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The nature of the Subluxation and the simple elegant complexity of The Adjustment: Not your Grandfather's waterhose

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Abstract: *Purpose:* To provide a scientific report using peer-reviewed scientific papers that will demonstrate the implications of brain function and plasticity and its correlation to Subluxation and hence the implications of brain function enhancement through chiropractic adjustments.

Methods: Analysis was undertaken of the literature reporting on brain plasticity related to brain function and its dependance on chemical changes within the brain. These were found to be highly related to a wide array of clinical outcomes. The literature demonstrates that now we can identify the chemical changes within the brain that are highly related to the same peripheral changes and central nervous system changes that we see with subluxation. Hence, the literature goes on to indicate that correction of these peripheral changes and central nervous system changes will in fact create changes in the biochemical function in the brain affecting brain plasticity for the better. It is inferred that the correction of brain plasticity will have outcomes affecting the entire body including brain function itself improving conditions such as anxiety, depression, addiction, personality conflicts, and learning disabilities. There is a question as well in most literature where it is suggested that changes in the brain chemistry and plasticity could very well aid in other problems such as MS, Alzheimer's, Parkinson's, etc.

Conclusions: It is reported here that there is a strong apparent connection between brain plasticity neurochemistry and Subluxation. We put forward that the chiropractic adjustment making changes in this neurochemistry will represent a profound change in brain plasticity, function, and learning. Further studies concerning this topic are needed to further corroborate our observations.

Indexing Terms: chiropractic; spinal adjustment; epigenetics; neuroplasticity; Dysponesis; zygapophysial joint.

Introduction

Discussed here is another layer of complexity to that phenomena that is subluxation. A large volume of recent studies indicates a plethora of changes in the body that occur due to subluxation; mechanically, neurologically, physiologically, and chemically.

Our focus here will be on the newer concept, brain functions and plasticity occurring with the cascade of all cerebral input, bioelectrical and chemical, during subluxation. There will be specific attention given to factors concerning interference distress, known as subluxation and the changes made through the

> *… The subluxation is not a phenomenon that affects only the local area, it is not solely a mechanical disruptor, as biochemical changes are intimately involved and direct brain impact is now obvious. It has been made clear that subluxation produces far reaching effects to the brain and even the DNA of each cell and how the adjustment corrects that'*

Chiropractic adjustment, eustress. We believe, and hope that this addition to the subluxation model will be universally accepted upon reading this paper, and that long gone is the explanation of the water hose theory in explaining the full function of Chiropractic. We know now that the complex and multifaceted biochemical changes that occur in subluxation are very similar to what we are seeing in concussion or traumatic brain injury, at least on a neurochemical level. When we speak of subluxation, perhaps we are discussing small concussive like injury incidents. The information offered here begs one to rethink the entire notion and the definition of the vertebral subluxation complex (VSC) as a purely an efferent phenomena.

Narrative

There is information concerning brain plasticity, memory optimisation, interruptions to, and malformations of, brain plasticity. Brain chemistry/ function and how that is impacted by proper nerve flow must be taken into consideration, looking as well at how brain chemistry is hindered and changed negatively by memory imprints created by maladaptive, erroneous nerve signalling

Understanding brain plasticity/memory/learning and how it is intimately related to the survival reaction is crucial. In the hierarchy of survival mechanisms, the maintenance of homeostasis within the body is primary. Hence, there is a highly coordinated multiplicity of control mechanisms of overlapping circuits of the limbic forebrain, hypothalamus, and brainstem. We must remember as well that the brain will respond to both physical and nonphysical stimulation. Nonphysical or psychogenic stimulation is based on prior experience (learning), personal thoughts, and innate programmed functions. (1)

Information input then into the brain must be of the highest quality, pro-survival nature. It has been known for some time that repetition of neural firing of brain cells form connections, synapses, and strengthens these connections through repetition making them permanent brain change. (2) Many studies demonstrate as well how aberrant neural firings over time will create maladaptation, improper brain wiring and hence maladaptive improper function. Furthermore, a multitude of studies have demonstrated how these maladaptations in brain plasticity can result in a broad array of neural connections in the brain, which may lead to many pathologic malfunctions. These cause the brain to manifest social conditions as anxiety depression, addictive behaviour; as well as visceral and motor dysfunction. (3, 4, 5, 6, 7) There has even been more profound and surprising changes demonstrated on the genetic level through neuroepigenetics. (8) Neuroepigenetics is the mechanism for modification of genetic code creating a new memory, through plasticity, changing the expression of the genetic code. This new concept opens doors to an entirely new avenue of thought concerning learning, plasticity/memory that encompassing the cellular/ DNA level as well.

Our goal is to delve into the causes of these brain /DNA changes and see how they are intimately related to subluxation and hence how specific chiropractic adjustments can help reform, through brain/DNA plasticity, brain function and cellular function and aid in the correction of maladaptive functions both behavioural and physiological.

Neuroplasticity

First, let us define brain plasticity as it has been understood. Neuroplasticity, also known as neural plasticity or brain plasticity, is a process that involves adaptive structural and functional changes to the brain. It is defined as '*the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganising its structure, functions, or connections*'. (9, 10) Brain plasticity is the ability of the neurons in the brain to connect, disconnect, and reconnect to other neurons in the brain creating synapse patterns for function. (11) This ability for the human brain to remodel itself is in part due to humans being born with an incompletely developed brain, as compared to other animals.

Not being totally preprogrammed at birth, with a full array of instinctual functions, has gifted the humans with a long 'educational' brain imprint window allowing humans to adjust to their environment and react to changes. 'I*t is what, perhaps, has allowed human beings to excel as a species*

while not being neither the strongest, biggest, nor quickest animal. Yet this brain malleability has allowed humans to create music, art, and science'. (12) As our brains receive input from our surroundings, we have observed on functional fMRI and PET scans, neuronal dendrites reaching out creating synapses connections to other neurons. It is observed that repetition of activity and repetition of thoughts will both reinforce these connections and create long-term synaptic pairing. (13) We have also found that surprisingly, this change in neuron connection can occur within minutes and can endure for years; or can change and dissipate in moments. This will depend upon the neuron activity among other variables.

Neurogenesis

It was historically believed, as per Hebbs, that brain plasticity was wholly the product of the brain's ability to make new different connections, synapses between existing neurons in the brain. (14) It was also believed that those existing neurons were created at birth and those are a set number of neurons in the brain.

We now know through multiple studies (15, 16, 17, 18, 19) that neurogenesis persists in the human throughout the aging process. Neurogenesis was found in the dentate gyrus of the hippocampal formation. (20) This finding has been considered to be one of the most controversial in the field of neurology.

Evidence is mounting and illustrating that neurons do in fact develop later in life and are necessary for learning and memory. As well it has been demonstrated that '*aberration in the production leads to memory impairments*'. (21) This was noted in studies corroborated by Boldrini (22) in 2018, previously cited by Levinson (23) in 2005. This was also found by Gould (24) in 1999. Boldrini and his group found that although in aging rodents and other primates the number of brain cells was fixed, it appears that numbers of intermediate neural progenitors and thousands of immature neurons were found in the hippocampal area of humans. Their conclusion was that '*Healthy older subjects without cognitive impairment, neuropsychiatric disease, or treatment for this, display preserved neurogenesis and ongoing hippocampal neurogenesis sustaining human specific cognitive function throughout life*'. This means that brain plasticity not only includes the connection and reconnection synaptically but also includes the creation of new neurons through stimulation to the hippocampal area. These new neurons migrate then to the cortex.

Epigenetic mechanisms

Levinson and his team (25) introduced the concept of epigenetic mechanisms in memory formation, i.e. *neural plasticity*. His group arrived at the opinion that epigenetic mechanisms probably have a role in synaptic plasticity and memory formation. Gould earlier on in 1999 (26) and his group demonstrated that learning enhances adult neurogenesis specifically in the hippocampal formation. His group found thousands of hippocampal neurons are 'born' (his term) in adulthood suggesting that new cells could be important to hippocampal function. They found that adult-generated hippocampal neurons are especially involved in associative memory formation.

Leuner (27) found that plasticity and learning enhances survival of these new neurons beyond the time that they might be required for trace memories only. We believe that this all demonstrates that learning, specifically survival learning, is going to involve the hippocampus and that the hypothalamus plays a huge role in brain plasticity through neurogenesis as we have described. Being an integral part of the limbic system, the hippocampus plays a vital role in regulating learning, memory encoding, memory consolidation, and spatial navigation. (28) In 2019 Maller (29) demonstrated the hippocampus as a key component of emotional and memory circuits and learning broadly connected throughout the brain. The strongest connection was through the ipsilateral thalamus. Those findings extended the collective knowledge of hippocampal anatomy highlighting the importance of the spinal limbic pathway.

Geisler and Dado (30) found direct spinal pathways to limbic system for nociceptive information. They reported that the hypothalamus is believed to play important roles in several aspects of nociception. Previously, nociceptive information was thought to reach hypothalamic neurons through

indirect, multisynaptic pathways. However, it was found and documented that thousands of neurons throughout the length of the spinal cord send axons directly into the hypothalamus. Many of these axons carry nociceptive information. The axons often follow a complex course, ascending through the contralateral spinal cord, brainstem, thalamus, and hypothalamus. They then cross the midline and enter the ipsilateral hypothalamus, turn posteriorly, and continue into the ipsilateral thalamus. (31) These axons provide nociceptive information to a variety of nuclei in the thalamus and hypothalamus bilaterally.

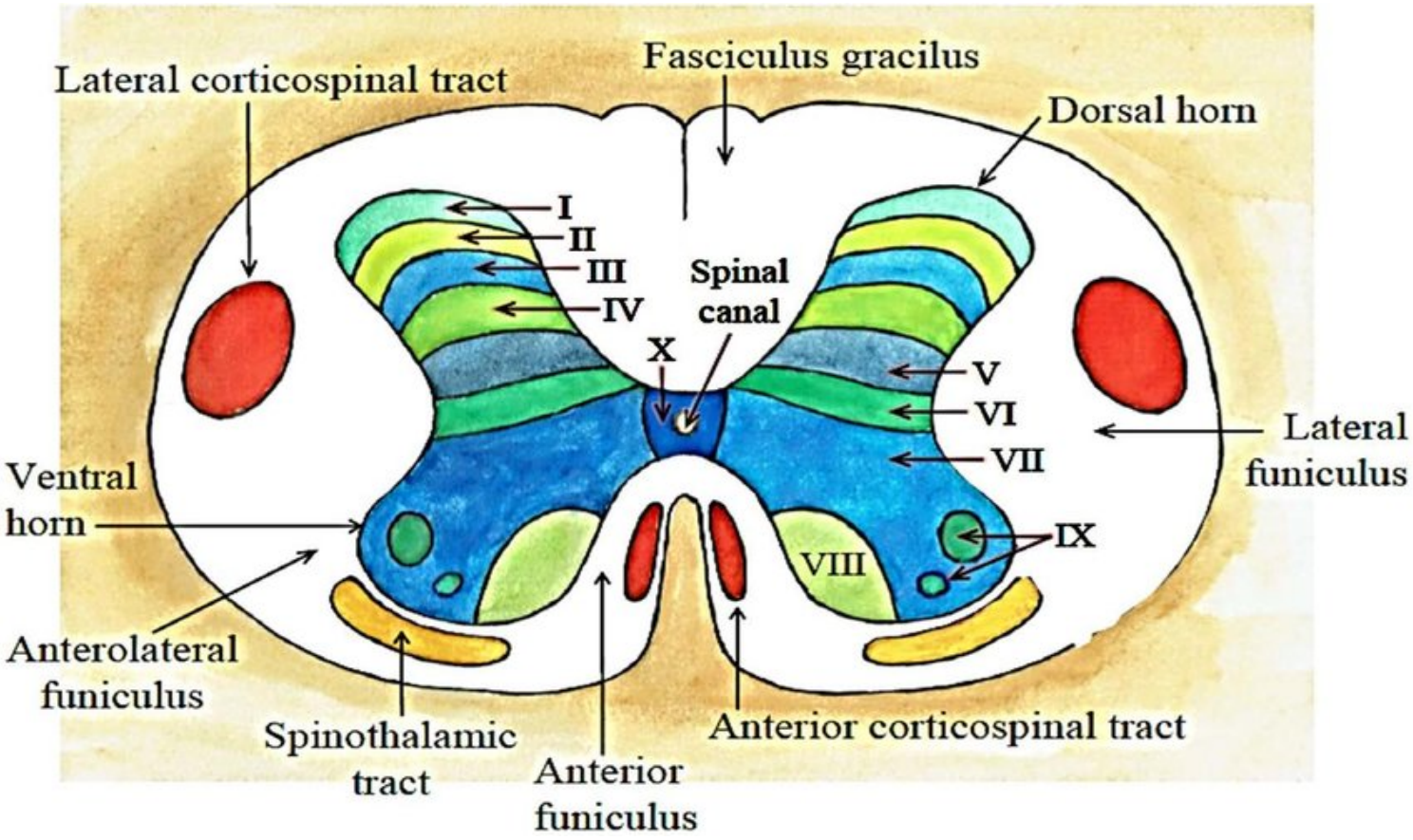
Recent anatomical studies have shown that a large number of neurons in the upper cervical spinal cord and caudal medulla project directly to the hypothalamus. (32, 33) Findings indicate that non nociceptive signals reach the hypothalamus primarily through the direct *Trigeminohypothalamic Tract* (THT) route, whereas nociceptive signals reach the hypothalamus through both the direct Trigeminohypothalamic Tract (THT) and the indirect *Reticulohypothalamic Tract* (RHT) routes. This suggests that highly prioritised painful signals are transferred in parallel channels to ensure that this critical information reaches the hypothalamus, a brain area that regulates homeostasis and other humoral responses required for the survival of the organism. Hence illustrating the importance for memory and changes in brain plasticity to allow for the imprinting of these memories. (34) Further noted were large numbers of collaterals from the *Spinohypothalamic Tract* (SHT) axons appears to project to a variety of targets in C1. (35)

> We are clearly wired to imprint important information to the brain for crucial plasticity. It becomes obvious to the observer that maladaptive imprinting through subluxation will affect survival-oriented function similarly.

Brainstem/hypothalamus mechanisms are multifaceted as are their connections. There is a direct sympathetic response that will involve reflex arcs communicating with the medulla (specifically rostral ventral), there are preganglionic sympathetic neurons in the interim mediolateral cell column of the spinal cord, this specifically observed between T7 and L1 that directly affect brain plasticity. There is also coordinated response from the parasympathetic branch that always occurs following stress altering stimulus; either direct systemic stressors or psychogenic stressors that are developed through learning plasticity. (36) The parasympathetic response is ultimately mediated by the nucleus ambiguous and dorsal motor nucleus of the vagal nerve (solitary tract NTS). Medullary and spinal systems impact higher-order autonomic integrated sites in the hindbrain (Raphe Pallidus, lateral parabrachial nucleus and Kolliker-Fuse nucleus). We see brain plasticity specifically affected through activation of the HPA axis through stimulation from C1 through C3 regions. (37)

More specifically, the Lateral spinothalamic tract carries pain and temperature information. The anterior spinothalamic tract carries crude touch and pressure information. Dorsal and ventral spinal cord and cerebellar area transmit and reception sensory information. The Lamina distribution of neurons in the cord germane to this topic is the lamina IV which extends dendrites to laminas II and III, whose axons enter to the spinothalamic tract. These areas specifically indicate direct communication between spinal cord and hypothalamus. (38)

Stackman and group (39) found hippocampal neurogenesis to be affected by vestibular input. They demonstrated that vestibular sensory information played an important role in brain/hippocampal activity and plasticity. Their work implied then that all sensory input employs the same mechanism.



As Chiropractors we immediately expect upper cervical and cervical sympathetic chain to influence this hippocampal brain activity. Surprisingly though, Kalkhoran and his group (40) found that even mild injury causing temporary impairment of the lower limbs cause a reduced neurogenesis in the properties in the hippocampus which is well associated with cognitive function deficit. Further this group found that on resolution of the mild lumbar nerve impairment the hippocampal function and neurogenesis were returned, and cognitive function returned as well.

This demonstrates a profound function of both subluxation and the adjustment

Kalkhoran's findings Corroborate Katter and Dado (41) who reported sacral spinal segments from L6 to S2 were involved in spinothalamic tract spinal limbic reactions. They found that systematic antidromic mapping techniques, mapping the axonal projections of 41 of these neurons within the diencephalon that, thirty-three neurons (80%) could be activated antidromically only from points in the contralateral thalamus. This while (20%) was activated antidromically from points in both the contralateral thalamus and hypothalamus.

Concerning the antidromic/orthodromic phenomenon and their effects to the CNS, it is important to explain the following. Dorsal root ganglion stimulation can follow the previously expect path from the periphery back to the CNS.(orthodromic); or now it seems can flow along an afferent nerve towards the periphery (antidromic). (42, 43) This antidromic flow can occur in motor nerve pathways as well (ventral root ganglion. (44) This antidromic phenomena is observed especially when the nerve is exposed to ACh. (45) Hubbard cites Diamond (46) and Katz (47) stating that ' *the release of potassium from damaged perineural tissues would follow with a ACh flow to endplate receptors and depolarise nerve terminals*'. Why might this be necessary, pro-survival?

It is suggested that message feedback is guaranteed by back-propagation mechanisms of action potentials (AP) endowed in the same feedforward circuits. (48) A significant fraction of APs is not coming from the canonical synapse-dendrite-soma signal flow, but instead from signals originating at the distal axon. Importantly, antidromic APs may carry information and can have a functional impact on the neuron, as they consistently depolarise the soma. Thus, plasticity or gene transduction mechanisms triggered by soma depolarisation can also be affected by these antidromic APs. Conduction velocity is asymmetrical, with antidromic conduction being slower than orthodromic. '*Altogether these findings have important implications for the study of neuronal function in vitro, reshaping our understanding of how information flows*'. (49, 50) This flow change is noted in the brain as well as in the spinal cord and peripherally. (51, 52) Affecting the nervous system at any point can still provide stimulation to the brain.

> It has been explained that another form of brain plasticity imprinting would be through long-term potentiation (LTP) or one could substitute the term, '*chronic subluxation*'

LTP increases synaptic efficiency creating a deeper memory link and memory storage. Shors' group (53) found that these LTP's, play a crucial role in the establishment of stable memories, a role consistent somewhat with 'Hebbian' descriptions of synaptic memory formation (Brain cells that fire together, wire together).

Other characteristics of LTP include rapid induction, persistence, and correlation with natural brain rhythms. This may be part of the cerebral loop of chronic pain, as seen with chronic subluxation. This might open the door to considering how many types of chronic pain, chronic subluxation patterns, might be products of a Complex Regional Pain Syndrome (CRPS) phenomenon.

Information found in these studies led Trettenbrein (54) to postulate that synaptic memory was much too simple a model. He argued that '*there is considerable literature on the neurobiology of learning and memory that shows the importance of synaptic plasticity as only a step in the chain of cellular and biochemical events involved in memory formation*', and that '*once memories are formed, then synaptic modification is essential for their expression*'. Studying those biochemical events Bakin and Weinberger (55) found that the physiological memory in the cerebral cortex was as well related to activation of *nucleus Basalis of Mynert* (nbM) and acetylcholine presence, this was corroborated by Maskos et al. (56)

The nbM contains a large population of cholinergic neurons that project their axons from the Basal Forebrain to the entire cortical mantle, the olfactory tubercle, and the amygdala. It has been functionally associated with the control of attention and maintenance of arousal, both key functions for appropriate learning and memory formation. (57) Furthermore, the nbM has been implicated in sharpening the acuity of sensory processing. These properties make the nbM key modulating pain perception and its plasticity. The nbM will not only respond to nociceptive stimuli but will undergo dynamic changes when transitioning to a chronic pain-like state. This makes a strong case concerning the relationship between nociceptive stimuli and brain change, i.e. plasticity; Indicating as well that the alleviation of the nociceptive stimuli, the adjustment, has a definitely positive effect on brain plasticity as well. (58, 59, 60, 61)

Concerning learning/brain plasticity, we are beginning to understand what goes on in 'learning' for the organism and how profound these changes must be. New information just begins to give us insight into how all-encompassing learning actually is. It's now put forward that the old model,

where learning will make changes only to synaptic organisation in brain (Hebbs), is not necessarily accurate. There has been found evidence of plasticity/learning on the genetic level.

Epigenetic changes to the genetic code through learned patterns demonstrate plasticity at the chromosomal level. (62) This was seen in the Dutch Hunger Winter study (63) where environmental changes to the pregnant mother, through starvation, created changes that were seen in the offspring for 4 generations after indicating genetic change. Those bodies learned through genetic modification to respond in conservation of fats, triglycerides, cholesterol management, and sugar metabolism differently than their peers. Common genetic markers found on their DNA group. Another study demonstrated as well, that when the father was affected, *Health Shocks of the Father and Longevity of the Children's Children*, (64) there was a learned association by preconception paternal health on perinatal outcomes.

This was seen again in Analysis of U.S. claims data. (65) These studies demonstrated that by reacting to environmental changes the organism 'learns' through neural modelling, i.e. *plasticity*, to change the way in which genetic code is expressed. In these cases, with the father, the change was passed only to the male offspring. This indicates chromosomal modification, i.e. plasticity particularly at the 'Y' chromosome.

Neural epigenetic learning

So, we must shift our focus on plasticity/memory not only as a brain-based phenomenon, but to see memory/learning/plasticity also reflected in the DNA and how it is expressed through neuroepigenetic changes. There appears to be two main mechanisms involved in neural epigenetic learning, they would be DNA methylation and histone modification. (66, 67, 68, 69, 70) It was reported in multiple studies that neuronal activity could induce changes in DNA methylation. And furthermore, it was cited that heavy signalling cascades falling on the receiving neuron, as seen in subluxation, can ultimately produce alterations in the epigenetic status of some genes. (71)

We know that changes in gene methylation will provide a potential mechanism for temporary recruitment or suppression of certain genes in memory formation. Histone modification, which can occur through methylation phosphorylation of histone. We have seen that one effect of DNA methylation is to recruit proteins that mediate histone modification. Histone acetylation, as through the coupling with acetylcholine, will as well cause epigenetic changes. (72) There is as well reports that Chiropractic and correcting the subluxation can impact DNA method methylation and therefore, acetyl choline presence. (73)

Dysponesis

We must understand the roles that the noxious and positive stimuli play in plasticity throughout the entire organism. The brain changes, expression of genetic code change, and changes at the cellular level all have a role concerning memory. All react to chiropractic care. (74) Even medical research validates the profound effect of subluxation, although they prefer to call it '*dysponesis*'. (75)

The presence of subluxation affects the brain's ability to appreciate its surroundings through obstruction of sensorial formation and tactile information, by subluxation's overstimulation of mechanical receptors, and stimulation of neuromodulators as we have previously stated. (76) The subluxation's stimulation of the release of neuromodulators, and stimulation of pain receptors both mechanical and chemical create an ambient change in the brain, and as we have demonstrated herein through epigenetics in our DNA expression as well. (77) Conversely, the adjustment in correcting the subluxation alleviates the localised inflammatory situation regulating cell apoptosis. The adjustment aids in the rebalancing of neuromodulators. The sensory input and pain input returned to normal.

But far more profound is the effect and changes that are made through modifications in the brain and chromosomal activity by rectifying erroneous receptor transmission. Rectifying erroneous stimulation to the genetic code will in the long run created a normalisation of neurohormones, neuromodulators, affecting the quality of new neurons generated. (78)

It is understood that this brain memory imprinting, for the most part, can be changed. There are some areas of the brain it would appear that tend not to re-imprint, these are areas that relate to speech, digestion, face recognition, the building blocks of vision, and perhaps the building blocks of grammar. We find that the brain imprints small strongly stable data. (79) Eagleman states that the brain changes relying on changing stimulus. Such stimulus relies on repetition and survival responses to create strong memories; repetition of changing stimulus creates new imprints.

Survival learning appears to be the most profound, important, and seems to rely heavily on the presence of Acetylcholine (ACh). (80) We see the importance of acetylcholine in the specificity of area in brain plasticity as noted by Kennedy (81) where they found that the acetylcholine through nicotinic receptors has a focusing effect on context learning. It has been found by many studies that the presence of acetylcholine in these areas of brain actually stimulates synaptic connection. (82) Stiver found that 'the bidirectional effects, i.e. destabilisation and stabilisation of memory connections, suggest a crucial influence of ACh on memory destabilisation and the updating functions of reconsolidation'. These results support the conclusion that the basal forebrain cholinergic projection to cortex is an important facilitator of synaptic plasticity in the mature cortex. (83)

The role of *acetylcholine* (ACh) in *synaptic plasticity* is well established. Studies using micro-iontophoretic application of acetylcholine in vivo and in vitro and electrical stimulation of the *basal forebrain* have demonstrated that ACh can produce long-lasting increases in neural responsiveness. (84, 85) '*Cholinergic neuromodulation is pivotal for arousal, attention, and cognitive processes. Loss or dysregulation of cholinergic inputs leads to cognitive impairments*'. (86) To form memory, many parts of the central nervous system (CNS) cooperate and the hippocampus plays an essential role. The function of the hippocampus is regulated by cholinergic neurons that come from many brain regions such as the prefrontal cortex, basal forebrain, and medial septum.

Acetylcholine as the first identified neurotransmitter and the main executor of the cholinergic nervous system, plays essential roles in learning and memory. However, inappropriate activation of the ACh-glutamate cascade impairs long-term memory consolidation. (87, 88) It has been shown that local elimination of ACh in the medial habenula (MHb) neurons alters glutamate co-release and presynaptic facilitation. Data demonstrate that ACh controls the quantal size and release frequency of glutamate at habenular synapses, and suggest that the synergistic functions of ACh and glutamate may be generally important for modulation of cholinergic circuit function and behaviour. (89)

ACh was recognised as a chemical that plays an important role in many different body functions. It is as well a *neurotransmitter*, and its main role is to communicate signals between neurons in the *central nervous system*(CNS) and the peripheral nervous system (PNS). (90) Acetylcholine is also found in many brain neurons where it plays a vital role in mental processes and human behaviours, such as memory and cognition. It is involved in attention, arousal, *neuroplasticity*, and REM sleep. Acetylcholine can affect behaviour by triggering sensory gating, a process that reduces or blocks background noise, and enhancing learning.

Neuroscientists at *Carnegie Mellon University* have, for the first time, used ACh to functionally rewire a dense matrix of neurons in the brain's cerebral cortex. They found that ACh can be targeted to turn on the normally silent network. Their research is published in *Neuron*. (91) There are other neurochemicals that facilitate or inhibit ACh. Dopamine, for example, acts as a reward signal and a positive reinforcement of behavior. Acetylcholine, on the other hand, correlates with attention, exploration, and spatial learning in general. Dopamine can be an acetylcholine inhibitor. (92) So we see this dynamic relationship between dopamine and acetylcholine during decision-making; ACh, released by cholinergic interneurons (CINs), drives the release of dopamine, and dopamine, in turn, inhibits the activity of acetylcholine CINs. (93) There is presented information how chiropractic through the reduction of the subluxation and through the spinothalamic tract impacts dopamine and acetylcholine production. (94, 95, 96) (see Figures)

Memory formation and memory retrieval are subject to complex cellular and molecular processes. Increasingly evidence exists that neuronal glucose metabolism and its control by the insulin signal transduction cascade are the main players in such processes. Acetylcholine synthesis depends on the availability of acetyl CoA, provided from glucose breakdown, and insulin, which controls the activity of acetylcholine transferase. ATP is necessary for both synaptic activity and plasticity. (97) ATP is a co-transmitter with glutamate, noradrenaline, GABA, acetylcholine, and dopamine in the brain. (98)

Data suggests that peripheral nerve entrapment increases DRG metabolism and tissue damage which causes ATP release. (99) ATP has now been identified as an excitatory co-transmitter in sympathetic and parasympathetic nerves. Now it appears that ATP acts as a co-transmitter in most, if not all, nerves in both the peripheral nervous system and central nervous system (CNS). ATP acts as a short-term signalling molecule in neurotransmission, neuromodulation, and neurosecretion. It also has potent, long-term (trophic) roles in cell proliferation, differentiation, and death, as well as in development and regeneration. (100)

Is ATP associated with subluxation?

Adenosine triphosphate (ATP) can sometimes act as a short-term trigger for long-term trophic events that become evident days or even weeks after the original challenge in synaptic transmission in ganglia and in the central nervous system. (101) The subluxation process might even begin with the initiation of irritation causing localised cell apoptosis which releases ATP. Peripheral terminals are activated by ATP released from local cells by mechanical deformation, cell damage, and subluxation. The receptors on fibres in the dorsal spinal cord and brain stem are activated and are involved in reflex control of visceral and cardiovascular activity, as well as relaying nociceptive impulses to pain centres. (102) We also understand the traditional role ATP plays a crucial part in providing energy to the mitochondria of all cells. In this case specifically for the dendritic mitochondria, stimulating dendritic synaptic firing.

The carotid body

Another important player in brain / DNA plasticity is the carotid body. The importance of the carotid body (CB) in relation to neuromodulators such as acetylcholine and ATP has been studied. Chemoreceptor cells in the carotid body (CB) depolarise and release neurotransmitters that excite afferent terminals of the carotid sinus nerve. Afferent signals are then relayed to the central pattern generator in the brainstem, leading to reflexes for homeostasis. (103)

The carotid body is the primary peripheral chemoreceptor in the body. It is suggested by Gold et al (104) that '*at an organ-level the carotid body is comparable to a miniature brain with compartmentalised discrete regions of clustered glomus cells defined by their neurotransmitter expression and receptor profiles*'. It has the connectivity to define reflex arcs that play a key role in initiating distinct physiological responses. This is similar in many ways to a switchboard that participates in the rudimentary components for synaptic plasticity, and learning/memory. The carotid body connects specific inputs to selective outputs.

A striking feature of the carotid body (CB) is its remarkable degree of plasticity in a variety of neurotransmitter/modulator systems in response to environmental stimuli, (105) particularly following hypoxia but also during other environmental experiences. Current evidence suggests that ACh and ATP are two major excitatory neurotransmitter candidates. (106) It has been found that efferent innervation to the carotid body comes from the superior cervical ganglion as well as sympathetic and parasympathetic nerves that are present with postganglionic neurons located within the CB or close to it in the form of paraganglia. (107) These modulate carotid body chemosensitivity through blood flow variation. (108) This demonstrates spinal nerve involvement in proper function of the carotid body.

Rethinking what happens

The traditional way of thinking then about the role of the spinal nerve system and its mechanism of affect may be outdated. What is now understood, is that in the sensory afferents following any nociceptive stimulus, its energy is transduced by a receptor (nociceptor) into a local generator

potentially expressed on the sensory afferent terminal. If the generator potential achieves threshold, action potentials are produced and conveyed orthodromically to the spinal cord.

However, an important property of nerve conduction, now understood, is that the excitable membrane can generate action potentials in both directions from a point of depolarisation. Thus, when primary afferent nerve fibres are activated distant from the receptor/terminal (mid-axonally or dorsal root ganglia (DRG)), they will generate action potentials that are conveyed bi-directionally, in the orthodromic direction to the spinal cord, and antidromically away from the cord along that nerve.

This was noted in this study by Sorkin (109) where they found that '*stimulation to the colon for example stimulated the bladder through what they found to be antidromic activity*'. They reported they were able to duplicate this phenomenon through irritation of the uterus referring sensation to the urinary bladder. There were reported other occurrences where DRG neurons projecting through different peripheral nerves to separate structures: as lumbar facets and areas of skin in the lumbar area and lumbar muscles, even to the knees and to various other parts of the viscera. It is offered that this could be the phenomenon behind visceral-somatic referred pain. (110, 111, 112)

Summary

So, it does appear that Orthodromic input to the spinal cord depolarises central terminals leading to a extracellular release of neurotransmitters into the tripartite synapse, onto second-order neurons as well as proximal glia. (113, 114) The antidromic flow can occur in motor nerve pathways as well (ventral root ganglion). (115) This antidromic phenomena is observed when the nerve is exposed to ACh. (116, 117, 118) The studies agree that the release of potassium from damaged perineural tissues would follow with a ACh flow to endplate receptors and depolarising nerve terminals. We see that stimulation of either sensory or motor, efferent or afferent nerves could create feedback to the CNS. This puts both dorsal root ganglia and ventral root ganglia in a new light.

The role of Chiropractic

We have demonstrated here the importance of plasticity, both brain and chromosomal, to learning/survival/function of the organism. We have described many mechanisms for stimulation of the changes to plasticity mechanical, neurological and chemical and how the nervous system, specifically the spinal nerves, impacts these mechanisms. It must be recognised that the impact of the subluxation and the correction of the subluxation is paramount to the process of plasticity in brain/DNA.

How does this impact our concept of subluxation and the adjustment?

The concept of subluxation is beginning to morph towards a new direction. Much is discussed about the implications of the intervertebral disk (IVD) or vertebral compression with and without bone spurs and that type of subluxation. One must look beyond that model.

For example, an interesting study looked at what goes on with subluxation at the zygapophysial joint (Z-joint) level. They macroscopically and histologically identified and illustrated that there are fibrous bands connecting the cervical nerve to the zygapophysial joint capsule and are an important factor in subluxation often overlooked: '*The fibrous bands are involved in the pathology of cervical spondylotic radiculopathy associated with the zygapophysial joints as dynamic factors*'. (119)

The presence of mechanoreceptive and nociceptive nerve endings in cervical facet capsules proves that these tissues are monitored by the central nervous system and implies that neural input from the facets is important to proprioception and pain sensation. (120) Innervation of the thoracic and lumbar facets is less consistent. (121) The cervical spine is loaded with sensory nerves as opposed to thoracic or lumbar since, it was found that biomechanical dysfunction of the cervical spinal column may lead to abnormal afferent (nerve impulses traveling towards the brain) information. (122) In another study the researchers remarked '*The cervical spine has an important role in providing proprioceptive input, and this is reflected in the abundance of cervical mechanoreceptors and their central and reflex connections to the vestibular, visual, and central nervous systems. Furthermore, it has*

been shown that body posture affects the way in which autobiographical memories are accessed and retained by both younger and older adults'. (123)

The zygapophysial joint

We observe again the importance of spinal integrity to brain plasticity. This crucial postural information is in great part provided by the Z-joints of the cervical spine. In the Z-joints we find encapsulated receptors, including the Pacinian corpuscles, Meissner's corpuscles, Krause endings and Ruffini endings that are all innervated by fast-conducting myelinated fibres. We understand how the mechanoreceptor continued firing will overload the proprioception to the brain. It will impede the inflow of sensory/proprioceptive information to the brain from the periphery as stated in *Melzack and Wall's Gate Theory*. As a matter of fact, Melzack and Wall appear to be discussing Chiropractic as they lay out their theory. Melzack and Wall said '*there is a transmission station in the spinal cord that influences the flow of nerve impulses to the brain*'. They called this transmission station a '*gate*'. '*This gate could be at the level of the substantia gelatinosa and the dorsal horn of the spinal cord will stop information from reaching the thalamus and cerebral cortex*.' (124)

'*Think of it as a gate you can open or close to get to your backyard*' they continue, '*Many factors can open or close the gate ... for example, positive mood, distraction, and deep relaxed breathing can act to close or partially close the gate while strong emotions like fear, anxiety, and expecting the worst can open the gate*'. The continual flooding of stimulus to the brain will cause Long Term Potentiation (LTP), causing rapid induction, persistence, correlation, and interference with natural brain rhythms. Again, this may be part of the cerebral loop of chronic pain seen with chronic subluxation, CRPS. (125)

Chronic clinical conditions

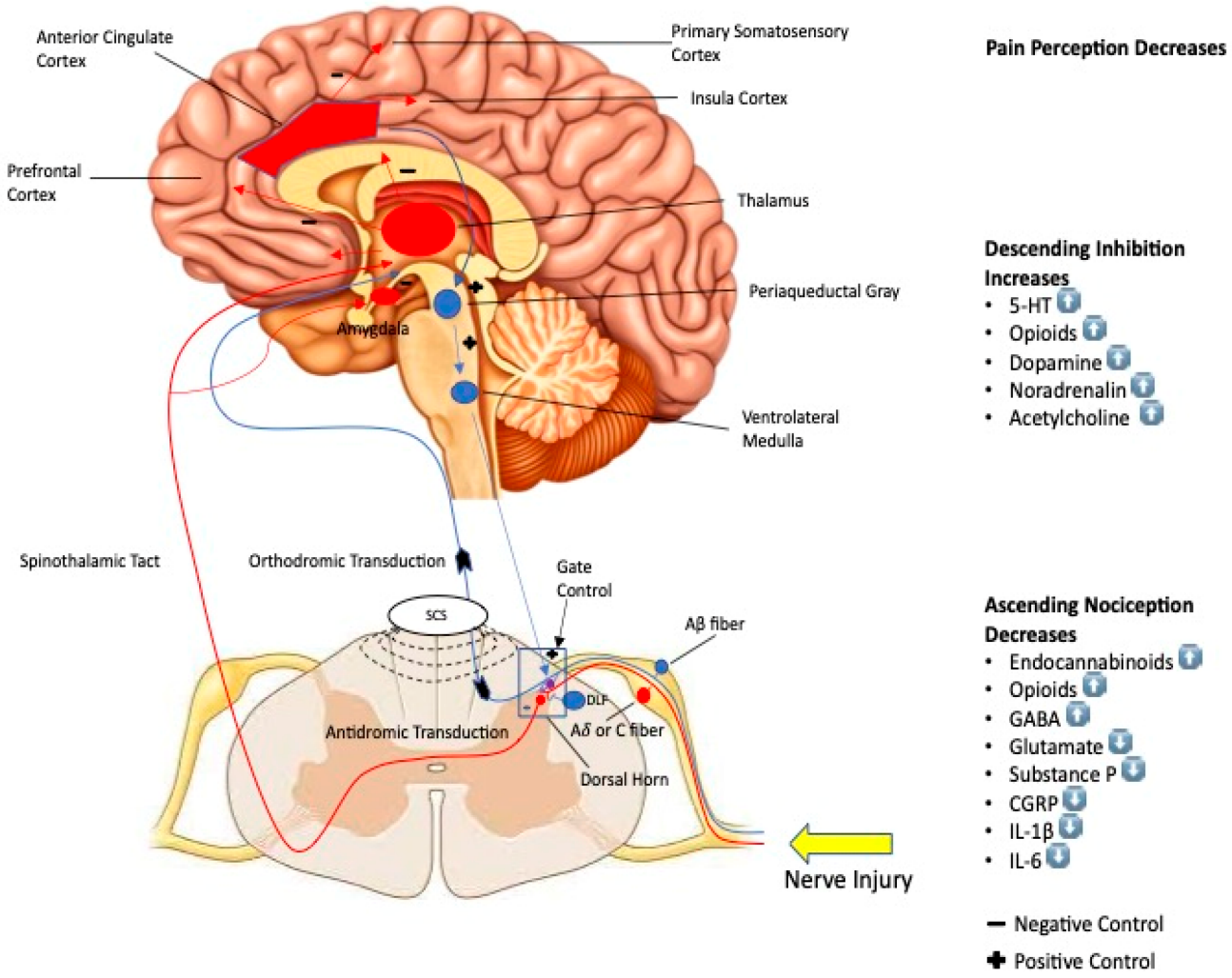
The recent experimental evidence has in fact demonstrated this neuronal/synaptic plasticity and, in particular, long-term potentiation (LTP) and long-term depression (LTD) in spinal neurons and the relation to chronic clinical conditions. The implications of these studies for possible mechanistic explanations of low back pain and its treatment by spinal manipulative therapy (SMT) are intriguing. (126)

The Boal study stated '*it is of monumental concern recognising the effect on neuroplasticity which is paramount to understanding the subluxation*'. Changes post-adjustment are not just localised to segments or dermatomes nor target organs:

> '*There is solid scientific evidence that adjusting the spine changes the manner in which the prefrontal cortex of the brain processes information. It demonstrates that the adjustment changes the way the brain works and shows that spinal function impacts brain function. One of the most interesting things about the changes we observed was that in the prefrontal cortex, which is responsible for behaviour, goal directed tasks, decision making, memory and attention, intelligence, processing of pain and emotional response to it, autonomic function, motor control, eye movements and spatial awareness, with the adjusting of a subluxation appears to begin an immediate corrective phenomenon*'. (127)

Chiropractic actually does impact plasticity through action via the autonomic nervous system (ANS). The ANS, responsible for many aspects of the survival mechanism, will stimulate or inhibit production of neurohormones. These neurohormones/neuromodulators, especially ACh and dopamine will have profound effects on brain plasticity. One such model is demonstrated in the figure below.

While ACh operates as a neurotransmitter in many parts of the body, it is most commonly associated with neuromuscular junction. The neuromuscular junction is where motor neurons located in the ventral spinal cord synapse with muscles in the body to activate them. Acetylcholine also functions as a neurotransmitter in the autonomic nervous system, acting both as the neurotransmitter between preganglionic and postganglionic neurons as well as being the final release product from parasympathetic postganglionic neurons. (128)

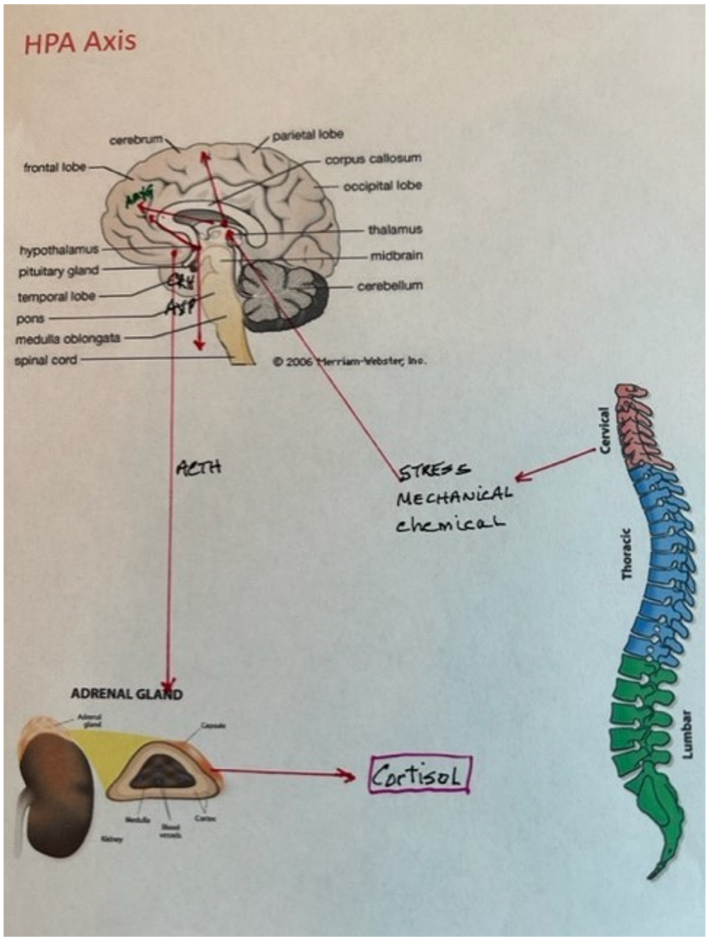


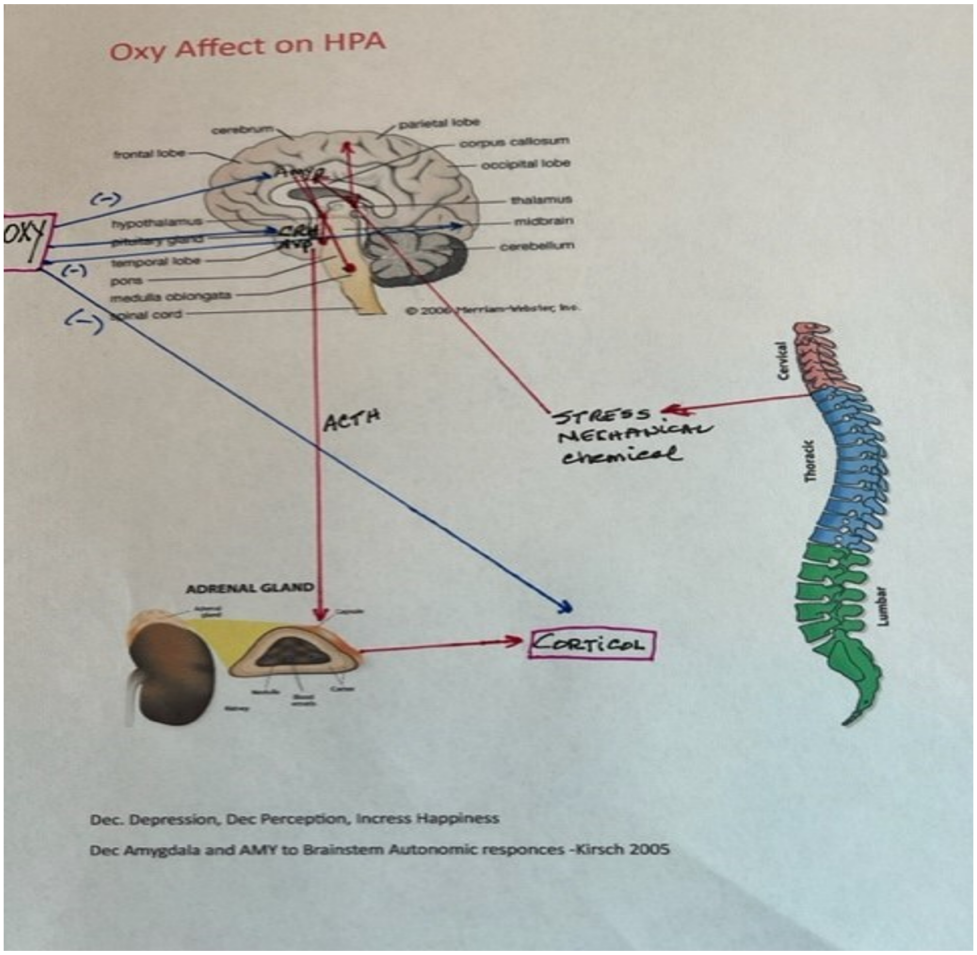
We have discussed here that ACh and ATP work synergistically as the ATP powers the mitochondria at the dendritic synaptic bulb, the Ach focuses where the activity will take place. ACh and Dopamine work together as well but Dopamine can inhibit the Ach function.

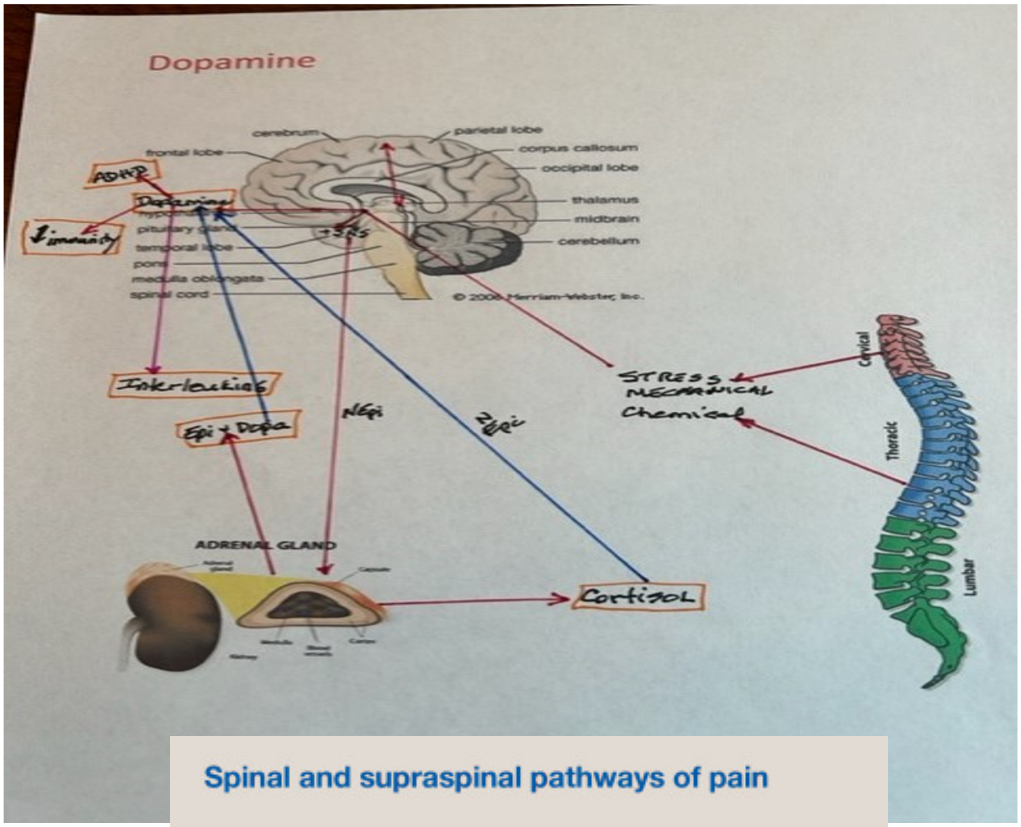
As for another neurohormone with control through the ANS, Cortisol is responsible for the accumulation of acetylcholine in these tissues. ACh exerts its action through the M3 ACh receptor, but an overproduction exacerbates tissue damage and oxidative stress and impairs regeneration. (129) We have seen studies where chiropractic can impact neuromodulators. (130) Lohman et al stated that '*mechanical stimulus provided through chiropractic specific manipulation modified neuropeptide expression by immediately increasing serum concentrations of multiple biomarkers except for Cortisol which was decreased*'. This will optimise ACh accumulation without an over production. (131) Sampath found that thoracic spinal manipulation can lead to different responses involving the sympathetic nervous system, the endocrine system and hypothalamic-pituitary axis releasing neurotrophic growth factor. Brain Derived Neurotrophic Factor (BDNF) is a key molecule involved in plastic changes related to learning and memory. (132)

How do spinal nerves affect neuromodulators?

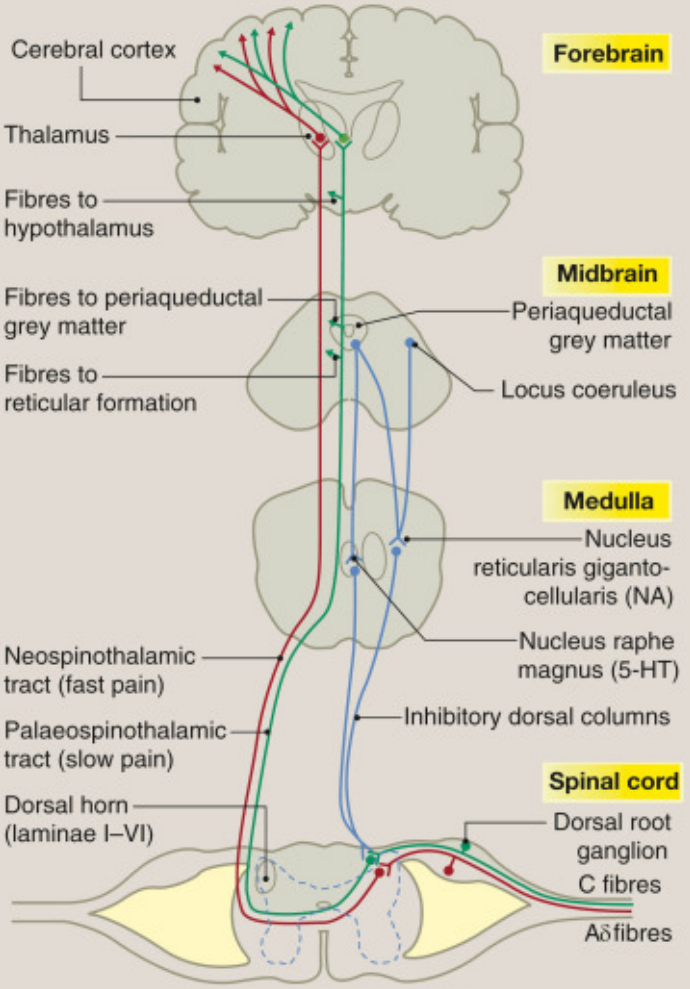
Part of our survival mechanisms relies on the spinothalamic tract. It is an ascending pathway of the spinal cord. Together with the medial lemniscus, it is one of the most important sensory pathways of the nervous system. It is responsible for the transmission of pain, temperature, and crude touch to the somatosensory region of the thalamus. The thalamus will communicate with all anterior brain and eventually cortical cells. The Hypothalamus can also generate new neurons, neurogenesis, as mentioned earlier. The connections can be observed in the following diagrams:


HPA Axis
cerebrum
parietal lobe
frontal lobe
corpus callosum
occipital lobe
thalamus
hypothalamus
midbrain
pituitary gland
cerebellum
temporal lobe
pons
medulla oblongata
spinal cord
© 2006 Merriam-Webster, Inc.
ACTH
STRESS
MECHANICAL
chemical
Cervical
Thoracic
Lumbar
ADRENAL GLAND
Cortisol


Oxy Affect on HPA
cerebrum
parietal lobe
frontal lobe
corpus callosum
occipital lobe
thalamus
midbrain
cerebellum
OXY
(-)
hypothalamus
pituitary gland
temporal lobe
pons
medulla oblongata
spinal cord
© 2006 Merriam-Webster, Inc.
ACTH
STRESS
MECHANICAL
chemical
Cervical
Thoracic
Lumbar
ADRENAL GLAND
CORTICOL
Dec. Depression, Dec Perception, Incress Happiness
Dec Amygdala and AMY to Brainstem Autonomic responces -Kirsch 2005



Spinal and supraspinal pathways of pain



Ascending nociceptive fast (red) and slow (green) pathways.
Descending inhibitory tracts (blue).
NA, noradrenaline; 5-HT, 5-hydroxytryptamine.

Chiropractors then by eliminating subluxation are normalising the stress placed on the CNS allowing for optimisation of neuromodulator function and imprinting of pro-survival information.

We cited here as well genetic plasticity. The ability of the body to modify genetic expression by turning certain genetic codes on or off. This learning/memory allows for dramatic change in each cell of the body in response to environmental shift, either internal or external, and moves the organism in a pro-survival pathway. There is also the possibility that through negative/nociceptive epigenetic stimulation, poor outcomes are created by turning some codes on or off. Moving the organism towards a pathway detrimental to survival.

Emerging evidence suggests the Chiropractic can affect genetic mechanisms through 5 Different avenues:

- environmental influences
- methylation processes
- elongation of DNA telomeres
- chromosomal oxidative stress reduction, and
- reducing emotional stress. (133)

Considering environmental influences, it has been stated 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*'. (134, 135, 136) This has been documented in medical literature as well, '*nerve impingement can interfere with the brain's ability to communicate with the muscles, organs, and cells and can result in loss of motor function, sensory function, or both*'. (137)

Concerning the methylation process, this is multi faceted as it applies to general neurophysiology as well as genetics. (138) Maltese and his group found that '*different studies with animal models have demonstrated that chiropractic therapies mediate neural plasticity, specifically through modulation of neurotrophins*'.

It has been reported that one of the effects of spinal manipulation during Chiropractic therapy is to stretch spinal muscles. Muscle stretch is a powerful stimulus for up regulation of a splice product (mechano-growth factor MGF) this promotes growth and repair both through myotrophism and neurotropism. (139)

Another pathway in which chiropractic affects neuromodulation is through neurotrophins via the HPA axis. The HPA axis relies on a series of signals from the sympathetic nervous system. If the brain continues to perceive danger, i.e. nociceptive stimulation from subluxation sites, hypothalamus releases corticotropin releasing hormone (CRH), which travels to pituitary gland triggering the release of adrenocorticotropin Hormone (ACH). This hormone travels to the adrenal glands stimulating the release of Cortisol. (140) We further understand the need for the modulation of the hypothalamus-pituitary-adrenal axis through chiropractic providing proper feedback regulation which allows the termination of the stress response as higher cortisol levels correlate with gross inflammatory responses and hyper-methylated sites on DNA causing deterioration and breakdown.

Another way in which chiropractic provides an epigenetic effect is through the protection of DNA telomeres. '*Telomeres on our linear DNA are very similar to the End of the Shoelaces*'. They are meant to protect the vital information contained within chromosomes, but over the years of cell division, telomeres shorten. Progressive shortening of telomeres leads to senescence, apoptosis, or oncogenic transformation of somatic cells, affecting the health and lifespan of an individual. (141) In the Case Study by Feforchuck (142) they reported correction of the vertebral subluxation and improvement of spinal alignment and posture may be associated with increased telomere length and further supports that chiropractic care may provide epigenetic salutogenic health benefits.

We can see how in the Feforchuck and McCoy study (143) the outcome was further reinforced by the study by Campbell and Kent (144) where they found that concerning oxidative stress, DNA repair

including preservation of telomeres was found with Chiropractic care. They stated '*serum Thiols are a measure of human health status. It is a surrogate estimate of DNA repair*'. This study demonstrated the effects of short-term and long-term chiropractic care on serum Thiol levels in asymptomatic subjects which positively affected DNA health.

Furthermore, a study by Kultur (145) found that oxidative stress causes inflammatory responses. These in turn increase cytokines and inflammation damage and lipoproteins damage specifically deoxyribonucleic acid (DNA). Oxidative stress-induced apoptosis may participate in chromosome rearrangements. (146) The Thiol-disulfide balance is a new method for determining oxidative stress. Spinal manipulation, the adjustment, is useful in returning Thiol-disulfide homeostasis and serum IMA levels to normal indicating reduction oxidative stress in patients. (147) This might be due to control of the cortisol/acetylcholine balance managing the inflammatory cycles.

Chiropractic's impact on emotional stress has been demonstrated in multiple studies the most outstanding study to date was by Blok (148) where they demonstrated that a simple amount of psychological stress seems to exacerbate pressure and discomfort on the volunteers' necks and lower backs with peak spinal loads on cervical vertebrae being 11.1% higher in compression, 9.4% higher in AP shear, and 19.3% higher in lateral shear. Weston and group stated '*this increased spine load occurred under just one condition of mild psychological stress and with a fairly light load. One can imagine what this would be like with more complex tasks or higher loads*'.

Physiological distress even in low rates was sufficient to create irritation and pressure in the nervous system enough to complicate the capacity for physical activity even in the light loads in previously asymptomatic individuals. It was further stated by Kinsella (149) that '*stress may stimulate genetic adaptations through epigenetics that in turn modulate the link between environment, human lifestyle factors, and the genes themselves*'.

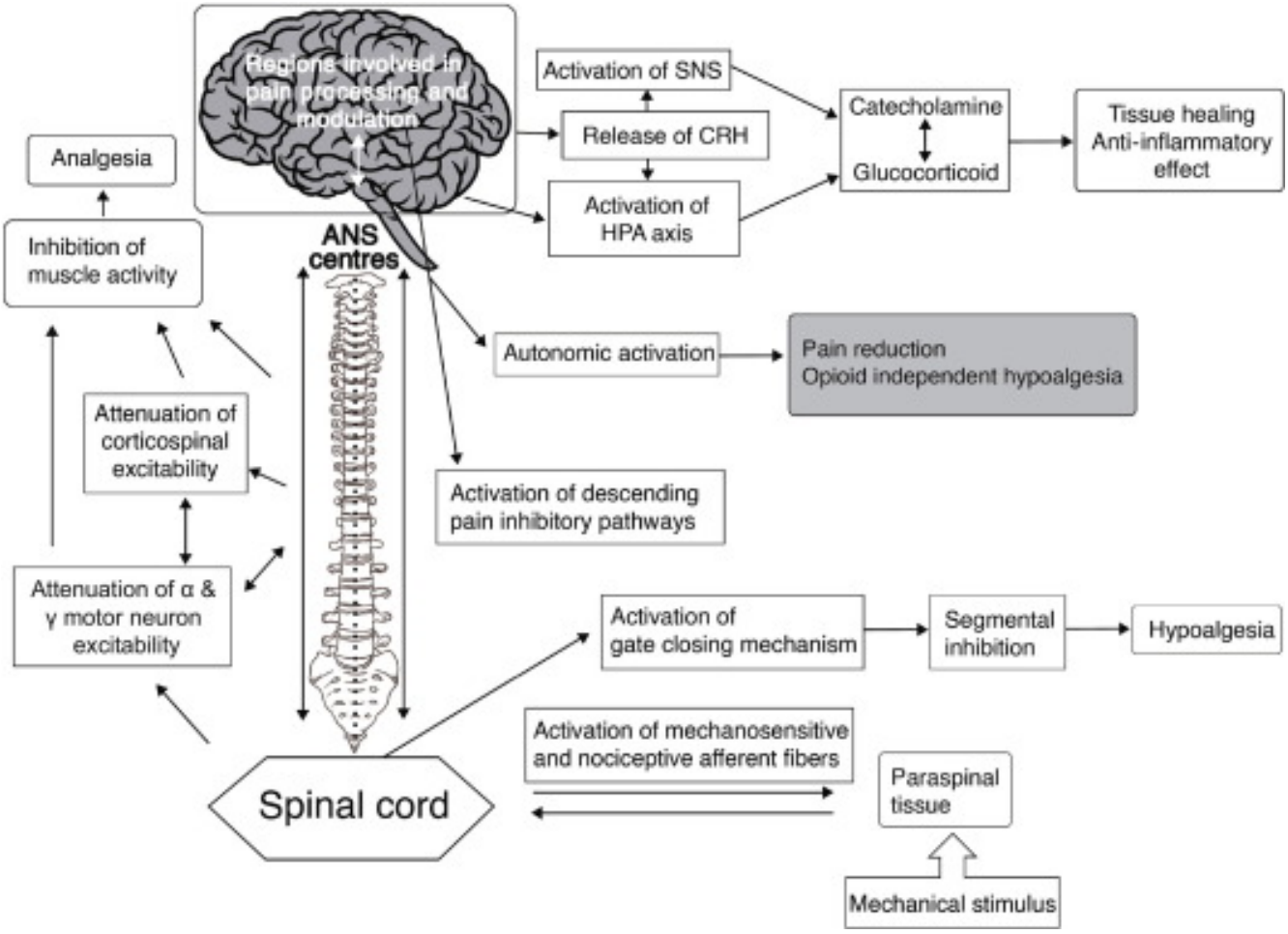
> The ability of Chiropractic to unburden the spine and relieve pressure on the nervous system undoubtedly relieves the outcome of physiological stress upon the nervous system.

Another study performed by Plaza-Monzano (150) demonstrated that Chiropractic adjustments have been shown to provide Eustress to the nervous system and entire body through stimulation and production of neurotensin and oxytocin, hence affecting mood through brain stimulation. This corroborated by another study by Duarte (151) where they found that spinal manipulation therapy, the adjustment, may impact neurotensin, oxytocin and immunological biomarkers.

Bringing it together

We observed upon reading all this information how all these factors appear interrelated. How environmental influences, emotional stress, affecting the HPA axis, triggers a flurry of neurochemical activity which will impact a large number of important factors such as methylation processes, chromosomal oxidative stress, and brain / DNA plasticity. By affecting both brain and DNA plasticity we affect the path of health that the individual will take immediately, in the future, and possibly impacting their future generations.

Concerning chiropractic, subluxation, and the adjustment, the data suggests that the improved clinical outcomes with Chiropractic that have been reported, are largely of neurophysiological origin. Wen and his group stated that '*it can be understood that Spinal Manipulation Therapy (SMT) is an effective treatment, and we suppose now that it might have been involved in modulating dysfunctional brain regions which are important for the processing of pain*'. (152)



This new model of some of the subluxation's results is one worth sharing. Granted it may not be as easy to share this model with one's patients, but the first step in our own minds as chiropractors is that we understand the profound changes that we are enabling in the body by applying the chiropractic adjustment.

In reviewing some of the models of subluxation over the course of chiropractic history we come across a few models which have been elaborated. In 1983 Leonard J Faye published his text, *Motion Palpation of the Spine*, in which he described the subluxation complex (SC) for supposedly the first time. (153)

Faye's model which was popular for a long time was also a five-part subluxation model

5-Part Subluxation Complex	Pathophysiological Changes
Neuropahtophysiology	• irritation/facilitation pathway via the Anterior, Lateral, or Posterior horn and • lead to hypertonic muscles • changes in the sympathetic vasomotor and sensory systems • may take the path of pressure/degeneration, • which leads to atrophy, sympatheticotonia, and anesthesia
Kinesiopathology	• Gillet's hypomobility • Illi's hypermobility • Mennel's loss of joint play • Compensation could lead to a combination of hyper and hypo mobility in the same motor unit.
Myopathology	• could be in the form of atonia or spasm, • which may be due to compensation • facilitation • or due to the feedback changes in the nerves controlling the muscles of the joint • Muscle spasm may lead to an activation of the viscero motor reflex.
Histopathology	• inflammatory process • edema
Biochemical	• related to the stress response including: • release of histamine, prostaglandins, and kinins

There have been many authors who have updated his model, some due to philosophy, some due to new scientific information, for examples Dishman's chiropractic subluxation complex (CSC) (154) and Lantz's vertebral subluxation complex (VSC). (155, 156)

New models were developed during this period. Examples include Barge's models; (157, 158) Gitelman's models; (159) Reinert's cervical, lumbar, and sacral models; (160) and Grostic's dentate ligament hypothesis. (161). Up until the 1990's there when there were further definitions of Chiropractic. There were even separate definitions offered by the ACA (162) and the ICA. (163)

> What we are illustrating here is that the definition of subluxation has been morphing, expanding all through chiropractic history. This is the natural process as new studies are published bringing new information to light. We cannot remain stagnant, resisting change to hold on to older models, Why? Those who came before us, those who established the definitions we hold so tightly to, they themselves continued to question and explore and redefine.

As we look at the description of the vertebral subluxation complex it still constitutes changes in the anatomy that will immediately begin stimulation to the brain at different levels both physically and biochemically as neuromodulators. Needless to say, we do not need to have all criteria to have a subluxation. Some may even understand the subluxation occurring first at the biochemical level when just the spilling off of ATP from damaged cells in the area begin to create biochemical interference at the cellular level.

As Chiropractors we feel primarily involved in neuromuscular changes. But one hopes that now one is cognisant of the greater array of neurophysiological changes. It would seem though that the priority scale that appears in Faye's model could be inverted and expanded as to properly present the levels of importance. One must respect the limitations of the science at the time Faye compiled this chart. It can be understood why the biochemical area falls at the shallow end of this chart. Much has been studied and understood since.

Conclusion

I have show how plasticity/learning/memory is imprinted not just in the brain, but in our very DNA. It has been discussed the pro-survival adaptations, and how they are formed. The anti-survival maladaptions have been discussed and how nociceptive input causes interference with plasticity, or detrimental imprinting. We understand that the way the brain is wired, it is always looking to make sense, look for patterns (patternicity), in the input received, apophenia. (164) In this way sensory input quality and accurateness is fundamental in directing brain /DNA imprinting. The detailed descriptions of the neuromodulator facilitation and disruption to plasticity has been discussed through neurohormonal production.

I have presented the now known mechanisms governing plasticity both brain and DNA, and how Chiropractic has been found to positively impact these mechanisms. It has been illuminated that the subluxation is not a phenomenon that affects only the local area of the subluxation. It is not solely a mechanical disruptor, as biochemical changes are intimately involved and direct brain impact is now obvious. It has been made clear that subluxation produces far reaching effects to the brain and even the DNA of each cell and how the adjustment corrects that. Hopefully, the material presented here will lead the reader to a new perspective on subluxation, and chiropractic as the only means of correcting the subluxation and establishing homeostasis in every spect of life throughout the body.

As one digests this new, albeit important, information it is of the utmost importance to develop a means of communicating this concept to the patient while still maintaining the conversation at a

level the patient can comprehend. There is a great need to develop such patient literature. We must ask ourselves, if are we misrepresenting possible outcomes from Chiropractic care to patients by continuing the water hose explanation and depriving them of insight into profound life altering opportunities?

Further study into this novel concept of subluxation and the adjustment and the vital importance for Chiropractic and overall health for the general population is indicated.

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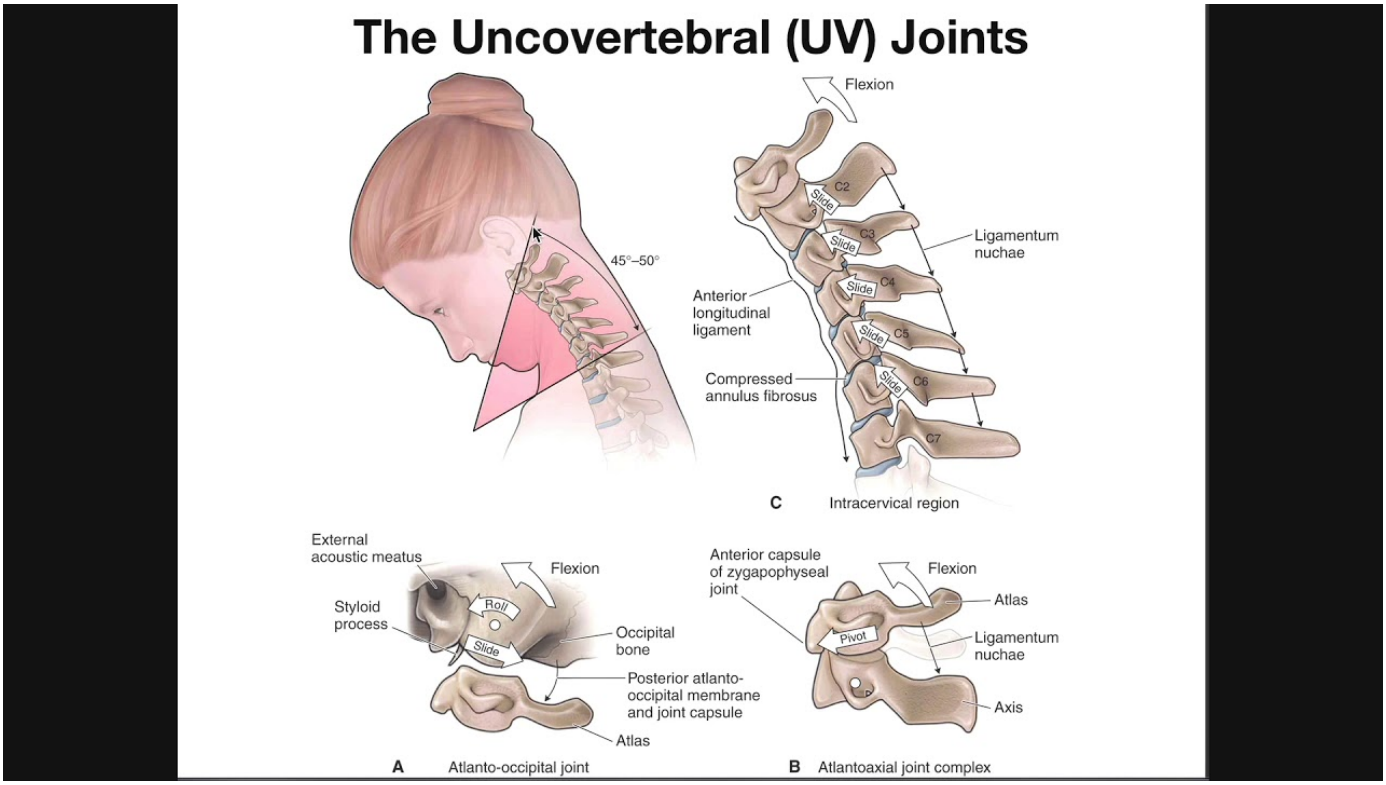
Editor's notes

Also in this issue, the paper '*Subluxation as a fuzzy narrative*' offers some answers to Weiner's proposition of improving the way Chiropractors communicate the ideas in this paper to their patients.

This video is a nice discussion on the cervical Z-joints.



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