

Heidi's Master Class

Update on Chiro-Neuro-Immune Connection

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 VP Research, Dean Research
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Key References

The Potential Mechanisms of High-Velocity, Low-Amplitude, Controlled Vertebral Thrusts on Neuroimmune Function: A Narrative Review

Heidi Haavik^{1,2}, Imran Khan Niazi^{1,2,3,4,5}, Nitika Kumari^{1,2,3}, Imran Amjad^{1,4,5}, Jenna Duehr¹ and Kelly Holt^{1,4,5}

Abstract: The current COVID-19 pandemic has necessitated the need for health-care workers that hold an expert remedy. There is some evidence that high-velocity, low-amplitude (HVLA) controlled vertebral thrusts have the potential to modulate immune responses. However, the mechanisms of the link between HVLA controlled vertebral thrusts and immunomodulation and the associated potential clinical implications are unclear. This review aims to elucidate the underlying mechanisms that are proposed for HVLA controlled vertebral thrusts and immunomodulation and discuss what this link implies for clinical practice and future research. A search for peer-reviewed articles published up until April 2021 was conducted. Twenty-three published papers were found that explored the impact of HVLA controlled vertebral thrusts on neuroimmune markers, which yielded a significant effect. These data, when analyzed, show that HVLA controlled vertebral thrusts influence the levels of immune markers in the body, including neuropeptides, inflammatory markers, and endocrine markers. This narrative review discusses the best likely mechanisms for how HVLA controlled vertebral thrusts could impact neuroimmune markers. The mechanisms are most likely due to the known changes in proprioceptive processing that occur within the central nervous system (CNS) in particular within the parabrachial nucleus, following HVLA spinal thrusts. The parabrachial nucleus is involved in the regulation of the autonomic nervous system, the hypothalamic-pituitary-adrenal axis and the immune system. The clinical and basic science literature are affected by a multitude of published studies. These studies suggest that HVLA controlled vertebral thrusts are beneficial for a wide range of conditions, including HVLA controlled vertebral thrusts have been proposed to modulate immune function. However, it is not yet known whether HVLA controlled vertebral thrusts have a clinically relevant impact on immunity. Further research is needed to explore the clinical impact of HVLA controlled vertebral thrusts on immune function.

Keywords: high-velocity, low-amplitude thrusts (HVLA), chiropractic, spinal manipulation, central nervous system, parabrachial nucleus, immune, endocrine, neuropeptides

1. Introduction

The COVID-19 pandemic has resulted in significant global morbidity and mortality by [1], especially amongst individuals who are immunocompromised, such as older people and those with underlying medical conditions [2]. The current pandemic and

Heidi Haavik, Imran Khan Niazi, Nitika Kumari, Imran Amjad, Jenna Duehr, Kelly Holt. (2021b) The potential mechanisms of High-Velocity, Low-Amplitude, Controlled Vertebral Thrusts on Neuroimmune Function: A narrative review. *Medicina* 2021, 57, 536. <https://doi.org/10.3390/medicina57060536>

Imran Amjad, Imran Khan Niazi, Nitika Kumari, Usman Ghani, Felipe Duarte, Federico For-tuna, Diego Gonzalez, Alex Sumich, Bibiana Fabre, Kelly Holt, Heidi Haavik. The effects of 12 weeks of chiropractic spinal adjustments on physiological biomarkers in adults: A pragmatic randomized controlled trial. *PLoS One*, 2025, 20(12), p.e0338730. <https://doi.org/10.1371/journal.pone.0338730>

Abstract

Background: Larger acute effects of chiropractic care on neuroplasticity, stress, and immune biomarkers remain unclear.

Objective: This study evaluates the effects of chiropractic care on physiological biomarkers, including brain-derived neurotrophic factor (BDNF), cortisol (saliva, blood, hair), and inflammatory cytokines (interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interleukin-gamma (IFN-γ), C-reactive protein (CRP), B-lymphocytes (CD19), T-helper cells (CD4), cytotoxic T cells (CD8), and natural killer cells (CD56) in subclinical spinal pain patients.

Methods: Parallel-group, pragmatic randomized controlled trial conducted at the Rehabilitation Center of Rijnland General Hospital, Rijnland, The Netherlands. Intervention: 12 weeks; follow-up: 16 weeks (May–December 2022). Participants with subclinical spinal pain were randomly assigned by using simple randomization to either 12 weeks of chiropractic or sham care. We aimed to recruit up to 150 participants over three months; however, given the pragmatic nature of the trial and logistical constraints, including the availability of chiropractors, the final number enrolled was determined.

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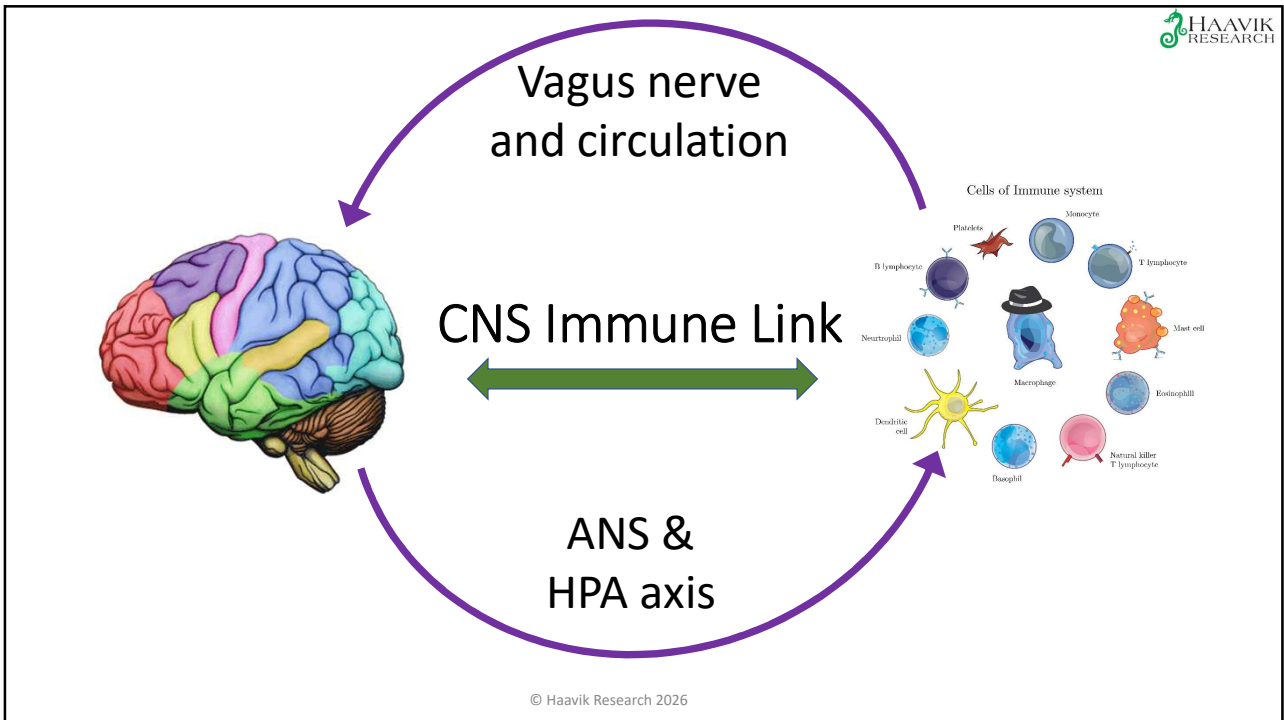
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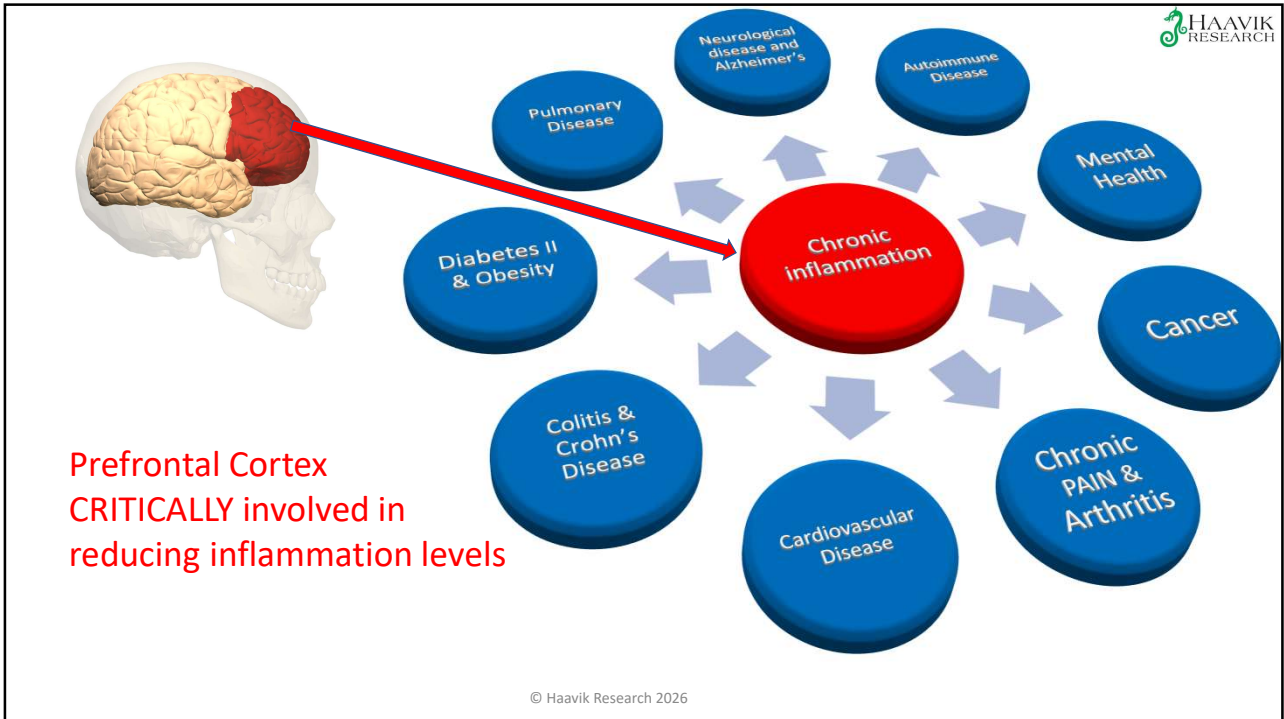
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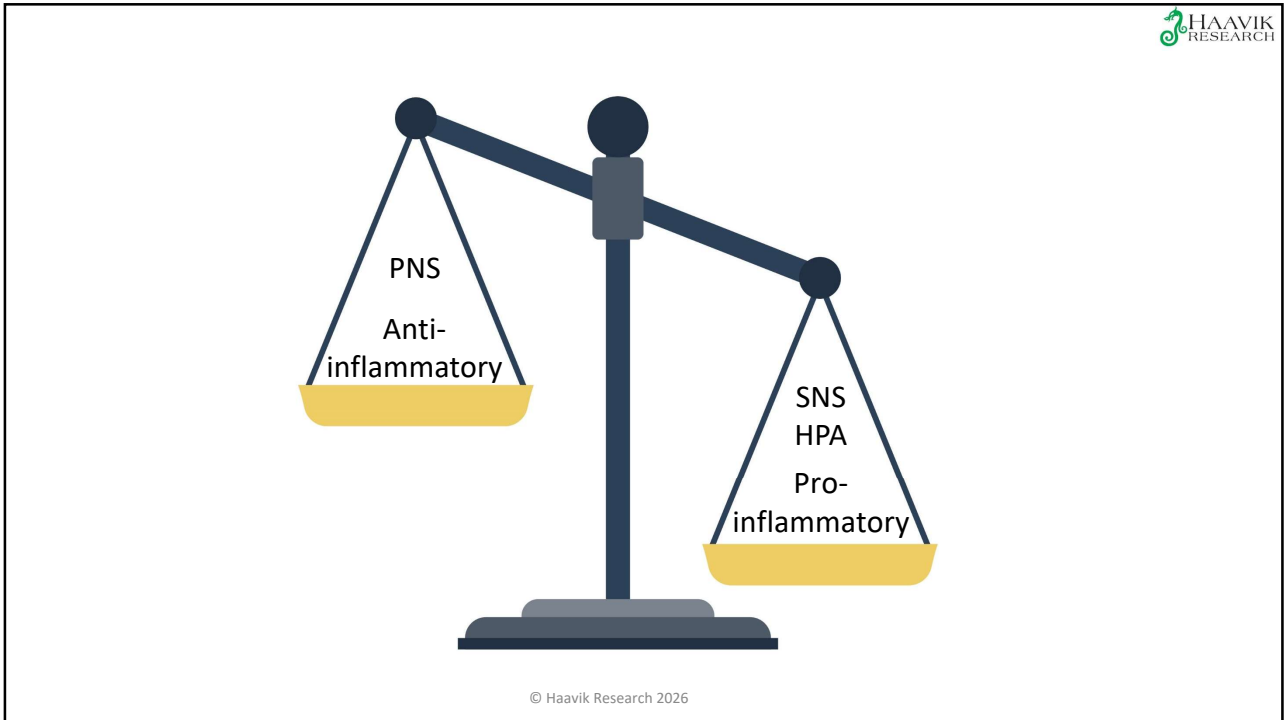
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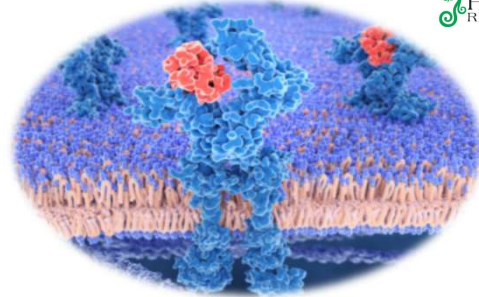


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Summary



- CNS – Immune Closely linked
- Bi-directional communication
- Rely on accurate perception of situation
- Appropriate / balanced response required (not too much or too little)
- Neuro-immune Cell Units around the body perceive immune threat
- Vagus afferents and blood convey inflammation levels to the brain
- Brain modulates immune response via HPA and ANS by releasing glucocorticoids and catecholamines which regulate immune cell function
- Stress impairs immune response

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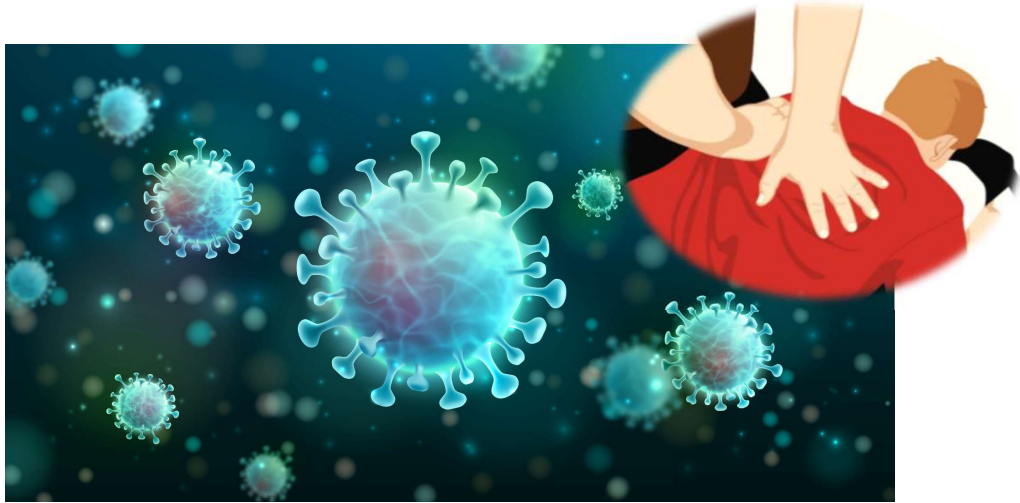
Take Home Messages

“There is substantial evidence that tells us the nervous system, the hormonal system and the immune system communicate with one another and are intimately linked in their functions. Stress affects our immune response and makes us more susceptible to infections such as respiratory diseases. And a part of the brain called the prefrontal cortex is critically involved in regulating the autonomic nervous system, the endocrine system and the immune system”.

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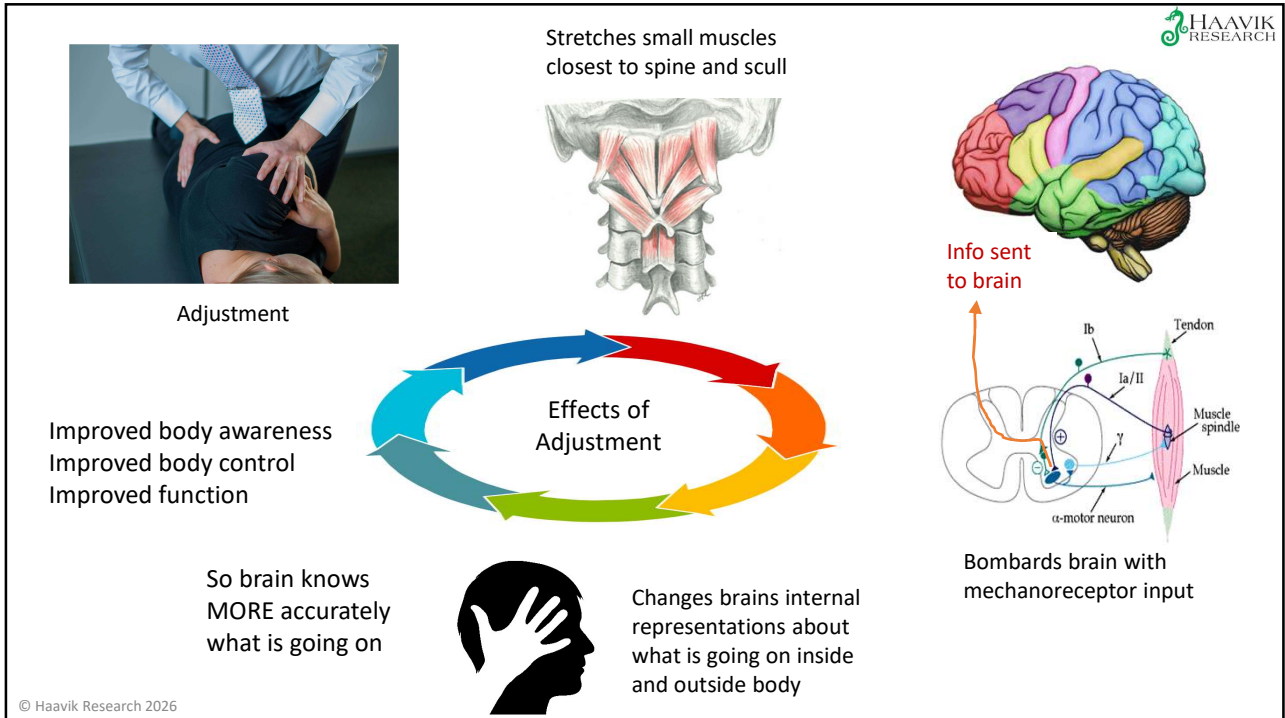
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Chiropractic and the Immune System

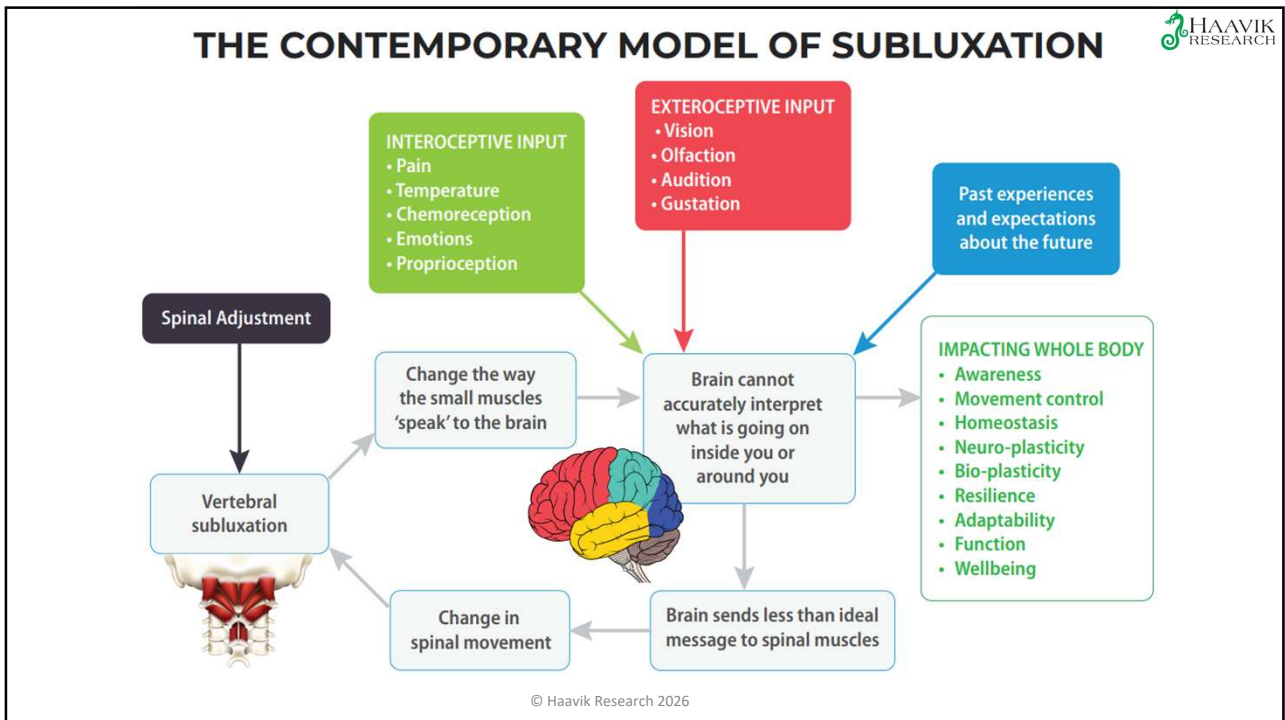


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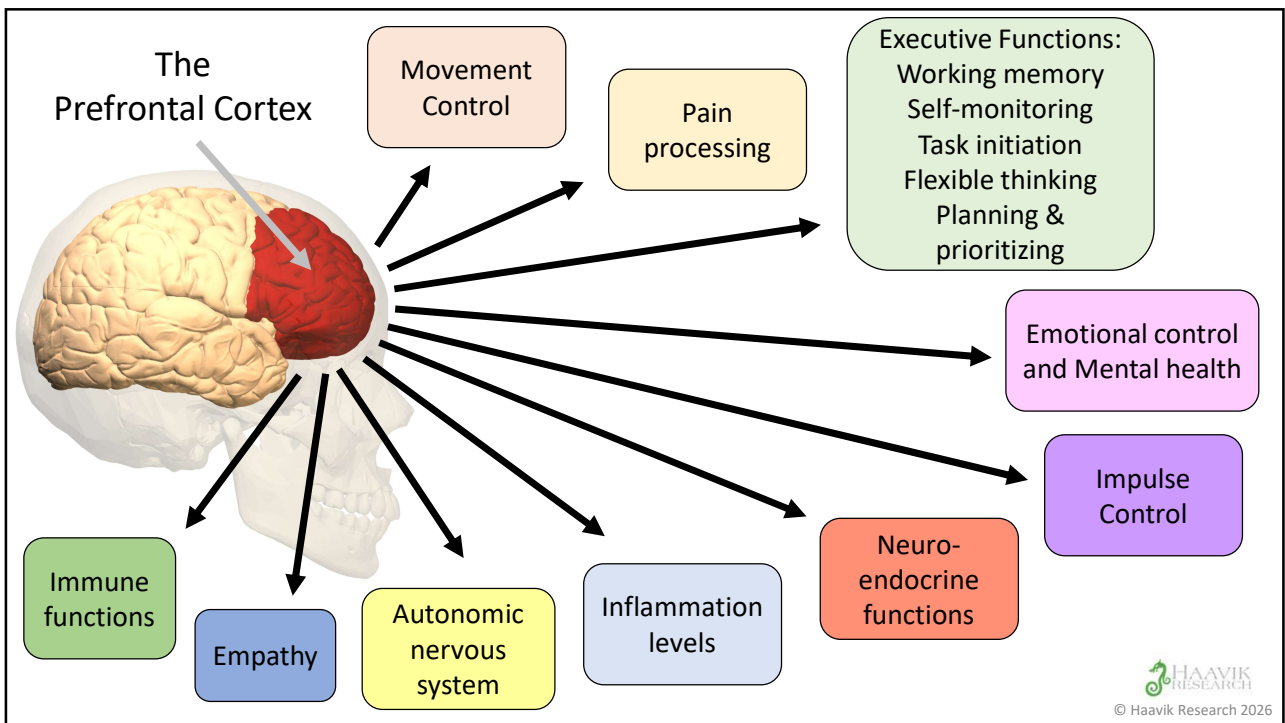
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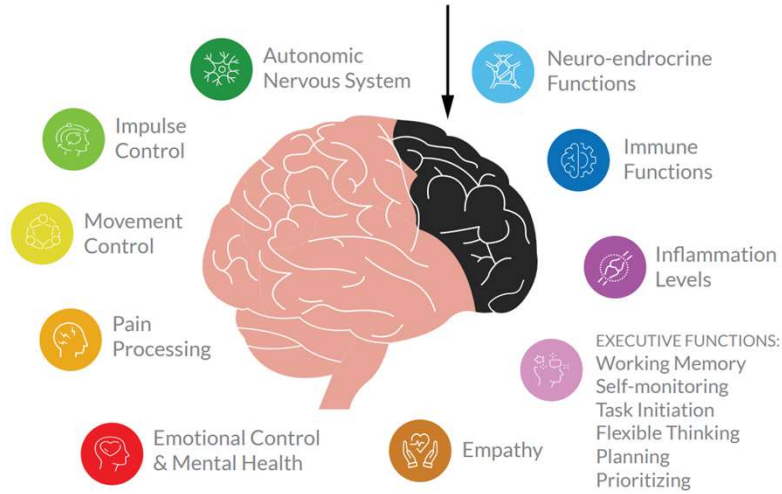


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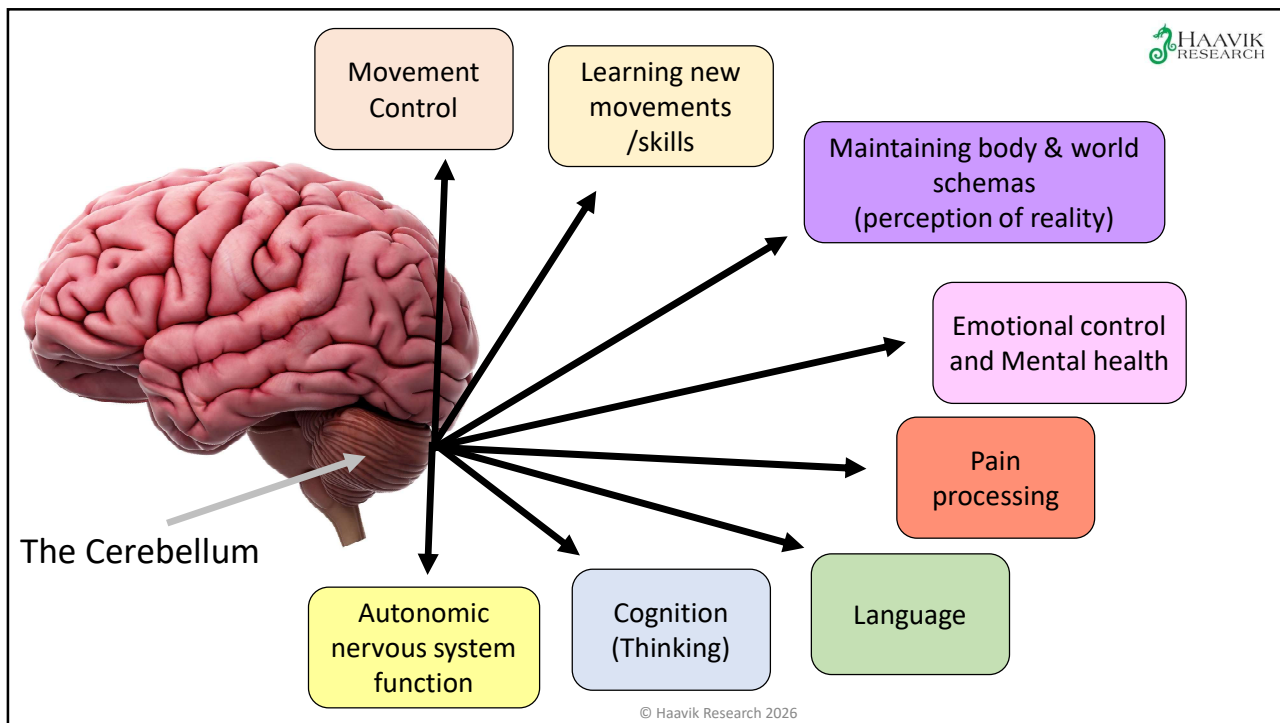
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THE PREFRONTAL CORTEX



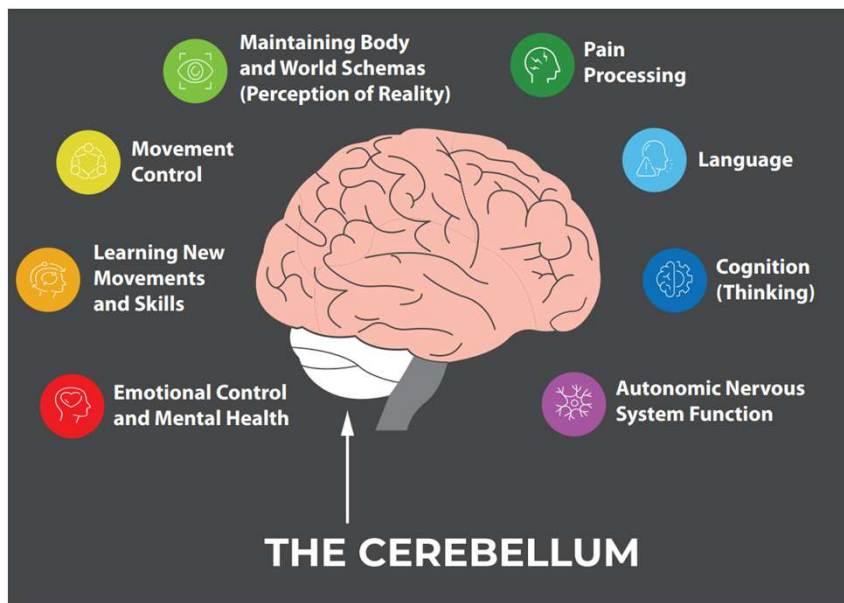
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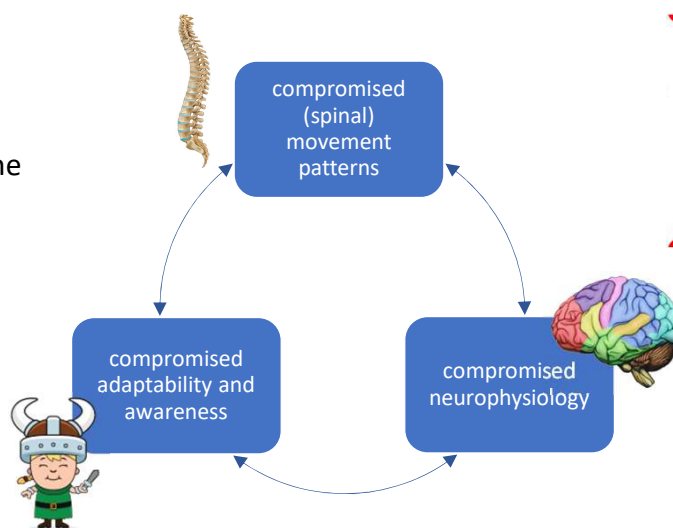


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The Brain Model – What evidence do we have?

✓
Basic Science
 Link chiro-neuro
 Link chiro-immune



~~NO LONGER NOTHING!!!!~~
 We now have a clinical trial!!!!

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Basic Science

vs

Clinical Science

- Is there a link between spinal function and neural function?
- Is there a link between spinal function and immune function?
- Can an adjustment impact neural function?
- Can an adjustment impact immune function?

- Can chiropractic care improve immune function by reducing susceptibility to getting sick
- Can chiropractic care improve immune function by improving outcomes if you do get sick (reduced symptoms, shorter recovery times, etc)

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Review 1 Conclusion

“spinal manipulation can increase substance-p, neurotensin, oxytocin and interleukin levels and may influence cortisol levels post-intervention”

“more research needs to be done to understand the clinical relevance of such changes”

Review article
Changes in biochemical markers following spinal manipulation-a systematic review and meta-analysis
 Kesava Kovanur-Sampath, M.D.^{1,2}, Ramakrishnan Mani, PhD¹, Jim Cotter, PhD³, Angela Spontelli Goseleman, PT⁴, Steve Tummally, PhD⁵
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ABSTRACT
 The aim of this meta-analysis was to determine the effectiveness of spinal manipulation in influencing various biochemical markers in healthy and/or symptomatic populations. Electronic databases (n = 10) were searched from inception till September 2016, and eight trials (222 participants) that met the inclusion criteria were included in the meta-analysis. Two authors independently extracted and assessed the risk of bias in included studies. Standardised mean differences for outcome measures were used to calculate effect sizes. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool was used for assessing the quality of the body of evidence for each outcome of interest. There was moderate quality evidence that spinal manipulation influenced biochemical markers. There was moderate quality evidence of significant difference that spinal manipulation is better (SMD -0.46, 95% CI -0.83 to -0.10) than control in eliciting changes in cortisol levels immediately after treatment. There was also a low quality evidence that spinal manipulation is better than control at post-treatment in increasing substance-P (SMD 0.44(0.02), 0.87 to 0.01), neurotensin (SMD 0.43(0.02), 0.28 to 0.60) and oxytocin levels (SMD 0.43(0.02), 0.30 to 0.57). However, low quality evidence indicated that spinal manipulation did not influence sympathetic (SMD 0.13(0.03), 0.06 to 0.20) nor parasympathetic (SMD 0.06(0.03), 0.17 to 0.26). The current review found that spinal manipulation can increase substance-p, neurotensin, oxytocin and cortisol levels and may influence cortisol levels post-intervention. However, future trials targeting symptomatic populations are required to understand the clinical importance of such changes. © 2017 Elsevier Ltd. All rights reserved.

1. Introduction
 Spinal manipulation (SM) is a specific hands-on approach used by several different therapeutic professions such as physiotherapy, osteopathy and chiropractic to commonly treat spinal pain (1). Kovanur et al. (2015). SM has been shown to be an effective treatment approach in low back and neck disorders (1). Kovanur et al. (2015). However, (2012). Recent systematic reviews have demonstrated the effectiveness of SM in treating spinal pain (Cromack et al., 2012; Coiro et al., 2015). Through the exact mechanism through which SM acts is still under scrutiny it has been widely accepted that SM initiates a cascade of neurophysiological changes including the peripheral nervous system, autonomic nervous system and the endocrine system (Dubboly et al., 2009). A key candidate mechanism responsible for the generation of pain is nociception that occurs at the site of tissue injury (Sivoni and Chavakis, 1997). Nociception is mediated by a range of healthy and normally produced biochemical markers, resulting in transmission of nociceptive impulses into the nervous system (Liu and Baskaran, 2011). These biochemical markers include various neuropeptides such as neurotensin, oxytocin, substance-P (SP) and oxytocin (Cohen, 2005). Neurotensin is produced in several regions of the CNS and spinal cord and it has several actions, including analgesia (1). Coiro et al., 2015). As these chemicals are primarily released at the injury site, they also result in initiation of inflammatory process which further results in the production of numerous pro-inflammatory and immune-regulatory cytokines and neurotransmitters (Cotter et al., 2017).

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Kovanur-Sampath, et al. 2017. *Musculoskeletal Science and Practice* 29: 120-131



Review 2 Conclusion

“Although spinal manipulations seem to trigger the activation of the neuro-immuno-endocrine system, the evidence supporting a biological account for the application of HVLAT in clinical practice is mixed and conflicting.

Further research on subjects with spinal MSK conditions with larger sample sizes are needed to obtain more insights about the biological effects of spinal manipulative therapy.”

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Review
The Effects Induced by Spinal Manipulative Therapy on the Immune and Endocrine Systems

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Abstract: Background and Objectives: Spinal manipulations are interventions widely used by different healthcare professionals for the management of musculoskeletal (MSK) disorders. While previous theoretical principles focused predominantly on biomechanical accounts, 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 modulation after the administration of spinal manipulative therapy (SMT). The aim of this paper is to provide an overview of the available evidence supporting the biological plausibility of high-velocity, low-amplitude thrust (HVLAT) on the immune-endocrine system. Materials and Methods: Narrative critical review. An electronic search on MEDLINE, PsycINFO, and Google Scholar followed by a hand and “snowballing” search were conducted to find relevant articles. Studies were included if they evaluated the effects of HVLAT on participants’ biomarkers. Results: The electronic search returned 13 relevant articles and two themes of discussion were developed. Nine studies investigated the effects of SMT on cortisol levels and five of them were conducted on asymptomatic populations. Four studies examined the effects of SMT on the immune system and all of them were conducted on healthy individuals. Conclusions: Although spinal manipulations seem to trigger the activation of the neuro-immunoendocrine system, the evidence supporting a biological account for the application of HVLAT in clinical practice is mixed and conflicting. Further research on subjects with spinal MSK conditions with larger sample sizes are needed to obtain more insights about the biological effects of spinal manipulative therapy.

Keywords: spinal manipulative therapy; immune system; endocrine system; back pain; neck pain; physiotherapy

1. Introduction

Spinal disorders are conditions affecting an increasing number of people, and their associated direct and indirect costs have dramatically grown around the globe [1]. The 12-month incidence of neck pain ranges between 10.4% and 21.2% [2], and more than 70% of people living in Western countries experience an episode of lower back pain in their lifetime [3].

Although economic and societal systems are striving to minimize the expenditures associated with their management, the US health care system alone devotes more than half of its total per annum for the treatment of these clinical entities [4]. Significant efforts are made by pain research to find effective interventions, yet these musculoskeletal conditions remain the leading causes for years lived with disabilities (YLDs) in most countries and territories. The Global Burden of Disease 2016 study reports that both the prevalence and the YLDs because of low back and neck pain have increased by more than 18% over the last decade [5].

Medicina 2019, 57, 448. doi:10.3390/med57080448

Colombi and Testa 2019. Medicina 55(8): 448.



Review 3 Conclusion

“There is substantial evidence suggesting that the nervous system, the hormonal system and the immune system communicate with one another and are intimately linked in their functions [70,93–97].

This communication is essential for the body’s ability to protect itself and involves a variety of immune mediators, including cytokines, neurotransmitters, hormones, and humoral factors [67,68,70,94,116,117,164,234].

Furthermore, the prefrontal cortex is critically involved in regulating the autonomic nervous system, the HPA axis, and the immune system [94,144–154].

Neuro-immune communication is affected by emotional or pain-related stress [69,144,151,195,260–262].

Stress activates the SNS and HPA axis to increase inflammation in the body. Stress also suppresses the prefrontal cortex, which in turn reduces its inhibitory control on the HPA axis and inhibits the anti-inflammatory PNS activity. This stress-induced inflammation weakens the immune response [95,98–112]. The stress-induced SNS activity also alters the muscle activation patterns to impair vertebral motor control [283–285], thus can cause the establishment of CSMC problems.

HVLA controlled vertebral thrusts have been shown to affect vertebral motor control [123–125,128,131,135], the prefrontal cortex [134], and the levels of immune mediators in the body that are important for a healthy immune response [15–32].”

Review
The Potential Mechanisms of High-Velocity, Low-Amplitude, Controlled Vertebral Thrusts on Neuroimmune Function: A Narrative Review

Heidi Haavik^{1,2}, Imran Khan Nizal^{1,2,3,4*}, Nikita Kumari^{1,2,3}, Imran Anjum^{1,4,5}, Jena Dasht¹ and Sofya Hain^{1,2,3}

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Abstract: The current COVID-19 pandemic has necessitated the need to find healthcare solutions that boost of support immunity. There is some evidence that high-velocity, low-amplitude (HVLA) controlled vertebral thrusts have the potential to modulate immune mediators. However, the mechanisms of the link between HVLA controlled vertebral thrusts and neuroimmune function and the associated potential clinical implications are less clear. This review aims to elucidate the underlying mechanisms that can explain the HVLA controlled vertebral thrusts’ neuroimmune link and discuss what this link implies for clinical practice and future research needs. A search for relevant articles published up until April 2021 was undertaken. Because three published papers were found that explained the impact of HVLA controlled vertebral thrusts on neuroimmune markers, of which only one stated a hypothesis. These two review studies show that HVLA controlled vertebral thrusts influence the levels of immune mediators in the body, including seroproteins, inflammatory markers, and endocrine markers. This narrative review discusses the most likely candidates for how HVLA controlled vertebral thrusts could impact these immune markers. The mechanisms are most likely due to the known changes in proprioceptive processing that occur within the central nervous system (CNS), in particular within the prefrontal cortex, following HVLA spinal thrusts. The prefrontal cortex is involved in the regulation of the autonomic nervous system, the hypothalamic-pituitary-adrenal axis and the immune system. Bi-directional neuro-immune interactions are affected by emotional or pain-related stress. Stress-induced sympathetic nervous system activity also alters vertebral motor control. Therefore, there are biologically plausible direct and indirect mechanisms that link HVLA controlled vertebral thrusts to the immune system, suggesting HVLA controlled vertebral thrusts have the potential to modulate immune function. However, it is not yet known whether HVLA controlled vertebral thrusts have a clinically relevant impact on immunity. Further research is needed to explore the clinical impact of HVLA controlled vertebral thrusts on immune function.

Keywords: high-velocity, low-amplitude thrust (HVLA); chiropractic; spinal manipulation; controlled vertebral thrusts; prefrontal cortex; immune system; endocrine system

1. Introduction

The COVID-19 pandemic has resulted in significant global morbidity and mortality [1], especially amongst individuals who are immunosuppressed, such as older people and those with underlying medical conditions [2–5]. The current pandemic and

Medicina 2021, 57, 536. https://doi.org/10.3390/med57080536

Haavik et al. 2021, Medicina 2021, 57, 536, p.15.

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HOT OFF THE PRESS 2025 PUBLICATION

- 106 SCSP participants
- 12 weeks of chiro care
- 4 week follow up
- EEG + Lots of clinical outcomes related to PFC
 - Immune
 - Emotions
 - Sleep
 - executive functions
 - Etc



Measurements taken at baseline, at 12 weeks and at 16 weeks

Amjad, Niazi, Kumari, Ghani, Rashid, Duarte, For-tuna, Gonzalez, Sumich, Fabre, Holt & Haavik. The effects of 12 weeks of chiropractic spinal adjustments on Physiological biomarkers in adults: A pragmatic randomized controlled trial. *PLoS One*, 2025, 20(12), p.e0338730.

<https://doi.org/10.1371/journal.pone.0338730>

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Study Design & Participants

- Pragmatic parallel-group RCT (Pakistan, 2022)
- Adults 20–60 with *subclinical spinal pain*
- 106 randomized → 88 completed 12 weeks → 73 completed follow-up
- **Groups:** 12 weeks chiropractic care vs sham care
- **Frequency:** ~3 sessions/week, 15–20 min each
- **Blinding:** Participants, assessors, and data analyst blinded
- **Blinding success:** 94% believed they received real chiropractic care
- **Outcomes measured at:** baseline, 12 weeks, 16-week follow-up



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Interventions & Biomarker Measures

- **Chiropractic care:** 12 weeks of adjusting vertebral subluxations
- **Sham care:** identical setup, positioning, and clicks with an activator — but *no thrusts* delivered
- **Primary outcome: Blood BDNF**
- **Secondary outcomes:**
Cortisol: saliva, blood, hair
Cytokines: IL-6, TNF- α , IFN- γ , CRP
Immune cells: CD4, CD8, CD19, CD56
- **Samples:** blood, saliva, hair (validated ELISA + chemiluminescent assays)
- **Analysis:** linear mixed-effects models with baseline adjustment



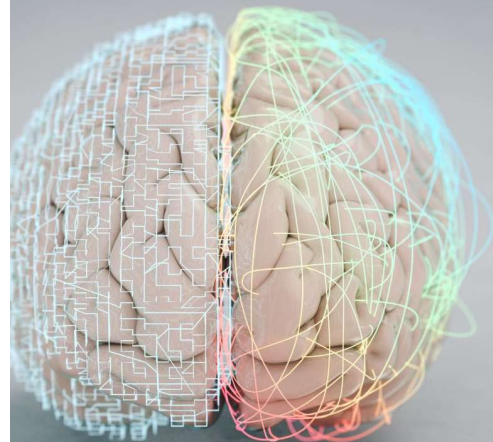
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BDNF

- Brain-Derived Neurotrophic Factor (BDNF)
- Key supporter of neuroplasticity
- Helps neurons survive, grow, and adapt
- Linked to learning, memory, mood, and pain modulation



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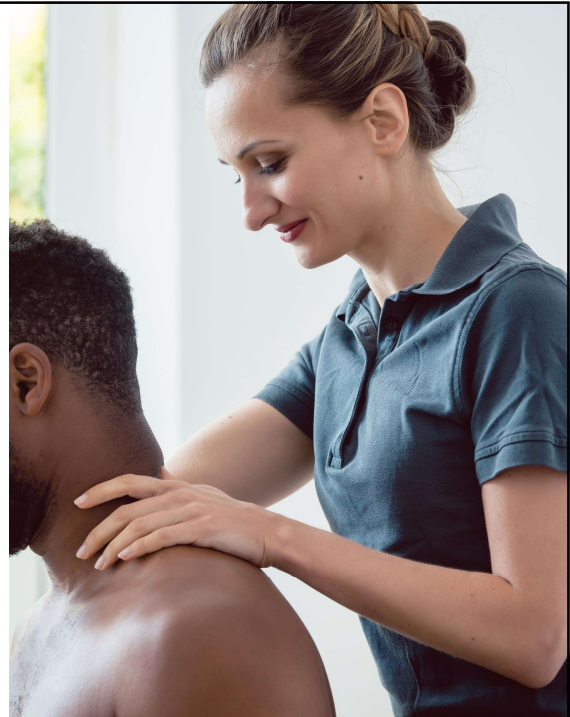
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BDNF changes with chiropractic care

- Primary outcome of the trial = blood BDNF at 12 weeks of chiropractic vs sham
- Higher BDNF in chiropractic group at 12 weeks +150 ± 60 (95% CI: 40 to 270), p = 0.009
- Trend for higher BDNF still at 16 weeks
- **Suggests enhanced neuroplastic activity in chiropractic group**

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What does this mean to us chiropractors?

- Adds biological weight to the “brain-based” chiropractic model
- 12 weeks of care → ↑ systemic neuroplasticity marker
- Potential relevance for:
 - Chronic pain
 - Stress resilience & healthy ageing
- Caution: Early evidence, effect sizes modest, needs replication
- **“There is emerging evidence that regularly caring for the spine appears to also support the brain’s capacity to adapt and reorganize, not just reduce symptoms.”**

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Cortisol

(Stress System – Hair, Blood, Saliva)

- Cortisol = main stress hormone (HPA axis)
- Short term: helps manage acute stress & inflammation
- Long term: chronically high cortisol can be harmful
- Measured in:
 - Blood & saliva → acute/short-term levels
 - Hair → longer-term, chronic stress load

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Cortisol Changes with Chiropractic Care

- **12 weeks:**
 - Blood cortisol: ↑ in **both** groups (no between-group difference)
 - Salivary cortisol: **higher in chiropractic** vs sham
 - $+5 \pm 2, p = 0.045$
 - Hair cortisol: **non-significant trend down** in chiropractic group
- **16 weeks (4 weeks after care stopped):**
 - Blood cortisol **lower in chiropractic vs sham**
 - -9 ± 4 (95% CI: -17 to -1), $p = 0.024$

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What does this mean for us chiropractors?

- Care may **engage** the stress system acutely (like exercise)
- Over time, chiropractic care may support **better regulation**
- Lower blood cortisol at 16 weeks = possible **reduce systemic stress load**
- Fits with a **neuroimmunomodulation / HPA axis** story
- *“There is emerging evidence that chiropractic care may help support healthier regulation of the stress system over time, not just symptom relief in the spine.”*



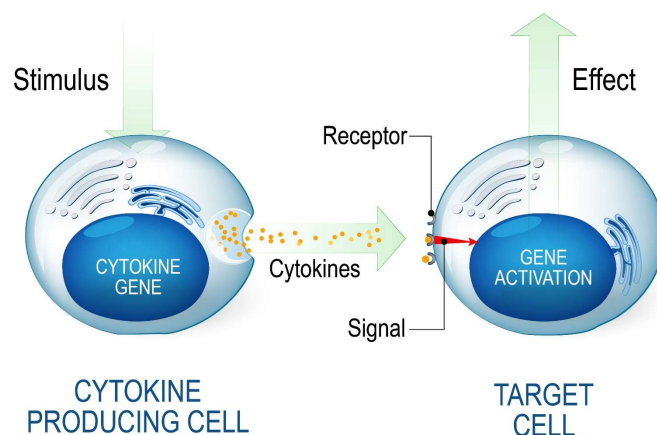
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Cytokines

- Proteins that are important in cell signaling.
- They are released by cells and affect the behavior of other cells.
- Cytokines include interferons, interleukins, lymphokines and other.
- Cytokines are produced by a broad range of cells, including immune cells: macrophages, B lymphocytes, T lymphocytes and mast cells.



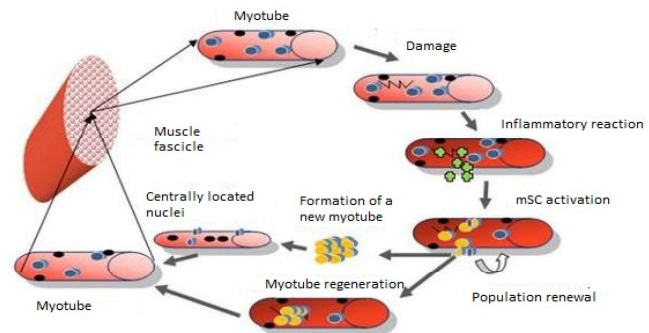
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IL-6 (Inflammation & Myokine)

- Interleukin-6 (IL-6) = **dual role** cytokine
- In disease: often **pro-inflammatory** (infection, autoimmunity)
- In muscle: acts as a **myokine** released during exercise
- Can support:
 - **Local tissue repair & regeneration**
 - **Regulation of acute phase response** (e.g., CRP)

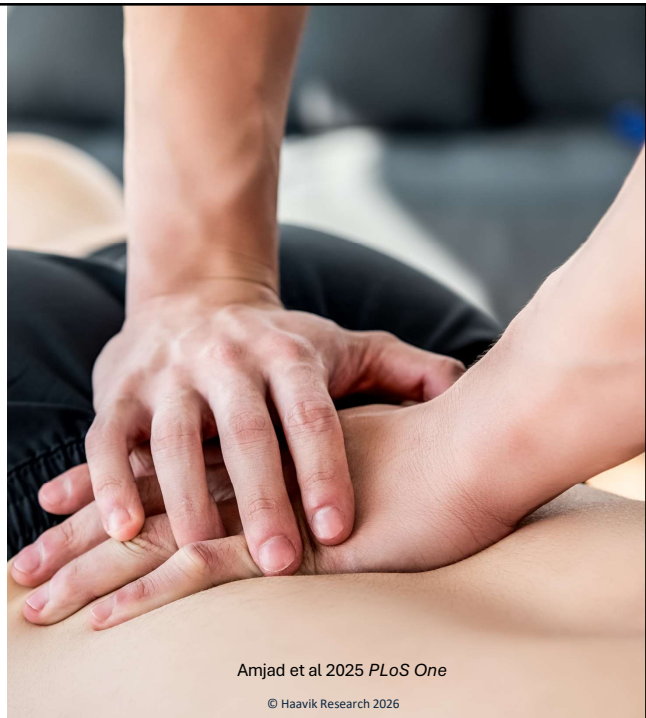


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IL-6 Changes with Chiropractic Care

- **Higher IL-6 in chiropractic group at 12 weeks**
 - $+1.0 \pm 0.3$ (95% CI: 0.5 to 1.5), $p < 0.001$
- Within chiropractic group:
 - IL-6 \uparrow at 12 and still \uparrow at 16 weeks
- No IL-6 change in sham at 12 weeks
- **CRP did NOT increase** in chiropractic group
- TNF- α actually **lower** in chiropractic group (see TNF slides)



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What does this mean for us chiropractors?

- HVLA adjustments may act like **“exercise”** for **deep paraspinal muscles**
- Repeated loading → **IL-6 myokine release** → muscle **repair & adaptation**
- No CRP rise + lower TNF- α → **not a harmful inflammatory spike**
- Supports model: adjusting dysfunctional segments = **mechanotherapy**
- Message: We may be **rehabilitating paraspinal tissues**, not just “putting bones back”



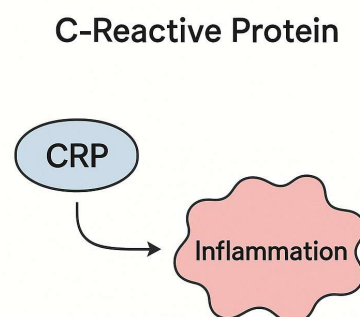
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CRP (Systemic Inflammation Marker)

- C-reactive protein (CRP)
- Produced by the liver in response to IL-6
- Widely used marker of **systemic inflammation**
- High CRP linked to:
 - Cardiometabolic risk
 - Chronic inflammatory states



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CRP Changes with Chiropractic Care

- No significant between-group differences at 12 or 16 weeks
- Within chiropractic:
 - Small increase at 12 weeks (borderline)
 - No sustained change at 16 weeks
- Within sham:
 - Similar small transient changes only
- Overall: **no clear CRP signal** favoring either group

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What does this mean for us chiropractors?

- Reassuring: no evidence of **harmful systemic inflammation** from care
- Supports the idea that IL-6 increase is **local muscle / myokine**, not systemic flare
- Chiropractic care appears **safe at the biomarker level** in this cohort
- Important message for:
 - **Interprofessional discussions**
 - Reassuring **patients** about safety



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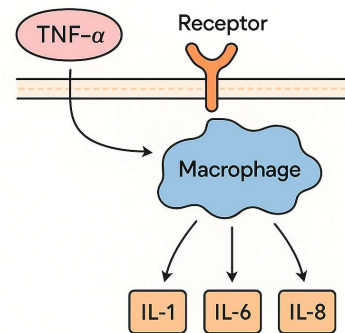
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TNF-alpha (Key Pro-Inflammatory Cytokine)

- Tumor Necrosis Factor-alpha (TNF- α)
- Major **pro-inflammatory cytokine**
- Helps initiate and propagate **acute inflammation**
- Chronically high TNF- α linked to:
 - **Chronic pain**
 - Autoimmunity
 - Tissue damage & degeneration

TNF- α and Inflammation



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TNF- α Changes with Chiropractic Care

- **Lower TNF- α in chiropractic vs sham at:**
 - 12 weeks: -2 ± 1 ; $p = 0.023$
 - 16 weeks: -2 ± 1 ; $p = 0.028$
- Within-group:
 - Sham group: TNF- α **increased significantly** over time
 - Chiropractic group: only modest, non-significant increase
- Overall: sham group became **more inflamed**, chiropractic group results consistent with reduced systemic inflammatory signaling.

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What does this mean for us chiropractors?

- 12 weeks of care → **favorable shift in a key inflammatory driver**
- Supports idea that chiropractic care may help **dampen chronic inflammation**
- Aligns with other work showing reduced TNF- α after manual therapies
- Potential relevance for:
 - **Chronic spinal pain**
 - **Multi-system inflammatory burden**
- *“There is preliminary evidence that regular chiropractic care may help support a more balanced inflammatory profile, including lower TNF-alpha.”*



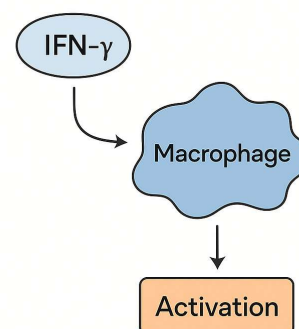
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INF- γ (gamma - Immune Activation & Defence)

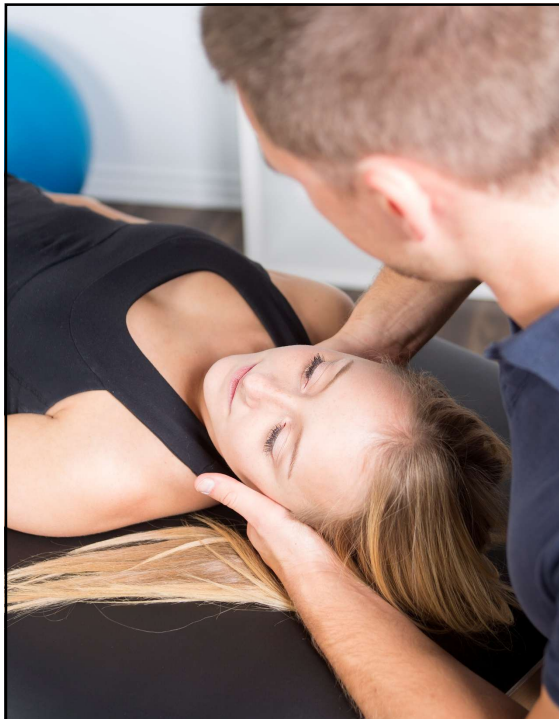
- Interferon-gamma (IFN- γ)
- Produced by T cells, NK cells, macrophages
- Activates cells that **kill infected or damaged cells**
- Important for **host defense**, but chronically high = **immune over-activation**



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IFN- γ Changes with Chiropractic Care

- 12 weeks:
 - No significant between-group difference
 - Chiropractic group: **modest IFN- γ increase**
- 16 weeks:
 - IFN- γ **significantly higher in sham vs chiropractic**
 - -22 ± 7 ; $p = 0.001$ (chiro < sham)
 - Driven by **big increase in sham group** between 12 and 16 weeks
- Chiropractic group did **not** show this late rise

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What does this mean for us chiropractors?

- If we put this together with the TNF-alpha and cortisol findings, a pattern emerges:
- The sham group progressively shows **more signs of immune activation and inflammation** – higher TNF-alpha, higher IFN-gamma, and higher cortisol at 16 weeks.
- The chiropractic group looks more like a system that has been challenged in a controlled way and has then **settled into a more regulated state**.
- That's exactly what we'd hope for if chiropractic care is supporting neuro-immune balance rather than simply being a placebo for pain.
- We're not 'suppressing' the immune system – we may be helping it to stay responsive but not over-reactive."



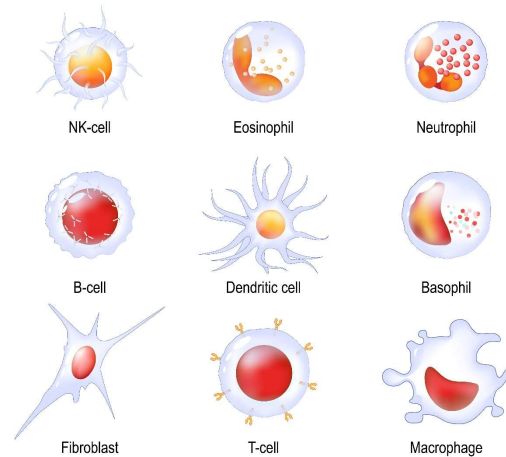
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Immune Cells:

- **CD19** – B-lymphocytes (antibody-producing cells)
- **CD4** – T-helper cells (coordinate immune responses)
- **CD8** – Cytotoxic T cells (kill infected/damaged cells)
- **CD56** – Natural killer (NK) cells (innate defence)

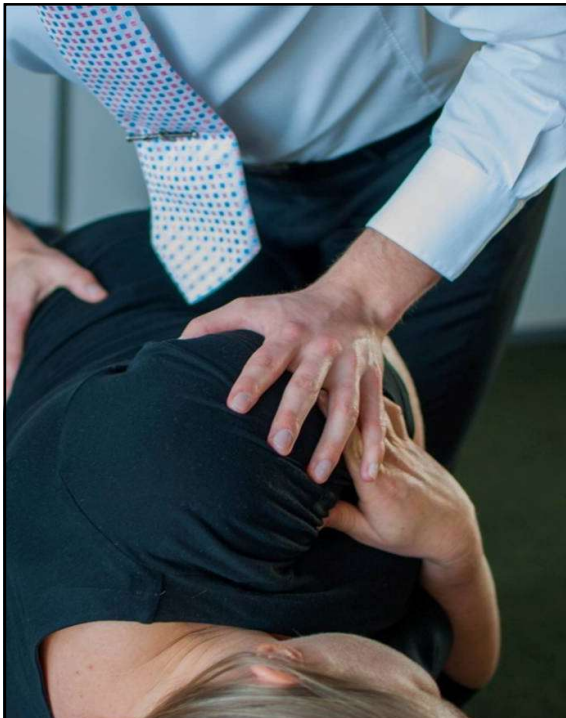


- CD4:CD8 ratio = indicator of **immune system activation/balance**

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Immune Cell Changes with Chiropractic Care

- **No significant between-group differences** (CD19, CD4, CD8, CD56) at 12 or 16 weeks
- **Within chiropractic group at 12 weeks:**
 - CD19 ↑ significantly
 - CD4 ↑ significantly
 - CD8 ↑ trend (non-significant)
 - CD56 ↑ (non-significant)
- Changes not sustained at 16 weeks

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What does this mean for us chiropractors?

- Suggests chiropractic care may **subtly tune immune cell activity**
- Patterns fit with:
 - Increased **immune competence**, not immune suppression
 - Balanced inflammatory picture alongside lower TNF-α & IFN-γ
- Very **early days** – hypothesis-generating, not definitive
- Message: another hint that chiropractic care interacts with the **neuro-immune network**



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Previous Research Also shown that HVLA thrusts alter:



Single thrust session studies mainly:

Neuropeptides

- Neurotensin ↑
- Oxytocin ↑
- Substance P ↑ (short-term)

Cytokines & Inflammatory Markers

- Pro-inflammatory cytokines ↓
- IL-1β ↓
- TNF-α ↓

These molecules influence:

- Inflammation
- Stress responses
- Neuroendocrine regulation
- Pain modulation

Anti-inflammatory cytokines ↑

- IL-2 ↑
- IL-10 ↑ (in some studies)

Endocrine Markers

- Cortisol responses are inconsistent, with some studies showing changes and others not.

Haavik et al. 2021. *Medicina* 2021, 57, 536.

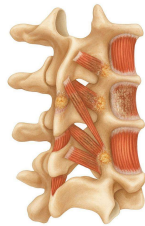
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Mechanisms from 2021 Review

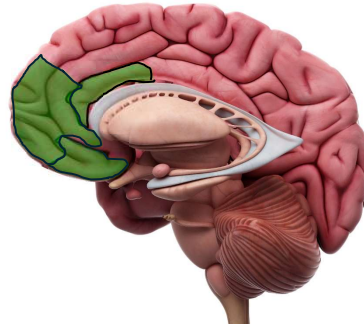
HVLA adjustments



Increase proprioceptive input from deep paraspinal muscles that are stretched rapidly during adjustments



Affect PFC activity



PFC regulates ANS, HPA axis, Immune system, Stress response, Emotions and pain modulation

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Mechanisms from 2025 RCT

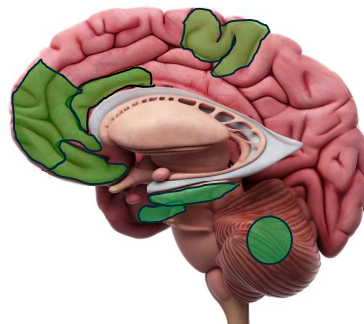
HVLA adjustments



Increase proprioceptive input from deep paraspinal muscles that are stretched rapidly during adjustments



Affect PFC, DMN activity, Cerebellum and SMI



PFC, DMN, Cerebellum and SMI impacts and regulates ANS, HPA axis, Immune system, Stress response, Emotions and pain modulation

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What you **CANNOT** say based on current science

- Cannot claim chiropractic care **treats, cures, or prevents** any inflammatory, immune, or neurological disease
- Cannot claim chiropractic care **directly boosts immunity**
- Cannot claim biomarker changes = **clinical outcomes** yet
- Cannot generalize beyond this **specific population** (subclinical spinal pain)
- Cannot infer long-term effects beyond **16 weeks**
- Cannot claim effects are large — current results show **modest effect sizes**
- Single RCT → requires **replication** before making broad clinical claims

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Take Home Messages from this latest publication

- First-ever **longer-term RCT** showing neuroplasticity + immune biomarker changes with chiropractic care
- **BDNF increased** → suggests enhanced neuroplastic activity
- **IL-6 increased** without CRP rise → consistent with **myokine / muscle repair response**, not harmful inflammation
- **TNF- α lower** in chiropractic group → potentially reduced systemic inflammatory load
- **Cortisol better regulated** over time (lower at 16 weeks)
- Sham group showed **worsening inflammatory/immune profile** (\uparrow TNF- α , \uparrow IFN- γ , \uparrow cortisol)
- No evidence of biomarker **harm** from chiropractic care
- Supports the **contemporary brain–immune–stress model** of chiropractic care

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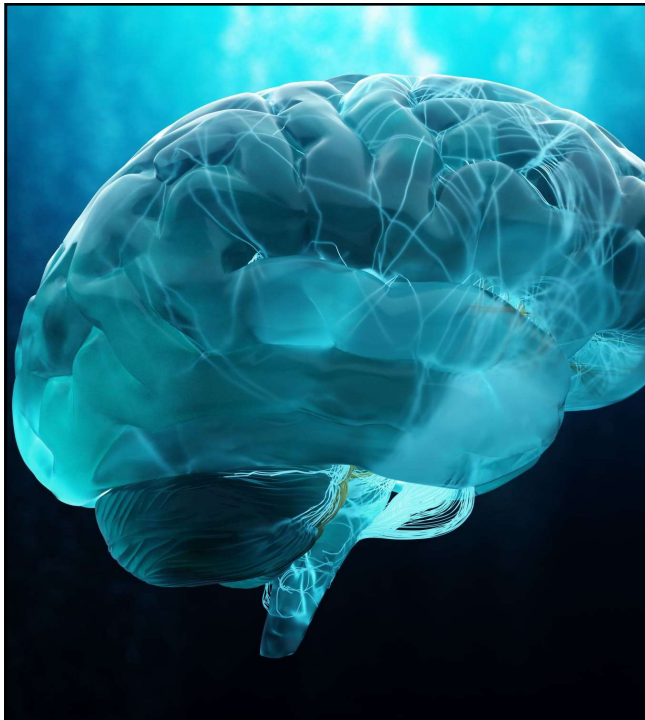
What we CAN claim based on this research



- Chiropractic care **modulated** key biomarkers (BDNF, IL-6, TNF- α , cortisol)
- Patterns suggest **neuroplastic, stress-regulatory, and immune-balancing** effects
- Changes occurred **over 12 weeks**, not just acutely
- Biomarker shifts were generally **favorable** (\uparrow BDNF, \downarrow TNF- α , \downarrow cortisol at follow-up)
- No evidence of **increased systemic inflammation or tissue damage**
- Findings **support**, but do not yet *prove*, broader health benefits
- More research needed \rightarrow larger sample, longer follow-up, integration with outcomes
- Safe, evidence-aligned message:
"Chiropractic care may influence neuroplasticity, stress physiology, and immune function."

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What is yet to come from this RCT

- Patient reported outcome measures (quality of life, stress, emotions)
- Sleep outcomes
- Executive functions outcomes
- Tripple Brain Network changes

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Gene Study Results HOT OFF THE PRESS (*NOT yet published*)

“Transcriptomic analysis identified key driver genes involved in oxidative stress regulation, oxygen transport, and immune modulation. The chiropractic group’s results suggests a more adaptive and regulated physiological state following chiropractic care compared with control group.”

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- Across two independent randomized studies we are observing convergent signals suggesting that chiropractic care may influence systemic neuroimmune regulation and cellular stress-response pathways.
- These effects appear to involve antioxidant regulation, immune modulation, and sensory signaling pathways, consistent with a shift toward a more adaptive physiological state.

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Questions?

