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EXPOSITION

Genetic aetiology of adolescent idiopathic scoliosis (AIS): Chiropractic's role

Gilbert Weiner and Charles Blum

Abstract: *Introduction:* Recent studies have demonstrated there are genetic and epigenetic underlying causes for adolescent idiopathic scoliosis (AIS). Apparently a genetic defect causing ciliary pathology in the neural canal can affect CSF flow and can result in scoliosis. A review of this emerging evidence demonstrates the need to re-evaluate the scoliosis-cerebral spinal fluid (CSF) relationship. Compelling studies have illustrated, as well, the dominant role played by epigenetic modifiers over the expression of genetic code. One fascinating study, in particular, has demonstrated definitively that scoliosis in zebra fish can be corrected through epigenetics.

Methods: The goal of this study was to revisit the current and newly published studies concerning scoliosis, epigenetics, as well as evaluating the currently available therapeutic alternatives for scoliosis treatment. The intent was to shed light on breakthrough studies and apply these finding to the chiropractic clinical practice.

Results: The position of chiropractic in this new arena of scoliosis and epigenetics is unfolding. These studies that were reviewed have demonstrated that chiropractic care can affect epigenetic mechanisms through five different avenues: environmental influences, methylation processes, elongating DNA telomeres, emotional stress reduction, and reducing chromosomal oxidative stress. Chiropractic management of scoliosis can be an effective tool for care, with minimal negative secondary effects. Recent studies are finding ineffectiveness of scoliosis bracing along with poor outcomes and serious secondary effects from surgical interventions for scoliosis treatment.

Conclusion: Therefore from a conservative, effective, low risk perspective chiropractic care appears to be an important consideration for scoliosis patients. Further study into this novel emerging field of care for scoliosis patients is indicated.

Indexing terms: Chiropractic; Adolescent Idiopathic Scoliosis (AIS); conservative care; cerebral spinal fluid (CSF); sacro-occipital technique.

Introduction

During 43 years of practicing chiropractic, observing, studying, and treating patients with scoliosis, its relation to temporomandibular dysfunction (TMD) and therefore cranial dysfunction, the focus was always on the restoration of cerebrospinal fluid (CSF) flow interrupted by the spinal/cranial distortions as a key in maintenance of health.

Utilising Sacro Occipital Technique (SOT) including cranial manipulation both SOT and Osteopathic (Upledger), Applied Kinesiology (AK), Feldenkrais Technique, Alexander Technique, Shiatsu, dental interventions, and foot orthotics all utilised attempting to seek structural balance. Always with the focus of believing in the importance of reestablishing the CSF flow disrupted

> *'... the mechanist idea of AIS is dated; here we present argument to the effect that chiropractors are well-placed to effect substantial change due to mechanisms involving epigenetics in addition to specific neural impacts on the developing spine ...'*

by the scoliotic distortions.

Following the science has always meant early on practicing with a structural interpretation of DD Palmer's '*Green Book*' principles. As the years rolled on and science appeared to 'catch up' to chiropractic philosophy, there was a shifting to a neurological interpretation. In the past few years, it has become very clear that chiropractic's basis; '*The Three Ts of Subluxation: Toxins, Traumas, and Thoughts*' do in fact have a great impact on our body systems; and now new studies help us to understand how they even impact our genetic health. It is our hope, that what is presented, will spark curiosity and stimulate further questioning and serve as a clarion call to action.

Methods

The goal of this study was to revisit the current and newly published studies concerning scoliosis, epigenetics, as well as evaluating the currently available therapeutic alternatives for scoliosis treatment. The intent was to shed light on breakthrough studies and apply these findings to the chiropractic clinical practice.

The impetus came from reading a study from *The Journal of Science* June 10 2016 conducted by Princeton University and University of Toronto titled '*Zebrafish models of idiopathic scoliosis link cerebrospinal fluid flow defects to spine curvature*'. (1, 2) The premise for treating scoliosis was turned on its head. This study followed up on a previous study published by Catanzariti, '*Adolescent idiopathic scoliosis (AIS), cerebrospinal fluid (CSF) flow and ciliopathy*'. (3) These studies clearly demonstrated that a genetic mutation creates ciliary defects within the neural canal which produces poor and stagnant CSF flow. This resulted in curvature of the spine, apparently in a compensatory effort, attempting to adapt to poor CSF flow by enhancing CSF flow through structural undulation. This Cerebral spinal fluid relationship to scoliosis has been observed on magnetic resonance imaging (MRI) as well. (4, 5, 6) This same ciliary genetic mutation it appears, is responsible for spermatic flagella failure as well as cilial failure in the fallopian tubes, both reasons for infertility and tubal pregnancy. (7) It is imagined that studies seeking to correlate this to incidence of infertility in scoliosis patients is the next step in investigation. (8)

The profoundly enlightening part was that the Zebrafish study by Burdine et al employed epigenetic modification. It was found that simply changing the temperature of the water the fish were in was sufficient to apply an epigenetic stimulation. The expression of the DNA code was altered and the cilia were repaired. This restored normal CSF flow, and 'straightened out' the spinal scoliosis. Their quote, '*if translatable to humans this could lead to a non-surgical approach to treating idiopathic scoliosis*'. No one is offering that a change in one's home thermostat might be a treatment for scoliosis. However, it does shine a blindingly bright light on aetiology of *Adolescent Idiopathic Scoliosis* (AIS) and a possible vehicle for correction.

So, the victim became the villain. The entire CSF flow-scoliosis connection was wrong. But where does that leave chiropractic if the aetiology is genetic? It places it front and center.

There are a plethora of recent studies demonstrating the effect chiropractic care has on epigenetic modification and we intend to discuss them herein. As stated, many times, '*Our DNA is not our destiny*'. Epigenetics can '*turn gene codes on or off*' modifying the manner in which our DNA is expressed. (9, 10) Furthermore, chiropractic has been proven to effect epigenetics in at least 5 ways.

Chiropractic and epigenetics

First, the concept of epigenetics is defined as, the way in which our body perceives the environment and hence how it responds to those external and internal environment conditions through the modification of the expression of our genetic code. (11) Fagiolini and Jensen in their

study stated that '*unequivocally, recent evidence suggests that the dynamic regulation of gene expression through epigenetic mechanisms is at the interface between environmental stimuli and long lasting molecular, cellular and complex behavioral phenotypes acquired during periods of developmental plasticity.'* (12) Epigenetic scientists including Dr Feinberg, professor of molecular medicine and director for Epigenetics at *Hopkins' Institute for Basic Biomedical Sciences*, have determined that '*the environment of the cell is the epigenetic control of the gene that determines the expression of the gene*'. (13) Epigenetic inheritance allows an organism to continually modify its gene expression to environmental change without affecting its DNA.

As chiropractors, it goes without saying that a nervous system unencumbered by subluxation will greatly enhance the way in which external and internal signalling reaches the nervous system and brain, and now we know even to the chromosomal level. (14, 15, 16, 17) This has been documented even in medical literature, '*Nerve impingement can interfere with the brain's ability to communicate with the muscles, organs, and cells and can result in the loss of motor function, sensory function, or both.*' (18) Different studies with animal models have demonstrated that chiropractic therapies mediate neuroplasticity, specifically through modulation of neurotrophins. '*Although, no studies have yet been published on the specificity of interaction between neurotrophin gene polymorphisms and chiropractic treatment; from the material collected, we identified a set of genes and some functional polymorphisms that could be correlated with better response to chiropractic therapy*'. (19)

Second, there are recent studies demonstrating how chiropractic impacts the methylation processes which are a prime mover in genetic transcription and replication. (20) Dr. Feinberg in his study stated '*Cellular biologists and epigenetic geneticists understand that methylation of the gene is a key to epigenetic control. This control is a result of the cell responding to a changing environment of the body either macro, micro, internal or external*.' (21) In the article '*Epigenetic Mechanisms of Integrative Medicine*', Riya Kanherkar, Deepak Chopra, et al, demonstrated the effects of alternative medicine including chiropractic have on the DNA methylation and epigenetic modification to DNA code. (22)

We know that these changes are not temporary. Kanherkar states from another study '*It is well known that epigenetic influences acting on a pregnant mother also affect the in-utero foetus*'. (23) This was supported by Barron-Cohen's work. (24) There is '*developmental plasticity*', where '*a single genotype, influenced by specific intrauterine events, has the capability to produce different phenotypes*'. (25). Furthermore, these epigenetic influences have been observed to span across at least 4 generations. Crossing four generations shows that genetic change is inherited. Therefore the study suggests a possible role for chiropractic treatment to the mother in promotion and enhancement of long-term foetal and infant health benefits through epigenetic pathways extending to future generations. We know that spinal manipulation techniques have been used to relieve symptoms arising from chronic low back pain, but they have also proven efficacy of treatment of vertebral subluxations in diabetic patients, (26) and this was substantiated in DeVocht's study. (27) There is research that even suggests that long-term chiropractic therapy may provide a tangible solution to chronic diseases that were previously thought to be genetic in nature. (28, 29)

Third, chiropractic has shown to maintain and elongate the telomere of the DNA creating greater DNA/cell health and lifespan. A ground breaking study by Fedorchuk and McCoy (30) found that '*correction of cervical lordosis and forward head position improved the sagittal spinal alignment and posture and was associated with lengthened telomeres, improvement in both quality of life, and autonomic nervous system function*.' There have been other studies discussing the epigenetic modification effect on previously considered genetic conditions. One such study discussing that the immune system is highly sensitive to shortening of telomeres as its competence depends strictly on cell renewal and clonal expansion of T- and B-cell populations.

(31) There has been mounting evidence of a causal role for telomere dysfunction in a number of degenerative disorders: '*Their manifestations encompass common disease states such as idiopathic scoliosis, pulmonary fibrosis and bone marrow failure. Although these disorders seem to be clinically diverse, collectively they comprise a single syndrome spectrum defined by the short telomere defect.*' (32)

Fourth, studies demonstrate how thoughts (emotional stress), as well as toxins and traumas (3 T's) produce epigenetic changes that modify the expression of the genetic code and is then passed down to at least 4 generations. (33, 34) Again, finding the genetic trait modified to the 4th generation is considered evidence that the change has been a genetic change and is not from '*nurture*'. Considering thoughts, i.e. mental stress, Dr. Rachel Yehuda, Director of the *Traumatic Stress Studies Division* at the *Icahn School of Medicine* at *Mount Sinai* in New York City, reported a study in 2015 on the children of 40 Holocaust survivors. She found that '*they had epigenetic changes to a gene linked to their levels of cortisol, a hormone involved in the stress response*'. She also found '*a distinctive pattern of DNA methylation*', another epigenetic marker. This study concluded that '*both parents and unborn children were affected on a genetic level*'. (35)

Another study highlighting stress as an epigenetic force was the seminal research on the *Dutch Hunger Winter*, an extended period of famine that took place towards the end of World War II when the Nazis blocked food supplies in October 1944, thrusting much of the Netherlands into famine. When the Dutch were liberated in May 1945 more than 20,000 had died of starvation. Pregnant women were particularly vulnerable, and the famine impacted their unborn children for the rest of their lives. Scientists found that those who had been in utero during the famine were a few pounds heavier than average.

The thinking goes that the mothers' bodies, because they were starving, underwent an epigenetic change that turned off a gene in their unborn children involved in burning the body's fuel. This study demonstrated that when the children reached middle age, they had higher LDL ('*bad*') cholesterol and triglyceride levels. They also suffered higher rates of obesity, diabetes, cardiovascular disease, and schizophrenia. When scientists looked into why, they found that '*these children carried a specific chemical marker, an epigenetic signature on one of their genes*'. (36)

Other studies have reported maternal stress causing epigenetic changes concerning the foetus' sensitivity to certain hormones. (37, 38) Contrarily, it has as well been put forward that Eu-stress (positive stressors) can positively affect health, reduce the ageing process and decrease the incidence of cancer through induced stress suppression through epigenetic mechanisms. '*We propose herein that stress may stimulate genetic adaptations through epigenetics that, in turn, modulate the link between the environment, human lifestyle factors, and genes*.' (39)

Plaza-Manzano states in his study that chiropractic adjustments have been shown to provide Eu-stress to the nervous system and entire body through stimulation and production of neurotensin, oxytocin, and cortisol. (40) Other studies have demonstrated how chiropractic affects mood through brain stimulation. (41) There have been studies documenting how stressors in the mother have caused genetic changes in the foetus. This was particularly enlightening as concerning autism. (42, 43) There have been multiple studies demonstrating how even stress on the father, not just the gestational mother, has affected further generations. This demonstrating once again epigenetic inheritance, not just in utero and/or nurture. Surprisingly this was passed only to the male offspring leaving the daughters unaffected, signalling a possible sex link pattern. (44)

There is much scientific support for the notion that chronic activation or deactivation of supra-spinal systems, as we know through subluxation, will lead to maladaptation of homeostatic mechanisms, causing the impairment of processes within the body, and ultimately leading to visceral disorders. Change in supra-spinal neurophysiological efferent activity is increasingly

being used to explain 'stress' related disease. These responses are often referred to as 'stress responses' and include the activation of the hypothalamic-pituitary-adrenal axis and sympatho-adrenal system, resulting in the consequential secretion of multiple hormones including corticotrophin releasing hormone, adrenocorticotropin hormone, cortisol, norepinephrine and epinephrine.

Once the stress response is activated, behavioural and physiological changes lead the way for the organism to adjust homeostasis within the body, attempting to increase its chances for survival. (45) A definitive study drawing a direct line between chiropractic and amygdala function, discusses '*the nodose ganglion of the vagus nerve and how dysfunction in this ganglion (a nerve message center) can move misinformation messages between the brain and body*'. (46) Recent neuroanatomical findings, as noted by Burnstein find anterograde tracing observations provide evidence for '*direct projections of spinal cord neurons to the amygdala and orbital cortex. Their laminar distribution in the spinal cord and the involvement of the amygdala and orbital cortex in limbic functions suggest that these pathways may play a role in neuronal circuits that enable somatosensory information, including pain, to affect autonomic, endocrine and behavioral functions*'. The *Vagus* nerve winds its way through the C1-C2 vertebrae complex: '*If the nerve is compressed, stretched, or damaged by cervical spine instability, a myriad of problems, including runaway emotions can occur*'. (47) It was stated earlier quoting Fagiolini, '*unequivocally, recent evidence suggests that the dynamic regulation of gene expression through epigenetic mechanisms is at the interface between environmental stimuli and long lasting complex behavioural phenotypes acquired during periods of developmental plasticity*.' (48)

The fifth level of epigenetic mechanisms are oxidative degeneration of chromosomes. Repair to these chromosomes was documented by reducing the oxidative stress. In a landmark study published in the *Journal of Vertebral Subluxation Research*, chiropractors collaborating with researchers at the *University of Lund* found that chiropractic care could influence basic physiological processes affecting oxidative stress and DNA repair. (49) '*Serum thiols are a measure of human health status. It is a surrogate estimate of DNA repair enzyme activity, most notably poly ADP – ribose polymerase or PARP. Campbell and Kent demonstrated the effects of short-term and long-term chiropractic care on serum thiol levels in asymptomatic subjects positively effecting DNA health*.' (50)

The implication is enormous for chiropractic because it has been proven that chiropractic care can promote epigenetic changes in the parent that will continue to change the genetics of future generations. What greater reason to care for young people of child bearing age and infants than this?

As one can see the nature and the etiology of scoliosis places chiropractic front and center. Chiropractic is shown to affect epigenetics through 5 different avenues of action.

What are the current allopathic therapeutic alternatives for patients in leu of chiropractic, and what about their outcomes?

Braces have been considered the least invasive therapeutic alternative. However, the sores and cutaneous ulcers they can cause are a serious side effect and a major cause for patient non-compliance. Bracing has been the standard method of trying to protect patients from needing surgery ever since a brace was developed in the 1940s, said Weinstein, MD, of the University of Iowa. '*But it has never really proven to be effective in any study. Many bracing treatments are unnecessary. We're unnecessarily bracing two patients to get the one patient who actually needs it. We are still over-treating patients*' Weinstein said, '*furthermore, on closer examination of the data we find that nearly half of the participants in the non-braced control group during the trial did not have curve progression to the point of needing surgery*'. The same was true for 41 percent of patients in the bracing group, who were non-compliant and actually spent very little time wearing

their braces. These statistics bring the efficacy of bracing into question. (51) A second meta study found that 60% to 70% of the patients referred to bracing are Risser 0 and 30% to 70% of this group will not wear the brace enough to ensure treatment efficacy. Furthermore, Risser 0 patients who reach the accelerated growth phase with a curve ≥40° are at 70% to 100% risk of curve progression to the fusion surgical threshold despite proper brace wear. Skeletally immature patients with relatively large magnitude scoliosis who are noncompliant are at a higher risk of failing brace treatment. (52)

In contemplating surgery as a viable therapeutic alternative, it is found that 40 % of operated patients with idiopathic scoliosis were legally defined as severely handicapped persons after surgery. (53) In their study, '*Rate of complications in scoliosis surgery – a systematic review of the Pub Med literature*', Weiss and Goodall found that, '*Scoliosis surgery has a varying but high rate of serious complications. A medical indication for this treatment cannot be established in view of the lack of evidence of efficacy. The rate of complications may even be higher than reported. Long-term risks of scoliosis surgery have not yet been reported upon in research. Trials with untreated control groups in the field of scoliosis raise ethical issues, as the control group could be exposed to the risks of undergoing such surgery*.' (54)

The fact that both surgically treated and brace-treated patients had more degenerative disc changes than the control participants as found by Danielsson and Nachemson is a concerning finding. (55) In evaluating the results of this study, the outcomes indicated that the initial average loss of the spinal correction offered by surgery was 3.2 degrees in the first year and 6.5 after two years with continued loss of 1 degree per year throughout life. It appears that in patients with a 50-degree curve, who were to undergo surgical correction, the curve would completely return after twenty years. This is observed through the need to repeat surgical intervention especially when the surgery was conducted on young children. An extremely potent declaration from none other than Dr. Paul Harington, inventor of the surgery for scoliosis with implanted metal rods, stated as far back as 1963, '*metal does not cure the disease of scoliosis, which is a condition involving much more than the spinal column*'. Report suggest that the Harrington rods will either bend, break loose from the wires, or worse, break completely in two as the spine continues in its scoliotic path, necessitating further surgical intervention and removal of the rods. Once the rod is removed, corrosion (rust) is found on two out of every three patients. (56) After the operation is performed, the average patient suffers a 25% reduction in their spinal ranges of motion. There was as well not noted any improvement of pulmonary or cardiac function in the surgical group. Keep in mind that the non-fused adult scoliosis patients do not demonstrate this same impairment. This flatly contradicts the claim that having a steel, stainless steel rod fused to your spine will not affect your mobility, physical activities, or quality of life. (57, 58, 59, 60)

Results

So, let us follow the science. The science is positioning chiropractic at the forefront in care for scoliosis, and perhaps other chronic conditions which have been linked to genetic predisposition. Science has also demonstrated that the conventional interventions offer poor outcomes with devastating and debilitating complications; further shinning the light on chiropractic as a primary choice of care as its side effects are negligible. (61, 62, 63) The most common side-effect of chiropractic scoliosis care reported in a medical study, who's initial intent was to discourage chiropractic care for scoliosis, was muscle soreness (accounting for 35.2 % of all side effects). The next common most side-effects were neck pain (13.6 % of side effects), back pain (12.0 %), headache (10.6 %), stiffness (7.8 %), and discomfort from the adjusting instrument (7.1 %). (64)

Chiropractic care has been found to be superior to bracing and possibly surgery. (65) This study found, '*Chiropractic treatment was associated with a reduction in the degree of curvature of adolescent idiopathic scoliosis in this case, after half a year of conventional medical treatment had*

failed to stop curve progression. This suggests that in at least some severe and progressive cases of scoliosis, chiropractic treatment including spinal manipulation may decrease the need for surgery.'

The possible secondary reactions to chiropractic care pale when compared with side effects of surgery which include, the syndrome of inappropriate antidiuretic hormone, pancreatitis, superior mesenteric artery syndrome, ileus, pneumothorax, hemothorax, chylothorax, fat embolism, urinary tract infections, wound infection, hardware failure, and death. (66) 21st century science has demonstrated what BJ Palmer stated over 100 years ago, '*We never know how far reaching something we may think, say or do today is, or how it will affect the lives of millions tomorrow*'.

The concept of the *Vertebral Subluxation Complex* has been made evident over and over again. Our 3 T's (thoughts, toxins, trauma) have been validated and illustrated to affect even cellular and chromosomal changes. (67) The medical research has begun to discuss the phenomenon of subluxation, but by renaming it '*dysponesis*' as not to lend any credibility to chiropractic. (68, 69) We now know that chiropractic can create profound changes in the body, not only neurological and structural, but epigenetic changes that will affect not only how our bodies function, but how the bodies of our children and our children's children will function.

Scoliosis is estimated to affect up to 5.2% of the general population. (70) Keep in mind that in typical year all cancers affect 4.39% of the population. (71) The average scoliosis patient will suffer a 14-year reduction in their average life expectancy, this is unacceptable, this is a problem of epidemic proportion if considering CDC statistic standards for epidemic. Chiropractic must step up and assume the leadership in scoliosis treatment understanding that as Dr. Harrington himself stated, '*scoliosis is a condition involving much more than the spinal column*'. Right now, the average chiropractic patient is a 39-year-old female. (72) This is wonderful, but does this position allow us to make the impact on health care in our communities, in our countries, in the world that we have an obligation to make?

I challenge our profession to come forward and care for not only the patient in your office, but their children, families, and affect people for generations to come. Let us embrace how science of the 21st century is validating our chiropractic principles. We must throw off the self-imposed shackles of being narrowly defined as mechanical pain-based care and embrace our roots as health-based care. Like the enormous adult elephant, restrained by a thin rope and a small wooden peg in the ground. Held there in place only by the conditioning of the small pup not having the strength to free itself. The enormous adult elephant has learned not even to try to free himself, not even recognising the power that it wields. Our power now comes from the science. There has been so much discussion of expanding our scope of practice. We should be concentrating on expanding our scope of demography.

Conclusion

Therefore, from a conservative, effective, low risk perspective chiropractic care appears to be the primary consideration for scoliosis patients. Further study into this novel emerging field of care for scoliosis patients as well as the importance of chiropractic care for children and overall health for the general population is indicated.

Charles L Blum
DC

Gilbert Weiner
DC
Private Practice
Bellingham , MA
drweiner@hotmail.com

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