Asia-Pacific Chiropractic Journal

EXPOSITION

# Long COVID: A Risk Factor for Scoliosis Incidence and Exacerbation? [Hypothesis]

Charles S Masarsky and Marion Todres-Masarsky

Abstract: With long COVID beginning to overtake acute COVID-19 infection as a public health concern, we hypothesize that long COVID is a risk factor for scoliosis incidence and exacerbation. We suggest mechanisms for this risk.

Emerging research suggests mitochondrial hijacking is a component of long COVID. This phenomenon can disturb osteoblast function. The resulting loss of structural integrity of the vertebra is expected to worsen scoliosis.

Reduced lung capacity due to both scoliosis and long COVID is expected to be mutually exacerbating. Breathing exercises are frequently part of the regimen of care for scoliosis patients, not only to improve lung capacity, but to help address the scoliosis itself by preserving rib cage flexibility. Reduced lung capacity due to long COVID would be expected to make this aspect of scoliosis care more difficult.

'Brain fog' and fatigue due to long COVID could reasonably be expected to increase the incidence of whiplash, slip-and-fall injuries, sports injuries, work-related accidents, and other forms of accidental trauma. Traumatic scoliosis could create new cases as well as exacerbating pre-existing scoliosis.

Methods of testing the hypothesis by standard epidemiological techniques, controlled clinical observational trials, and case reports are discussed. If the null hypothesis is found to be rejected, and this hypothesis accepted, the importance of intensified screening for both scoliosis and long COVID are discussed. We discuss the possible role of dietary interventions and chiropractic adjustments in the clinical care of scoliosis patients also suffering from long COVID.

Indexing Terms: chiropractic; Long COVID; scoliosis; mitochondria; hypothesis

## Introduction & Background

*Concerns shifting from acute COVID-19*

Liu et al recently suggested that an increase in the prevalence of idiopathic scoliosis can be a consequence of the COVID-19 pandemic. (1) The basis of the Liu et al hypothesis was previous research in which neuro-inflammation triggered idiopathic scoliosis in experimental animals. The relevance of this finding lies in the ability of COVID-19 infection to generate inflammatory responses in many sites, including neurological tissue. Hypothetically, neuro-inflammation caused by COVID-19 infection would provoke idiopathic scoliosis in humans by mechanisms similar to those responsible for the aforementioned results in experimental animals.

> *... It is thought the possible relationship between COVID-19 and scoliosis will emerge during the next decade using standard epidemiological techniques. We propose a hypothesis in this regard and recommend its testing'*

Exacerbation of existing scoliosis may have been an additional consequence of acute COVID-19. During the height of the pandemic, there was an understandable reluctance to keep up with in-person check-ups for fear of infection. (2) This may have led to a greater amount of scoliosis progression than would have occurred had regular care not been interrupted. Also, the reduced lung capacity in significant scoliosis and in COVID-19 infection could have been mutually exacerbating conditions. This would reasonably be expected to disturb rib cage flexibility and mechanics, increasing the risk of scoliosis progression.

Now that concern in many parts of the world is beginning to shift from the acute infections of the pandemic to long COVID, the neuro-inflammation discussed by Liu et al in terms of scoliosis risk continues to be a concern. In this paper we propose a number of mechanisms in addition to neuro-inflammation by which the chronic sequelae of the disease could be generating increased incidence and exacerbation of scoliosis.

## Bone integrity and mitochondrial hijacking

Sun et al reviewed emerging evidence pointing to mitochondrial hijacking as a significant mechanism in both acute and long COVID. (3) This is a complex and incompletely understood phenomenon still under active investigation. Briefly, COVID-19 infection of mitochondria inhibits mitochondrial fission, rendering the cell unable to produce new mitochondria. (4) This leads to accumulation of aged and damaged mitochondria in the cell. The virus also appears to interfere with mitochondrial biosynthesis of coenzyme Q-10 (ubiquinone). (5) These phenomena begin during the acute infection and can continue into long COVID.

While the exact mechanism of mitochondrial hijacking is not fully understood, this major disruption in cellular energy production has many consequences. Sun et al suggested mitochondrial hijacking as a cause of reduced female fertility in long COVID. (3) The constellation of cognitive dysfunctions in long COVID often referred to as 'brain fog' as well as chronic fatigue could also result from mitochondrial hijacking. (6) It is plausible that mitochondrial hijacking is a major factor in the success of the COVID-19 virus as a pathogen, given that robust mitochondrial function is an important factor in anti-viral defense.

In addition to these multi-system consequences of mitochondrial hijacking, Ajaz et al found that mitochondrial hijacking is associated with increased blood plasma levels of fibroblast growth factor 21. (7) Increased plasma levels of fibroblast growth factor 21 is associated with suppression of osteoblast function. This would undoubtedly impair the structural integrity of bone tissue throughout the body. In terms of spinal structure, deformation of vertebral bodies would be expected due to asymmetrical weight bearing affecting those segments in lateral flexion. This would cause the scoliotic curvatures to progress. This would be the case whether the scoliosis is of the most common idiopathic adolescent variety or not. Therefore, children, adolescents, and adults with scoliosis would all be at risk.

The same mechanism could also promote the development of other spinal distortions such as kyphosis. The risk of compression fracture would be expected to increase due to reduced osteoblast function. Healing from fractures of any sort would be impaired.

## Long COVID and trauma risk

In the course of everyday life, a person's alertness, balance, and orientation in space are critically important in preventing trauma from such sources as whiplash, slip-and-fall accidents, sports injuries, and work-related accidents. The brain fog, vestibular dysfunction, and fatigue that frequently plague the long COVID victim would be expected to interfere with these protective neurological functions.

With increased incidence of trauma will come increased incidence of traumatic scoliosis. Some of this incidence will involve individuals with no previous history of scoliosis. Stable scoliosis can be destabilized by superimposed traumatic scoliosis. Traumatic scoliosis will complicate the challenge

of stabilizing patients in the active phase of idiopathic adolescent scoliosis. The severity of any trauma would surely be increased in the presence of decreased bone integrity, as described above.

Disturbance of vestibular function related to long COVID is problematic even without trauma. The normal integration of visual, vestibular, and proprioceptive input is required to achieve postural compensation for adolescent idiopathic scoliosis, according to a recent review of the literature. (8) Disturbance of vestibular function could cause decompensation of previously stable scoliosis.

## Long COVID pulmonary dysfunction and scoliosis

Maintenance of breathing capacity is a major concern in caring for the scoliosis patient. Physical therapy approaches to scoliosis as taught by major schools including those originating from France, Germany, Italy, Spain, Poland, and the United Kingdom all include breathing exercises. (9) These exercises are designed not only to improve breathing capacity, but also to reduce scoliotic curvature and maintain the flexibility and normal mechanics of the spine and rib cage.

Dyspnea, wheezing, and chest tightness are commonly reported indications of long COVID pulmonary dysfunction. (10) This dysfunction could reasonably be expected to make reduction or stabilization of scoliotic curves more difficult, while making progression of scoliosis more probable.

## The hypothesis

That: '*Long COVID is a risk factor for scoliosis incidence and exacerbation*', expressed as the Null Hypothesis for testing as '*there is no association between long COVID and scoliosis incidence'*.

### *Testing the hypothesis*

Liu et al suggest that the possible relationship between COVID-19 and scoliosis will emerge during the next decade using standard epidemiological techniques. (1) Long COVID cases will be emerging for some time yet, so the time frame for standard epidemiological evidence may in fact take longer than one decade.

In the meantime, preliminary tests of the hypothesis may be possible. One approach is a randomized controlled observational trial in which patients with idiopathic scoliosis matched as closely as possible for age, gender, scoliosis severity at the onset of care, and overall health would be divided into two groups. One group would be those with a history of long COVID and the other group would have no such history. The hypothesis predicts a poorer outcome among those with the long COVID history.

Aside from the usual difficulties in setting up such a study, a simple check of history would not capture patients whose acute and possibly long COVID is asymptomatic. Even if a person has not noticed headache, brain fog, dyspnea, dizziness/vertigo or other long COVID symptoms, the sequelae of the asymptomatic acute infection may be sufficient to disturb the body's resistance to scoliotic progression. Also, relatively mild symptoms may be noticed by the patient, but not deemed significant enough to report to health care providers treating scoliosis, which many lay people would consider unrelated to long COVID. These problems with history could result in patients with long COVID inadvertently grouped with those patients without long COVID. This would severely confound the results.

Perhaps a blood marker such as 'fibroblast growth factor 21' could be used as an additional criterion. Elevated plasma levels consistent with mitochondrial hijacking would be a reason to include a subject in the long COVID group. The same general approach could be used if a more appropriate marker of long COVID can be identified.

A different type of test would be to follow school systems that routinely screen for adolescent idiopathic scoliosis. If the percentage of the student population positive for scoliosis is significantly greater for the four years 2021-2025 compared to 2015-2019, that would be consistent with the hypothesis. This is a simple comparison of prevalence as with the statistic for 'excess deaths'.

Certain components of the hypothesis could be tested. For example, if whiplash and other injuries are more prevalent among long COVID patients than the general population, that would be consistent

with the hypothesis. Drilling a bit deeper, if traumatic scoliosis is more prevalent among post-trauma patient with long COVID than without, that would be supportive of our hypothesis.

Case reports, while lacking statistical power, could nevertheless be useful as early tests of the hypothesis. For example, a scoliosis patient completely stabilized for years demonstrating progression of the scoliotic curvatures after developing long COVID would be consistent with the hypothesis.

Especially valuable would be a description of the follow-up: what measures succeed and what measures fail in the effort to re-stabilize such a patient? If the most successful approach or approaches not only addressed the scoliosis as such, but also addressed aspects of long COVID (dyspnea, dizziness/vertigo, etc.) that would also be consistent with the hypothesis.

Again, a history of long COVID is not always easy to capture. This is especially the case in the adolescent age group, where the initial infection is often asymptomatic. In these cases, long COVID might not be recognized as such. In case where previously stabilized scoliosis begins to progress, the attending clinician could test for 'fibroblast growth factor 21' or some other marker of long COVID. The resulting case report could contribute to our knowledge of the interactions between long COVID and scoliosis.

## Clinical significance of this hypothesis

### *Implications for Public Health Screening*

If the hypothesis is supported, screening for scoliosis should be intensified in populations where long COVID is common. Also, screening for COVID-19 antibodies and long COVID should be intensified for patients already diagnosed with scoliosis.

### *Implications for Clinical Intervention*

For reasons discussed above, not every scoliosis patient will know whether or not they are suffering from long COVID. Therefore, measures to address aspects of long COVID should be routine in scoliosis intervention. Fortunately, breathing exercises and vestibular training are already common aspects of scoliosis intervention, and these should be emphasized.

Other measures are not yet common in scoliosis care. Liu et al suggested pharmaceutical interventions to reduce neuro-inflammation. (1) Along these lines, foods and nutritional supplements that contain antioxidants capable of crossing the blood-brain barrier can be part of the scoliosis care regimen. *Curcumin* found in turmeric, *shagaol* found in ginger, *catechin* found in green tea, *rutin* and *Vitamin C* (ascorbic acid) found in cranberries, citrus and many other fruit sources, and *resveratrol* found in red grapes and many berries are all in this category. (11, 12, 13, 14, 15, 16) In some cases, dietary advice and/or supplementation along these lines may render pharmaceutical anti-inflammatories unnecessary.

It is possible that neurological deficits due to mitochondrial hijacking could be partially counteracted by improving the scoliosis patient's level of coenzyme Q-10 (*ubiquinol*). A diet high in coenzyme Q-10, possibly augmented by supplementation could be instituted. Meat, fish (especially salmon and sardines), seeds, nuts, broccoli, and avocados are some of the foods rich in coenzyme Q-10. Other nutrients necessary for the support of cellular respiration such as the B-complex and omega-3 fatty acids could be included in this regimen. Foods such as animal protein, whole grains, and brewer's yeast are rich in the B vitamins. Omega-3 fatty acids are abundant in nuts such as walnuts, olives and olive oil, fatty fish such as salmon and sardines, and avocados, to mention just a few.

Statins have been reported to be helpful in the acute stage of COVID-19. (17, 18) While the short-term benefits may be encouraging, long term statin use, whether for COVID-19 treatment or cardiovascular management, potentially interferes with biosynthesis of coenzyme Q-10 within the mitochondrion. (19, 20) If the hypothesis is supported, clinicians should be cautious about prescribing statins to scoliosis patients. If a scoliosis patient is already taking statins, the prescribing

clinician should weigh the risks and benefits of reducing the dosage of the medication or discontinuing it altogether.

Chiropractic adjustments are not often included in the regimen of the scoliosis patient. Yet, there are published studies in which these patients benefited from chiropractic adjustments. For example, Chung and Salminen reported the results of a series of six upper cervical adjustments over a 25-week period in the care of a ten-year-old female scoliosis patient. (21) A ten-degree reduction in scoliotic curvature was confirmed by a medical radiologist's independent examination.

In another report, a fifteen-year-old female scoliosis patient with a Cobb angle of 44° was adjusted one time to correct biomechanical dysfunction at the first cervical vertebra. (22) Five months after this adjustment, the Cobb angle had reduced to 32°.

The importance of correcting cervical dysfunction in scoliosis patients was confirmed by a physical therapy study in which seventy-one patients with adolescent idiopathic scoliosis underwent manual therapy for the cervical spine. (23) Improvement was noted in 94% of the patients, with an average correction of 8°. This investigator suggests that adolescent idiopathic scoliosis can be in part a compensation to keep the ears (and therefore the inner ear vestibular apparatus) level in the face of cervical dysfunction. Correcting the cervical dysfunction renders the scoliosis unnecessary, thereby allowing it to spontaneously reduce.

We note that measurement of the Cobb angle can be done via magnetic resonance imaging with the patient upright, where that is available. This may be an attractive alternative to multiple x-ray exposures, especially in adolescents.

The vestibular disturbance that occurs in many patients with long COVID would exacerbate the vestibular disturbance caused by any cervical dysfunction. Correcting this dysfunction, while important for scoliosis patients in general, would be especially relevant to those with long COVID, if our hypothesis is supported.

Chiropractic adjustments have been reported to improve forced vital capacity and forced expiratory volume in one second. (24, 25, 26, 27, 28, 29) Therefore, these adjustments could augment breathing exercises already part of many scoliosis care regimens. The importance of this would certainly increase in the face of pulmonary dysfunction commonly encountered in the long COVID patient.

Chiropractic clinical literature on the care of long COVID patients is in its earliest stages. A 59-year-old female long COVID patient presented with complaints of headache, and 'brain fog', including deficits in memory and attention (30). She was unable to read without provoking a headache. After three chiropractic adjustments over an eighteen-day period, substantial improvement was noted. Improvement in memory and attention span was demonstrated by increase in reverse digit span with less distress at follow-up compared to presentation. Old recipes, which she had difficulty remembering and following prior to care became easier to work with post-intervention.

At follow-up, the patient reported the ability to read an entire book over a two-day period with no ill effects. While this patient did not have a history of scoliosis, the potential of the chiropractic adjustment to improve a patient's ability to cope with long COVID is relevant to the scoliosis patient if our hypothesis is supported.

Marion Todres-Masarsky
BA, MA, DC
Private Practice of Chiropractic, Vienna, VA

Charles S. Masarsky
B.S. Biology, DC
Private Practice of Chiropractic, Vienna, VA
e: viennachiropractic@verizon.net

*Cite:* Masarsky CS, Todres-Masarsky M. Long COVID: A Risk Factor for Scoliosis Incidence and Exacerbation? [Hypothesis] URL Asia-Pac Chiropr J. 2023;3.3. URL apcj.net/Papers-Issue-3-3/#MasarskyLongCovidScoliosis

*Conflict of interest*

The authors declare no conflict of interest regarding this paper.

## References

1. Liu Z, Jaing W, Hai Y, et al. Will the COVID-19 Pandemic Increase the Prevalence of Idiopathic Scoliosis? Med Hypotheses, 2021; 147: 110477.
2. Moreno CAM, Camelo CG, Sampaio PHMDA, et al. Effect of the COVID-19 pandemic on patients with inherited neuromuscular disorders. Arq. Neuro-Psiquiatr. 80 (6) • June 2022. URL https://doi.org/10.1590/0004-282X-ANP-2021-0166.
3. Sun J, Liu Q, Zhang X, et l. Mitochondrial hijacking: A potential mechanism for SARS-CoV-2 to impair female fertility. Medical Hypotheses, 2022 (March); 160: 110778. URL https://www.sciencedirect.com//science/article/pii/S0306987722000184?via%3Dihub.
4. Holder K, Reddy PH. The COVID-19 Effect on the Immune System and Mitochondrial Dynamics in Diabetes, Obesity, and Dementia. Neurosci Rev J Bring Neurobiol Neurol Psychiatry, 2021; 27(4): 331-339. URL 10.1177/1073858420960443.
5. Gvozdjakova A, Klauco F, Kurcharska J, et al. Is mitochondrial bioenergetics and coenzyme Q10 the target of a virus causing COVID-19? Bratisl Lek Listy, 2020; 121(11): 775-778. At 10.4149/bll_2020_126.
6. Stefano GB, Buttiker P, Weissenberger S, et al. Editorial: The Pathogenesis of Long-Term Neuropsychiatric COVID-19 and the Role of Microglia, Mitochondria, and Persistent Neuroinflammation: A Hypothesis. Med Sci Monit, 2021 (May 10); 27: e933015. URL https://www.medscimonit.com//abstract/full/idArt/933015.
7. Ajaz S, McPhail MJ, Singh KK, et al. Mitochondrial metabolic manipulation by SARS-CoV-2 in peripheral blood mononuclear cells of patients with COVID-19. Am J Physiol-Cell Physiol, 2021; 320(1): C57-C65. URL https://journals.physiology.org/doi/full/10.1152/ajpcell.00426.2020.
8. Cristancho DCG, Trujillo GJ, Manrique IF, et al. Neurological Mechanisms Involved in Idiopathic Scoliosis. Systematic Review of the Literature. Neurocirugia (Astur: Engl Ed), 2022; Mar 4: S2529-8496(22)00018-1. URL https://pubmed.ncbi.nlm.nih.gov/35256329/#affiliation-1.
9. Berdishevsky H, Lebel VA, Bettany-Saltikov J, et al. Physiotherapy Scoliosis-Specific Exercises – A Comprehensive Review of Seven Major Schools. Scoliosis Spinal Disord, 2016; 4(11): 20. URL https://scoliosisjournal.biomedcentral.com/articles/10.1186/s13013-016-0076-9
10. Aiyegbusi OL, Hughes SE, Turner G, et al. Symptoms, Complications and Management of Long COVID: A Review. J R Soc Med, 2021; 114(9): 428-442. At 10.1177/01410768211032850
11. Wang O, Sun AY, Simonyi A, et al. Neuroprotective mechanisms of curcumin against cerebral ischemia-induced neuronal apoptosis and behavioral deficits. J Neurosci Res, 2005; 82(1): 138-148. URL http://www.ncbi.nlm.nih.gov/pubmed/16075466
12. Moon M, Kim HG, Choi JG, et al. 6-Shogaol, An Active Constituent of Ginger, Attenuates Neuroinflammation And Cognitive Deficits in Animal Models of Dementia. Biochem Biophys Res Commun, 2014; 449: 8-13. URL http://www.ncbi.nlm.nih.gov/pubmed/24796668.
13. Huang Q, Wu LJ, Tashiro S, et al. Catechin, an ingredient of green tea, protects murine microglia from oxidative stress-induced DNA damage and cell cycle arrest. J Pharmacol Sci, 98(1): epub 2005 May. URL http://www.ncbi.nlm.nih.gov/pubmed/15879681.
14. Koda T, Kuroda Y, Imai H. Rutin supplementation in the diet has protective effects against toxicant induced hippocampal injury by suppression of microglial activation and pro-inflammatory cytokines. Cell Mol Neurobiol, 2009 e-pub Jan 21. URL http://www.ncbi.nlm.nih.gov/pubmed/19156514.
15. Shah SA, Yoon GH, Kim HO, et al. Vitamin C Neuroprotection Against Dose-Dependent Glutamate-Induced Neurodegeneration in the Postnatal Brain. Neurochem Res, 2015; 40: 875-884. URL http://www.ncbi.nlm.nih.gov/pubmed/25701025.
16. Candelario-Jalil E, de Oliveira ACP, Gräf S, et al. Resveratrol potently reduces prostaglandin E2 production and free radical formation in lipopolysaccharide-activated primary rat microglia. J Neuroinflammaton, 2007;4:25. URL http://www.jneuroinflammation.com/content/4/1/25.
17. Kouhpeikar H, Tabasi HK, Khazir Z, et al. Statin Use in COVID-19 Hospitalized Patients and Outcomes: A Retrospective Study. Front Cardiovasc Med, 2022 Feb 24;9:820260. URL https://www.frontiersin.org/articles/10.3389/fcvm.2022.820260/full.

18. Soldevila L, Valerio-Sallent L, Roure S, et al. Drug exposure may have a substantial influence on COVID-19 prognosis among residents of long-term care facilities: an exploratory analysis. Int J Infect Dis, 2021 Aug;109:192-194. URL https://www.ijidonline.com/article/S1201-9712(21)00562-2/fulltext.

19. Passi S, Stancato A, Aleo E, Dmitrieva A, Littarru GP. Statins lower plasma and lymphocyte ubiquinol/ubiquinone without affecting other antioxidants and PUFA. Biofactors 2003;18(1-4):113-24. URL https://pubmed.ncbi.nlm.nih.gov/14695926/.

20. Gutierrez-Mariscal F, De La Cruz-Ares S, Torres-Pena J, Alcala-Diaz J, Yubero-Serrano E, Lopez-Miranda J. Coenzyme Q-10 and Cardiovascular Diseases. Antioxidants, 2021; 10(6): 906. URL https://www.mdpi.com//2076-3921/10/6/906/htm.

21. Chung J, Salminen B. Reduction in scoliosis in a 10 year-old female undergoing upper cervical chiropractic care: a case report [case report] J Pediatr Matern & Fam Health – Chiropr, 2011; 1: 23-30. URL https://www.chiroindex.org/?search_page=articles&action=&articleId=22749&search1=scoliosis&search2=upper%20cervical.

22. Khauv KB, Dickholtz M. Improvement in Adolescent Idiopathic Scoliosis in a Patient Undergoing Upper Cervical Chiropractic Care: A Case Report. J Pediatr Matern & Fam Health-Chiropr, 2010; 4: 136-142. URL https://www.chiroindex.org/?search_page=articles&action=&articleId=21590&search1=scoliosis.

23. Polak J. Adolescent Idiopathic Scoliosis: A 71 Cases Study Ascertaining that Straightening is Possible, and a New Etiological Hypothesis. Asian Spine J, 2013; 7(4): 282-288. URL https://doi.org/10.4184/asj.2013.7.4.282.

24. Engel R, Gonski P, Vemulpad S,et al The medium-term effect of spinal manipulative therapy for chronic obstructive pulmonary disease: a randomized controlled trial. In: Lawrence DJ. ACC Research Agenda Conference 2018: Peer Reviewer Acknowledgments and Abstracts of Proceedings. J Chiropr Educ, 2018; 32(1): 50–81. URL https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5834302/.

25. Kessinger R. Changes In Pulmonary Function Associated with Upper Cervical Specific Chiropractic Care. J Vertebral Subluxation Res, 1997; 1(3):43-49. URL https://vertebralsubluxationresearch.com/2017/09/10/changes-in-pulmonary-function-associated-with-upper-cervical-specific-chiropractic-care/.

26. Masarsky CS, Weber M. Chiropractic and Lung Volumes – A Retrospective Study. ACA J Chiropr, 1986; 20(9): 65.

27. Masarsky CS, Weber M. Chiropractic Management of Chronic Obstructive Pulmonary Disease. J Manipulative Physiol Ther, 1988: 11: 505-510. URL https://www.ncbi.nlm.nih.gov/pubmed/3253396.

28. Masarsky CS, Weber M. Screening Spirometry in the Chiropractic Examination. ACA J Chiropractic, 1989 (FEB); 23:67-68.

29. Masarsky CS, Weber M. Somatic Dyspnea and the Orthopedics of Respiration. Chiropractic Technique, 1991; 3:26-29.

30. Masarsky CS, Todres-Masarsky M. Long Haul COVID-19 and Subluxation: A case report.Asia-Pac Chiropr J. 2022;2.6. URL https://apcj.rocketsparkau.com/site_files/4725/upload_files/MasarskyLongCOVIDCR.pdf?dl=1.