Pathophysiological Mechanisms and Clinical Implications of Upper Cervical Vertebral Subluxations (Neurological Disorders with Craniocervical Dysfunction)

Jonathan Verderame [1] , M. Shakib Arslan [2*]

Abstract

Background: The craniocervical junction is a critical neuro-anatomical region, playing a significant role in health and disease due to its vulnerability. Upper cervical vertebral subluxations, defined as alterations in the atlanto-axial motion and/or position relative to the cranium and cervical spine, can disrupt normal physiological processes. This article aims to provide a comprehensive overview of the fundamental science, clinical models, and pathophysiology related to upper cervical vertebral subluxation. Methods: This review article synthesizes existing literature on upper cervical vertebral subluxation. It examines various models and mechanisms, including subluxation degeneration, the subluxation complex model, compression of the brainstem and neural structures, dysafferentation, the neurodystrophic model, and segmental facilitation. Neurobiological mechanisms such as dyskinesia, dysgenesis, dysautonomia, dysafferentation, neuroplasticity, and ephaptic transmission are also explored. Results: The review identifies and interprets multiple neurobiological mechanisms associated with upper cervical vertebral subluxations. Each model and mechanism highlights the potential impact on neurophysiology and overall health. The article discusses how these subluxations can lead to various systemic consequences, providing evidence from both fundamental science and clinical perspectives. Conclusion: Upper cervical vertebral subluxations have significant implications for health due to their potential to interfere with normal physiology through various neurobiological mechanisms. Understanding these mechanisms and their clinical relevance can enhance diagnostic and therapeutic approaches, ultimately improving patient outcomes. Further research is needed to deepen our understanding of these complex interactions and their broader implications for health and disease.

Keywords: Craniocervical junction, Vertebral subluxation, Neurobiological mechanisms, Chiropractic care, Cervical spine alignment, Atlanta axial joint, segmental dysfunction

Significance | This review discusses upper cervical vertebral subluxations' neurobiological mechanisms, enhancing diagnosis and treatment in chiropractic care.

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Introduction

Craniocervical subluxation, characterized by abnormal alignment or movement between the skull and the upper cervical spine, particularly involving the C1 atlas and C2 axis vertebrae, can arise from various causes such as trauma, degenerative changes, congenital abnormalities, or inflammatory conditions

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affecting the cervical spine. Understanding the underlying pathophysiological mechanisms of this condition is crucial for accurate diagnosis, effective management, and the prevention of potential complications. Chiropractors, as primary healthcare providers, play a unique and vital role in analyzing and correcting vertebral subluxation (VS), as demonstrated by (Hart, 2016; Nelson, 1997). VS is broadly defined as a condition where a vertebra loses its proper alignment with adjacent segments, causing less severe displacement than a luxation but still interfering with the body's adaptability and homeostasis (Henderson, 2005). According to Kwon et al. (2023), the prevalence of VS is 78.55%. While some within the chiropractic profession view VS as a historical concept (Senzon, 2018), there is a consensus that correcting VS is a defining feature of the profession. The assessment and correction of VS are core clinical objectives in chiropractic practice (Gatterman, 2005; Russell, 2019).

The scientific literature includes 500 potential synonyms for VS, which some authors argue can be detrimental to the professional identity (Rome, 1996). There is no suitable metonym for vertebral subluxation (VS) as common language fails to encompass the full scope of the pathophysiology involved. Therefore, the term vertebral subluxation should remain central in clinical practice, research, and public policy within the chiropractic profession. Although the concept and neurobiological mechanisms of VS are not fully understood, the body of knowledge has grown since its first definition in 1902. Dishman (1985) and Lantz (1995) initially introduced and popularized the five-component model known as the "vertebral subluxation complex," which includes spinal kinesiopathology, neuropathology, myopathology, histopathology, and biochemical changes. This framework was later expanded to a nine-component model to further explain the pathological processes associated with VS, now encompassing angiology, neurology, myology, inflammatory response, anatomy, physiology, kinesiology, biochemistry, and connective tissue physiology.

Lantz's concept of the vertebral subluxation complex integrates all facets of chiropractic clinical management into a cohesive conceptual framework, often referred to as a "unified field theory of chiropractic." Each component of this model delineates the specific anatomical, physiological, and biochemical changes associated with VS, encompassing the potential pathophysiological and neurobiological dysregulation involved. Research on the effects of VS has produced varied results due to a lack of randomized controlled trials. However, the past decade has seen a significant increase in the understanding of VS in peer-reviewed literature, highlighting the need for an updated and comprehensive review (Kent, 2019). The objective of this paper is to describe novel pathophysiological mechanisms of VS.

Analysis

The biomechanics underlying craniocervical subluxation involve complex interactions among the skull, atlas (C1), axis (C2), and the surrounding ligaments and muscles. Misalignments, such as the anterior or posterior displacement of C1 relative to C2, can result in altered spinal curvature, increased joint stress, and reduced spinal stability. Additionally, factors like ligament laxity, muscle weakness, and irregular loading patterns contribute to the development of craniocervical subluxation. Radiographs were annotated with the atlas plane line, the frontal cephalic line, and the cervical spine line, and orthogonality values were derived from these annotations. The adjustment radiographs shown in Figure 1 were used for this purpose, and adjusting vectors were then calculated.

The concept of "subluxation" remains a dynamic blend of theory, practical application, and ongoing research. Despite the challenges faced by the theory of vertebral subluxation, as previously examined, exploring contemporary literature could enhance the clinical relevance of vertebral subluxation as a primary reason for seeking chiropractic care (Vernon, 2010). The mechanisms by which spinal derangements produce clinically significant neurological and other systemic effects are not yet fully understood. Without a comprehensive understanding of the potential neurobiological components involved, assessing the epidemiological impact remains elusive. Kent introduced an operational model for evaluating neuro-dysregulation associated with vertebral subluxation, comprising four key elements:

Dysafferentation: Altered facet joint nociceptive/mechanoreceptive functions that regulate postural changes and cortical function.

Dyskinesia: This includes impaired regional and global ranges of movement, pathomechanical degenerative changes resulting in vertebral artery compromise, cerebral spinal fluid circulation, spinal cord compression, and/or autonomic dysfunction.

Dysponesis: Refers to abnormal tonicity of muscle activity and errors in the action potential.

Dysautonomia: Spinal dysfunction results in abnormal regulation of organs, glands, and blood vessels. Neural dysregulation causes neurodystrophic modulation of both specific and nonspecific immunity, leading to reduced vagal tone (Kent, 2017; Christopher, 1996).

This operational definition enables an objective, reliable, and replicable assessment of the potential effects associated with vertebral subluxation (VS) in both clinical practice and research. Kent's model of chiropractic subluxation theory includes neurological, somatovisceral, myological, biomechanical, and biochemical effects. The pathophysiological mechanisms of VS reviewed in this paper encompass neuroplastic changes, vagal tone, cerebrospinal fluid hemodynamics, cerebral blood flow,

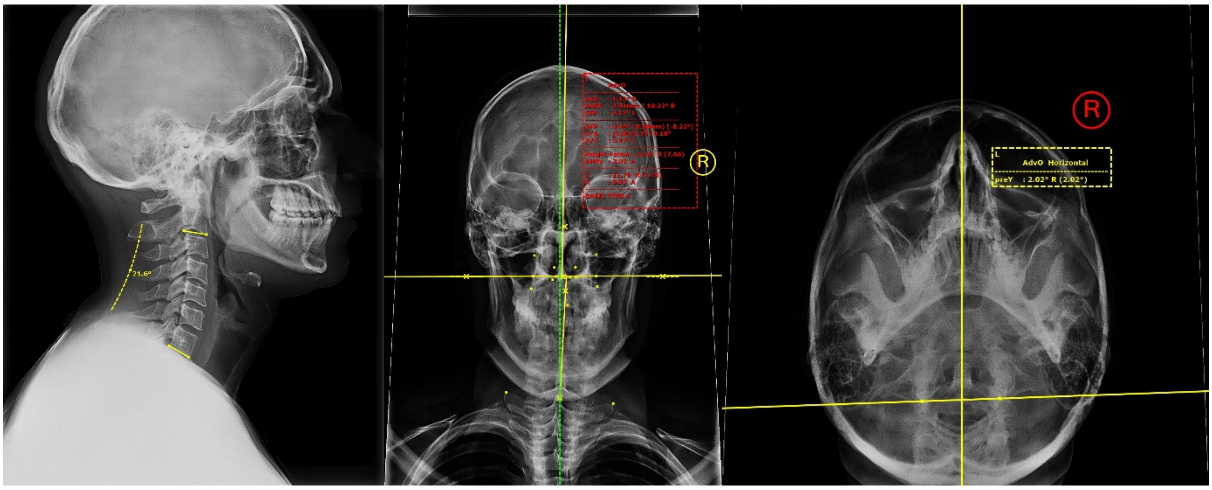

Figure 1. Radiographic geometry

venous drainage, and biochemical changes related to immunity (Kent, 2017; Christopher, 1996).

Neuroplasticity

Chiropractic adopts a salutogenic approach to healthcare, emphasizing adaptability and health promotion rather than merely treating symptoms. Coined in 1979, the salutogenic model focuses on the origins of health rather than the origins of disease (Kent, 2018). Craniocervical subluxation can exert significant pressure on adjacent neural structures, including the spinal cord and cranial nerves. Compression or impingement of these tissues may manifest as symptoms such as neck pain, headaches, dizziness, and sensory or motor impairments. In severe cases, craniocervical subluxation can lead to spinal cord injury, myelopathy, or brainstem compression, necessitating prompt medical intervention. In 2011, health was redefined as "the ability to adapt and self-manage" Huber et al. (2016).

Traditional chiropractic theory and clinical applications aim to improve overall health and neurological integrity rather than treating specific diseases. The salutogenic theory describes the essential framework of neuroplasticity, whereby the organism is remodeled by sensory input. Neuroplastic dysfunction is common in degenerative brain conditions such as Alzheimer's disease and dementia. Electroencephalography, functional MRI, and somatosensory-evoked potentials have all been used to quantify the neuroplastic changes involved in chiropractic intervention. Spinal dysfunction alters afferent input to the central nervous system, resulting in maladaptive neural plasticity. One potential brain region affected is the prefrontal cortex Lelic et al. (2016), partially explaining chiropractic's impact on mental health. Correction of spinal misalignment can also affect pain perception Gay et al. (2014). Restoring normal cervical lordosis impacts autonomic regulation, disability, and sensorimotor control Moustafa et al. (2021). Multiple studies, including several randomized controlled trials, have shown that chiropractic intervention can correct cervical and lumbar lordosis Moustafa et al. (2021).

Neuro-inflammatory reflex loop

Vagal tone and somatovisceral dysfunction occur when abnormal tensile forces on the dura mater, central nervous system, and spinal nerve roots are caused by sagittal lordotic spinal curves and vertebral subluxations. This results in nerve fiber swelling and changes in action potential, leading to somatovisceral dysfunction. A case study by Fedorchuk et al. (2017) showed an increase in telomere length after chiropractic intervention, promoting healthy longevity. The posterior cervical muscles are crucial for spinal cord stabilization, sensorimotor control, and managing cervicocephalic pain. Myo-dural bridges, which connect the fascia of the suboccipital muscles to the dura across the cervical epidural space, play a significant role in both passive and active anchoring of the spinal cord. These bridges monitor dural tension to maintain spinal cord patency and prevent dural "infolding." Failure of this system can lead to cervicocephalic headaches, altered cerebrospinal fluid flow, sensorimotor function changes, and duration-related diseases, as highlighted by Enix et al. (2014).

Côté et al. (2020) concluded that chiropractic care does not affect immunity, citing a lack of valid clinical and scientific evidence. However, numerous credible studies excluded from their publication suggest that chiropractic care and spinal dysfunction do influence and/or alter immune function Fornari et al. (2017). It is well established that stress compromises the immune response, and a study by Organ et al. (2011) found that mean salivary amylase levels (a stress biomarker) significantly decreased after chiropractic intervention. Chiropractic spinal adjustments (SA) appear to modulate the neuroendocrine system, as evidenced by increased levels of glutathione peroxidase and superoxide dismutase after five weeks of SA, both of which are essential for the immune system. Additionally, chiropractic adjustments alter biochemical markers such as substance P, neurotensin, and oxytocin, which play important roles in immune health Sampath et al. (2015).

A potential route of neuroimmune regulation involves the vagus nerve, which modulates inflammation and inflammatory biomarkers, thus regulating inflammatory cytokine receptors. Heart rate variability (HRV) is used to monitor the impact of chiropractic interventions on vagal tone Budgell and Polus, (2006). A study by Win et al. (2015) demonstrated that HRV analysis is a useful, noninvasive method to evaluate changes in sympathovagal regulation related to alterations in hemodynamics and numeric pain scale scores. These initial findings suggest that adjustments in the lower cervical region may enhance sympathetic activity dominance, while adjustments in the upper cervical region may boost parasympathetic activity predominance, particularly in individuals with neck pain who received both upper and lower cervical adjustments.

A study by Zhang et al. (2006) conducted in a multi-clinic setting concluded that a single chiropractic adjustment increased HRV and reduced pain as measured by a visual analog scale (VAS). Chiropractic spinal adjustments (SA) may activate the parasympathetic nervous system to counterbalance the activity of the sympathetic nervous system. This neurological stimulation releases neurotrophins essential for anti-depressive treatments, suggesting that chiropractic care may be beneficial for treating major depression Kiani et al. (2020). Abnormal tensile forces on the dura mater, central nervous system, and spinal nerve roots caused by craniocervical subluxation can lead to somatovisceral dysfunction. Chiropractic intervention may influence telomere length and alleviate symptoms associated with cervical musculature dysfunction.

Role of Cerebrospinal fluid circulation, Venous and hemodynamic obstruction

The internal jugular vein descends from the jugular foramen alongside the carotid artery and the vagus nerve, all of which are in close contact with the diagonal process of the atlas. Biomechanical dysfunction in this region can compromise hemodynamics (Seoane & Rhoton, 1999). Compression of the internal jugular vein by the transverse process of the atlas after supratentorial craniotomy can lead to cerebellar hemorrhage, local irritation of the vagus nerve, and distant end-organ dysfunction. Misalignment of the atlas vertebra increases intracranial venous pressure and disrupts cerebral circulation, impairing nutrient delivery to the brain and affecting cerebral hemodynamics. These alterations can contribute to various disease processes, including neurological diseases, neurodegeneration, brain injury, stroke, and secondary brain lesions (Bor-Seng-Shu et al., 2012).

In a study by Rectenwald et al. (2018), a patient with Bow Hunter Syndrome received treatment using the Atlas Orthogonal chiropractic technique over eight visits in six weeks. Post-treatment, the patient showed a significant increase in blood flow volume: 8.2% in the left vertebral artery and 22.2% in the right vertebral artery. Improvements were also noted in transient visual impairment and a reduction in rotational misalignment of the first and second cervical vertebrae, as shown by radiographic examination. These results suggest that reducing rotational misalignment may have contributed to enhanced blood flow in the vertebral arteries when the head was in a neutral position.

Ding et al. (2020) found vascular stenosis in 69 out of 92 internal jugular veins, with 50.7% (35/69) of the stenotic vessels compressed solely by the transverse process of C1 and 44.9% (31/69) compressed by both the transverse process of C1 and the styloid process. Compression by the transverse process of C1 was more common in unilateral internal jugular vein stenosis (69.6% vs. 41.3%, $P = 0.027$), while compression involving both the transverse process of C1 and the styloid process was more prevalent in bilateral internal jugular vein stenosis (52.2% vs. 30.4%, $P = 0.087$).

Bakris et al. (2007) conducted a randomized controlled trial that examined anatomical abnormalities of the cervical spine at the level of the atlas vertebra. They found that these abnormalities were correlated with relative ischemia of the brain stem circulation and an increase in blood pressure (BP). The study observed that manual atlas realignment to an orthogonal position was associated with a decrease in arterial pressure. It concluded that restoring the alignment of the atlas vertebra correlates with a substantial and sustained decrease in BP, similar to the effects of a two-drug combination therapy.

In fetuses with transposition of the large vessels, there is a decreased flow of oxygen-rich blood to the heart and brain, initiating the asphyxia cascade. This condition can lead to craniocervical dysfunction, particularly involving the C0-C2 region. The craniocervical junction (CCJ) encloses the encephalic vasculature, the cerebrospinal fluid (CSF) system, and the central nervous system. Deformity of the CCJ may impede blood and CSF circulation (Rosa & Baird, 2015; McPartland & Brodeur, 1999). Chronic ischemia, edema, and hydrocephalus may contribute to neurodegenerative diseases, with the CCJ potentially playing a role in conditions like Alzheimer's disease, Parkinson's disease, ALS, and multiple sclerosis (Flanagan, 2015).

Misalignments of the C1-2 vertebrae can disrupt normal cerebrospinal fluid (CSF) flow and blood flow in the vertebrobasilar system. Reducing misalignments at the CCJ may restore spinal integrity, improve CSF flow, and enhance venous outflow in conditions like chronic cerebrospinal venous insufficiency and multiple sclerosis (Rosa et al., 2018). Biomechanical dysfunction at the craniocervical junction can compromise hemodynamics and cerebral circulation, potentially contributing to neurological diseases. Restoring spinal integrity through chiropractic adjustments may improve cerebrospinal fluid circulation, venous outflow, and cerebral blood flow, thereby offering therapeutic benefits.

Cerebral blood flow

Rotational misalignments or anatomical deformation of the craniocervical junction (CCJ) can contribute to reduced blood flow in the vertebrobasilar system (Fiester et al., 2021). Cerebellar tonsillar ectopia disrupts cerebrospinal fluid (CSF) dynamics, obstructing venous outflow and causing intracerebral venous congestion, which reduces intracerebral compliance and blood flow. This condition, compounded by the failure of both principal and collateral venous outflow tracts, increases venous pressure and leads to cerebral blood flow insufficiency. Although CSF shunting can temporarily improve blood flow, it may eventually result in veno-congestive brain edema and other complications (Ravindra et al., 2015).

The natural lordotic curvature of the cervical spine is considered optimal for cervical spine posture, as the absence of cervical lordosis disrupts biomechanics and leads to significant neurobiological implications (Bulut et al., 2016). Loss of cervical spine lordosis is associated with reduced vertebral artery hemodynamics. Given the close anatomical relationship between the cervical spine, vertebral arteries, and cerebral vasculature, it is suggested that improving cervical lordosis enhances collateral cerebral artery hemodynamics and circulation (Katz et al., 2019).

The development of a computational tool represents a significant advancement in understanding the dynamics of hemodynamic alterations in cerebral blood flow. This tool not only aids in comprehending the evolution of these changes but also provides insights into the pathology of collateral circulation and middle cerebral artery (MCA) stenosis. Its potential implications extend to enhancing diagnostic capabilities and informing therapeutic strategies for conditions related to cerebral blood flow abnormalities (Kang, 2023).

Clinical Manifestations

Clinical manifestations of craniocervical subluxation vary depending on the underlying etiology, severity of the condition, and individual patient factors. Common signs and symptoms include neck stiffness, limited range of motion, radicular pain, and neurological deficits. Diagnosis typically involves a thorough clinical evaluation, including physical examination, imaging studies (e.g., X-ray, MRI), and neurological testing.

Treatment Approaches

The promptness of diagnosis plays a crucial role in shaping the prognosis of craniocervical subluxation, directly influencing the potential for non-surgical interventions such as bloodless reduction or surgical treatments (Gonzalez et al., 2022). The management of craniocervical subluxation focuses on alleviating symptoms, restoring spinal alignment, and preventing disease progression. Conservative treatment methods include physical therapy, chiropractic manipulation, cervical traction, and analgesic medications. However, if conservative approaches fail to achieve the desired outcomes or if there is neurological compromise, surgical interventions such as decompression, fusion, or stabilization procedures may become necessary.

Conclusion

We have analyzed novel processes involved in the pathophysiological mechanisms of VS which include neuroplastic changes, vagal tonality, cerebral spinal fluid hemodynamics, vascular pathology, cerebral blood flow, venous drainage, as well as biochemical changes associated with immunity. Biomechanical dysfunction, particularly around the CCJ, occludes foramen, obstructs cerebral circulatory modulation, and alters neurological processes. VS has a multitude of pathophysiological consequences beyond musculoskeletal pain. Improved clinical approaches might result from more studies in this field. The study underscores the varied clinical manifestations of craniocervical subluxation and proposes diverse treatment approaches, ranging from non-surgical interventions like physical therapy and chiropractic manipulation to surgical procedures in refractory cases or neurological compromise.

Author Contributions

J. V. and M.S.A. conceptualized the study. J. V. and M.S.A. conducted the formal analysis. M.S.A. carried out the investigation. J. V. and M.S.A. re-graphically represented and added analysis of the data. Both J. V. and M.S.A. wrote the review draft. M.S.A. edited the review. J. V. re-validated the results. Furthermore, both authors equally contributed to the writing and proofreading of the paper.

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Competing financial interests

The authors have no conflict of interest

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