

Review

A Scoping Review of Chiropractic, Vertebral Subluxation and Immune Function with Implications for Development of a Protocol for Measurement of Immune Biomarkers in Chiropractic Research & the Development of Related Policy

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Abstract

Objective: To discuss the existing literature on chiropractic, vertebral subluxation and immune function in order to inform the development of an integrative review of the literature, a review of immune biomarkers in relation to chiropractic, development of a research protocol, the implementation of future studies and the development of related policy.

Methods/Results: We conducted a scoping review of existing literature available to the authors and conducted further searches and gathering of documents based on that available literature. 125 papers were gathered and included in this review.

Conclusions: This is a scoping review of the literature regarding chiropractic and its relationship to neuroimmunology. It is intended to inform a larger project and give that team as much background as possible in a short period of time. The results of the already available research demands that we further explore the neuro-immuno-regulatory effects of chiropractic, adjustment and spinal manipulation and it provides a starting point for doing so. While adjustments reduce pain and inflammation, they also improve immune-regulatory function. How and to what extent is the subject of this current multi-pronged project.

Key Words: *Chiropractic, immunity, neuroimmunity, neuroimmunology, psychoneuroimmunology, neuroimmunoendocrine system, immune biomarkers, supersystem, vertebral subluxation, adjustment, spinal manipulation*

Introduction

It is well established that the nervous system controls and coordinates all functions and systems of the human body including immunity and the immune system.¹ Many in chiropractic consider that this relationship confers salutogenic benefits in people undergoing chiropractic care.²⁻⁴

Recent events related to the Coronavirus Pandemic have brought this relationship to the forefront within and outside of the chiropractic profession. This includes assertions by researchers within the chiropractic profession that there is no credible evidence supporting claims of effectiveness of spinal adjustment and/or manipulation in boosting or strengthening the immune system and that there is no credible, scientific

evidence that spinal adjustment and/or manipulation has any clinically relevant effect on the immune system.⁵

As a result of the assertions by these researchers, some chiropractic regulatory boards, chiropractic trade organizations and chiropractic educational institutions from around the world are claiming that there exists no credible, scientific evidence that would permit claims of effectiveness for conferring or enhancing immunity through spinal adjustment and/or manipulation to be made in communications by chiropractors.⁶ Essentially, chiropractors have been effectively muzzled and banned from discussing any connection between the nervous and immune systems.

The conclusions of the highly circulated document have been refuted along with exposing the biases of the authors and the flaws of the process itself.⁷ This refutation of the highly flawed document has led to the development of a plan for a more robust examination of the actual existing literature and a related multi-prong plan for addressing this issue moving forward. This paper is part of that effort.

The objectives of this multi-pronged project are to complete a review, develop protocols, conduct studies and develop policy. An integrative review of the literature, a review of immune biomarkers in relation to chiropractic, development of protocols, the implementation of studies and the development of policy are proceeding simultaneously alongside each other in the interest of time.

The following is a brief review of chiropractic, vertebral subluxation and immune function followed by a focused review of salivary tests for our current biomarkers of interest: *Immunoglobulin A, Cortisol and C-Reactive Protein*. This is a scoping review of the literature regarding chiropractic and its relationship to neuroimmunology. It is intended to inform a larger project and give that team as much background as possible in a short period of time in order to address the urgency of the matter.

Review of Chiropractic, Vertebral Subluxation and Immune Function

Vertebral Subluxation Theory, Neurology and Immune Function

According to Rome:

". . . evidential support for the hypothesis of an association of a physiological and pathophysiological neurovertebral influence upon visceral function does exist in the health professions. This evidence consists of empirical observations, anecdotal reports, through to blinded randomised controlled trials and pure neurophysiological research"⁸

Rome argues further that there is more published evidence in favor of chiropractic involvement in the management of a number of visceral conditions than there is for many of the musculoskeletal conditions managed by manipulative therapy.

Despite this, Rome contends that ". . . the management of somato-autonomic related visceral conditions remains somewhat contentious, even though there would appear to be a similar degree of anecdotal efficacy, patient acceptance and satisfaction – as well as the more formal research."

The original chiropractic theory is centered on the principle that obstruction or interference in the nervous system caused by vertebral subluxation can affect internal physiological function and the propagation of mental impulses and therefore plays a role in pathophysiology and dis-ease.⁹

The theory is based on the premise that the nervous system can be adversely affected by vertebral subluxation which can adversely affect the autonomic nervous system and therefore influence the internal milieu. Correction or reduction of the biomechanical component of the vertebral subluxation through

specific chiropractic adjustment may positively influence associated pathophysiological conditions - doing so through afferent and efferent somatosensory and autonomic reflexes.⁹⁻¹¹

According to Haldeman:

"Stimulation of a visceral receptor can cause reactions in the viscera themselves, can send afferent impulses to the medulla and higher centres, and can affect the somatic musculature. Stimulation of the somatic afferents similarly can have a widespread effect on sympathetic outflow to the viscera."¹²

Rome contends that the hypothesis has four integrally linked steps:⁸

1. That there can be sufficient somatic disturbance to alter the normal sensory input at that segmental level.
2. That this aberration would primarily consist of a bombardment of noxious somatic sensory input, and resulting in modulation of normal autonomic (ANS) activity
3. That resultant altered efferent somatovisceral activity may then interfere with the physiology of the innervated structures(s) involving that reflex level. This may be via central processing, neurologically directly onto that structure – or other mechanisms.
4. That in the case of that structure being an organ, such interference may be in the form of physiologic dysfunction, with associated symptoms, simulated disease of that organ, or possibly degrees of, or predisposition to pathology.

Chiropractic and the Neuro-Immune Connection

Interest in the autonomic-immune and somato-autonomic-immune association has been growing for some time. Cevikbas et al assert that autonomic nerves are involved in innate and adaptive immune pathways during allergic and atopic skin diseases.¹³

Sato reports on Kimira in 1994 who stated that somatic afferent stimulation produces a reflex effect on immune function, with autonomic nerves acting as the efferent pathway.¹⁴

According to Johnson, reviewing the sensory and sympathetic nerve supply within the cervical spine, ". . . the neuropeptide levels in the cell bodies located within the dorsal root ganglion of sensory nerves fluctuate according to the physiological state of the zygapophysial joint."¹⁵

Rome opines that:

"This observation would tend to support the concept of a connection between the state of the somatic component – importantly a vertebral articulation, and at least the sympathetic nervous system – a somatosympathetic neurological circuit."⁸

Sato in his paper on modulation of visceral functions by somatic afferent activity urges the reader:

"In this study of body homeostasis and environmental adaptation it would seem very important to further analyse the contribution of somatic afferent input to the autonomic nervous and hormonal regulation of visceral organ activity... (and)... that visceral functions can be moderated by somatic afferent input via various degrees of integration of autonomic nerves, hormones, and immunological processes."¹⁶

In a paper on modulation of the immune system by the autonomic nervous system and its implication in immunological changes, Nagatomi et al state that the autonomic nervous system plays a major role in the regulation of the immune system.¹⁷ Taken together, they assert:

"... the sympathetic nervous system does not simply suppress the immune system but might help organize the immune response sequentially and spatially by modulating the distribution of immunocompetent cells."

As Rome points out:

"There is a valid basis for the concept of a somatosensory-autonomic-visceral role in chiropractic and published formal research by chiropractic and other professions, as well as clinical observations, have contributed towards substantiating this foundation. In fact, there is far more evidence in support of this chiropractic hypothesis, with virtually none refuting it."⁸

Khalsa in a 2005 conference on the biology of manual therapies discussed the evidence that manual care triggers "... a cascade of cellular, biomechanical, neural, and/or extracellular events as the body adapts to the external stress." They stress that this leads to responses by the central and autonomic nervous systems that lead to observed changes in circulating levels of various neuropeptides and regulatory proteins.¹⁸

In a 2008 paper, Cohn reviewed the literature on the connections between the nervous and the immune systems, and explored the contention that chiropractic adjustments may affect neuroimmune function. He concluded that there appear to be numerous modes of communication between the nervous system and the immune system. It also appears, not only in theory but in practice, that chiropractic adjustments may have a beneficial effect on the functioning of both the nervous and the immune system.¹⁹

Brown, in a review of the field of psychoneuroimmunology and chiropractic noted chiropractic's non-surgical, drugless form of health care that seeks to optimize health and wellness via the relationship between structure, primarily the spine, and function, primarily the nervous system of the human body. Brown concluded his review asserting that chiropractic is well positioned to make a unique contribution to the field of psychoneuroimmunology.²⁰

In a study looking at long term assessment of blood indices and immune panel profiling of subjects receiving chiropractic care, Boone and his colleagues found significant changes in blood indices and the immune profile in the study group suggesting that the positive correlation was a reflection of the hosts' resistance to viral infection and destruction of virus

infected cells. The relationship among lymphocyte subpopulations may have reflected a natural balancing or redistribution of the overall lymphocyte subpopulation as individual cell types respond to a variety of immune challenges.²¹

In another study by Boone and colleagues over a 9 month period, subjects received chiropractic adjustments, completed a self-reported quality of life questionnaire and had complete blood counts and immune panels. Subjects demonstrated significant reductions in all chiropractic indicators compared to baseline. A positive change in Life Enjoyment occurred and they concluded that the subjects appear to have maintained a healthy physiology based on the complete blood count and immune profile throughout the duration of the study.²²

In a study of 650 children undergoing chiropractic the data revealed a pattern of subluxation correlated with numerous somatic, visceral and immune complaints that were helped following chiropractic care prompting the authors to recommend that these subluxations be discovered as early as possible in a child's development in order to effect a correction.²³

In a review of objective physiologic changes and associated health benefits of chiropractic adjustments in asymptomatic subjects Hannon reported statistically significant improvements in respiration, range of motion, heart rate variability and autonomic function, endocrine function, cardiovascular function, immune function, muscle strength and overall athletic ability of "healthy" or "normal" individuals.²⁴

According to Hannon other studies have documented statistically significant increases or improvements in neurocognitive functions such as reaction-time and information processing, visual acuity, stress and reproductive hormones, healing / recovery time, general health of senior citizens, and reduced labor times of pregnant women following or during chiropractic care.

Hannon asserted that "considering that these initial findings document objectively measured physiologic changes and their associated health benefits in nearly every major system of the human body, it is plausible that chiropractic care may benefit every function of the body. Furthermore, these data are congruent with numerous subjective studies that suggest chiropractic care is associated with accruing, long-term, overall health benefits."²⁴

In a study of 57 people looking at long term remission and alleviation of symptoms in allergy and Crohn's disease patients following spinal adjustment for reduction of vertebral subluxations Takeda and his colleagues addressed the association between visceral disease and immune dysfunction from sympathetic segmental disturbances secondary to vertebral subluxation.²⁵

Of the 17 patients who received spinal adjustments, 12 showed long-term and stable remission of their symptoms and of these, 9 experienced an alleviation effect. They found that vertebral subluxation is a common and characteristic finding in patients with allergies and Crohn's disease.

The authors concluded that according to the results of their study ". . . the possibility may be considered that chronic nerve compression secondary to vertebral subluxation in the thoracic and lumbar regions had a significant effect on the immune function of these allergy and Crohn's disease patients. It is further postulated that this nerve compression leads to a chronic functional disorder having a significant effect on digestion, absorption of nutrients and liquids, conveyance of food as well as various other functions of the digestive tract extending to excretion."²⁵

In a comparative study of the health status of children raised under the health care models of chiropractic and allopathic medicine, Van Breda reported that those children raised under chiropractic care had less infections and took less antibiotics than their medical counterparts.²⁶

The improved quality of life and improved health outcomes in relation to immune related health challenges by people undergoing chiropractic care mentioned above is further supported by similar outcomes reported by parents and their children in numerous studies conducted by Alcantara and his team at the International Chiropractic Pediatric Association (ICPA) through a Practice Based Research Network (PBRN) involving thousands of children.^{27,28}

These studies are further buttressed by numerous case reports published in the peer reviewed literature showing improved health outcomes following chiropractic for allergies, asthma, sinusitis, sinus congestion, chronic colds, dermatitis and IgE levels.²⁹⁻⁴⁵

Positive health outcomes related to immune function is further reinforced by numerous case studies on otitis media and immune function in general.⁴⁶⁻⁶⁵

Based on just this cursory review there appears to be ample support for a biologically plausible and beneficial relationship between vertebral subluxation reduction, the nervous system and immune function. In the following section we will review the impact of chiropractic on immune biomarkers.

Impact of Chiropractic on Immune Biomarkers

In the most recent review of the effects induced by spinal manipulation on the immune and endocrine systems, Columbi and Testa included studies if they evaluated the effects of manipulation on participants' biomarkers.⁶⁶

The authors state that ". . . recent models propose that the observed pain modulatory effects of this form of manual therapy may be the result of more complex mechanisms. It has been suggested that other phenomena like neurophysiological responses and the activation of the immune-endocrine system may explain variability in pain inhibition after the administration of spinal manipulative therapy (SMT)."⁶⁶

The aim of their paper was "to provide an overview of the available evidence supporting the biological plausibility of high-velocity, low-amplitude thrust (HVLAT) on the immune-endocrine system". Their search retrieved 13 relevant articles and two themes of discussion were developed. Nine studies investigated the effects of manipulation on cortisol levels and

four studies examined the effects of manipulation on the immune system.

They concluded that spinal manipulation seems to trigger the activation of the neuroimmunoendocrine system and encouraged further research to obtain more insights about the biological effects of spinal manipulative therapy.⁶⁶

Cytokines are cell signaling protein molecules secreted by cells of the immune system and are a category of signaling molecules used in intercellular communication. Spinal manipulation has been shown to reduce the production of pro-inflammatory cytokines and increase the blood levels of cytokines that are immuno-regulatory in nature.

Brennan, et al., demonstrated that upper thoracic spinal manipulation resulted in a significant increase in phagocytic activity of neutrophils and monocytes when compared to a sham manipulation or soft-tissue treatment.⁶⁷ In another study by Brennan, et al., they found that spinal manipulation results in viscerosomatic responses that affect the phagocytic activity of both neutrophils and mononuclear cells.⁶⁸

In a small study by Selano and Grostic, it was found that upper cervical adjustments increased CD4 helper T-cell counts by 48 percent over the six-month duration of the study.⁶⁹

Teodorczyk-Injeyan showed that chiropractic treated subjects have also shown attenuation of lipopolysaccharide induced production of the inflammatory cytokines unrelated to systemic levels of the neurotransmitter substance P.⁷⁰

Research has explored the relationship of spinal manipulation, spino-autonomic reflexes and their influence on activity of immune and inflammatory cells. This research has shown a reduction in pro-inflammatory cytokines after spinal manipulation. This includes reduction of inflammatory cytokines, tumor necrosis factor and interleukin-1 β .⁷¹

Spinal manipulation down-regulates inflammatory-type responses via a central mechanism and manipulation ameliorates the physiological responses of blood cells to an inflammatory stimulus suggesting that spino-visceral reflexes alter the functional activity of cells in the immune and inflammatory systems.

In 2010, Roy, et al., did pre- and post-intervention measures from blood samples and detected a reduction in pro-inflammatory cytokines interleukin 6 (IL-6) and C-reactive protein (CRP) after a series of nine chiropractic manipulations from T12-L5 using an adjusting instrument and related protocol in 10 chronic low back pain patients and 10 healthy subjects. Both IL-6 and CRP levels were lowered toward the values in healthy subjects showing that chiropractic is capable of attenuating the inflammatory response. The authors of the study suggest that it is plausible the inflammatory process can be reversed in those receiving adjustments.⁷²

Increased secretion of interleukin-2 (IL-2) has also been found following chiropractic care. IL-2 is an important cytokine in T-cell-dependent immune responses. It also plays a role in the development, maintenance and survival of regulatory T cells making it critically important in immune tolerance. IL-2 is an

immune-regulatory cytokine and signaling molecule necessary for the response to microbial infection as well as the body's ability to discriminate between self and non-self.

In one study, 76 asymptomatic subjects were randomized to receive an upper thoracic manipulation with cavitation or without cavitation, or were included in a control group. All subjects had their blood drawn before, 20 minutes and two hours after the intervention. Induced secretion of IL-2 increased significantly with the T-lymphocyte response becoming enhanced after spinal manipulation suggesting that manipulation may influence IL-2 immune regulated biological responses.⁷³

In another study of 74 subjects the increased production of interleukin-2 as a result of thoracic manipulation was associated with increased antibody synthesis from monocytes. The study showed that there was increased synthesis of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies in peripheral blood mononuclear cells in those subjects who received thoracic manipulation. This means that antibody synthesis (IgG and IgM) induced by interleukin-2 is increased after manipulation.⁷⁴

Studies demonstrate evidence indicating that chiropractic and spinal manipulation may influence immune system response. Studies suggest that manipulation consistently reduces the production of pro-inflammatory mediators associated with tissue damage and pain from articular structures. Other studies provide evidence that manipulation may induce and enhance production of the immune-regulatory cytokine IL-2 and the production of immunoglobulins.

In a study examining the effect of chiropractic spinal manipulative therapy on salivary cortisol levels by Tuchin, nine subjects received chiropractic over six weeks revealing reduction of salivary cortisol over the complete time frame of the study.⁷⁵

According to Tuchin a number of studies have analyzed the relationship of salivary cortisol with stressful events. These studies, he suggests, have shown that salivary cortisol levels often increase in relation to increases in the level of stress. From this it has been demonstrated that the level of stress of a patient can be correlated with secreted cortisol levels.

In another study involving chiropractic and cortisol levels, plasma levels of beta-endorphin, adrenocorticotrophic hormone (ACTH), and cortisol before and after intervention chiropractic was performed in 40 male subjects. Levels of immune-reactive ACTH, immune-reactive beta-endorphin, and cortisol were measured. No differences in ACTH or beta-endorphin were found between sham and treated groups, or between pre-and post-intervention in any group; cortisol levels fell over the course of the study in all groups. According to the authors of the study the findings suggest that manipulation is not a stressor that activates the hypothalamo-pituitary-adrenal axis.⁷⁶

Whelan studied whether basal salivary cortisol levels can be properly detected and whether chiropractic manipulation has any direct effect on basal salivary cortisol levels in humans. Subjects were adult male students attending a chiropractic

college. Salivary samples were collected for 5 weeks. During Week 1, samples were collected by the students at home upon waking. During Weeks 2 through 5, home samples were collected upon waking and were followed by an additional time course of samples collected in a laboratory setting before and after manipulation.⁷⁷

According to the study's authors chiropractic manipulative therapy did not significantly change basal salivary cortisol levels. A decrease in salivary cortisol was detected over time on each trial testing day. Overall, cortisol levels significantly decreased from the time of the home samples until the pretreatment laboratory measurement). Cortisol levels subsequently decreased from pretreatment to 15 minutes after treatment. After treatment, there were progressive decreases in cortisol levels. The authors concluded that neither the anticipation of manipulation nor the spinal manipulative procedure itself induces a state of stress or anxiety.⁷⁷

In a study to assess the effects of short-term and long-term chiropractic care on serum thiol levels in asymptomatic subjects, researchers found statistically significant differences in the serum thiol levels in three groups. Mean serum thiol levels were lowest in patients with active disease as well as patients with initial musculoskeletal complaints. Asymptomatic subjects under chiropractic care demonstrated higher mean serum thiol levels than patients with active disease. The researchers concluded that asymptomatic or primary wellness subjects under chiropractic care demonstrated higher mean serum thiol levels than patients with active disease and produced some values that were higher than normal wellness values.⁷⁸ Serum thiols are a measure of human health status and are a surrogate estimate of DNA repair enzyme activity, most notably poly ADP – ribose polymerase or PARP.

To be sure, the literature base supporting the clinical role of chiropractic in supporting immune function is widespread and it is buttressed by the expanded depth and breadth of the literature on those manual methods, in general, that are directed at improving the structure and function of the spine and nervous system. Osteopathy serves as an example of another profession that has devoted time and effort at researching this topic.

Osteopathy and Immunity

Osteopaths have long managed their patients with an eye toward immune support as have physical therapists, massage therapists and a host of other manual practitioners.

In osteopathic studies of Immunoglobulin A (IgA) it has been shown that Osteopathic Manipulative Therapy (OMT) has a positive effect on IgA levels in persons experiencing high stress. Results suggest that OMT may then have therapeutic preventive and protective effects on both healthy and hospitalized patients, especially those experiencing high levels of emotional or physiological stress and those at higher risk of acquiring upper respiratory tract infections.⁷⁹

OMT has also been shown to aid in the recovery from pneumonia by enhancing the functioning of the immune system, and maximizing the effects of antibiotics. In addition,

OMT has been associated with decreased hospital-stay duration, decreased use of intravenous antibiotics, and decreased incidence of respiratory failure or death in elderly patients hospitalized with pneumonia.⁸⁰⁻⁹⁸

Not surprisingly based on the above studies, osteopathy has also been credited with providing improved health outcomes during the 1918 Flu Pandemic.⁹⁹⁻¹⁰¹

Smith reported that mortality among a total of 110,120 patients with influenza treated by the 2445 members who reported “authenticated detailed case reports” to the American Osteopathic Association was 0.25%. Mortality due to influenza in patients receiving traditional medical care, however, was ultraconservatively estimated at 5% to 6%. Among patients with pneumonia treated medicinally, mortality was estimated at 33%, and even as high as between 68% and 78% in some large centers. The death rate due to pneumonia among 6258 patients cared for by osteopathic physicians was 10%.¹⁰¹

Chiropractic & the Spanish Flu Pandemic of 1918

In turn, no review of the role of chiropractic and immune function would be complete without addressing its role during the 1918 Flu Pandemic.¹⁰²⁻¹⁰³ While some in the chiropractic profession have dismissed these pandemic flu related data out of hand because they have not reviewed the actual data, the osteopathic profession does not seem to have any trouble promoting its success in a similar fashion and those same chiropractors refrain from criticizing the osteopaths or attempting to silence their discussions of it.

According to Rhodes:¹⁰²

In Davenport, Iowa, 50 medical doctors treated 4,953 cases, with 274 deaths. In the same city, 150 chiropractors including students and faculty of the Palmer School of Chiropractic, treated 1,635 cases with only one death.

In the state of Iowa, medical doctors treated 93,590 patients, with 6,116 deaths - a loss of one patient out of every 15. In the same state, excluding Davenport, 4,735 patients were treated by chiropractors with a loss of only 6 cases - a loss of one patient out of every 789.

National figures show that 1,142 chiropractors treated 46,394 patients for influenza during 1918, with a loss of 54 patients - one out of every 886.

Reports show that in New York City, during the influenza epidemic of 1918, out of every 10,000 cases medically treated, 950 died; and in every 10,000 pneumonia cases medically treated 6,400 died. These figures are exact, for in that city these are reportable diseases.

In the same epidemic, under drugless methods, only 25 patients died of influenza out of every 10,000 cases; and only 100 patients died of pneumonia out of every 10,000 cases.

In the same epidemic reports show that chiropractors in Oklahoma treated 3,490 cases of influenza with only 7 deaths. In Oklahoma there is a clear record showing that chiropractors

were called in 233 cases where medical doctors had cared for the patients, and finally gave them up as lost. The chiropractors saved all these lost cases but 25.

So powerful were the results seen by chiropractors that those results and the outpouring of support by the public were seen as a survival factor for a fledgling chiropractic profession seeking public acceptance.

Rhodes stated:

The first survival factor for chiropractic: they were the legal and legislative salvation. But the fabulous success of chiropractic in combating the 1917-1918 influenza outbreak was the public relations breakthrough that can certainly be called the second great survival factor. Better acceptance by the public followed and more patients meant financial safety for practicing chiropractors. Dedicated chiropractors came into the profession in increasing numbers and they had a sure sense of certainty, heady conviction, and a great willingness to fight for the cause.¹⁰²

Ron Pero's Research

One final area of contention among those who criticize the state of the evidence related to chiropractic and immune function is the work of Ronald Pero. The highly flawed and biased review by the World Federation of Chiropractic's Research Committee⁵ included an out of hand rejection of Pero's work stating:

Numerous attempts have failed to retrieve this study. Without the original study to review, no scientific assessment of its claims can be made. Therefore, the "Pero and Fleisa" study does not constitute credible, scientific evidence that spinal adjustment/manipulation enhances or confers immunity nor should it be used as a basis to provide care.

And though they failed in their “numerous attempts” to secure data and though they admit they have no citation, they nevertheless formed an opinion about documents they never reviewed.

The WFC Research Committee's failure at their claimed “numerous attempts” to locate data on Pero's work and their failure to accomplish that despite the involvement of 9 researchers with apparently extensive experience in literature searching and retrieval along with the combined resources of their collective libraries - leaves one to wonder how hard they actually looked. Given their failure to locate actual data they chose instead to review internet memes in order to arrive at their rejection.

While Pero's research was not published in a peer reviewed indexed journal, the hypothesis and findings of his study were published along with writings and transcripts of presentations he gave on the topic.¹⁰⁴⁻¹⁰⁶ These are the apparent sources of data used in memes highly circulated among the chiropractic profession. Pero and Fleisa put together a testable hypothesis for chiropractic stating:

“It is clear from the literature review and the data presented above that spinal pathomechanics can cause hormonal changes

that, in turn can lead to genotoxic responses, altered physiological states of health and disease. Hence it becomes imperative to research the possible scientific molecular basis for chiropractic.”¹⁰⁴

Pero and Fleisa laid out the reasoning:

1. Spinal pathomechanical stress to the nervous system induces neurohormonal imbalance that can lead to other hormonal changes.
2. Either or both of the above may cause pathometabolic events resulting in a measurable increase in genotoxicity.
3. Genotoxicity leads to significantly altered physiological states of health via mutagenic or cytotoxic events.
4. Therefore, spinal pathomechanical stress leads to significantly altered physiologic states of health.
5. Spinal pathomechanics can be improved, corrected, and/or prevented by appropriate chiropractic intervention.
6. Therefore, appropriate chiropractic intervention can lead to significant lessening of mutagenic or cytotoxic events.

Pero and Fleisa concluded:

“We feel there is sufficient evidence available for interested scientists to proceed with the validation of the hypothesis that chiropractic intervention can prevent accumulation of DNA damage in cells and thereby reduce the incidence of altered physiologic states of health by such damage.”¹⁰⁴

Some of Pero's work was contemporaneously reported in the November 1989 issue of the East West Journal. Referring to Pero's study, which he collaborated on with Fleisa and with a grant from the Chiropractic Basic Science Research Foundation (CBSRF), they reported on the conduct of a study to gauge resistance to hazardous environmental chemicals hypothesizing that people with cancer would have a suppressed immune response to toxic burdens. While they hypothesized that healthy people and people receiving chiropractic care should have a relatively enhanced response.¹⁰⁶

Measuring 107 individuals who had received long term chiropractic care, Pero's team found that all chiropractic patients were "genetically normal" meaning they had no genetic reasons for increased resistance or susceptibility to disease. Any difference therefore had to be accounted for by environmental or therapeutic factors.

It was reported that the chiropractic patients had a 200% greater immune-competence than people who had not received chiropractic care and a 400% greater immune competence than people with cancer or other serious diseases. It was reported that the immune competence did not show a decline with age.

Pero concluded that "chiropractic may optimize whatever genetic abilities you have" so that you can fully resist serious disease. He stated: "I'm very excited to see that without chemical intervention this particular group of patients under

chiropractic care did show a very improved response. These changes come from chiropractic treatment.”¹⁰⁶

Conclusion

This is a scoping review of the literature regarding chiropractic and its relationship to neuroimmunology. It is intended to inform a larger project and give that team as much background as possible in a short period of time. We believe this to be an urgent matter.

In the end it is really not a scientific or research deficit that brings us to this confrontation. It is instead due to differing interpretations of the well-entrenched model of evidence informed practice by factions within the chiropractic profession. The segment of the profession that holds to an “RCT” only standard and at the same time does not consider the desires of the patient, their values and the expertise of clinicians happens to be in general control of the regulatory, educational and research aspects of the profession. This faction of the profession has sought for several decades to restrict the practice of chiropractic to a musculoskeletal, pain based model and they have done so by limiting the acceptable evidence for chiropractic to randomized controlled clinical trials and through an embrace of extreme scientism.¹⁰⁷⁻¹¹⁰

This faction within the profession is intentionally attempting to suppress the evidence that does exist and they provide false and misleading interpretation and commentary on that evidence. That false narrative has been adopted/endorsed by state regulatory boards, trade organizations and chiropractic schools to be used against chiropractors who say the words “nervous system” and “immune system” in the same sentence when communicating with patients and the public.

Senzon has written extensively on this issue in a 10 part series demonstrating that a small group of academics in the profession are staging a coup d'état by trying to “cleanse” the chiropractic lexicon.¹¹¹⁻¹²¹ These claims are supported by the critique and analysis of Villanueva-Russell.¹²² In an evidence-based approach to historical writing, Senzon examines the flaws, breaks down historical errors that arguments rest upon, and lays out the rationale for establishing a shared base of knowledge for the entire profession. Senzon attempts to correct the errors in the literature regarding vertebral subluxation placed by numerous “subluxation deniers” who have peppered the scientific and historical literature with unreferenced and unsupported statements regarding the nature and historical issues surrounding vertebral subluxation.

Though the combined conclusions in regards to these musculoskeletal outcomes following manipulation is poor it is promoted within the profession by that faction as if the science is settled.¹²³⁻¹²⁵ In addition to the intellectual dishonesty of failing to acknowledge the weakness in their own arguments and the literature supporting it - they engage in misdirection by pointing instead to chiropractors who, for over 100 years, have witnessed improved health outcomes from providing manual care and how they are talking about immunity and then demand through flawed “research” that they should be silenced. No mention is made of similar health outcomes and practices from the physical therapists, massage therapists, manual medicine practitioners or osteopathy.

Another issue that plagues the chiropractic literature is one of semantic pathology. Kent addressed this in his review of vertebral subluxation, semantic pathology, epistemic trespassing, and ethics.¹²⁶

A function of language is differentiation. Language should be a tool for minimizing ambiguity, and establishing precision in communication. This necessitates the use of terminology that communicates the uniqueness of the thing being described. The use of terms that homogenize rather than differentiate foster ambiguity and imprecision. The practice of conflating terms, such as vertebral subluxation, joint dysfunction, adjustment, and spinal manipulation has ethical and political implications. One example is the suggestion that the terms vertebral subluxation, joint fixation, joint dysfunction are interchangeable. They are not the same thing. There are significant operational and epistemological differences. Implicit in the term vertebral subluxation are both biomechanical and neurological elements. Vertebral subluxation is a relational neurological process that impacts the human experience, not merely a fixated joint. A fixated or tender joint might represent one manifestation of vertebral subluxation, not a synonym for vertebral subluxation. The notion that they are the same leads to confusion and ambiguity.

These issues will need to be addressed in any research protocol that involves assessing for the presence of vertebral subluxation and its relationship to changes in immune biomarkers.

An error is made in many studies of the effects of “manipulation” by lumping together all “hands on” techniques, while failing to address key issues, such as the examination criteria used to determine the presence of “manipulable lesions,” and how the investigators determine that the “manipulative treatment” was successful. Research designs based upon the haphazard application of ill-defined interventions selected by utilizing examination procedures whose reliability has not been established cannot be considered “scientific.”

An operational definition is a description of the procedures used to determine the means for measuring or observing something. To assess the effect of vertebral subluxation correction on a dependent variable (EEG activity, H-reflexes, health outcomes, etc) one must:

1. Define how the presence of vertebral subluxation will be determined. The methods used must be reliable (reproducible within and between examiners) and valid (measure what they claim to measure).
2. Define the intervention used to attempt correction of the vertebral subluxation.
3. Perform a pre-adjustment examination.
4. Apply the intervention (adjustment, placebo, control).
5. Perform a post-adjustment examination to determine that the subluxation has been reduced or corrected according to the criteria of the operational definition

Whether or not the chiropractic profession will address this political problem remains to be seen but even a cursory review of the available evidence as has been done here reveals the

science supporting the clinical evidence so many chiropractors observe regularly in practice. The results of this research demands that we further explore the neuro-immuno-regulatory effects of chiropractic, adjustment and spinal manipulation and it provides a starting point for doing so. While adjustments reduce pain and inflammation, they also improve immune-regulatory function. How and to what extent is the subject of this current multi-pronged project.

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