 effectively lowers fasting plasma homocysteine in healthy elderly persons who are folate and riboflavin replete. Am J Clin Nutr. 2001;73:759-64.
- 108. Wu JT. Circulating homocysteine is an inflammation marker and a risk factor of life-threatening inflammatory diseases. J Biomed Lab Sci. 2007;19:107-11.
- 109. Li T, Chen Y, Li J, Yang X, Zhang H, Qin X, et al. Serum homocysteine concentration Is significantly associated with inflammatory/immune factors. PLoS One. 2015;10:e0138099.
- 110. Wiberg JMM, Nordsteen J, Nilsson N. The short-term effectof spinal manipulation in the treatment of infantile colic: A randomized controlled trial with a blinded observer. J Manipulative Physiol Ther. 1999;22:517-22.
- 111. Kokjohn K, Schmid DM, Triano JJ, Brennan PC. The effect of spinal manipulation on pain and prostaglandin levels in women with primary dysmenorrhea. J Manipulative Physiol Ther. 1992;15:279-85.
- 112. Plaugher G, Long CR, Alcantara J, Silverus AD, Wood H, Lotun K, et al. Practice-based randomized controlledcomparison clinical trial of chiropractic adjustments and brief massage treatment at sites of subluxation in subjects with essential hypertension: Pilot study. J Manipulative Physiol Ther. 2002;25:221-39.
- 113. Bronfort G, Evans RL, Kubic P, Filkin P. Chronic pediatric asthma and chiropractic spinal manipulation: A prospective clinical series and randomized clinical pilot study. J Manipulative Physiol Ther. 2002;24:369-77.
- 114. Fallon JM. The role of the chiropractic adjustment in the care and treatment of 332 children with otitis media. Journal of Clinical Chiropractic Pediatrics. 1997;2:167-83.
- 115. Pollard H, Ward G, Hoskins W, Hardy K. The effect of a manual therapy knee protocol on osteoarthritic knee pain: A randomised controlled trial. J Can Chiropr Assoc. 2008;52:229-42.
- 116. Goertz CM, Hurwitz EL, Murphy BA, Coulter ID. Extrapolating beyond the data in a systematic review of spinal manipulation for nonmusculoskeletal disorders: A fall from the summit. J Manipulative Physiol Ther. 2021;44:271-9.
- 117. Rosner AL. Evidence-based medicine: revisiting the pyramid of priorities. J Bodyw Mov Ther. 2012;16:42-9.
- 118. Teodorczyk-Injeyan JA, Injeyan HS, Ruegg R. Spinal manipulative therapy reduces inflammatory cytokines but not substance P production in normal subjects. J Manipulative Physiol Ther. 2006;29:14-21.
- 119. Teodorczyk-Injeyan JA, Injeyan S, Ruegg R. Spinal manipulative therapy (SMT) augments production of antiinflammatory cytokine IL-10 in normal subjects. World Federation of Chiropractic 9th Biennial Congress. Vilamoura, Portugal; 2007; p. 143-4.
- 120. Koch A, Zacharowski K, Boehm O, Stevens M, Lipfert P, von Giesen HJ, et al. Nitric oxide and pro-inflammatory cytokines correlate with pain intensity in chronic pain patients. Inflamm Res. 2007;56:32-7.
- 121. Teodorczyk-Injeyan JA, Triano JJ, Gringmuth R, DeGraauw C, Chow A, Injeyan HS. Effects of spinal manipulative therapy on inflammatory mediators in patients with non-specific low back pain: A non-randomized controlled clinical trial. Chiropr Man Therap. 2021;29:3.
- 122. McEwen BS. Physiology and neurobiology of stress and adaptation: Central role of the brain. Physiol Rev. 2007;87:873-904.
- 123. Danese A, Caspi A, Williams B, Ambler A, Sugden K, Mika J, et al. Biological embedding of stress through inflammation processes in childhood. Mol Psychiatry. 2011;16:244-6.
- 124. Hassett AL, Clauw DJ. The role of stress in rheumatic diseases. Arthritis Res Ther. 2010;12:123.
- 125. Marsland AL, Bachen EA, Cohen S, Rabin B, Manuck SB. Stress, immune reactivity and susceptibility to infectious

disease. Physiol Behav. 2002;77:711-6.

- 126. Marsland AL, Walsh C, Lockwood K, John-Henderson NA. The effects of acute psychological stress on circulating and stimulated inflammatory markers: A systematic review and meta-analysis. Brain Behav Immun. 2017;64:208-19.
- 127. Walker S. Neuro emotional technique seminar manual. Encinitas, CA; 2006.
- 128. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: Bibliographic study of patient assessed health outcome measures. BMJ. 2002;324:1417.
- 129. Bablis P, Pollard H, Rosner AL. Stress reduction via neuro-emotional technique to achieve the simultaneous resolution of chronic low back pain with multiple inflammatory and biobehavioural indicators: A randomized, double-blinded, placebo-controlled trial. J Integr Med. 2022;20:135-44.
- 130. Murphy B, Dawson N, Slack J. Sacroiliac joint manipulation decreases the H-reflex. Electromyogr Clin Neurophysiol. 1995;35:87-94.
- 131. Herzog W, Scheele D, Conway PJ. Electromyographic responses of back and limb muscles associated with spinal manipulative therapy. Spine (Phila Pa 1976). 1999;24:146-52; discussion 53.
- 132. Suter E, McMorland G, Herzog W, Bray R. Decrease in quadriceps inhibition after sacroiliac joint manipulation in patients with anterior knee pain. J Manipulative Physiol Ther. 1999;22:149-53.
- 133. Niazi IK, Turker KS, Flavel S, Kinget M, Duehr J, Haavik H. Changes in H-reflex and V-waves following spinal manipulation. Exp Brain Res. 2015;233:1165-73.
- 134. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: Scientific advances and future directions. Psychol Bull. 2007;133:581-624.
- 135. Waddell G. Low back pain: A twentieth century health care enigma. Spine (Phila Pa 1976). 1996;21:2820-5.
- 136. Pelletier R, Higgins J, Bourbonnais D. Is neuroplasticity in the central nervous system the missing link to our understanding of chronic musculoskeletal disorders? BMC Musculoskelet Disord. 2015;16:25.
- 137. Haavik H, Kumari N, Holt K, Niazi IK, Amjad I, Pujari AN, et al. The contemporary model of vertebral column joint dysfunction and impact of high-velocity, low-amplitude controlled vertebral thrusts on neuromuscular function. Eur J Appl Physiol. 2021;121:2675-720.
- 138. Liu CZ, Kong J, Wang K. Acupuncture therapies and neuroplasticity. Neural Plast. 2017:6178505.
- 139. Haavik H. The contemporary understanding of the chiropractic subluxation. In: Plaugher G, Anrig C, editors. Pediatric Chiropractic, 3rd Edition. Philadelphia, PA: Walters Kluwer; 2023. p. 29-89.
- 140. McDowall D, Emmanuel E, Grace S, Chaseling M. Tone as a health concept: An analysis. Complement Ther Clin Pract. 2017;29:27-34.
- 141. Pascual-Leone A, Amedi A, Fregni F, Merabet LB. The plastic human brain cortex. Annu Rev Neurosci. 2005;28:377-401.
- 142. Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Hauser W. Nociplastic pain: Towards an understanding of prevalent pain conditions. Lancet. 2021;397:2098-110.
- 143. Hiraga SI, Itokazu T, Nishibe M, Yamashita T. Neuroplasticity related to chronic pain and its modulation by microglia. Inflamm Regen. 2022;42:15.
- 144. Costigan M, Scholz J, Woolf CJ. Neuropathic pain: A maladaptive response of the nervous system to damage. Annu Rev Neurosci. 2009;32:1-32.
- 145. Apkarian VA, Hashmi JA, Baliki MN. Pain and the brain: Specificity and plasticity of the brain in clinical chronic pain. Pain. 2011;152:S49-S64.
- 146. Carter LE, McNeil DW, Vowles KE, Sorrell JT, Turk CL, Ries BJ, et al. Effects of emotion on pain reports, tolerance and physiology. Pain Res Manag. 2002;7:21-30.
- 147. Zweyer K, Velker B, Ruch W. Do cheerfulness, exhilaration, and humor production moderate pain tolerance? A FACS study. 2004.
- 148. Ceunen E, Vlaeyen JW, Van Diest I. On the origin of interoception. Front Psychol. 2016;7:743.
- 149. Tinazzi M, Zanette G, Volpato D, Testoni R, Bonato C, Manganotti P, et al. Neurophysiological evidence of neuroplasticity at multiple levels of the somatosensory system in patients with carpal tunnel syndrome. Brain. 1998;121 (Pt 9):1785-94.
- 150. Lee H, Nicholson LL, Adams RD. Cervical range of motion associations with subclinical neck pain. Spine (Phila Pa 1976). 2004;29:33-40.
- 151. Lee HY, Wang JD, Yao G, Wang SF. Association between cervicocephalic kinesthetic sensibility and frequency of subclinical neck pain. Man Ther. 2008;13:419-25.
- 152. Lee H, Nicholson LL, Adams RD, Bae SS. Proprioception and rotation range sensitization associated with subclinical neck pain. Spine (Phila Pa 1976). 2005;30:E60-7.
- 153. Farid B, Yielder P, Holmes M, Haavik H, Murphy BA. Association of subclinical neck pain with altered multisensory integration at baseline and 4-week follow-up relative to asymptomatic controls. J Manipulative Physiol Ther. 2018;41:81-91.
- 154. Haavik H, Murphy B. Subclinical neck pain and the effects of cervical manipulation on elbow joint position sense. J Manipulative Physiol Ther. 2011;34:88-97.
- 155. Llinas R, Welsh JP. On the cerebellum and motor learning. Curr Opin Neurobiol. 1993;3:958-65.

- 156. Manzoni D. The cerebellum and sensorimotor coupling: looking at the problem from the perspective of vestibular reflexes. Cerebellum. 2007;6:24-37.
- 157. Manzoni D. The cerebellum may implement the appropriate coupling of sensory inputs and motor responses: Evidence from vestibular physiology. Cerebellum. 2005;4:178-88.
- 158. Marshall JF. Brain function: neural adaptations and recovery from injury. Annu Rev Psychol. 1984;35:277-308.
- 159. Andrew D, Yielder P, Haavik H, Murphy B. The effects of subclinical neck pain on sensorimotor integration following a complex motor pursuit task. Exp Brain Res. 2018;236:1-11.
- 160. Haavik-Taylor H, Murphy B. Cervical spine manipulation alters sensorimotor integration: A somatosensory evoked potential study. Clin Neurophysiol. 2007;118:391-402.
- 161. Taylor HH, Murphy B. Altered central integration of dual somatosensory input after cervical spine manipulation. J Manipulative Physiol Ther. 2010;33:178-88.
- 162. Tinazzi M, Priori A, Bertolasi L, Frasson E, Mauguiere F, Fiaschi A. Abnormal central integration of a dual somatosensory input in dystonia. Evidence for sensory overflow. Brain. 2000;123 (Pt 1):42-50.
- 163. Abbruzzese G, Berardelli A. Sensorimotor integration in movement disorders. Mov Disord. 2003;18:231-40.
- 164. Taylor HH, Murphy B. The effects of spinal manipulation on central integration of dual somatosensory input observed after motor training: A crossover study. J Manipulative Physiol Ther. 2010;33:261-72.
- 165. Strutton PH, Theodorou S, Catley M, McGregor AH, Davey NJ. Corticospinal excitability in patients with chronic low back pain. J Spinal Disord Tech. 2005;18:420-4.
- 166. Waberski TD, Lamberty K, Dieckhofer A, Buchner H, Gobbele R. Short-term modulation of the ipsilateral primary sensory cortex by nociceptive interference revealed by SEPs. Neurosci Lett. 2008;435:137-41.
- 167. Rossi S, della Volpe R, Ginanneschi F, Ulivelli M, Bartalini S, Spidalieri R, et al. Early somatosensory processing during tonic muscle pain in humans: Relation to loss of proprioception and motor 'defensive' strategies. Clin Neurophysiol. 2003;114:1351-8.
- 168. Lelic D, Niazi IK, Holt K, Jochumsen M, Dremstrup K, Yielder P, et al. Manipulation of dysfunctional spinal joints affects sensorimotor integration in the prefrontal cortex: A brain source localization study. Neural Plast. 2016;2016:3704964.
- 169. Daligadu J, Haavik H, Yielder PC, Baarbe J, Murphy B. Alterations in cortical and cerebellar motor processing in subclinical neck pain patients following spinal manipulation. J Manipulative Physiol Ther. 2013;36:527-37.
- 170. Baarbe JK, Yielder P, Haavik H, Holmes MWR, Murphy BA. Subclinical recurrent neck pain and its treatment impacts motor training-induced plasticity of the cerebellum and motor cortex. PLoS One. 2018;13:e0193413.
- 171. Palmgren PJ, Sandstrom PJ, Lundqvist FJ, Heikkila H. Improvement after chiropractic care in cervicocephalic kinesthetic sensibility and subjective pain intensity in patients with nontraumatic chronic neck pain. J Manipulative Physiol Ther. 2006;29:100-6.
- 172. Palmgren PJ, Lindeberg A, Nath S, Heikkila H. Head repositioning accuracy and posturography related to cervical facet nerve blockade and spinal manipulative therapy in healthy volunteers: A time series study. J Manipulative Physiol Ther. 2009;32:193-202.
- 173. Palmgren PJ, Andreasson D, Eriksson M, Hagglund A. Cervicocephalic kinesthetic sensibility and postural balance in patients with nontraumatic chronic neck pain--a pilot study. Chiropr Osteopat. 2009;17:6.
- 174. Haavik H, Niazi IK, Jochumsen M, Sherwin D, Flavel S, Türker KS. Impact of spinal manipulation on cortical drive to upper and lower limb muscles. Brain sciences. 2016;7:2.
- 175. Christiansen TL, Niazi IK, Holt K, Nedergaard RW, Duehr J, Allen K, et al. The effects of a single session of spinal manipulation on strength and cortical drive in athletes. Eur J Appl Physiol. 2018;118:737-49.
- 176. Karason AB, Drysdale IP. Somatovisceral response following osteopathic HVLAT: a pilot study on the effect of unilateral lumbosacral high-velocity low-amplitude thrust technique on the cutaneous blood flow in the lower limb. J Manipulative Physiol Ther. 2003;26:220-5.
- 177. Driscoll MD. Arterial tonometry and assessment of cardiovascular alterations with chiropractic spinal manipulative therapy. J Manipulative Physiol Ther. 1997;20:47-55.
- 178. Pelissier AL, Gantenbein M, Bruguerolle B. Nicotine-induced perturbations on heart rate, body temperature and locomotor activity daily rhythms in rats. J Pharm Pharmacol. 1998;50:929-34.
- 179. Sachar K, Goel R, Weiss AP. Acute and chronic effects of nicotine on anastomotic patency following ischemia/ reperfusion. J Reconstr Microsurg. 1998;14:179-84.
- 180. Sauro HM. Control and regulation of pathways via negative feedback. J R Soc Interface. 2017;14.
- 181. Waddell G. The Back Pain Revolution. Edinburgh, Scotland: Churchill Livingstone; 2004.
- 182. Wadell G, Feder G, McIntosh A, Lewis M, Hutchinson A. Low Back Pain Evidence Review, 1st Edition. London, United Kingdom: Royal College of General Practitioners; 1996.
- 183. Pert CB. The Molecules of Emotion : Why We Feel the Way We Feel. New York, NY: Scribner; 1997.
- 184. Viner R. Putting stress in life: Hans Selye and the making of stress theory. Social Studies Science. 1999;29:391-410.
- 185. Selye H. The Stress of Life. New York: McGraw-Hill; 1956.
- 186. Kovacs KJ, Mikos IH, Bali B. Psychological and physiological stressors. In: Steckler T, Kalin H, Reul JMHM, editors. Handbook of Stress and the Brain: Elsevier BV; 2005; p. 775-92.

- 187. Nurlson R. The neurobiology of stress. In: al'Alosi M, Flaten MA, editors. Neuroscience of Pain, Stress, and Emotion: Psychological and Clinical Applications. New York, NY: Academic Press; 2016. p. 29-49.
- 188. Graham JE, Christian LM, Kiecolt-Glaser JK. Stress, age, and immune function: toward a lifespan approach. J Behav Med. 2006;29:389-400.
- 189. Bernton EW, Meltzer MS, Holaday JW. Suppression of macrophage activation and T-lymphocyte function in hypoprolactinemic mice. Science. 1988;239:401-4.
- 190. Amiercan Chiropractic Association. Five Things Physicians and Patients Should Question. Choosing Wisely: ABIM Foundation; June 1, 2019.
- 191. Taylor JAM. The Role of Radiopgraphy in Evaluating Subluxation. St Louis, MO: Elsevier Mosby; 2005.
- 192. Taylor JA. Full-spine radiography: A review. J Manipulative Physiol Ther. 1993;16:460-74.
- 193. Hildebrandt RW. Chiropractic Spinographology, 2nd Edition. Baltimore, MD: Williams & Wilkins; 1985.
- 194. Howe J. Facts and fallacies, myths and misconceptions in spinography. J Clin Chiro Archives Edition. 1972;2:1-7.
- 195. Hildebrandt RW Chiropractic spinography and postural roentgenography. II. Clinical basis. J Manipulative Physiol Ther. 1981;4:191-201.
- 196. Grice A. Radiographic, biomechanical, and clinical factors in lumbar lateral flexion: Part I. J Manipulative Physiol Ther. 1979;2:26-34.
- 197. Dupuis PR, Yong-Hing K, Cassidy JD, Kirkaldy-Willis WH. Radiologic diagnosis of degenerative lumbar spinal instability. Spine (Phila Pa 1976). 1985;10:262-76.
- 198. Gitelman R. A chiropractice approach to biomechanical disorders of the lumbar spine and pelvis. Norwalk, CT: Appleton-Century Crofts; 1980.
- 199. Breen AC, Teyhen DS, Mellor FE, Breen AC, Wong KW, Deitz A. Measurement of intervertebral motion using quantitative fluoroscopy: Report of an international forum and proposal for use in the assessment of degenerative disc disease in the lumbar spine. Adv Orthop. 2012;2012:802350.
- 200. Breen A, Breen A. Accuracy and repeatability of quantitative fluoroscopy for the measurement of sagittal plane translation and finite centre of rotation in the lumbar spine. Med Eng Phys. 2016;38:607-14.
- 201. Jenkins HJ, Downie AS, Moore CS, French SD. Current evidence for spinal X-ray use in the chiropractic profession: A narrative review. Chiropr Man Therap. 2018;26:48.
- 202. Ferrari R. Imaging studies in patients with spinal pain: Practice audit evaluation of Choosing Wisely Canada recommendations. Can Fam Physician. 2016;62:e129-37.
- 203. Oakley PA, Harrison DE. Are restrictive medical radiation imaging campaigns misguided? It seems so: A case example of the American Chiropractic Association's adoption of "Choosing Wisely". Dose Response. 2020;18:1559325820919321.
- 204. George Chiropractic Council. GCC Board Rejects ABIM Foundation Choosing Wisely Campaign. Unanimously Adopts ICA's PCCR X-Ray Protocols in Best Practices; 2018.
- 205. Haneline M, Cooperstein R, Young M, Birkeland K. An annotated bibliography of spinal motion palpation reliability studies. J Can Chiropr Assoc. 2009;53:40-58.
- 206. Haneline MT, Cooperstein R, Young M, Birkeland K. Spinal motion palpation: a comparison of studies that assessed intersegmental end feel vs excursion. J Manipulative Physiol Ther. 2008;31:616-26.
- 207. Hestbaek L, Leboeuf-Yde C. Are chiropractic tests for the lumbo-pelvic spine reliable and valid? A systematic critical literature review. J Manipulative Physiol Ther. 2000;23:258-75.
- 208. Seffinger MA, Najm WI, Mishra SI, Adams A, Dickerson VM, Murphy LS, et al. Reliability of spinal palpation for diagnosis of back and neck pain: A systematic review of the literature. Spine (Phila Pa 1976). 2004;29:E413-25.
- 209. Marcotte J, Normand MC, Black P. Measurement of the pressure applied during motion palpation and reliability for cervical spine rotation. J Manipulative Physiol Ther. 2005;28:591-6.
- 210. Billis EV, Foster NE, Wright CC. Reproducibility and repeatability: errors of three groups of physiotherapists in locating spinal levels by palpation. Man Ther. 2003;8:223-32.
- 211. Huijbregts PA. Spinal motion palpation: A review of reliability studies. J Man Manip Ther. 2002;10:24-39.
- 212. Cooperstein R, Haneline MT. Spinous process palpation using the scapular tip as a landmark vs a radiographic criterion standard. J Chiropr Med. 2007;6:87-93.
- 213. Cooperstein R, Haneline MT, Young MD. The location of the inferior angle of the scapula in relation to the spinal level of prone patients. J Can Chiropr Assoc. 2009;53:121-8.
- 214. Haneline MT, Cooperstein R, Young MD, Ross J. Determining spinal level using the inferior angle of the scapula as a reference landmark: A retrospective analysis of 50 radiographs. J Can Chiropr Assoc. 2008;52:24-9.
- 215. Chakraverty R, Pynsent P, Isaacs K. Which spinal levels are identified by palpation of the iliac crests and the posterior superior iliac spines? J Anat. 2007;210:232-6.
- 216. Cooperstein R, Young M, Haneline M. Interexaminer reliability of cervical motion palpation using continuous measures and rater confidence levels. J Can Chiropr Assoc. 2013;57:156-64.
- 217. Cooperstein R, Young M. The reliability of lumbar motion palpation using continuous analysis and confidence ratings: Choosing a relevant index of agreement. J Can Chiropr Assoc. 2016;60:146-57.
- 218. Cooperstein R, Young M. The reliability of spinal motion palpation determination of the location of the stiffest spinal

site is influenced by confidence ratings: A secondary analysis of three studies. Chiropr Man Therap. 2016;24:50.

- 219. Cooperstein R, Haneline M, Young M. Interexaminer reliability of thoracic motion palpation using confidence ratings and continuous analysis. J Chiropr Med. 2010;9:99-106.
- 220. Woerman AL, Binder-Macleod SA. Leg length discrepancy assessment: accuracy and precision in five clinical methods of evaluation. J Orthop Sports Phys Ther. 1984;5:230-9.
- 221. Still A. Manual of Osteopathic Technique, 2nd Edition. London, United Kingdom: Hutchinson Company; 1959.
- 222. Holt KR, Russell DG, Hoffmann NJ, Bruce BI, Bushell PM, Taylor HH. Interexaminer reliability of a leg length analysis procedure among novice and experienced practitioners. J Manipulative Physiol Ther. 2009;32:216-22.
- 223. Triano JJ, Budgell B, Bagnulo A, Roffey B, Bergmann T, Cooperstein R, et al. Review of methods used by chiropractors to determine the site for applying manipulation. Chiropr Man Therap. 2013;21:36.
- 224. Cooperstein R, Morschhauser E, Lisi AJ. Cross-sectional validity study of compressive leg checking in measuring artificially created leg length inequality. J Chiropr Med. 2004;3:91-5.
- 225. French SD, Green S, Forbes A. Reliability of chiropractic methods commonly used to detect manipulable lesions in patients with chronic low-back pain. J Manipulative Physiol Ther. 2000;23:231-8.
- 226. Schneider M, Homonai R, Moreland B, Delitto A. Interexaminer reliability of the prone leg length analysis procedure. J Manipulative Physiol Ther. 2007;30:514-21.
- 227. Schmitt WH, Jr., Yanuck SF. Expanding the neurological examination using functional neurologic assessment: part II neurologic basis of applied kinesiology. Int J Neurosci. 1999;97:77-108.
- 228. Goodheart GJ. Applied Kinesiology Research Manuals. Detroit, MI; 1964-1998.
- 229. Cuthbert SC, Goodheart GJ, Jr. On the reliability and validity of manual muscle testing: A literature review. Chiropr Osteopat. 2007;15:4.
- 230. Walther DS. Applied Kinesiology Synopsis, 2nd Edition. Shawnee Mission, KS: International College of Applied Kinesiology; 2000.
- 231. Haas M, Cooperstein R, Peterson D. Disentangling manual muscle testing and Applied Kinesiology: Critique and reinterpretation of a literature review. Chiropr Osteopat. 2007;15:11.
- 232. Conable KM. Intraexaminer comparison of applied kinesiology manual muscle testing of varying durations: A pilot study. J Chiropr Med. 2010;9:3-10.
- 233. Rosner AL, Leisman G, Gilchriest J, Charles E, Keschner MG, Minond M. Reliability and validity of therapy localization as determined from multiple examiners and instrumentation. Functional Neurology, Rehabilitation, and Ergonomics. 2015;5:365.
- 234. Caruso W, Leisman G. A force/displacement analysis of muscle testing. Percept Mot Skills. 2000;91:683-92.
- 235. Schwartz SA, Utts J, Spottiswoode SJ, Shade CW, Tully L, Morris WF, et al. A double-blind, randomized study to assess the validity of applied kinesiology (AK) as a diagnostic tool and as a nonlocal proximity effect. Explore (NY). 2014;10:99-108.
- 236. Rosner AL, Cuthbert SC. Applied kinesiology: distinctions in its definition and interpretation. J Bodyw Mov Ther. 2012;16:464-87.
- 237. Ochoa-Cacique D, Cordoba-Mosqueda ME, Aguilar-Calderon JR, Garcia-Gonzalez U, Ibarra-De la Torre A, Reyes-Rodriguez VA, et al. Double crush syndrome: Epidemiology, diagnosis, and treatment results. Neurochirurgie. 2021;67:165-9.
- 238. Phan A, Shah S, Hammert W, Mesfin A. Double Crush Syndrome of the upper extremity. J Bone Joint Surg. 2021;9.
- 239. Ren HJ, Ye X, Li PY, Shen YD, Qiu YQ, Xu WD. Outcomes of ulnar nerve decompression for double crush syndrome. Br J Neurosurg. 2021:1-9.
- 240. Barbu BA, Handra C-M, Bădoiu S, Nica SA. A case of bilateral "double/multiple crush" entrapment syndrome of the upper limbs in a violinist. Romanian Journal of Occupational Medicine. 2020;71:49-58.
- 241. Siu G, Jaffe JD, Rafique M, Weinik MM. Osteopathic manipulative medicine for carpal tunnel syndrome. J Osteopath Med. 2012;112:127-39.
- 242. Burnham T, Higgins DC, Burnham RS, Heath DM. Effectiveness of osteopathic manipulative treatment for carpal tunnel syndrome: A pilot project. J Osteopath Med. 2015;115:138-48.
- 243. Davis PT, Hulbert JR, Kassak KM, Meyer JJ. Comparative efficacy of conservative medical and chiropractic treatments for carpal tunnel syndrome: A randomized clinical trail. J Manipulative Physiol Ther. 1998;21:317-26.
- 244. Bergman GJ, Winters JC, Groenier KH, Pool JJ, Meyboom-de Jong B, Postema K, et al. Manipulative therapy in addition to usual medical care for patients with shoulder dysfunction and pain: A randomized, controlled trial. Ann Intern Med. 2004;141:432-9.
- 245. Bergman GJ, Winter JC, van Tulder MW, Meyboom-de Jong B, Postema K, van der Heijden GJ. Manipulative therapy in addition to usual medical care accelerates recovery of shoulder complaints at higher costs: Economic outcomes of a randomized trial. BMC Musculoskelet Disord. 2010;11:200.
- 246. McHardy A, Hoskins W, Pollard H, Onley R, Windsham R. Chiropractic treatment of upper extremity conditions: A systematic review. J Manipulative Physiol Ther. 2008;31:146-59.
- 247. Brantingham JW, Cassa TK, Bonnefin D, Pribicevic M, Robb A, Pollard H, et al. Manipulative and multimodal therapy for upper extremity and temporomandibular disorders: A systematic review. J Manipulative Physiol Ther.

2013;36:143-201.

- 248. Pollard H, Ward G, Hoskins W, Hardy K. The effect of a manual therapy knee protocol on osteoarthritic knee pain: A randomised controlled trial. J Can Chiropractic Assoc. 2008;52:229.
- 249. Hoskins W, McHardy A, Pollard H, Windsham R, Onley R. Chiropractic treatment of lower extremity conditions: A literature review. J Manipulative Physiol Ther. 2006;29:658-71.
- 250. Brantingham JW, Globe G, Pollard H, Hicks M, Korporaal C, Hoskins W. Manipulative therapy for lower extremity conditions: expansion of literature review. J Manipulative Physiol Ther. 2009;32:53-71.
- 251. Brantingham JW, Bonnefin D, Perle SM, Cassa TK, Globe G, Pribicevic M, et al. Manipulative therapy for lower extremity conditions: Update of a literature review. J Manipulative Physiol Ther. 2012;35:127-66.
- 252. Upledger JE, Vredevogt J. Craniosacral Therapy. Seattle, WA: Eastland Press; 1983.
- 253. Greenman P, Mein EA, Andary M. Craniosacral manipulation. Phys Med Rehabil Clin N Am. 1996;7:872-96.
- 254. Cutler MJ, Holland BS, Stupski BA, Gamber RG, Smith ML. Cranial manipulation can alter sleep latency and sympathetic nerve activity in humans: A pilot study. J Altern Complement Med. 2005;11:103-8.
- 255. Miana L, Bastos VH, Machado S, Arias-Carrion O, Nardi AE, Almeida L, et al. Changes in alpha band activity associated with application of the compression of fourth ventricular (CV-4) osteopathic procedure: A qEEG pilot study. J Bodyw Mov Ther. 2013;17:291-6.
- 256. Green C, Marti CW, Bassett K, Kazanjian A. A Systematic Review and Critical Appraisal of the Scientific Evidence on Craniosacral Therapy. Joint Health Technology Assessment Series. Vancouver, British Columbia, Canada: University of British Columbia; 1999.
- 257. Haller H, Lauche R, Sundberg T, Dobos G, Cramer H. Craniosacral therapy for chronic pain: a systematic review and meta-analysis of randomized controlled trials. BMC Musculoskelet Disord. 2019;21:1.
- 258. The Rubicon Group. 2002.
- 259. Margach RW. Chiropractic functional neurology: An introduction. Integr Med (Encinitas). 2017;16:44-5.
- 260. Functional Neurology: What is it And Where is the Evidence? : Australian Spinal Research Foundation; 2018.261. Demortier M, Leboeuf-Yde C. Unravelling functional neurology: An overview of all published documents by FR
- Carrick, including a critical review of research articles on its effect or benefit. Chiropr Man Therap. 2020;28:9.
- 262. Rosner A. In support of evidence-informed functional neurology. Journal of Integrative Medicine. Submitted for publication, January 2023.
- 263. Beck RW. Functional Neurology for Practitioners of Manual Medicine, 2nd Edition. Oxford, United Kingdom: Elsevier; 2011.
- 264. Meyer AL, Meyer A, Etherington S, Leboeuf-Yde C. Unravelling functional neurology: A scoping review of theories and clinical applications in a context of chiropractic manual therapy. Chiropr Man Therap. 2017;25:19.
- 265. Behrman S, Ebmeier K. Can exercise prevent cognitive decline? The Practitioner. 2014;258:17-21, 2-3.
- 266. Barnes JN. Exercise, cognitive function, and aging. Adv Physiol Educ. 2015;39:55-62.
- 267. Biondi M, Zannino LG. Psychological stress, neuroimmunomodulation, and susceptibility to infectious diseases in animals and man: A review. Psychother Psychosom. 1997;66:3-26.
- 268. Ader R, Cohen N, Felten D. Psychoneuroimmunology: Interactions between the nervous system and the immune system. Lancet. 1995;345:99-103.
- 269. Rotenberg VS, Sirota P, Elizur A. Psychoneuroimmunology: Searching for the main deteriorating psychobehavioral factor. Genetic Social And General Psychology Monographs. 1996;122:329-46.
- 270. Morgan L. Psychoneuroimmunology, the placebo effect and chiropractic. J Manipulative Physiol Ther. 1998;21:484-91.
- 271. Brimhall J. Memo to David Chapman-Smith, Secretary General of the World Federation of Chiropractic. 2005.
- 272. Senzon SA. The Roots of Subluxation. Today's Chiropractic Lifestyle. New York, NJ Montclair, NJ: Slow Burn Personal Training System; 2008; p. 38,40.
- 273. International Federation of Chiropractors and Organizations. Position Paper on Vertebral Subluxation as a Sole Rational for Care. Saratoga Springs, NY: IFCO.
- 274. Foundation for Vertebral Subluxation. Home Page. Kennesaw, GA; 2018.
- 275. International Chiropractors Association. ICA Policy Statement on Chiropractic Diagnosis. Arlington, VA; 2017.
- 276. International Chiropractors Association. Policy Handbook and Code of Ethics, 2nd Edition. Arlington, VA: International Chiropractors Association; 1991.
- 277. American Chiropractic Association. Core Beliefs, Policies, Positions, and Guidelines. Arlington, VA: American Chiropractic Association; 2021.
- 278. FAQ Canadian Chiropractic Association. Toronto, Ontario, Canada: Canadian Chiropractic Association.
- 279. Keating JC, Jr., Charlton KH, Grod JP, Perle SM, Sikorski D, Winterstein JF. Subluxation: Dogma or science? Chiropr Osteopat. 2005;13:17.
- 280. News Staff. Australian Chiropractors Association Bans Info on Chiropractic & Immunity Conference from Facebook Page. The Chronicle of Chiropractic. Kennesaw, GA; 2020.
- 281. World Health Organization. WHO Guidelines on Basic Training and Safety in Chiropractic. Geneva, Switzerland; 2005.

- 282. New Zealand Chiropractic Association. Vertebral Subluxation. Richmond, Nelson, New Zealand.
- 283. Association of Chiropractic Colleges. Issues in Chiropractic, Position Paper #1. In: Association of Chiropractic Colleges, editor. Bethesda, MD: Association of Chiropractic Colleges; 1996. p. 1.
- 284. Council of Chiropractic Education. CCE Accreditation Standards: Principles, Processes & Requirements for Accreditation. Scottsdale, AZ; 2018. p. 28.
- 285. Council of Chiropractic Education. CCE Accreditation Standards: Principles, Processes & Requirements for Accreditation. Scottsdale, AZ: Council on Chiropractic Education; 2013.
- 286. National Board of Chiropractic Examiners. About Chiropractic. 2014.
- 287. Rademacher W. Recognizing Subluxation. In: Federation of Chiropractic Licensing Boards, editor. 94th Annual Congress. Virtual 2021; p. 1.
- 288. General Chiropractic Council. GCC Registrant Guidance Claims made for the Chiropractic Vertebral Subluxation Complex. February 2017 Edition. London, United Kingdom: General Chiropractic Council; 2017.
- 289. Federation for Vertebral Subluxation. ECU President Calls Subluxation Concept Outdated. The Chronicle of Chiropractic; Kennesaw, Georgia; 2012.
- 290. Consensus Statement. 6th Biennial World Federation of Chiropractic Congress. Paris, France; 2001.
- 291. World Federation of Chiropractic. Our Principles; 2019.
- 292. International Chiropractic Education Collaboration. Clinical and Professional Chiropractic Education: A Position Statement.In: International Chiropractic Education Collaboration, editor; 2014.
- 293. National Board of Chiropractic Examiners. Pratice Analysis of Chiropractic. Greeley, CO: National Board of Chiropractic Examiners; 2010.
- 294. Institute for Alternative Futures. Chiropractic 2025: Divergent Futures. Alexandria, VA; 2013.
- 295. Institute for Alternative Futures. Explore.Aspire.Create.Evolve. Institute for Alternative Futures; 2022.
- 296. Funk MF, Frisina-Deyo AJ, Mirtz TA, Perle SM. The prevalence of the term subluxation in chiropractic degree program curricula throughout the world. Chiropr Man Therap. 2018;26:24.
- 297. New Zealand College of Chiropractic. Course Summary. Auckland, New Zealand.
- 298. Association of Chiropractic Colleges. Position Paper #1. J Manipulative Physiol Ther. 1996;19:634-5.
- 299. Foundation for Vertebral Subluxation. The Chronicle of Chiropractic. Kennesaw, GA; 2015.
- 300. Homola S. Pseudoscience in the use of manipulation by chiropractors. Focus on Alternative and Complementary Therapies. 2013;18:89-94.
- 301. Howick J, Koletsi D, Pandis N, Fleming PS, Loef M, Walach H, et al. The quality of evidence for medical interventions does not improve or worsen: a metaepidemiological study of Cochrane reviews. J Clin Epidemiol. 2020;126:154-9.
- 302. Hill AB. The environment and disease: association or causation? 1965. J R Soc Med. 2015;108:32-7.
- 303. Fedak KM, Bernal A, Capshaw ZA, Gross S. Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology. Emerg Themes Epidemiol. 2015;12:14.
- 304. Essex C. Ulysses syndrome. BMJ. 2005;330:1268.
- 305. Segren JC, Stauffer J. The Patients' Guide to Medical Tests. New York, NY: Facts on File; 1998.
- 306. Meadows K. Patient-reported outcome measures A call for more narrative evidence. J Patient Exp. 2021;8:23743735211049666.
- 307. Enkin MW, Jadad AR. Using anecdotal information in evidence-based health care: Heresy or necessity? Ann Oncol. 1998;9:963-6.
- 308. Ebrall P. A more inclusive evidence hierarchy for chiropractic. Asia-Pacific chiropr J. 2021;2.
- 309. Rome P, Waterhouse JD. Is anecdotal evidence undervalued? Asia-Pacific Chiropr J. 2022;3.
- 310. Haavik H, Niazi IK, Holt K, Murphy B. Effects of 12 weeks of chiropractic care on central integration of dual somatosensory input in chronic pain patients: A preliminary study. J Manipulative Physiol Ther. 2017;40:127-38.
- 311. Holt K, Niazi IK, Nedergaard RW, Duehr J, Amjad I, Shafique M, et al. The effects of a single session of chiropractic care on strength, cortical drive, and spinal excitability in stroke patients. Sci Rep. 2019;9:2673.
- 312. Masarsky CS, Todres-Masarsky M. Somatovisceral Aspects of Chiropractic: An Evidence-Based Approach. New York: Churchill Livingstone; 2001.
- 313. Oxford Languages. Oxford, United Kingdom: Oxford University Press; 2022.
- 314. Homola S. Is the chiropractic subluxation theory a threat to public health. Scientific Review of Alt Med. 2001;5:45-53.
- 315. Haavik Taylor H, Murphy BA. Altered cortical integration of dual somatosensory input following the cessation of a 20 min period of repetitive muscle activity. Exp Brain Res. 2007;178:488-98.
- 316. Baarbé JK, Holmes MW, Murphy HE, Haavik H, Murphy BA. Influence of subclinical neck pain on the ability to perform a mental rotation task: a 4-week longitudinal study with a healthy control group comparison. J Manipulative Physiol Ther. 2016;39:23-30.
- 317. Haavik H, Ozyurt MG, Niazi IK, Holt K, Nedergaard RW, Yilmaz G, et al. Chiropractic manipulation increases maximal bite force in healthy individuals. Brain Sci. 2018;8.
- 318. Navid MS, Niazi IK, Lelic D, Amjad I, Kumari N, Shafique M, et al. Chiropractic spinal adjustment increases the

cortical drive to the lower limb muscle in chronic stroke patients. Front Neurol. 2021;12:747261.

319. Holt K, Niazi IK, Amjad I, Kumari N, Rashid U, Duehr J, et al. The effects of 4 weeks of chiropractic spinal adjustments on motor function in people with stroke: A randomized controlled trial. Brain Sci. 2021;11.